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(54) **2-(1H-INDAZOL-3-YL)-3H-IMIDAZO[4,5-B]PYRIDINE AND THERAPEUTIC USES THEREOF**

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(57) **ABSTRACT**

Indazole compounds for treating various diseases and pathologies are disclosed. More particularly, the present invention concerns the use of an indazole compound or analogs thereof, in the treatment of disorders characterized by the activation of Wnt pathway signaling (e.g., cancer, abnormal cellular proliferation, angiogenesis, fibrotic disorders, bone or cartilage diseases, and osteoarthritis), the modulation of cellular events mediated by Wnt pathway signaling, as well as genetic diseases and neurological conditions/disorders/diseases due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Also provided are methods for treating Wnt-related disease states.

2-(1H-INDAZOL-3-YL)-3H-IMIDAZO[4,5-B]PYRIDINE AND THERAPEUTIC USES THEREOF

RELATED APPLICATIONS

[0001] This application is a divisional application of U.S. application Ser. No. 14/847,336, filed Sep. 8, 2015, and claims the benefit of U.S. Provisional Application No. 62/047,401, filed Sep. 8, 2014, each of which is incorporated herein by reference in its entirety.

BACKGROUND

Technical Field

[0002] This disclosure relates to inhibitors of one or more proteins in the Wnt pathway, including inhibitors of one or more Wnt proteins, and compositions comprising the same. More particularly, it concerns the use of an indazole compound or salts or analogs thereof, in the treatment of disorders characterized by the activation of Wnt pathway signaling (e.g., cancer, abnormal cellular proliferation, angiogenesis, fibrotic disorders, bone or cartilage diseases, and osteoarthritis), the modulation of cellular events mediated by Wnt pathway signaling, as well as genetic diseases and neurological conditions/disorders/diseases due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Also provided are methods for treating Wnt-related disease states.

Background

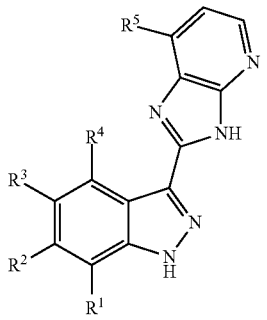
[0003] The Wnt growth factor family includes more than 10 genes identified in the mouse and at least 19 genes identified in the human. Members of the Wnt family of signaling molecules mediate many short- and long-range patterning processes during invertebrate and vertebrate development. The Wnt signaling pathway is known for its role in the inductive interactions that regulate growth and differentiation, and it also plays roles in the homeostatic maintenance of post-embryonic tissue integrity. Wnt stabilizes cytoplasmic β-catenin, which stimulates the expression of genes including c-myc, c jun, fra-1, and cyclin D1. In addition, misregulation of Wnt signaling can cause developmental defects and is implicated in the genesis of several human cancers. The Wnt pathway has also been implicated in the maintenance of stem or progenitor cells in a growing list of adult tissues including skin, blood, gut, prostate, muscle, and the nervous system.

SUMMARY

[0004] The present disclosure provides methods and reagents, involving contacting a cell with an agent, such as an indazole compound, in a sufficient amount to antagonize a Wnt activity, e.g., to reverse or control an aberrant growth state or correct a genetic disorder due to mutations in Wnt signaling components.

[0005] Some embodiments disclosed herein include Wnt inhibitors containing an indazole core. Other embodiments disclosed herein include pharmaceutical compositions and methods of treatment using these compounds.

[0006] One embodiment disclosed herein includes a compound having the structure of Formula I:



I

[0007] as well as prodrugs and pharmaceutically acceptable salts thereof.

[0008] In some embodiments of Formula (I):

[0009] R^1, R^2, and R^4 are independently selected from the group consisting of H and halide;

[0010] R^3 is selected from the group consisting of -heteroaryl$(R^6)_q$ and -heterocyclyl$(R^7)_h$;

[0011] R^5 is selected from the group consisting of H, -heteroaryl$(R^8)_q$, -heterocyclyl$(R^9)_h$, and -aryl$(R^{10})_k$;

[0012] each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of halide, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl$(R^{11})_h$, —(C_{1-4} alkylene)$_p$carbocyclyl$(R^{12})_j$, —(C_{1-4} alkylene)$_p$aryl$(R^{13})_k$, —$NHC(=O)R^{14}$, —$NR^{15}R^{16}$, —(C_{1-6} alkylene)$NR^{17}R^{18}$, and —OR^{24};

[0013] each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0014] each R^8 is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-6} alkyl), halide, —CF_3, —OCH_3, —CN, and —$C(=O)R^{19}$;

[0015] each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-6} alkyl), halide, —CF_3, —CN, and —OCH_3;

[0016] each R^{10} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-6} alkyl), halide, —CF_3, —CN, —OCH_3, —(C_{1-6} alkylene)$_p$$NHSO_2R^{19}$, —$NR^{15}$($C_{1-6}$alkylene)$NR^{15}R^{16}$, —($C_{1-6}$ alkylene)$_p$$NR^{15}R^{16}$, and —$OR^{27}$;

[0017] each R^{11} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0018] each R^{12} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0019] each R^{13} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0020] each R^{14} is independently selected from the group consisting of —(C_{1-9} alkyl), -heteroaryl$(R^{20})_q$, -aryl$(R^{21})_k$, —CH_2aryl$(R^{21})_k$, -carbocyclyl(R^{22}), —CH_2carbocyclyl$(R^{22})_j$, —(C_{1-4} alkylene)$_p$$NR^{25}R^{26}$, -heterocyclyl$(R^{23})_h$, and —$CH_2$heterocyclyl$(R^{23})_h$;

[0021] each R^{15} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

[0022] each R^{16} is independently selected from the group consisting of H, —(C_{1-6} alkyl), —CH_2aryl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$;

[0023] each R^{17} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

[0024] each R^{18} is independently selected from the group consisting of H, —(C_{1-6} alkyl), —CH_2aryl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$;

[0025] each R^{19} is a —(C_{1-6} alkyl);

[0026] each R^{20} is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0027] each R^{21} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0028] each R^{22} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0029] each R^{23} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

[0030] each R^{24} is independently selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{23})$_h$, —(C_{1-4} alkylene)$_p$carbocyclyl(R^{22})$_j$, —(C_{1-4} alkylene)$_p$aryl(R^{21})$_k$, and —(C_{1-6} alkylene)$_p$$NR^{25}R^{26}$;

[0031] each R^{25} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

[0032] each R^{26} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

[0033] each R^{27} is independently selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{23})$_h$, and —(C_{1-6} alkylene)$_p$$NR^{25}R^{26}$;

[0034] each p is independently 0 or 1;

[0035] each q is independently 0 to 4;

[0036] each h is independently 0 to 10;

[0037] each k is independently 0 to 5; and

[0038] each j is independently 0 to 12.

[0039] Some embodiments include stereoisomers and pharmaceutically acceptable salts of a compound of Formula (I).

[0040] Some embodiments include pro-drugs of a compound of Formula (I).

[0041] Some embodiments of the present disclosure include pharmaceutical compositions comprising a compound of Formula (I) and a pharmaceutically acceptable carrier, diluent, or excipient.

[0042] Other embodiments disclosed herein include methods of inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins by administering to a patient affected by a disorder or disease in which aberrant Wnt signaling is implicated, such as cancer and other diseases associated with abnormal angiogenesis, cellular proliferation, cell cycling and mutations in Wnt signaling components, a compound according to Formula (I). Accordingly, the compounds and compositions provided herein can be used to treat cancer, to reduce or inhibit angiogenesis, to reduce or inhibit cellular proliferation and correct a genetic disorder due to mutations in Wnt signaling components.

[0043] Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, anklyosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, osteochondrodysplasia, Alzheimer's disease, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-Amelia syndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

[0044] Some embodiments of the present disclosure include methods to prepare compounds of Formula (I).

[0045] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

DETAILED DESCRIPTION

[0046] Provided herein are compositions and methods for inhibiting one or more members of the Wnt pathway, including one or more Wnt proteins. Other Wnt inhibitors and methods for using the same are disclosed in U.S. application Ser. Nos. 12/852,706; 12/968,505; 13/552,188; 13/800,963; 13/855,874; 13/887,177 13/938,691; 13/938,692; 14/019,103; 14/019,147; 14/019,940; 14/149,948; 14/178,749; 14/331,427; and Ser. No. 14/334,005; and U.S. Provisional Application Ser. Nos. 61/232,603; 61/288,544; 61/305,459; 61/620,107; 61/642,915; and 61/750,221, all of which are incorporated by reference in their entirety herein.

[0047] Some embodiments provided herein relate to a method for treating a disease or disorder including, but not limited to, cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, anklyosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, bone and cartilage diseases, Alzheimer's disease, lung disease, osteoarthritis, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

[0048] In some embodiments, non-limiting examples of bone and cartilage diseases which can be treated with the

compounds and compositions provided herein include bone spur (osteophytes), craniosynostosis, fibrodysplasia ossificans progressive, fibrous dysplasia, giant cell tumor of bone, hip labral tear, meniscal tears, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), osteochondritis dissecans, osteochondroma (bone tumor), osteopetrosis, relapsing polychondritis, and Salter-Harris fractures.

[0049] In some embodiments, pharmaceutical compositions are provided that are effective for treatment of a disease of an animal, e.g., a mammal, caused by the pathological activation or mutations of the Wnt pathway. The composition includes a pharmaceutically acceptable carrier and a compound as described herein.

Definitions

[0050] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of ordinary skill in the art to which this disclosure belongs. All patents, applications, published applications, and other publications are incorporated by reference in their entirety. In the event that there is a plurality of definitions for a term herein, those in this section prevail unless stated otherwise.

[0051] As used herein, "alkyl" means a branched, or straight chain chemical group containing only carbon and hydrogen, such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl and neo-pentyl. Alkyl groups can either be unsubstituted or substituted with one or more substituents. Alkyl groups can be saturated or unsaturated (e.g., containing —C═C— or —C≡C— subunits), at one or several positions. In some embodiments, alkyl groups include 1 to 9 carbon atoms (for example, 1 to 6 carbon atoms, 1 to 4 carbon atoms, or 1 to 2 carbon atoms).

[0052] As used herein, "alkylene" means a bivalent branched, or straight chain chemical group containing only carbon and hydrogen, such as methylene, ethylene, n-propylene, iso-propylene, n-butylene, iso-butylene, sec-butylene, tert-butylene, n-pentylene, iso-pentylene, sec-pentylene and neo-pentylene. Alkylene groups can either be unsubstituted or substituted with one or more substituents. Alkylene groups can be saturated or unsaturated (e.g., containing —C═C— or —C≡C— subunits), at one or several positions. In some embodiments, alkylene groups include 1 to 9 carbon atoms (for example, 1 to 6 carbon atoms, 1 to 4 carbon atoms, or 1 to 2 carbon atoms).

[0053] As used herein, "carbocyclyl" means a cyclic ring system containing only carbon atoms in the ring system backbone, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cyclohexenyl. Carbocyclyls may include multiple fused rings. Carbocyclyls may have any degree of saturation provided that at least one ring in the ring system is not aromatic. Carbocyclyl groups can either be unsubstituted or substituted with one or more substituents. In some embodiments, carbocyclyl groups include 3 to 10 carbon atoms, for example, 3 to 6 carbon atoms.

[0054] As used herein, "lower alkyl" means a subset of alkyl having 1 to 3 carbon atoms, which is linear or branched. Examples of lower alkyls include methyl, ethyl, n-propyl and isopropyl. Likewise, radicals using the terminology "lower" refer to radicals having 1 to about 3 carbons in the alkyl portion of the radical.

[0055] As used herein, "aryl" means a mono-, bi-, tri- or polycyclic group with only carbon atoms present in the ring backbone having 5 to 14 ring atoms, alternatively 5, 6, 9, or 10 ring atoms; and having 6, 10, or 14 pi electrons shared in a cyclic array; wherein at least one ring in the system is aromatic. Aryl groups can either be unsubstituted or substituted with one or more substituents. Examples of aryl include phenyl, naphthyl, tetrahydronaphthyl, 2,3-dihydro-1H-indenyl, and others. In some embodiments, the aryl is phenyl.

[0056] As used herein, "arylalkyl" means an aryl-alkyl-group in which the aryl and alkyl moieties are as previously described. In some embodiments, arylalkyl groups contain a C_{1-4}alkyl moiety. Exemplary arylalkyl groups include benzyl and 2-phenethyl.

[0057] As used herein, the term "heteroaryl" means a mono-, bi-, tri- or polycyclic group having 5 to 14 ring atoms, alternatively 5, 6, 9, or 10 ring atoms; and having 6, 10, or 14 pi electrons shared in a cyclic array; wherein at least one ring in the system is aromatic, and at least one ring in the system contains one or more heteroatoms independently selected from the group consisting of N, O, and S. Heteroaryl groups can either be unsubstituted or substituted with one or more substituents. Examples of heteroaryl include thienyl, pyridinyl, furyl, oxazolyl, oxadiazolyl, pyrrolyl, imidazolyl, triazolyl, thiodiazolyl, pyrazolyl, isoxazolyl, thiadiazolyl, pyranyl, pyrazinyl, pyrimidinyl, pyridazinyl, triazinyl, thiazolyl benzothienyl, benzoxadiazolyl, benzofuranyl, benzimidazolyl, benzotriazolyl, cinnolinyl, indazolyl, indolyl, isoquinolinyl, isothiazolyl, naphthyridinyl, purinyl, thienopyridinyl, pyrido[2,3-d]pyrimidinyl, pyrrolo[2,3-b]pyridinyl, quinazolinyl, quinolinyl, thieno[2,3-c]pyridinyl, pyrazolo[3,4-b]pyridinyl, pyrazolo[3,4-c]pyridinyl, pyrazolo[4,3-c]pyridine, pyrazolo[4,3-b]pyridinyl, tetrazolyl, chromane, 2,3-dihydrobenzo[b][1,4]dioxine, benzo[d][1,3]dioxole, 2,3-dihydrobenzofuran, 2,3-dihydrobenzo[b][1,4]oxathiine, and others. In some embodiments, the heteroaryl is selected from thienyl, pyridinyl, furyl, pyrazolyl, imidazolyl, pyranyl, pyrazinyl, and pyrimidinyl.

[0058] As used herein, "halo", "halide" or "halogen" is a chloro, bromo, fluoro, or iodo atom radical. In some embodiments, a halo is a chloro, bromo or fluoro. For example, a halide can be fluoro.

[0059] As used herein, "haloalkyl" means a hydrocarbon substituent, which is a linear or branched, alkyl, alkenyl or alkynyl substituted with one or more chloro, bromo, fluoro, and/or iodo atom(s). In some embodiments, a haloalkyl is a fluoroalkyls, wherein one or more of the hydrogen atoms have been substituted by fluoro. In some embodiments, haloalkyls are of 1 to about 3 carbons in length (e.g., 1 to about 2 carbons in length or 1 carbon in length). The term "haloalkylene" means a diradical variant of haloalkyl, and such diradicals may act as spacers between radicals, other atoms, or between a ring and another functional group.

[0060] As used herein, "heterocyclyl" means a nonaromatic cyclic ring system comprising at least one heteroatom in the ring system backbone. Heterocyclyls may include multiple fused rings. Heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, heterocycles have 5-7 members. In six membered monocyclic heterocycles, the heteroatom(s) are selected from one to three of O, N or S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, or S. Examples of hetero-

cyclyl include azirinyl, aziridinyl, azetidinyl, oxetanyl, thietanyl, 1,4,2-dithiazolyl, dihydropyridinyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-dioxolanyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl, pyrrolidinyl, tetrahydrofuryl, tetrahydropyridinyl, oxazinyl, thiazinyl, thiinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, piperidinyl, pyrazolidinyl imidazolidinyl, thiomorpholinyl, and others. In some embodiments, the heterocyclyl is selected from azetidinyl, morpholinyl, piperazinyl, pyrrolidinyl, and tetrahydropyridinyl.

[0061] As used herein, "monocyclic heterocyclyl" means a single nonaromatic cyclic ring comprising at least one heteroatom in the ring system backbone. Heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, heterocycles have 5-7 members. In six membered monocyclic heterocycles, the heteroatom(s) are selected from one to three of O, N or S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, or S. Examples of heterocyclyl include azirinyl, aziridinyl, azetidinyl, oxetanyl, thietanyl, 1,4,2-dithiazolyl, dihydropyridinyl, 1,3-dioxanyl, 1,4-dioxanyl, 1,3-dioxolanyl, morpholinyl, thiomorpholinyl, piperazinyl, pyranyl, pyrrolidinyl, tetrahydrofuryl, tetrahydropyridinyl, oxazinyl, thiazinyl, thiinyl, thiazolidinyl, isothiazolidinyl, oxazolidinyl, isoxazolidinyl, piperidinyl, pyrazolidinyl imidazolidinyl, thiomorpholinyl, and others.

[0062] The term "substituted" refers to moieties having substituents replacing a hydrogen on one or more non-hydrogen atoms of the molecule. It will be understood that "substitution" or "substituted with" includes the implicit proviso that such substitution is in accordance with permitted valence of the substituted atom and the substituent, and that the substitution results in a stable compound, e.g., which does not spontaneously undergo transformation such as by rearrangement, cyclization, elimination, etc. Substituents can include, for example, —(C_{1-9} alkyl) optionally substituted with one or more of hydroxyl, —NH_2, —NH(C_{1-3} alkyl), and —N(C_{1-3} alkyl)$_2$; —(C_{1-9} haloalkyl); a halide; a hydroxyl; a carbonyl [such as —C(O)OR, and —C(O)R]; a thiocarbonyl [such as —C(S)OR, —C(O)SR, and —C(S)R]; —(C_{1-9} alkoxyl) optionally substituted with one or more of halide, hydroxyl, —NH_2, —NH(C_{1-3} alkyl), and —N(C_{1-3} alkyl)$_2$; —$OPO(OH)_2$; a phosphonate [such as —$PO(OH)_2$ and —$PO(OR')_2$]; —OPO(OR')R"; —NRR'; —C(O)NRR'; —C(NR)NR'R"; —C(NR')R"; a cyano; a nitro; an azido; —SH; —S—R; —OSO_2(OR); a sulfonate [such as —SO_2(OH) and —SO_2(OR)]; —SO_2NR'R"; and —SO_2R; in which each occurrence of R, R' and R" are independently selected from H; —(C_{1-9} alkyl); C_{6-10} aryl optionally substituted with from 1-3 R'"; 5-10 membered heteroaryl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with from 1-3 R'"; C_{3-7} carbocyclyl optionally substituted with from 1-3 R'"; and 3-8 membered heterocyclyl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with from 1-3 R'"; wherein each R'" is independently selected from —(C_{1-6} alkyl), —(C_{1-6} haloalkyl), a halide (e.g., F), a hydroxyl, —C(O)OR, —C(O)R, —(C_{1-6} alkoxyl), —NRR', —C(O)NRR', and a cyano, in which each occurrence of R and R' is independently selected from H and —(C_{1-6} alkyl). In some embodiments, the substituent is selected from —(C_{1-6} alkyl), —(C_{1-6} haloalkyl), a halide (e.g., F), a hydroxyl, —C(O)OR, —C(O)R, —(C_{1-6} alkoxyl), —NRR', —C(O)NRR', and a cyano, in which each occurrence of R and R' is independently selected from H and —(C_{1-6} alkyl).

[0063] As used herein, when two groups are indicated to be "linked" or "bonded" to form a "ring", it is to be understood that a bond is formed between the two groups and may involve replacement of a hydrogen atom on one or both groups with the bond, thereby forming a carbocyclyl, heterocyclyl, aryl, or heteroaryl ring. The skilled artisan will recognize that such rings can and are readily formed by routine chemical reactions. In some embodiments, such rings have from 3-7 members, for example, 5 or 6 members.

[0064] The skilled artisan will recognize that some structures described herein may be resonance forms or tautomers of compounds that may be fairly represented by other chemical structures, even when kinetically, the artisan recognizes that such structures are only a very small portion of a sample of such compound(s). Such compounds are clearly contemplated within the scope of this disclosure, though such resonance forms or tautomers are not represented herein.

[0065] The compounds provided herein may encompass various stereochemical forms. The compounds also encompass diastereomers as well as optical isomers, e.g., mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art. Unless otherwise indicated, when a disclosed compound is named or depicted by a structure without specifying the stereochemistry and has one or more chiral centers, it is understood to represent all possible stereoisomers of the compound.

[0066] The term "administration" or "administering" refers to a method of providing a dosage of a compound or pharmaceutical composition to a vertebrate or invertebrate, including a mammal, a bird, a fish, or an amphibian, where the method is, e.g., orally, subcutaneously, intravenously, intralymphatic, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonarilly, vaginally, rectally, ontologically, neuro-otologically, intraocularly, subconjuctivally, via anterior eye chamber injection, intravitreally, intraperitoneally, intrathecally, intracystically, intrapleurally, via wound irrigation, intrabuccally, intraabdominally, intra-articularly, intra-aurally, intrabronchially, intracapsularly, intrameningeally, via inhalation, via endotracheal or endobronchial instillation, via direct instillation into pulmonary cavities, intraspinally, intrasynovially, intrathoracically, via thoracostomy irrigation, epidurally, intratympanically, intracisternally, intravascularly, intraventricularly, intraosseously, via irrigation of infected bone, or via application as part of any admixture with a prosthetic device. The method of administration can vary depending on various factors, e.g., the components of the pharmaceutical composition, the site of the disease, the disease involved, and the severity of the disease.

[0067] A "diagnostic" as used herein is a compound, method, system, or device that assists in the identification or characterization of a health or disease state. The diagnostic can be used in standard assays as is known in the art.

[0068] The term "mammal" is used in its usual biological sense. Thus, it specifically includes humans, cattle, horses,

monkeys, dogs, cats, mice, rats, cows, sheep, pigs, goats, and non-human primates, but also includes many other species.

[0069] The term "pharmaceutically acceptable carrier", "pharmaceutically acceptable diluent" or "pharmaceutically acceptable excipient" includes any and all solvents, co-solvents, complexing agents, dispersion media, coatings, isotonic and absorption delaying agents and the like which are not biologically or otherwise undesirable. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. In addition, various adjuvants such as are commonly used in the art may be included. These and other such compounds are described in the literature, e.g., in the Merck Index, Merck & Company, Rahway, N.J. Considerations for the inclusion of various components in pharmaceutical compositions are described, e.g., in Gilman et al. (Eds.) (2010); *Goodman and Gilman's: The Pharmacological Basis of Therapeutics,* 12th Ed., The McGraw-Hill Companies.

[0070] The term "pharmaceutically acceptable salt" refers to salts that retain the biological effectiveness and properties of the compounds provided herein and, which are not biologically or otherwise undesirable. In many cases, the compounds provided herein are capable of forming acid and/or base salts by virtue of the presence of amino and/or carboxyl groups or groups similar thereto. Many such salts are known in the art, for example, as described in WO 87/05297. Pharmaceutically acceptable acid addition salts can be formed with inorganic acids and organic acids. Inorganic acids from which salts can be derived include, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like. Organic acids from which salts can be derived include, for example, acetic acid, propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. Pharmaceutically acceptable base addition salts can be formed with inorganic and organic bases. Inorganic bases from which salts can be derived include, for example, sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum, and the like; particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Organic bases from which salts can be derived include, for example, primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines, basic ion exchange resins, and the like, specifically such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

[0071] "Solvate" refers to the compound formed by the interaction of a solvent and a compound as provided herein or a salt thereof. Suitable solvates are pharmaceutically acceptable solvates including hydrates.

[0072] "Patient" as used herein, means a human or a non-human mammal, e.g., a dog, a cat, a mouse, a rat, a cow, a sheep, a pig, a goat, a non-human primate, or a bird, e.g., a chicken, as well as any other vertebrate or invertebrate. In some embodiments, the patient is a human.

[0073] A "therapeutically effective amount" or "pharmaceutically effective amount" of a compound as provided herein is one which is sufficient to achieve the desired physiological effect and may vary according to the nature and severity of the disease condition, and the potency of the compound. "Therapeutically effective amount" is also intended to include one or more of the compounds of Formula I in combination with one or more other agents that are effective to treat the diseases and/or conditions described herein. The combination of compounds can be a synergistic combination. Synergy, as described, for example, by Chou and Talalay, *Advances in Enzyme Regulation* (1984), 22, 27-55, occurs when the effect of the compounds when administered in combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a synergistic effect is most clearly demonstrated at sub-optimal concentrations of the compounds. It will be appreciated that different concentrations may be employed for prophylaxis than for treatment of an active disease. This amount can further depend upon the patient's height, weight, sex, age and medical history.

[0074] A therapeutic effect relieves, to some extent, one or more of the symptoms of the disease.

[0075] "Treat," "treatment," or "treating," as used herein refers to administering a compound or pharmaceutical composition as provided herein for therapeutic purposes. The term "therapeutic treatment" refers to administering treatment to a patient already suffering from a disease thus causing a therapeutically beneficial effect, such as ameliorating existing symptoms, ameliorating the underlying metabolic causes of symptoms, postponing or preventing the further development of a disorder, and/or reducing the severity of symptoms that will or are expected to develop.

[0076] "Drug-eluting" and/or controlled release as used herein refers to any and all mechanisms, e.g., diffusion, migration, permeation, and/or desorption by which the drug(s) incorporated in the drug-eluting material pass therefrom over time into the surrounding body tissue.

[0077] "Drug-eluting material" and/or controlled release material as used herein refers to any natural, synthetic or semi-synthetic material capable of acquiring and retaining a desired shape or configuration and into which one or more drugs can be incorporated and from which incorporated drug(s) are capable of eluting over time.

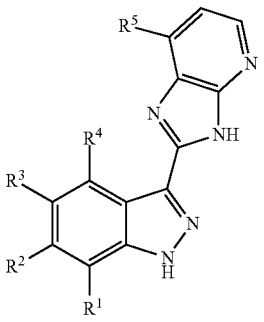
[0078] "Elutable drug" as used herein refers to any drug or combination of drugs having the ability to pass over time from the drug-eluting material in which it is incorporated into the surrounding areas of the body.

[0079] The term "comprising" as used herein is synonymous with "including," "containing," or "characterized by," and is inclusive or open-ended and does not exclude additional, unrecited elements or method steps.

[0080] Compounds

[0081] The compounds and compositions described herein can be used as anti-proliferative agents, e.g., anti-cancer and anti-angiogenesis agents, and/or as inhibitors of the Wnt signaling pathway, e.g., for treating diseases or disorders associated with aberrant Wnt signaling. In addition, the compounds can be used as inhibitors of one or more kinases, kinase receptors, or kinase complexes. Such compounds and compositions are also useful for controlling cellular proliferation, differentiation, and/or apoptosis.

[0082] Some embodiments of the present disclosure include compounds of Formula



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or salts, pharmaceutically acceptable salts, or prodrugs thereof.

[0083] In some embodiments, R^1, R^2, and R^4 are independently selected from the group consisting of H and halide.

[0084] In some embodiments, R^3 is selected from the group consisting of -pyridinyl$(R^6)_q$ and -pyrimidinyl$(R^7)_q$.

[0085] In some embodiments, R^3 is selected from the group consisting of -piperidinyl$(R^7)_h$ and -tetrahydropyridinyl$(R^7)_h$.

[0086] In some embodiments, R^3 is selected from the group consisting of -pyridinyl$(R^6)_q$, -pyrimidinyl$(R^6)_q$, -pyrazinyl$(R^6)_q$, -pyrazolyl$(R^6)_q$, and -imidazolyl$(R^6)_q$.

[0087] In some embodiments, R^3 is selected from the group consisting of -heteroaryl$(R^6)_q$ and -heterocyclyl$(R^7)_h$.

[0088] In some embodiments, R^5 is selected from the group consisting of H, -heteroaryl$(R^8)_q$, -heterocyclyl$(R^9)_h$, and -aryl$(R^{10})_k$.

[0089] In some embodiments, R^5 is selected from the group consisting of H, -pyridinyl(R^8), -imidazolyl(R^8), -furanyl$(R^8)_q$, -thiophenyl$(R^8)_q$, -piperidinyl$(R^9)_h$, -piperazinyl$(R^9)_h$, and -phenyl$(R^{10})_k$.

[0090] In some embodiments, each R^6 is one substituent attached to the pyridinyl and is independently selected from the group consisting of H, halide, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{11})_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{12})_j$, —$(C_{1-4}$ alkylene$)_p$aryl$(R^{13})_k$, —NHC(═O)R^4, —$NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)NR^{17}R^{18}$, and —OR^{24}.

[0091] In some embodiments, each R^6 is one substituent attached to the pyridinyl and is independently selected from the group consisting of halide, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{11})_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{12})_j$, —$(C_{1-4}$ alkylene$)_p$aryl$(R^{13})_k$, —NHC(═O)R^4, —$NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)NR^{17}R^{18}$, and —OR^{24}.

[0092] In some embodiments, each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of H, halide, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{11})_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{12})_j$, —$(C_{1-4}$ alkylene$)_p$aryl$(R^{13})_k$, —NHC(═O)R^4, —$NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)NR^{17}R^{18}$, and —OR^{24}.

[0093] In some embodiments, each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of halide, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{11})_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{12})_j$, —$(C_{1-4}$ alkylene$)_p$aryl$(R^{13})_k$, —NHC(═O)R^4, —$NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)NR^{17}R^{18}$, and —OR^{24}.

[0094] In some embodiments, each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of F, -Me, -Et, —(CH_2)heterocyclyl$(R^{11})_h$, -heterocyclyl$(R^{11})_h$, —(CH_2)carbocyclyl$(R^2)_j$, —(CH_2)aryl$(R^3)_k$, —NHC(═O)$(C_{1-5}$ alkyl), —NHC(═O)phenyl$(R^{21})_k$, —NHC(═O)(CH_2)phenyl$(R^{21})_k$, —NHC(═O)carbocyclyl$(R^{22})_j$, —NHC(═O)(CH_2)heterocyclyl$(R^{23})_h$, —NH_2, —$N(C_{1-3}$ alkyl$)_2$, —$NH(C_{1-4}$ alkyl), —$(CH_2)N(C_{1-3}$ alkyl$)_2$, —$(CH_2)NH(C_{1-4}$ alkyl), —OH, —$O(C_{1-3}$ alkyl), —Ocarbocyclyl$(R^{22})_j$, —Oheterocyclyl$(R^{23})_h$, —$O(CH_2CH_2)$heterocyclyl$(R^{23})_h$, —$O(CH_2CH_2)N(C_{1-3}$ alkyl$)_2$, and —$O(CH_2)$phenyl$(R^{21})_k$.

[0095] In some embodiments, each R^7 is one substituent attached to the pyrimidinyl and is independently selected from the group consisting of H, halide, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{11})_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{12})_j$, —$(C_{1-4}$ alkylene$)_p$aryl$(R^{13})_k$, —NHC(═O)R^4, —$NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)NR^{17}R^{18}$, and —OR^{24}.

[0096] In some embodiments, each R^7 is one substituent attached to the pyrimidinyl and is independently selected from the group consisting of halide, —$(C_{1-6}$ alkyl), —$(C_{1-4}$ alkylene$)_p$heterocyclyl$(R^{11})_h$, —$(C_{1-4}$ alkylene$)_p$carbocyclyl$(R^{12})_j$, —$(C_{1-4}$ alkylene$)_p$aryl$(R^{13})_k$, —NHC(═O)R^4, —$NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)NR^{17}R^{18}$, and —OR^{24}.

[0097] In some embodiments, each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of H, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0098] In some embodiments, each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0099] In some embodiments, each R^8 is one substituent attached to the heteroaryl and is independently selected from the group consisting of H, —$(C_{1-6}$ alkyl), halide, —CF_3, —OCH_3, —CN, and —C(═O)R^{19}.

[0100] In some embodiments, each R^8 is one substituent attached to the heteroaryl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —OCH_3, —CN, and —C(═O)R^{19}.

[0101] In some embodiments, each R^8 is one substituent attached to the heteroaryl and is independently selected from the group consisting of H, -Me, -Et, F, —CF_3, —OCH_3, —CN, and —C(═O)$(C_{1-3}$ alkyl).

[0102] In some embodiments, each R^8 is one substituent attached to the heteroaryl and is independently selected from the group consisting of -Me, -Et, F, —CF_3, —OCH_3, —CN, and —C(═O)$(C_{1-3}$ alkyl).

[0103] In some embodiments, each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of H, —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, and —OCH_3.

[0104] In some embodiments, each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, and —OCH_3.

[0105] In some embodiments, each R^{10} is one substituent attached to the aryl and is independently selected from the group consisting of H, —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, —OCH_3, —$(C_{1-6}$ alkylene$)_p NHSO_2R^{19}$, —$NR^{15}(C_{1-6}$ alkylene$)NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)_p NR^{15}R^{16}$, and —OR^{27}.

[0106] In some embodiments, each R^{10} is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-6}$ alkyl), halide, —CF_3, —CN, —OCH_3, —$(C_{1-6}$ alkylene$)_p NHSO_2R^{19}$, —$NR^{15}(C_{1-6}$ alkylene$)NR^{15}R^{16}$, —$(C_{1-6}$ alkylene$)_p NR^{15}R^{16}$, and —OR^{27}.

[0107] In some embodiments, each R^{10} is one substituent attached to the aryl and is independently selected from the

group consisting of H, -Me, -Et, F, —CF_3, —CN, —OCH_3, —$(CH_2CH_2)NHSO_2(C_{1-3}$ alkyl), —$NH(CH_2CH_2)N(C_{1-3}$ alkyl)$_2$, —OH, —$O(C_{1-3}$ alkyl), —$O(CH_2CH_2)$heterocyclyl $(R^{23})_h$, and —$O(CH_2CH_2)N(C_{1-3}$ alkyl)$_2$.

[0108] In some embodiments, each R^{10} is one substituent attached to the aryl and is independently selected from the group consisting of -Me, -Et, F, —CF_3, —CN, —OCH_3, —$(CH_2CH_2)NHSO_2(C_{1-3}$ alkyl), —$NH(CH_2CH_2)N(C_{1-3}$ alkyl)$_2$, —OH, —$O(C_{1-3}$ alkyl), —$O(CH_2CH_2)$heterocyclyl $(R^{23})_h$, and —$O(CH_2CH_2)N(C_{1-3}$ alkyl)$_2$.

[0109] In some embodiments, each R^{11} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of H, amino, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0110] In some embodiments, each R^{11} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0111] In some embodiments, each R^{11} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, Me, Et, F, Cl, and —CF_3.

[0112] In some embodiments, each R^{12} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of H, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0113] In some embodiments, each R^{12} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0114] In some embodiments, each R^{12} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

[0115] In some embodiments, each R^{13} is one substituent attached to the aryl and is independently selected from the group consisting of H, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0116] In some embodiments, each R^{13} is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0117] In some embodiments, each R^{13} is one substituent attached to the aryl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

[0118] In some embodiments, each R^{14} is independently selected from the group consisting of —$(C_{1-9}$ alkyl), -heteroaryl$(R^{20})_q$, -aryl$(R^{21})_k$, —CH_2aryl$(R^{21})_k$, -carbocyclyl $(R^{22})_j$, and —CH_2carbocyclyl$(R^{22})_j$.

[0119] In some embodiments, each R^{14} is independently selected from the group consisting of —$(C_{1-9}$ alkyl), -heteroaryl$(R^{20})_q$, -aryl$(R^{21})_k$, —CH_2aryl$(R^{21})_k$, -carbocyclyl $(R^{22})_j$, —CH_2carbocyclyl$(R^{22})_j$, —$(C_{1-4}$ alkylene$)_pNR^{25}R^{26}$, -heterocyclyl$(R^{23})_h$, and —CH_2heterocyclyl $(R^{23})_h$.

[0120] In some embodiments, each R^{14} is independently selected from the group consisting of —$(C_{1-5}$ alkyl), -phenyl $(R^{21})_k$, —(CH_2)phenyl$(R^{21})_k$, -carbocyclyl$(R^{22})_j$, —(CH_2) carbocyclyl$(R^{22})_j$, —$(CH_2)N(C_{1-3}$ alkyl)$_2$, and —(CH_2)heterocyclyl$(R^{23})_h$.

[0121] In some embodiments, each R^{15} is independently selected from the group consisting of H and —$(C_{1-6}$ alkyl).

[0122] In some embodiments, each R^{15} is independently selected from the group consisting of H and —$(C_{1-3}$ alkyl).

[0123] In some embodiments, each R^{16} is independently selected from the group consisting of H, —$(C_{1-6}$ alkyl), —CH_2aryl$(R^{21})_k$, and —CH_2carbocyclyl(R^{22}).

[0124] In some embodiments, each R^{16} is independently selected from the group consisting of H, —$(C_{1-3}$ alkyl), —CH_2phenyl$(R^{21})_k$, and —CH_2carbocyclyl$(R^{22})_j$.

[0125] In some embodiments, each R^{17} is independently selected from the group consisting of H and —$(C_{1-6}$ alkyl).

[0126] In some embodiments, each R^{17} is independently selected from the group consisting of H and —$(C_{1-3}$ alkyl).

[0127] In some embodiments, each R^{18} is independently selected from the group consisting of H, —$(C_{1-6}$ alkyl), —CH_2aryl$(R^{21})_k$, and —CH_2carbocyclyl(R^{22}).

[0128] In some embodiments, each R^{18} is independently selected from the group consisting of H, —$(C_{1-3}$ alkyl), —CH_2phenyl$(R^{21})_k$, and —CH_2carbocyclyl$(R^{22})_j$.

[0129] In some embodiments, each R^{19} is independently a —$(C_{1-6}$ alkyl).

[0130] In some embodiments, each R^{19} is independently a —$(C_{1-3}$ alkyl).

[0131] In some embodiments, each R^{20} is one substituent attached to the heteroaryl and is independently selected from the group consisting of H, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0132] In some embodiments, each R^{20} is one substituent attached to the heteroaryl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0133] In some embodiments, each R^{20} is one substituent attached to the heteroaryl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

[0134] In some embodiments, each R^{21} is one substituent attached to the aryl and is independently selected from the group consisting of H, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0135] In some embodiments, each R^{21} is one substituent attached to the aryl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0136] In some embodiments, each R^{21} is one substituent attached to the aryl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

[0137] In some embodiments, each R^{22} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of H, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0138] In some embodiments, each R^{22} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0139] In some embodiments, each R^{22} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

[0140] In some embodiments, each R^{23} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of H, —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0141] In some embodiments, each R^{23} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —$(C_{1-4}$ alkyl), halide, —CF_3, and —CN.

[0142] In some embodiments, each R^{23} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of Me, Et, F, Cl, and —CF_3.

[0143] In some embodiments, R^{24} is selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{23})$_h$, —(C_{1-4} alkylene)$_p$carbocyclyl(R^{22})$_j$, —(C_{1-4} alkylene)$_p$aryl(R^{21})$_k$, and —(C_{1-6} alkylene)$_p$$NR^{25}R^{26}$.

[0144] In some embodiments, R^{24} is selected from the group consisting of H, -Me, -Et, -iPr, -heterocyclyl(R^{23})$_h$, —(CH_2CH_2)heterocyclyl(R^{23})$_h$, -carbocyclyl(R^{22})$_j$, —(CH_2)phenyl(R^{21})$_k$, and —(CH_2CH_2)N(C_{1-3} alkyl)$_2$.

[0145] In some embodiments, each R^{25} is independently selected from the group consisting of H and —(C_{1-6} alkyl).

[0146] In some embodiments, each R^{25} is independently selected from the group consisting of Me and Et.

[0147] In some embodiments, each R^{26} is independently selected from the group consisting of H and —(C_{1-6} alkyl).

[0148] In some embodiments, each R^{26} is independently selected from the group consisting of Me and Et.

[0149] In some embodiments, R^{27} is selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl(R^{23})$_h$, and —(C_{1-6} alkylene)$_p$$NR^{25}R^{26}$.

[0150] In some embodiments, R^{27} is selected from the group consisting of H, -Me, -Et, -iPr, —(CH_2CH_2)heterocyclyl(R^{23})$_h$, and —(CH_2CH_2)N(C_{1-3} alkyl)$_2$.

[0151] In some embodiments, each p is independently 0 or 1; in some embodiments, each p is 0; in some embodiments, each p is 1.

[0152] In some embodiments, each q is independently 0 to 4; in some embodiments, each q is 0; in some embodiments, each q is 1; in some embodiments, each q is 2; in some embodiments, each q is 3; in some embodiments, each q is 4.

[0153] In some embodiments, each h is independently 0 to 10; in some embodiments, each h is 0; in some embodiments, each h is 1; in some embodiments, each h is 2; in some embodiments, each h is 3; in some embodiments, each h is 4.

[0154] In some embodiments, each k is independently 0 to 5; in some embodiments, each k is 0; in some embodiments, each k is 1; in some embodiments, each k is 2; in some embodiments, each k is 3.

[0155] In some embodiments, each j is independently 0 to 12; in some embodiments, each j is 0; in some embodiments, each j is 1; in some embodiments, each j is 2; in some embodiments, each j is 3; in some embodiments, each j is 4.

[0156] In some embodiments, each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-3} alkyl), —CH_2heterocyclyl(R^{11})$_h$, —NHC(=O)R^{14}, —$NR^{15}R^{16}$, and —$CH_2NR^{17}R^{18}$.

[0157] In some embodiments, at least one R^{11} is halide.

[0158] In some embodiments, R^{14} is selected from the group consisting of —(C_{1-5} alkyl), -phenyl(R^{21})$_k$, —CH_2phenyl(R^{21})$_k$, and -carbocyclyl(R^{22})$_j$.

[0159] In some embodiments, each R^{15} and R^{16} are independently selected from H and —(C_{1-5} alkyl).

[0160] In some embodiments, each R^{17} and R^{18} are independently selected from H and —(C_{1-5} alkyl).

[0161] In some embodiments, k is 1 or 2 and each R^{10} is independently a halide.

[0162] In some embodiments, k is 2 and one R^{10} is halide and the other R^{10} is —$CH_2NHSO_2R^9$.

[0163] In some embodiments, R^{19} is —(C_{1-3} alkyl).

[0164] In some embodiments, k is 2 and one R^{10} is halide and the other R^{10} is —$NHCH_2CH_2NR^{15}R^{16}$.

[0165] In some embodiments, each R^{15} and R^{16} are independently selected from H and —(C_{1-3} alkyl).

[0166] In some embodiments, R^5 is selected from the group consisting of -pyridinyl(R^8)$_q$, -imidazolyl(R^8)$_q$, -furanyl(R^8)$_q$, and -thiophenyl(R^8)$_q$.

[0167] In some embodiments, q is 0 or 1, and R^8 is selected from the group consisting of halide, —(C_{1-3} alkyl), —C(=O)R^{19}, wherein R^{19} is —(C_{1-2} alkyl).

[0168] In some embodiments, R^5 is selected from the group consisting of -piperidinyl(R^9)$_h$ and -piperazinyl(R^9)$_h$.

[0169] In some embodiments, q is 1, and R^9 is selected from the group consisting of H and —(C_{1-3} alkyl).

[0170] In some embodiments, R^1 is H; in other embodiments, R^1 is halide, e.g. F.

[0171] In some embodiments, R^2 is H; in other embodiments, R^2 is halide, e.g. F.

[0172] In some embodiments, R^4 is H; in other embodiments, R^4 is halide, e.g. F.

[0173] In some embodiments, R^2 and R^4 are H, and R^1 is F; in some embodiments, R^1 and R^4 are H, and R^2 is F; in some embodiments, R^1 and R^2 are H, and R^4 is F; in some embodiments, R^2 and R^4 are F, and R^1 is H; in some embodiments, R^1 and R^4 are F, and R^2 is H; in some embodiments, R^1 and R^2 are F, and R^4 is H; in some embodiments, R^1, R^2, and R^4 are H; in some embodiments, R^1, R^2, and R^4 are F.

[0174] In some embodiments, R^3 is -heteroaryl(R^6)$_q$.

[0175] In some embodiments, R^3 is -pyridinyl(R^6)$_q$.

[0176] In some embodiments, R^3 is -pyridin-3-yl(R^6)$_q$.

[0177] In some embodiments, R^3 is -pyrimidinyl(R^6)$_q$.

[0178] In some embodiments, R^3 is -pyrimidin-5-yl(R^6)$_q$.

[0179] In some embodiments, R^3 is -pyrimidin-5-yl(R^6)$_q$ and q is 0.

[0180] In some embodiments, R^3 is -pyrazinyl(R^6)$_q$.

[0181] In some embodiments, R^3 is -pyrazolyl(R^6)$_q$.

[0182] In some embodiments, R^3 is -pyrazol-4-yl(R^6)$_q$, q is 1, and R^6 is Me.

[0183] In some embodiments, R^3 is -pyrazol-4-yl(R^6)$_q$ and q is 0.

[0184] In some embodiments, R^3 is -imidazolyl(R^6)$_q$.

[0185] In some embodiments, R^3 is -imidazol-5-yl(R^6)$_q$, q is 1, and R^6 is Me.

[0186] In some embodiments, R^3 is -imidazol-5-yl(R^6)$_q$, q is 2, and both R^6 are Me.

[0187] In some embodiments, R^3 is -heterocyclyl(R^7)$_h$.

[0188] In some embodiments, R^3 is -piperidinyl(R^7)$_h$.

[0189] In some embodiments, R^3 is -piperidin-4-yl(R^7)$_h$.

[0190] In some embodiments, R^3 is -piperidin-4-yl(R^7)$_h$, and h is 0.

[0191] In some embodiments, R^3 is -tetrahydropyridinyl(R^7)$_h$.

[0192] In some embodiments, R^3 is -1,2,3,6-tetrahydropyridinyl(R^7)$_h$.

[0193] In some embodiments, R^3 is -1,2,3,6-tetrahydropyridinyl(R^7)$_h$, and h is 0.

[0194] In some embodiments, R^5 is H.

[0195] In some embodiments, R^5 is -heteroaryl(R^8)$_q$.

[0196] In some embodiments, R^5 is -heterocyclyl(R^9)$_h$.

[0197] In some embodiments, R^5 is -piperidinyl(R^9)$_h$.

[0198] In some embodiments, R^5 is -piperazinyl(R^9)$_h$.

[0199] In some embodiments, R^5 is -aryl(R^{10})$_k$.

[0200] In some embodiments, R^5 is -phenyl(R^{10})$_k$.

[0201] In some embodiments, R^5 is -pyridinyl(R^8)$_q$.

[0202] In some embodiments, R^5 is -pyridin-3-yl(R^8)$_q$.

[0203] In some embodiments, R^5 is -pyridin-4-yl$(R^8)_q$.

[0204] In some embodiments, R^5 is -pyridin-5-yl$(R^8)_q$.

[0205] In some embodiments, R^5 is -pyridin-3-yl$(R^8)_q$ and q is 0.

[0206] In some embodiments, R^5 is -pyridin-4-yl$(R^8)_q$ and q is 0.

[0207] In some embodiments, R^5 is -pyridin-5-yl$(R^8)_q$ and q is 0.

[0208] In some embodiments, R^5 is -imidazolyl$(R^8)_q$.

[0209] In some embodiments, R^5 is -imidazol-1-yl$(R^8)_q$, q is 1, and R^8 is —(C_{1-3} alkyl).

[0210] In some embodiments, R^5 is -imidazol-1-yl$(R^8)_q$, q is 1, and R^8 is methyl.

[0211] In some embodiments, R^5 is -furanyl$(R^8)_q$.

[0212] In some embodiments, R^5 is -furan-2-yl$(R^8)_q$.

[0213] In some embodiments, R^5 is -furan-2-yl$(R^8)_q$ and q is 0.

[0214] In some embodiments, R^5 is -furan-3-yl$(R^8)_q$.

[0215] In some embodiments, R^5 is -furan-3-yl$(R^8)_q$ and q is 0.

[0216] In some embodiments, R^5 is -thiophenyl$(R^8)_q$.

[0217] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$.

[0218] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$ and q is 0.

[0219] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1 or 2, and each R^8 is independently a halide.

[0220] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1 or 2, and R^8 is F.

[0221] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1 or 2, and each R^8 is independently a —(C_{1-6} alkyl).

[0222] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1 or 2, and each R^8 is independently a —(C_{1-2} alkyl).

[0223] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1 or 2, and R^8 is methyl.

[0224] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1 or 2, and R^8 is —CF_3.

[0225] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1 or 2, and R^8 is CN.

[0226] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1, and R^8 is —C(=O)R^9.

[0227] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1, R^8 is —C(=O)R^{19}, and R^{19} is —(C_{1-6} alkyl).

[0228] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1, R^8 is —C(=O)R^{19}, and R^{19} is —(C_{1-4} alkyl).

[0229] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1, R^8 is —C(=O)R^{19}, and R^{19} is —(C_{1-2} alkyl).

[0230] In some embodiments, R^5 is -thiophen-2-yl$(R^8)_q$, q is 1, R^8 is —C(=O)R^{19}, and R^{19} is methyl.

[0231] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$.

[0232] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$ and q is 0.

[0233] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1 or 2, and each R^8 is independently a halide.

[0234] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1 or 2, and R^8 is F.

[0235] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1 or 2, and each R^8 is independently a —(C_{1-6} alkyl).

[0236] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1 or 2, and each R^8 is independently a —(C_{1-2} alkyl).

[0237] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1 or 2, and R^8 is methyl.

[0238] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1 or 2, and R^8 is —CF_3.

[0239] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1 or 2, and R^8 is CN.

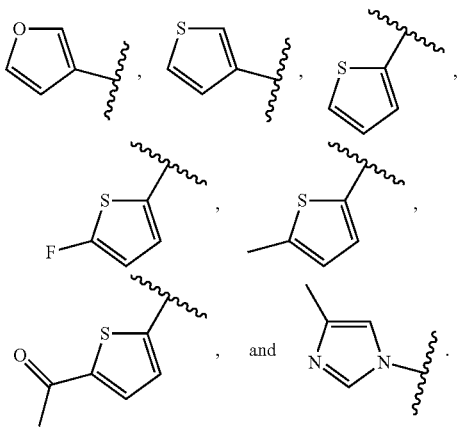
[0240] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1, and R^8 is —C(=O)R^9.

[0241] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1, R^8 is —C(=O)R^{19}, and R^{19} is —(C_{1-4} alkyl).

[0242] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1, R^8 is —C(=O)R^{19}, and R^{19} is —(C_{1-2} alkyl).

[0243] In some embodiments, R^5 is -thiophen-3-yl$(R^8)_q$, q is 1, R^8 is —C(=O)R^{19}, and R^{19} is methyl.

[0244] In some embodiments, R^5 is selected from the group consisting of:



[0245] In some embodiments, R^5 is -phenyl$(R^{10})_k$.

[0246] In some embodiments, R^5 is -phenyl$(R^{10})_k$ and k is 0.

[0247] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 1 or 2, and each R^{10} is independently a halide.

[0248] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 1 or 2, and R^{10} is F.

[0249] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 1, and R^{10} is F.

[0250] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is a halide and the other R^{10} is —(C_{1-6} alkylene)$_p$$NHSO_2R^9$.

[0251] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is a halide and the other R^{10} is —(C_{1-4} alkylene)$_p$$NHSO_2R^{19}$, and p is 1.

[0252] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is a halide and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$, and p is 1.

[0253] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is a halide and the other R^{10} is —$CH_2NHSO_2R^{19}$.

[0254] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is a halide and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is —(C_{1-4} alkyl).

[0255] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is a halide and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is —(C_{1-2} alkyl).

[0256] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is a halide and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is methyl.

[0257] In some embodiments, R^5 is -phenyl$(R^{10})_k$, k is 2, one R^{10} is F and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is —(C_{1-2} alkyl).

[0258] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is F and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is methyl.

[0259] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —NR^{15}(C_{1-6} alkylene) $NR^{15}R^{16}$.

[0260] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —NR^{15}(C_{1-5} alkylene) $NR^{15}R^{16}$.

[0261] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —NR^{15}(C_{1-4} alkylene) $NR^{15}R^{16}$.

[0262] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —NR^{15}(C_{1-3} alkylene) $NR^{15}R^{16}$.

[0263] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$NR^{15}CH_2CH_2NR^{15}R^{16}$.

[0264] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$NHCH_2CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently a —(C_{1-6} alkyl).

[0265] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$NHCH_2CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently a —(C_{1-4} alkyl).

[0266] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$NHCH_2CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently a —(C_{1-2} alkyl).

[0267] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$NHCH_2CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are both methyl.

[0268] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is F and the other R^{10} is —$NHCH_2CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are independently a —(C_{1-2} alkyl).

[0269] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is F and the other R^{10} is —$NHCH_2CH_2NR^{15}R^{16}$, and R^{15} and R^{16} are both methyl.

[0270] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$OCH_2CH_2NR^{25}R^{26}$.

[0271] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$OCH_2CH_2NR^{25}R^{26}$, and R^{25} and R^{26} are independently a —(C_{1-2} alkyl).

[0272] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$OCH_2CH_2NR^{25}R^{26}$, and R^{25} and R^{26} are both methyl.

[0273] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is F and the other R^{10} is —$OCH_2CH_2NR^{25}R^{26}$, and R^{25} and R^{26} are both methyl.

[0274] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is —(C_{1-4} alkyl).

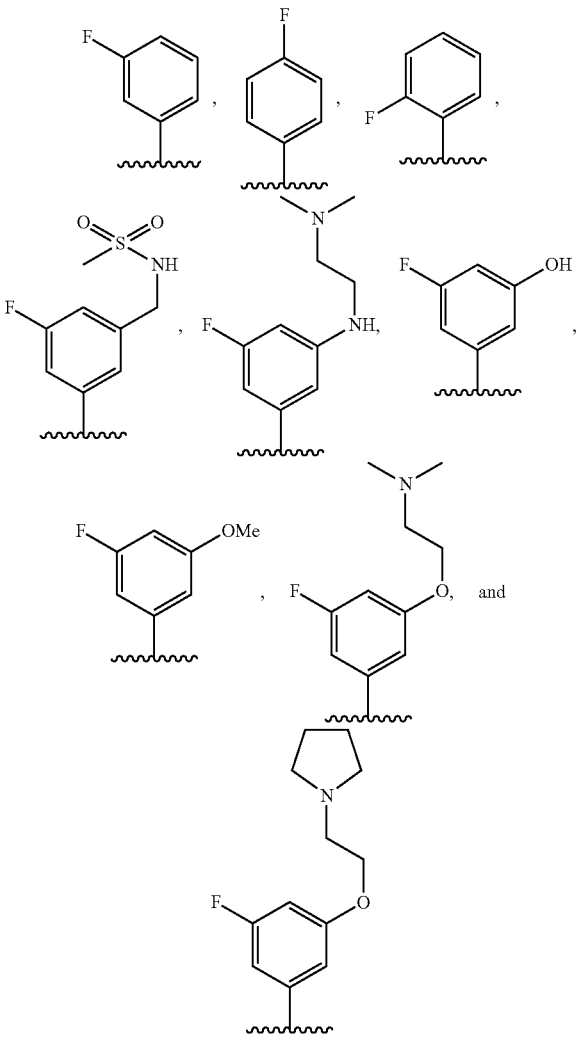
[0275] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is —(C_{1-2} alkyl).

[0276] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is halide and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is methyl.

[0277] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is F and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is —(C_{1-2} alkyl).

[0278] In some embodiments, R^5 is -phenyl(R^{10})$_k$, k is 2, one R^{10} is F and the other R^{10} is —$CH_2NHSO_2R^{19}$, and R^{19} is methyl.

[0279] In some embodiments, R^5 is selected from the group consisting of:



[0280] In some embodiments, R^5 is -piperidinyl(R^9)$_h$.

[0281] In some embodiments, R^5 is -piperidin-1-yl(R^9)$_h$.

[0282] In some embodiments, R^5 is -piperidin-1-yl(R^9)$_h$ and h is 0.

[0283] In some embodiments, R^5 is -piperidin-1-yl(R^9)$_h$, h is 1 or 2, and each R^9 is independently selected from a halide.

[0284] In some embodiments, R^5 is -piperazinyl(R^9)$_h$.

[0285] In some embodiments, R^5 is -piperazin-1-yl(R^9)$_h$.

[0286] In some embodiments, R^5 is -piperazin-1-yl(R^9)$_h$, h is 1, and R^9 is C_{1-3} alkyl.

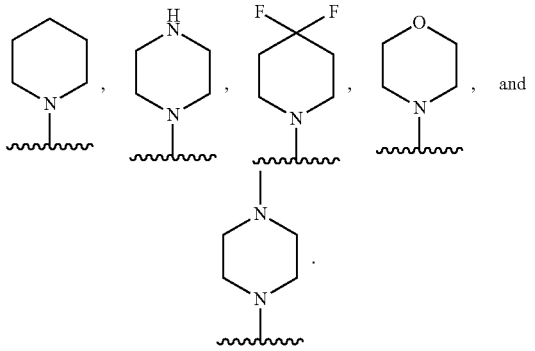
[0287] In some embodiments, R^5 is -piperazin-1-yl(R^9)$_h$, h is 1, and R^9 is methyl.

[0288] In some embodiments, R^5 is -morpholinyl(R^9)$_h$.

[0289] In some embodiments, R^5 is -morpholin-1-yl(R^9)$_h$.

[0290] In some embodiments, R^5 is -morpholin-1-yl(R^9)$_h$ and h is 0.

[0291] In some embodiments, R^5 is selected from the group consisting of:



[0292] In some embodiments, q is 0.

[0293] In some embodiments, at least one R^6 is a halide.

[0294] In some embodiments, at least one R^6 is a F.

[0295] In some embodiments, R^6 is F.

[0296] In some embodiments, at least one R^6 is —(C_{1-6} alkyl).

[0297] In some embodiments, at least one R^6 is —(C_{1-5} alkyl).

[0298] In some embodiments, at least one R^6 is —(C_{1-4} alkyl).

[0299] In some embodiments, at least one R^6 is —(C_{1-3} alkyl).

[0300] In some embodiments, at least one R^6 is —(C_{1-2} alkyl).

[0301] In some embodiments, at least one R^6 is methyl.

[0302] In some embodiments, R^6 is a methyl.

[0303] In some embodiments, at least one R^6 is —(C_{1-4} alkylene)$_p$heterocyclyl(R^{11})$_h$ and p is 0 or 1.

[0304] In some embodiments, at least one R^6 is —(C_{1-3} alkylene)$_p$heterocyclyl(R^{11})$_h$ and p is 0 or 1.

[0305] In some embodiments, at least one R^6 is —(C_{1-2} alkylene)$_p$heterocyclyl(R^{11})$_h$ and p is 0 or 1.

[0306] In some embodiments, at least one R^6 is —CH_2pyrrolidinyl(R^{11})$_h$.

[0307] In some embodiments, at least one R^6 is —CH_2pyrrolidinyl(R^{11})$_h$ and h is 0.

[0308] In some embodiments, R^6 is a —CH_2pyrrolidinyl (R^{11})$_h$ and h is 0.

[0309] In some embodiments, at least one R^6 is —CH_2pyrrolidinyl(R^{11})$_h$, h is 1 or 2, and at least one R^{11} is a halide.

[0310] In some embodiments, at least one R^6 is —CH_2pyrrolidinyl(R^{11})$_h$, h is 1 or 2, and at least one R^{11} is F.

[0311] In some embodiments, R^6 is a —CH_2pyrrolidinyl (R^{11})$_h$, h is 1 or 2, and at least one R^{11} is halide.

[0312] In some embodiments, R^6 is —CH_2pyrrolidinyl (R^{11})$_h$, h is 1 or 2, and at least one R^{11} is F.

[0313] In some embodiments, R^6 is a —CH_2pyrrolidinyl (R^{11})$_h$, h is 1 or 2, and each R^{11} is F.

[0314] In some embodiments, at least one R^6 is —CH_2piperidinyl(R^{11})$_h$.

[0315] In some embodiments, at least one R^6 is —CH_2piperidinyl(R^{11})$_h$ and h is 0.

[0316] In some embodiments, R^6 is a —CH_2piperidinyl (R^{11})$_h$ and h is 0.

[0317] In some embodiments, at least one R^6 is —CH_2piperidinyl(R^{11})$_h$ and at least one R^{11} is a halide.

[0318] In some embodiments, at least one R^6 is —CH_2piperidinyl(R^{11})$_h$ and at least one R^{11} is F.

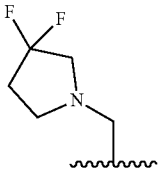
[0319] In some embodiments, at least one R^6 is —CH_2piperidinyl(R^{11})$_h$, h is 1 or 2, and each R^{11} is a halide.

[0320] In some embodiments, at least one R^6 is —CH_2piperidinyl(R^{11})$_h$, h is 1 or 2, and each R^{11} is F.

[0321] In some embodiments, R^6 is —CH_2piperidinyl (R^{11})$_h$, h is 1 or 2, and each R^{11} is a halide.

[0322] In some embodiments, R^6 is a —CH_2piperidinyl (R^{11})$_h$, h is 1 or 2, and each R^{11} is F.

[0323] In some embodiments, R^6 is a



[0324] In some embodiments, at least one R^6 is —(C_{1-4} alkylene)$_p$carbocyclyl(R^{12})$_j$.

[0325] In some embodiments, at least one R^6 is —(C_{1-4} alkylene)$_p$carbocyclyl(R^{12})$_j$ and j is 0 or 1.

[0326] In some embodiments, at least one R^6 is —(C_{1-3} alkylene)$_p$carbocyclyl(R^{12})$_j$ and j is 0 or 1.

[0327] In some embodiments, at least one R^6 is —(C_{1-2} alkylene)$_p$carbocyclyl(R^{12})$_j$ and j is 0 or 1.

[0328] In some embodiments, at least one R^6 is —CH_2carbocyclyl(R^2)$_j$.

[0329] In some embodiments, R^6 is a —CH_2carbocyclyl (R^2)$_j$.

[0330] In some embodiments, at least one R^6 is —(C_{1-4} alkylene)$_p$aryl(R^{13})$_k$ and k is 0 or 1.

[0331] In some embodiments, at least one R^6 is —(C_{1-3} alkylene)$_p$aryl(R^{13})$_k$ and k is 0 or 1.

[0332] In some embodiments, at least one R^6 is —(C_{1-2} alkylene)$_p$aryl(R^{13})$_k$ and k is 0 or 1.

[0333] In some embodiments, at least one R^6 is —CH_2aryl (R^{13})$_k$.

[0334] In some embodiments, at least one R^6 is —CH_2phenyl(R^3)$_k$.

[0335] In some embodiments, R^6 is a —CH_2phenyl(R^{13})$_k$.

[0336] In some embodiments, at least one R^6 is —NHC(=O)R^{14}.

[0337] In some embodiments, R^6 is a —NHC(=O)R^{14}.

[0338] In some embodiments, at least one R^6 is —NHC(=O)R^{14} and R^{14} is —(C_{1-9} alkyl).

[0339] In some embodiments, at least one R^6 is —NHC(=O)R^{14} and R^{14} is —(C_{1-8}alkyl).

[0340] In some embodiments, at least one R^6 is —NHC(=O)R^{14} and R^{14} is —(C_{1-7} alkyl).

[0341] In some embodiments, at least one R^6 is —NHC(=O)R^{14} and R^{14} is —(C_{1-6} alkyl).

[0342] In some embodiments, at least one R^6 is —NHC(=O)R^{14} and R^{14} is —(C_{1-5} alkyl).

[0343] In some embodiments, R^6 is a —NHC(=O)R^{14} and R^{14} is —(C_{1-5} alkyl).

[0344] In some embodiments, at least one R^6 is —NHC(=O)R^{14} and R^{14} is —(C_{1-4} alkyl).

[0345] In some embodiments, R^6 is a —NHC(═O)R^{14} and R^{14} is —(C_{1-4} alkyl).

[0346] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is —(C_{1-3} alkyl).

[0347] In some embodiments, R^6 is a —NHC(═O)R^{14} and R^{14} is —(C_{1-3} alkyl).

[0348] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is —(C_{1-2} alkyl).

[0349] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is —(C_{2-5} alkyl).

[0350] In some embodiments, R^6 is a —NHC(═O)R^{14} and R^{14} is —(C_{2-5} alkyl).

[0351] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is —(C_{3-4} alkyl).

[0352] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is -aryl$(R^{21})_k$.

[0353] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is -phenyl$(R^{21})_k$, and k is 0.

[0354] In some embodiments, R^6 is a —NHC(═O)R^{14}, R^{14} is -phenyl$(R^{21})_k$, and k is 0.

[0355] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is —CH_2aryl$(R^{21})_k$.

[0356] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is —CH_2phenyl$(R^{21})_k$, and k is 0.

[0357] In some embodiments, R^6 is a —NHC(═O)R^{14}, R^{14} is —CH_2phenyl$(R^{21})_k$, and k is 0.

[0358] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is -heteroaryl$(R^{20})_q$.

[0359] In some embodiments, at least one R^6 is —NHC(═O)R^{14} and R^{14} is -carbocyclyl$(R^{22})_j$.

[0360] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is -carbocyclyl$(R^{22})_j$, and j is 0.

[0361] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is -cyclopropyl$(R^{22})_j$, and j is 0.

[0362] In some embodiments, R^6 is a —NHC(═O)R^{14}, R^{14} is -cyclopropyl(R^{22}), and j is 0.

[0363] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is -cyclobutyl$(R^{22})_j$, and j is 0.

[0364] In some embodiments, R^6 is a —NHC(═O)R^{14}, R^{14} is -cyclobutyl$(R^2)_j$, and j is 0.

[0365] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is -cyclopentyl$(R^{22})_j$, and j is 0.

[0366] In some embodiments, R^6 is a —NHC(═O)R^{14}, R^{14} is -cyclopentyl$(R^{22})_j$, and j is 0.

[0367] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is -cyclohexyl$(R^{22})_j$, and j is 0.

[0368] In some embodiments, R^6 is a —NHC(═O)R^{14}, R^{14} is -cyclohexyl(R^{22})), and j is 0.

[0369] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is —CH_2carbocyclyl(R^{22})), and j is 0.

[0370] In some embodiments, at least one R^6 is —NHC(═O)R^{14}, R^{14} is —CH_2cyclopropyl$(R^{22})_j$, and j is 0.

[0371] In some embodiments, R^6 is a —NHC(═O)R^{14}, R^{14} is —CH_2cyclopropyl$(R^{22})_j$, and j is 0.

[0372] In some embodiments, at least one R^6 is —$NR^{15}R^{16}$.

[0373] In some embodiments, at least one R^6 is —$NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-6} alkyl).

[0374] In some embodiments, at least one R^6 is —$NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-5} alkyl).

[0375] In some embodiments, at least one R^6 is —$NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-4} alkyl).

[0376] In some embodiments, at least one R^6 is —$NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-3} alkyl).

[0377] In some embodiments, at least one R^6 is —$NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and —(C_{1-2} alkyl).

[0378] In some embodiments, at least one R^6 is —$NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and methyl.

[0379] In some embodiments, R^6 is a —$NR^{15}R^{16}$, and R^{15} and R^{16} are independently selected from the group consisting of H and methyl.

[0380] In some embodiments, at least one R^6 is —NH_2.

[0381] In some embodiments, R^6 is a —NH_2.

[0382] In some embodiments, at least one R^6 is —NHR^{16} and R^{16} is —(C_{1-4} alkyl).

[0383] In some embodiments, at least one R^6 is —NHR^{16} and R^{16} is —(C_{1-3} alkyl).

[0384] In some embodiments, R^6 is —NHR^{16} and R^{16} is —(C_{1-2} alkyl).

[0385] In some embodiments, at least one R^6 is —NHR^{16} and R^{16} is —CH_2aryl$(R^{21})_k$.

[0386] In some embodiments, R^6 is —NHR^{16}, R^{16} is —CH_2phenyl$(R^{21})_k$, and k is 0.

[0387] In some embodiments, at least one R^6 is —NHR^{16} and R^{16} is —CH_2carbocyclyl$(R^{22})_j$.

[0388] In some embodiments, at least one R^6 is —NHR^{16}, R^{16} is —CH_2cyclopropyl$(R^{22})_j$, and j is 0.

[0389] In some embodiments, R^6 is a —NHR^{16}, R^{16} is —CH_2cyclopropyl$(R^{22})_j$, and j is 0.

[0390] In some embodiments, at least one R^6 is —NHR^{16}, R^{16} is —CH_2cyclobutyl$(R^{22})_j$, and j is 0.

[0391] In some embodiments, R^6 is a —NHR^{16}, R^{16} is —CH_2cyclobutyl$(R^{22})_j$, and j is 0.

[0392] In some embodiments, at least one R^6 is —NHR^{16}, R^{16} is —CH_2cyclopentyl$(R^{22})_j$, and j is 0.

[0393] In some embodiments, R^6 is a —NHR^{16}, R^{16} is —CH_2cyclopentyl$(R^{22})_j$, and j is 0.

[0394] In some embodiments, at least one R^6 is —NHR^{16}, R^{16} is —CH_2cyclohexyl$(R^{22})_j$, and j is 0.

[0395] In some embodiments, R^6 is a —NHR^{16}, R^{16} is —CH_2cyclohexyl$(R^{22})_j$, and j is 0.

[0396] In some embodiments, at least one R^6 is —(C_{1-6} alkylene)$NR^{17}R^{18}$.

[0397] In some embodiments, at least one R^6 is —(C_{1-5} alkylene)$NR^{17}R^{18}$.

[0398] In some embodiments, at least one R^6 is —(C_{1-4} alkylene)$NR^{17}R^{18}$.

[0399] In some embodiments, at least one R^6 is —(C_{1-3} alkylene)$NR^{17}R^{18}$.

[0400] In some embodiments, at least one R^6 is —(C_{1-2} alkylene)$NR^{17}R^{18}$.

[0401] In some embodiments, at least one R^6 is —$CH_2NR^{17}R^{18}$.

[0402] In some embodiments, R^6 is a —$CH_2NR^{17}R^{18}$.

[0403] In some embodiments, at least one R^6 is —$CH_2NR^{17}R^{18}$, and R^{17} and R^{18} are independently selected from the group consisting of H and —(C_{1-6} alkyl).

[0404] In some embodiments, at least one R^6 is —$CH_2NR^{17}R^{18}$, and R^{17} and R^{18} are independently selected from the group consisting of H and —(C_{1-5} alkyl).

[0405] In some embodiments, at least one R^6 is $—CH_2NR^{17}R^{18}$, and R^{17} and R^{18} are independently selected from the group consisting of H and $—(C_{1-4}$ alkyl).

[0406] In some embodiments, at least one R^6 is $—CH_2NR^{17}R^{18}$, and R^{17} and R^{18} are independently selected from the group consisting of H and $—(C_{1-3}$ alkyl).

[0407] In some embodiments, at least one R^6 is $—CH_2NR^{17}R^{18}$, and R^{17} and R^{18} are independently selected from the group consisting of H and $—(C_{1-2}$ alkyl).

[0408] In some embodiments, at least one R^6 is $—CH_2NR^{17}R^{18}$, and R^{17} and R^{18} are independently selected from the group consisting of H and methyl.

[0409] In some embodiments, R^6 is a $—CH_2NR^{17}R^{18}$, and R^{17} and R^{18} are independently selected from the group consisting of H and methyl.

[0410] In some embodiments, at least one R^6 is $—CH_2NH_2$.

[0411] In some embodiments, R^6 is a $—CH_2NH_2$.

[0412] In some embodiments, at least one R^6 is $—CH_2NMe_2$.

[0413] In some embodiments, R^6 is a $—CH_2NMe_2$.

[0414] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$ and R^{18} is $—(C_{1-4}$ alkyl).

[0415] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$ and R^{18} is $—(C_{1-3}$ alkyl).

[0416] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$ and R^{18} is $—(C_{1-2}$ alkyl).

[0417] In some embodiments, R^6 is a $—CH_2NHR^{18}$ and R^{18} is $—(C_{1-2}$ alkyl).

[0418] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$ and R^{18} is $—CH_2aryl(R^{21})_k$.

[0419] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$, R^{18} is $—CH_2phenyl(R^{21})_k$, and k is 0.

[0420] In some embodiments, R^6 is a $—CH_2NHR^{18}$, R^{18} is $—CH_2phenyl(R^{21})_k$, and k is 0.

[0421] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$ and R^{18} is $—CH_2carbocyclyl(R^{22})_j$.

[0422] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclopropyl(R^{22})_j$, and j is 0.

[0423] In some embodiments, R^6 is a $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclopropyl(R^{22})_j$, and j is 0.

[0424] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclobutyl(R^{22})_j$, and j is 0.

[0425] In some embodiments, R^6 is a $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclobutyl(R^{22})_j$, and j is 0.

[0426] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclopentyl(R^{22})_j$, and j is 0.

[0427] In some embodiments, R^6 is a $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclopentyl(R^{22})_j$, and j is 0.

[0428] In some embodiments, at least one R^6 is $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclohexyl(R^{22})$, and j is 0.

[0429] In some embodiments, R^6 is a $—CH_2NHR^{18}$, R^{18} is $—CH_2cyclohexyl(R^{22})_j$, and j is 0.

[0430] In some embodiments, at least one R^6 is $—OR^{24}$.

[0431] In some embodiments, at least one R^6 is —OH.

[0432] In some embodiments, R^6 is a —OH.

[0433] In some embodiments, at least one R^6 is $—OR^{24}$ and R^{24} is $—(C_{1-3}$ alkyl).

[0434] In some embodiments, at least one R^6 is $—OR^{24}$ and R^{24} is $—(C_{1-2}$ alkyl).

[0435] In some embodiments, at least one R^6 is —OMe.

[0436] In some embodiments, R^6 is a —OMe.

[0437] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is -heterocyclyl$(R^{23})_h$, and h is 0.

[0438] In some embodiments, R^6 is a $—OR^{24}$, R^{24} is -heterocyclyl$(R^{23})_h$, and h is 0.

[0439] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is -carbocyclyl$(R^{22})_j$, and j is 0.

[0440] In some embodiments, R^6 is a $—OR^{24}$, R^{24} is -carbocyclyl$(R^{22})_j$, and j is 0.

[0441] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is $—(C_{1-4}$ alkylene)heterocyclyl$(R^{23})_h$, and h is 0.

[0442] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is $—(CH_2CH_2)$heterocyclyl$(R^{23})_h$, and h is 0.

[0443] In some embodiments, R^6 is a $—OR^{24}$, R^{24} is $—(CH_2CH_2)$heterocyclyl$(R^{23})_h$, and h is 0.

[0444] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is $—(C_{1-4}$ alkylene)$NR^{25}R^{26}$ and R^{25} and R^{26} are independently a $—(C_{1-4}$ alkyl).

[0445] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is $—(CH_2CH_2)NR^{25}R^{26}$ and R^{25} and R^{26} are independently a $—(C_{1-2}$ alkyl).

[0446] In some embodiments, at least one R^6 is $—OR^{24}$, and R^{24} is $—(CH_2CH_2)NMe_2$.

[0447] In some embodiments, R^6 is a $—OR^{24}$, and R^{24} is $—(CH_2CH_2)NMe_2$.

[0448] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is $—(C_{1-4}$ alkylene)aryl$(R^{21})_k$, k is 0 or 1 and R^{21} is halide.

[0449] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is $—(CH_2CH_2)$phenyl$(R^{21})_k$, k is 0 or 1 and R^{21} is a halide.

[0450] In some embodiments, R^6 is a $—OR^{24}$, R^{24} is $—(CH_2CH_2)$phenyl$(R^{21})_k$, k is 0 or 1 and R^{21} is a halide.

[0451] In some embodiments, at least one R^6 is $—OR^{24}$, R^{24} is $—(CH_2)$phenyl$(R^{21})_k$, k is 0 or 1 and R^{21} is a halide.

[0452] In some embodiments, R^6 is a $—OR^{24}$, R^{24} is $—(CH_2)$phenyl$(R^{21})_k$, k is 0 or 1 and R^{21} is a halide.

[0453] In some embodiments, h is 0.

[0454] In some embodiments, at least one R^7 is a halide.

[0455] In some embodiments, at least one R^7 is a F.

[0456] In some embodiments, at least one R^7 is $—(C_{1-6}$ alkyl).

[0457] In some embodiments, at least one R^7 is $—(C_{1-5}$ alkyl).

[0458] In some embodiments, at least one R^7 is $—(C_{1-4}$ alkyl).

[0459] In some embodiments, at least one R^7 is $—(C_{1-3}$ alkyl).

[0460] In some embodiments, at least one R^7 is $—(C_{1-2}$ alkyl).

[0461] In some embodiments, at least one R^7 is methyl.

[0462] In some embodiments, at least one R^8 is a halide.

[0463] In some embodiments, at least one R^8 is a F.

[0464] In some embodiments, at least one R^8 is $—(C_{1-4}$ alkyl).

[0465] In some embodiments, at least one R^8 is $—(C_{1-3}$ alkyl).

[0466] In some embodiments, at least one R^8 is $—(C_{1-2}$ alkyl).

[0467] In some embodiments, at least one R^8 is methyl.

[0468] In some embodiments, R^8 is a methyl.

[0469] In some embodiments, at least one R^8 is $—C(=O)(C_{1-3}$ alkyl).

[0470] In some embodiments, at least one R^8 is $—C(=O)$Me.

[0471] In some embodiments, R^8 is a $—C(=O)$Me.

[0472] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; and R^{10} is F.

[0473] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$NHSO$_2$$R^{19}$; p is 1; and R^{19} is —(C_{1-3} alkyl).

[0474] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)N$R^{15}$$R^{16}$; and R^{15} and R^{16} are independently selected from —(C_{1-3} alkyl).

[0475] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is —(C_{2-5}alkyl); R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(=O)R^{19}; R^{19} is —(C_{1-3} alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

[0476] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; and R^9 is selected from the group consisting of halide and —(C_{1-2} alkyl).

[0477] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; R^{10} is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0478] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$NHSO$_2$$R^{19}$; p is 1; R^{19} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0479] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)N$R^{15}$$R^{16}$; R^{15} and R^{16} are independently selected from —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0480] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(=O)R^{19}; R^{19} is C_{1-3} alkyl; the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0481] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(=O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; R^9 is selected from the group consisting of halide and —(C_{1-2} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0482] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —N$R^{15}$$R^{16}$ and —CH_2N$R^{17}$$R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$, wherein k and j are 0; R^5 is -phenyl(R^{10})$_k$, wherein k is 1 or 2; R^{10} is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0483] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —N$R^{15}$$R^{16}$ and —CH_2N$R^{17}$$R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$, wherein k and j are 0; R^5 is -phenyl(R^{10})$_k$, wherein k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$NHSO$_2$$R^{19}$; p is 1; R^{19} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0484] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —N$R^{15}$$R^{16}$ and —CH_2N$R^{17}$$R^{18}$, wherein R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl), and R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$, wherein k and j are 0; R^5 is -phenyl(R^{10})$_k$, wherein k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)N$R^{15}$$R^{16}$, wherein R^{15} and R^{16} are independently selected from —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0485] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is selected from the group consisting of —N$R^{15}$$R^{16}$ and —CH_2N$R^{17}$$R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$; k and j are 0; R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(=O)R^{19}; R^{19} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0486] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —N$R^{15}$$R^{16}$ and —CH_2N$R^{17}$$R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$; k and j are 0; R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; each R^9 is independently selected from the group consisting of halide and —(C_{1-2} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0487] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; R^{10} is F; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0488] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$; p is 1; R^9 is —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0489] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)$NR^{15}R^{16}$; R^{15} and R^{16} are independently selected from —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0490] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(═O)R^{19}; R^{19} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0491] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$, wherein h is 0-2; R^{11} is F; R^5 is -heterocyclyl(R^9)$_h$, wherein h is 1 or 2; each R^9 is independently selected from the group consisting of halide and —(C_{1-2} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0492] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$; q is 0; R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; and R^{10} is F.

[0493] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyrimidinyl(R^6); q is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$; p is 1; and R^{19} is —(C_{1-3} alkyl).

[0494] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$; q is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)$NR^{15}R^{16}$; and R^{15} and R^{16} are independently a —(C_{1-3} alkyl).

[0495] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$, wherein q is 0; R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(═O)R^{19}; R^{19} is —(C_{1-3} alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

[0496] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$; q is 0; R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; each R^9 is independently selected from the group consisting of halide and —(C_{1-2}alkyl).

[0497] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; and R^{10} is F.

[0498] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$; p is 1; and R^{19} is —(C_{1-3} alkyl).

[0499] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)$NR^{15}R^{16}$; and R^{15} and R^{16} are independently a —(C_{1-3} alkyl).

[0500] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^8 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(═O)R^{19}; R^{19} is —(C_{1-3} alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

[0501] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is —(C_{2-5} alkyl); R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; and each R^9 is independently selected from the group consisting of halide and —(C_{1-2} alkyl).

[0502] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; R^{10} is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0503] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$; p is 1; R^{19} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0504] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)$NR^{15}R^{16}$; R^{15} and R^{16} are independently a —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0505] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is -carbocyclyl(R^{22})$_j$; j is 0; R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(═O)R^{19}; R^{19} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0506] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —NHC(═O)R^{14}; R^{14} is -carbocyclyl(R^2); j is 0; R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; each R^9 is independently selected from the group consisting of halide and —(C_{1-2} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0507] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —$NR^{15}R^{16}$ and —$CH_2NR^{17}R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$, wherein k and j are 0; R^5 is -phenyl(R^{10})$_k$, wherein k is 1 or 2; R^{10} is F; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0508] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —$NR^{15}R^{16}$ and —$CH_2NR^{17}R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected

from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$, wherein k and j are 0; R^5 is -phenyl(R^{10})$_k$, wherein k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$; p is 1; R^{19} is —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0509] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —$NR^{15}R^{16}$ and —$CH_2NR^{17}R^{18}$, wherein R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl), and R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$, wherein k and j are 0; R^5 is -phenyl(R^{10})$_k$, wherein k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)$NR^{15}R^{16}$, wherein R^{15} and R^{16} are independently selected from —(C_{1-3} alkyl); and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0510] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is selected from the group consisting of —$NR^{15}R^{16}$ and —$CH_2NR^{17}R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})); k and j are 0; R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(═O)R^{19}; R^{19} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0511] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is selected from the group consisting of —$NR^{15}R^{16}$ and —$CH_2NR^{17}R^{18}$; R^{15} and R^{17} are independently selected from the group consisting of H and —(C_{1-3} alkyl); R^{16} and R^{18} are independently selected from the group consisting of H, —(C_{1-3} alkyl), —CH_2phenyl(R^{21})$_k$, and —CH_2carbocyclyl(R^{22})$_j$; k and j are 0; R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; each R^9 is independently selected from the group consisting of halide and C_{1-2} alkyl; and the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

[0512] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; R^{10} is F; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0513] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$; p is 1; R^{19} is —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0514] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)$NR^{15}R^{16}$; R^{15} and R^{16} are independently selected from —(C_{1-3} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0515] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$, wherein q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$; h is 0-2; R^{11} is F; R^5 is -heteroaryl(R^8)$_q$, wherein q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(═O)R^{19}; R^{19} is —(C_{1-3} alkyl); the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole; and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0516] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —CH_2heterocyclyl(R^{11})$_h$, wherein h is 0-2; R^{11} is F; R^5 is -heterocyclyl(R^9)$_h$, wherein h is 1 or 2; R^9 is selected from the group consisting of halide and —(C_{1-2} alkyl); and the heterocyclyl is selected from the group consisting of pyrrolidine and piperidine.

[0517] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$; q is 0; R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; and R^{10} is F.

[0518] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$; q is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —(C_{1-2} alkylene)$_p$$NHSO_2R^{19}$; p is 1; and R^{19} is —(C_{1-3} alkyl).

[0519] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$; q is 0; R^5 is -phenyl(R^{10})$_k$; k is 2; one R^{10} is F and the other R^{10} is —NH(C_{1-6} alkylene)$NR^{15}R^{16}$; and R^{15} and R^{16} are independently selected from —(C_{1-3} alkyl).

[0520] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$, wherein q is 0; R^5 is -heteroaryl(R^8)$_q$; q is 1; R^8 is selected from the group consisting of halide, —(C_{1-2} alkyl), and —C(═O)R^{19}; R^{19} is —(C_{1-3} alkyl); and the heteroaryl is selected from the group consisting of pyridine, furan, thiophene, and imidazole.

[0521] In some embodiments, R^2 is F; R^1 and R^4 are H; R^3 is -pyrimidinyl(R^6)$_q$; q is 0; R^5 is -heterocyclyl(R^9)$_h$; h is 1 or 2; R^9 is selected from the group consisting of halide and —(C_1-2 alkyl).

[0522] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyrazol-4-yl(R^6)$_q$; q is 0 or 1; R^6 is —(C_{1-3} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; and R^{10} is F.

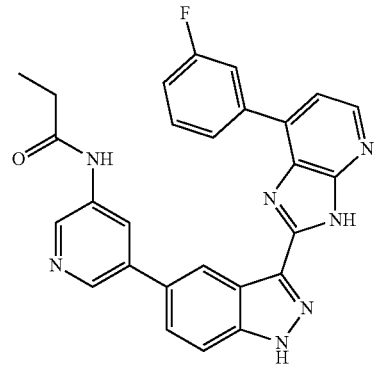
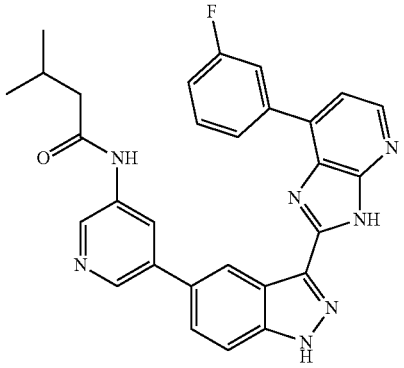
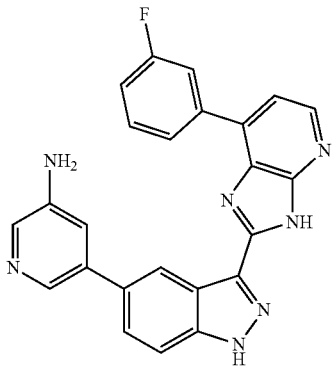
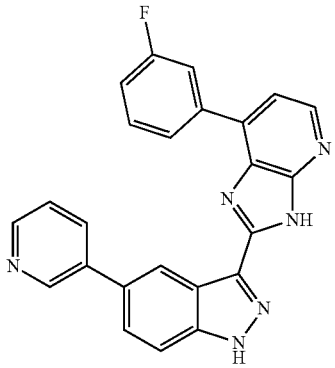
[0523] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -imidazol-5-yl(R^6)$_q$; q is 1 or 2; each R^6 is independently selected from —(C_{1-3} alkyl); R^5 is -phenyl(R^{10})$_k$; k is 1 or 2; and R^{10} is F.

[0524] In some embodiments, R^1, R^2, and R^4 are H; R^3 is -pyridin-3-yl(R^6)$_q$; q is 1; R^6 is —OR^{24}; R^{24} is selected from the group consisting of H and —(C_{1-3} alkyl); R^5 is -phenyl (R^{10})$_k$;

[0525] k is 1 or 2; and R^{10} is F.

[0526] Illustrative compounds of Formula (I) are shown in Table 1.

TABLE 1

1	
2	
3	
4	

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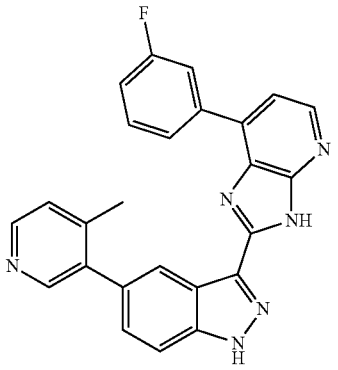
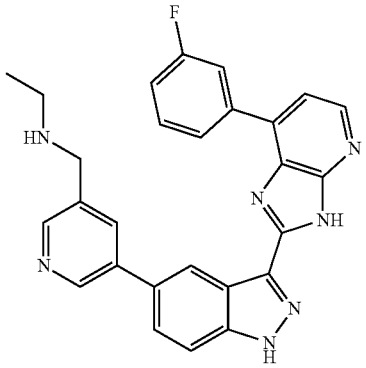
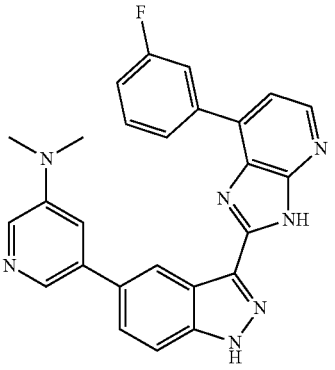
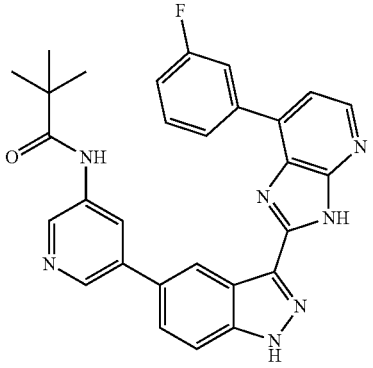
5	
6	
7	
8	

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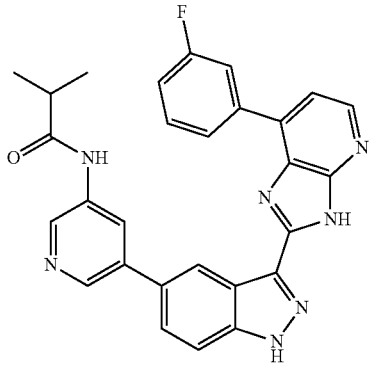
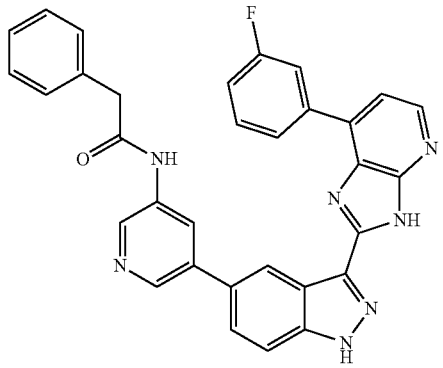
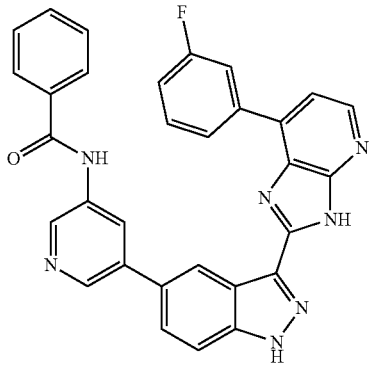
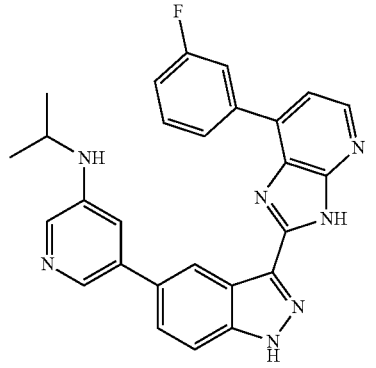
9	
10	
11	
12	

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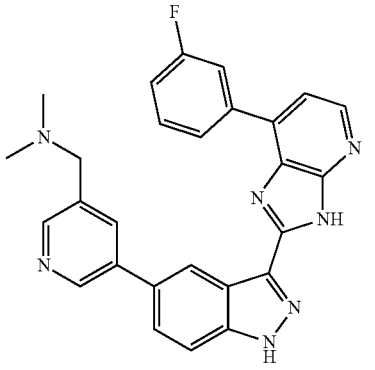
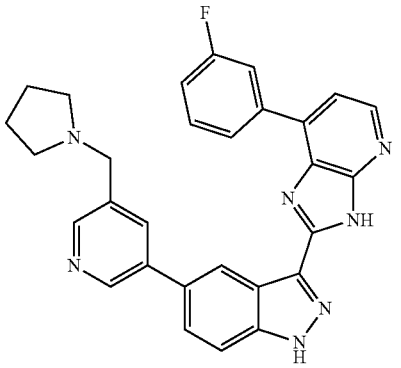
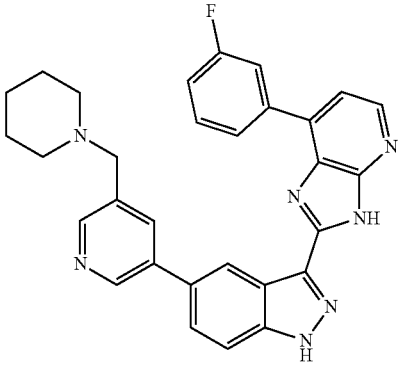
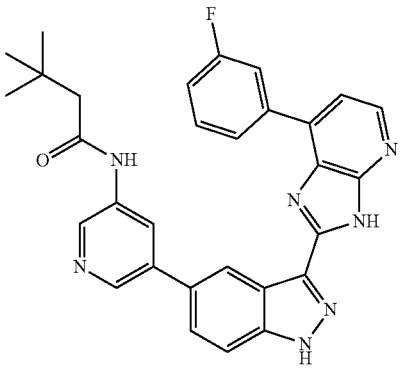
13	
14	
15	
16	

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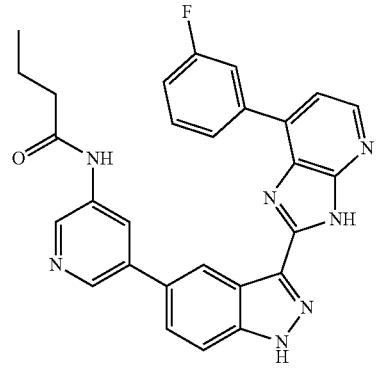
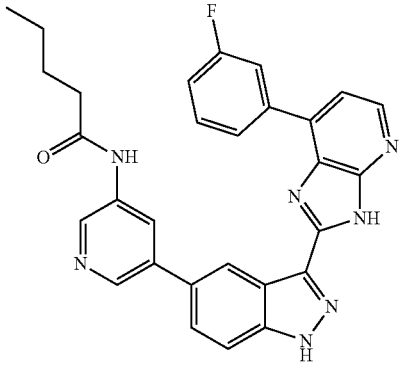
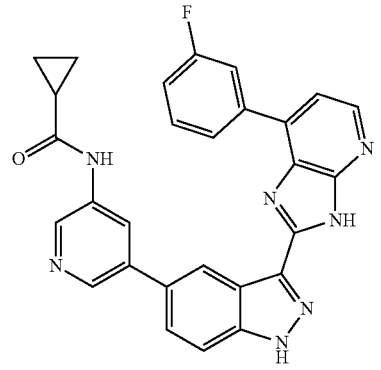
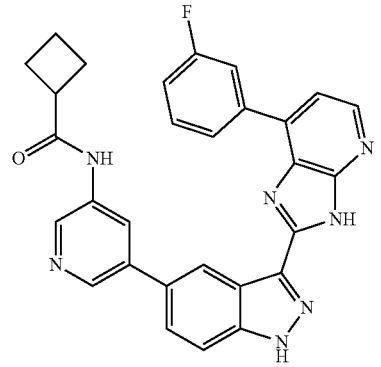
17	
18	
19	
20	

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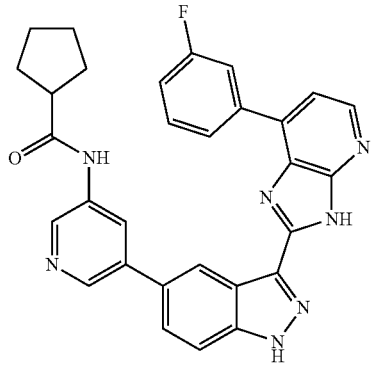
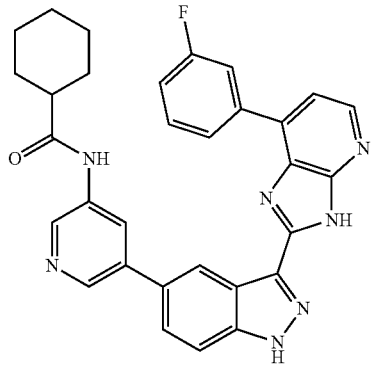
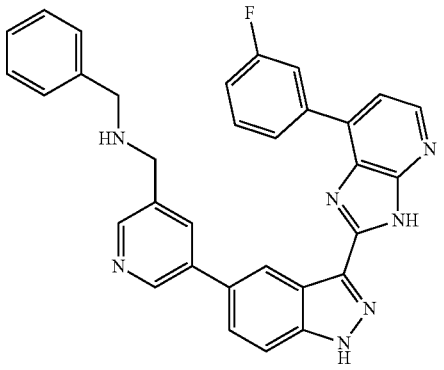
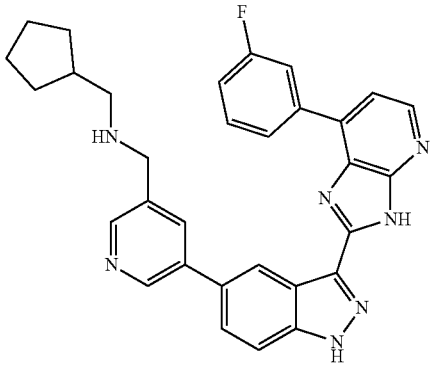
21	
22	
23	
24	

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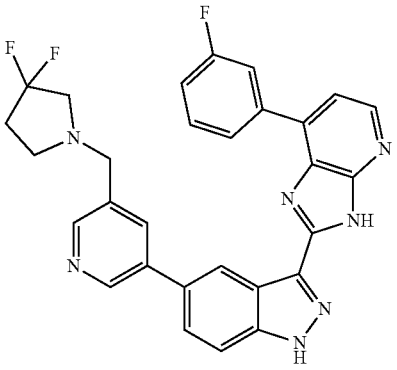
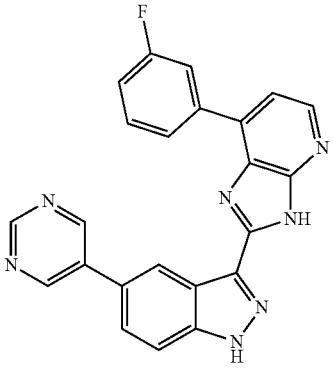
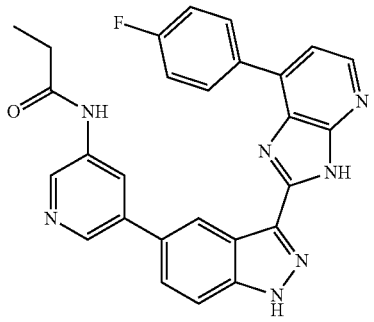
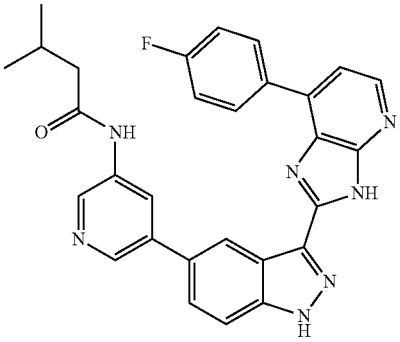
25	
26	
27	
28	

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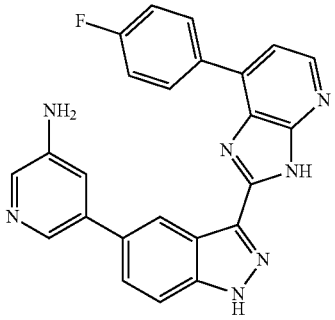
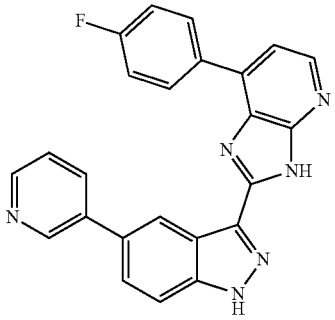
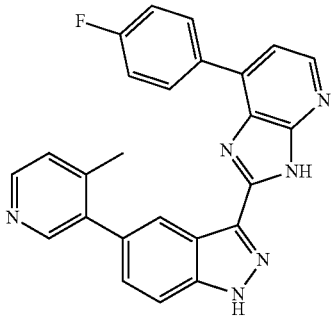
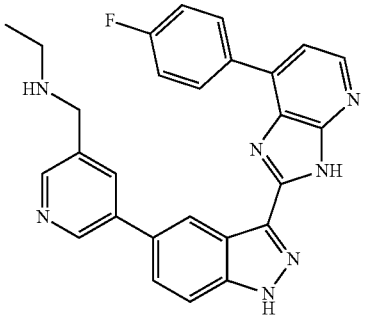
29	
30	
31	
32	

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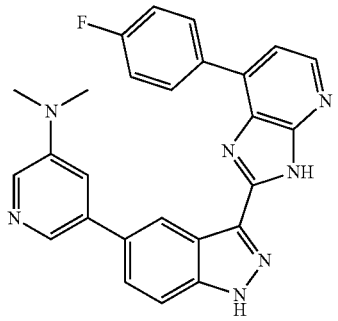
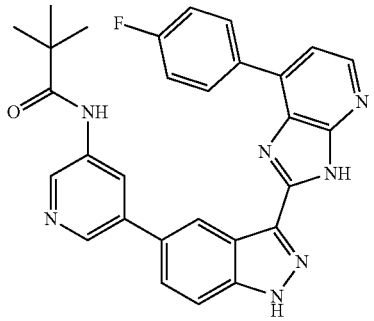
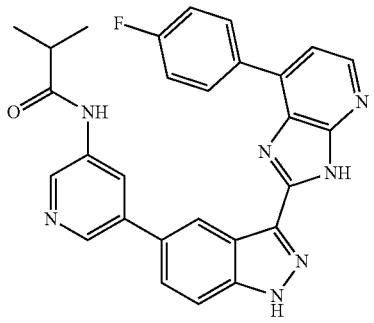
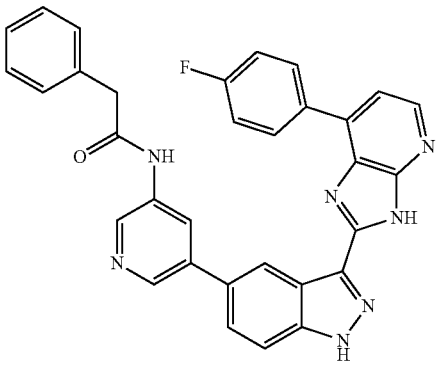
33	
34	
35	
36	

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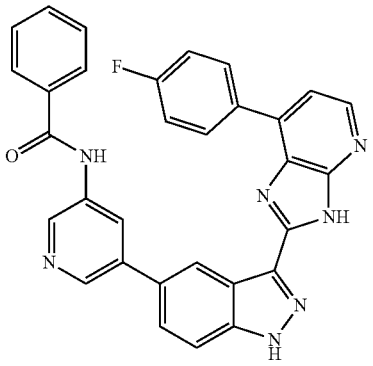
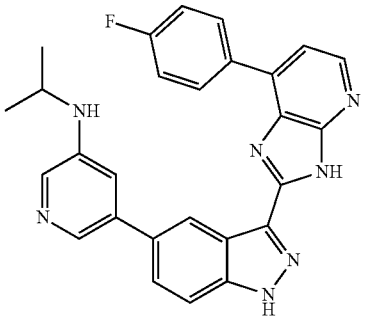
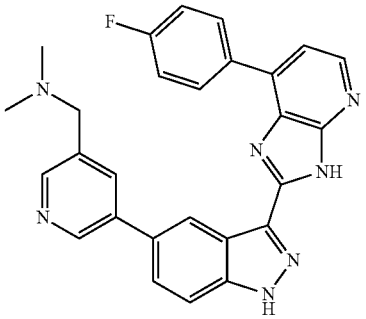
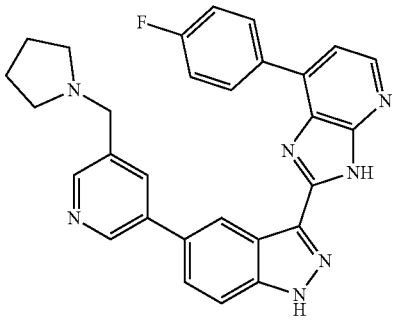
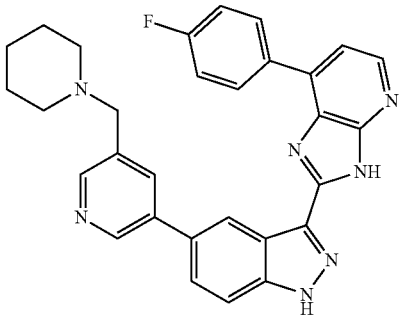
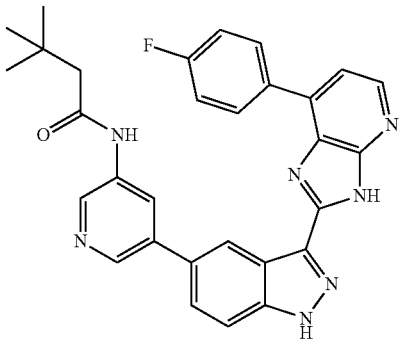
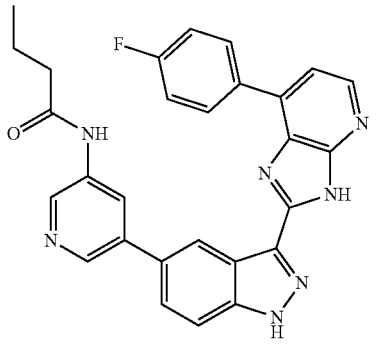
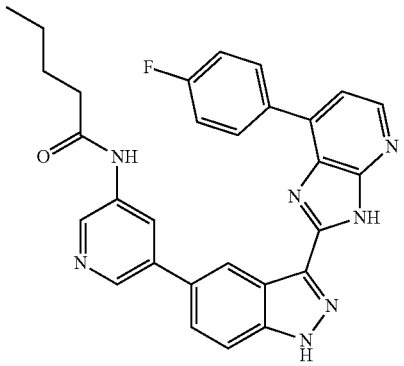
37	
38	
39	
40	

TABLE 1-continued

41	
42	
43	
44	

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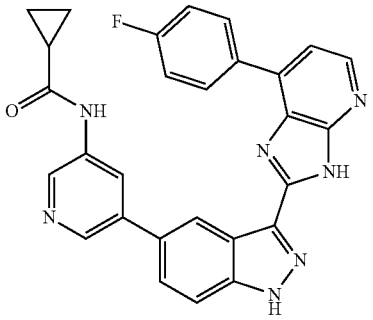
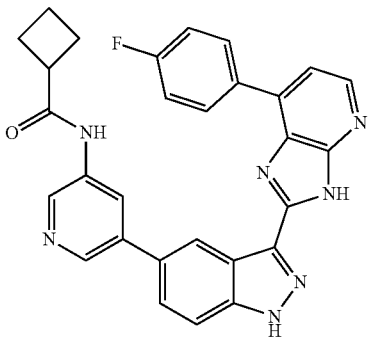
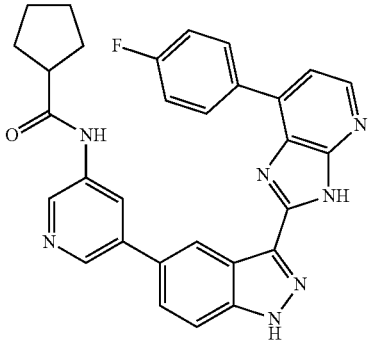
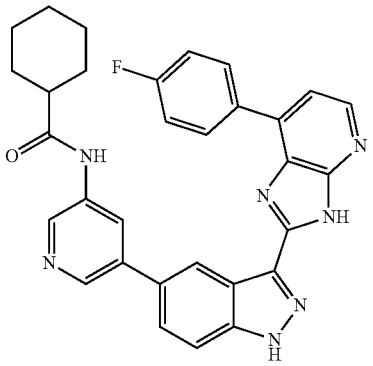
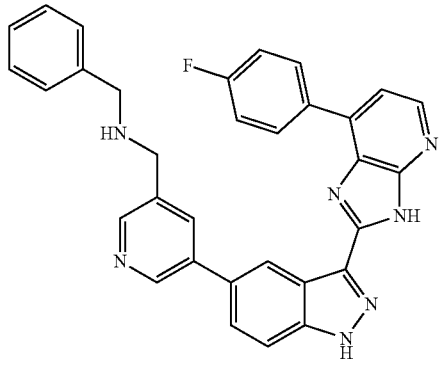
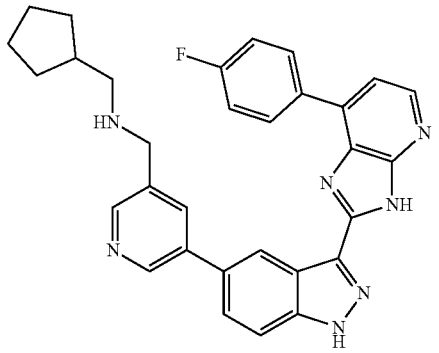
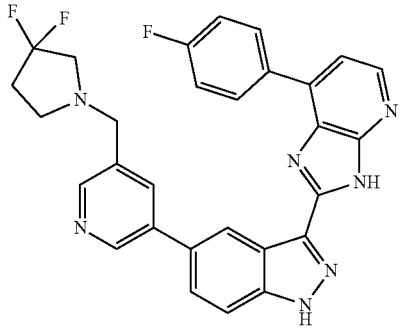
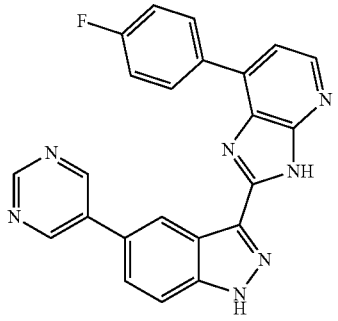
45	
46	
47	
48	

TABLE 1-continued

49	
50	
51	
52	

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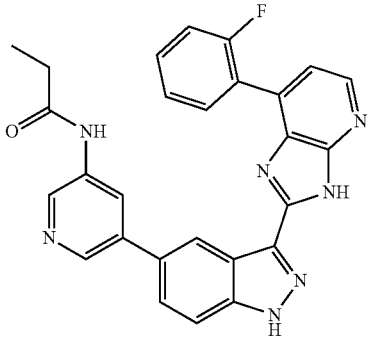
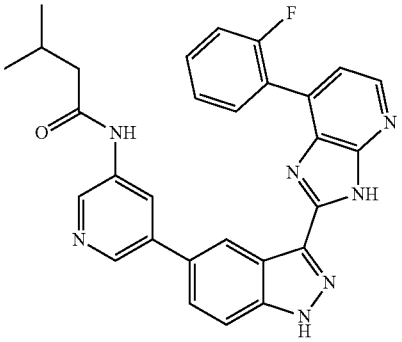
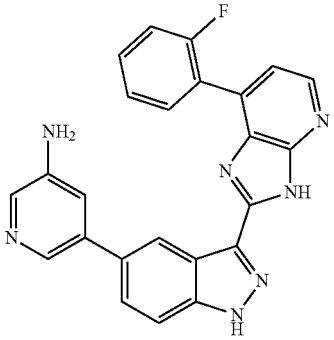
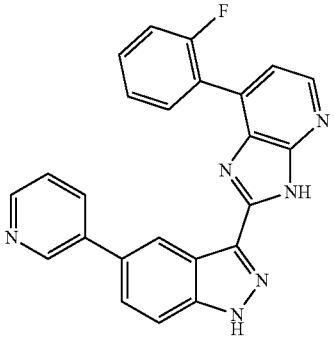
53	
54	
55	
56	

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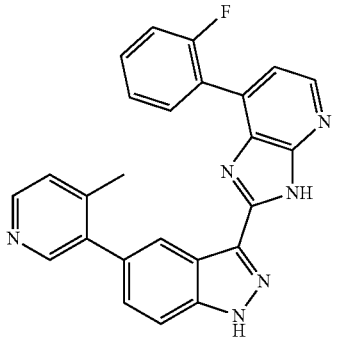
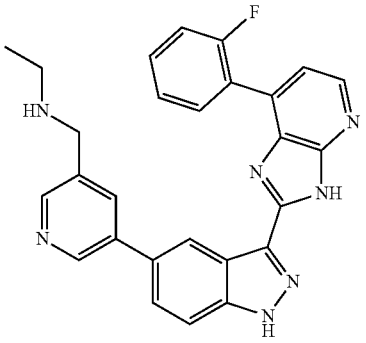
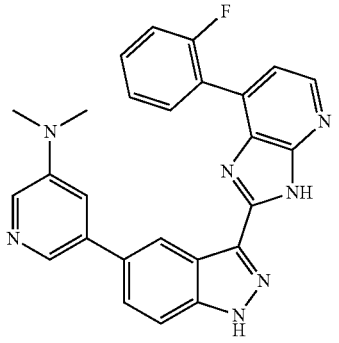
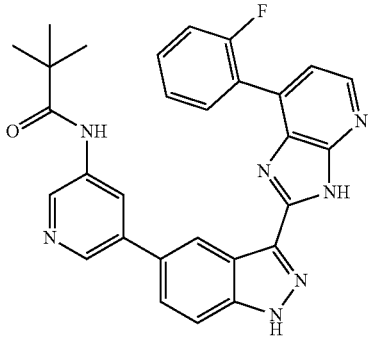
57	
58	
59	
60	

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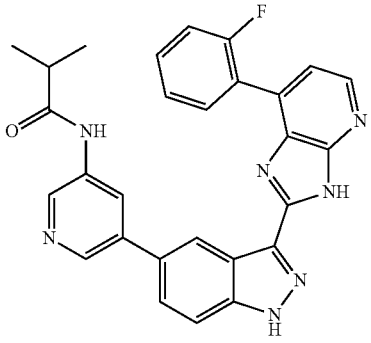
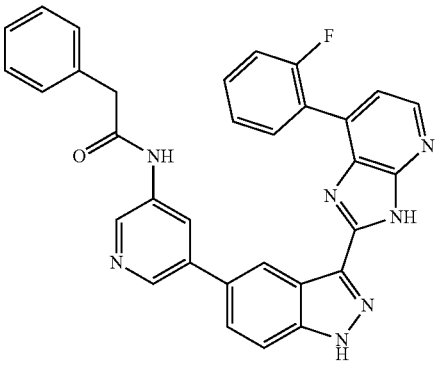
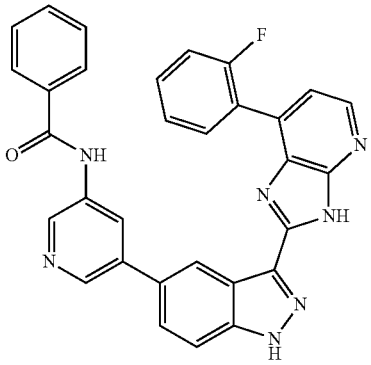
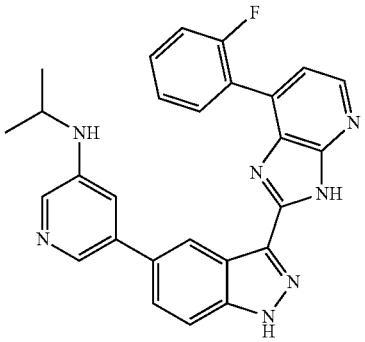
61	
62	
63	
64	

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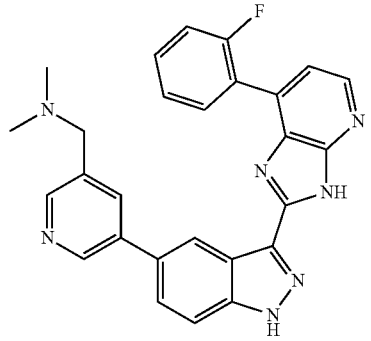
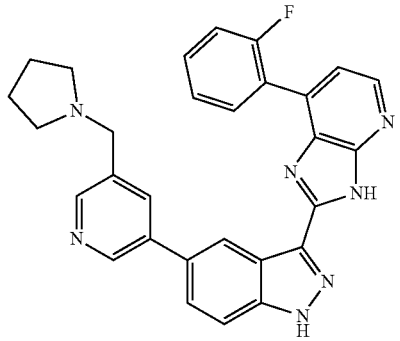
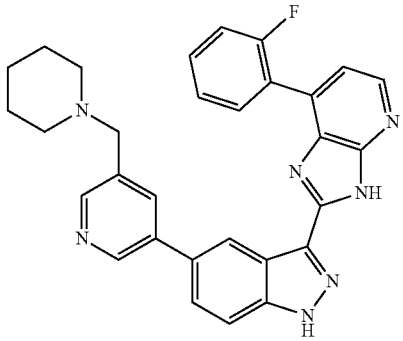
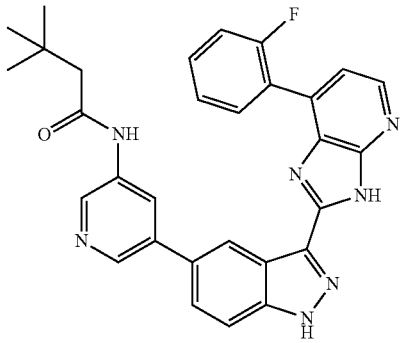
65	
66	
67	
68	

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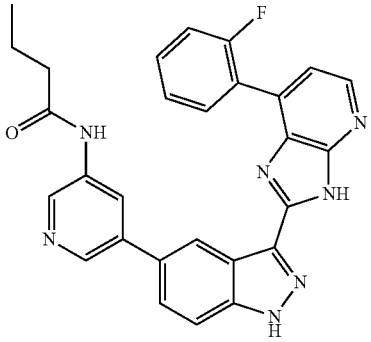
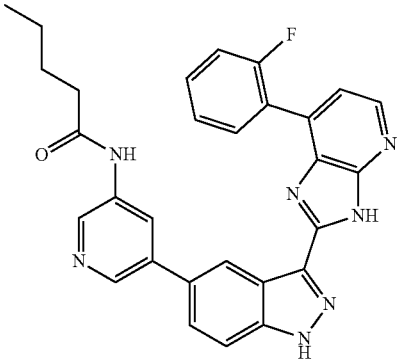
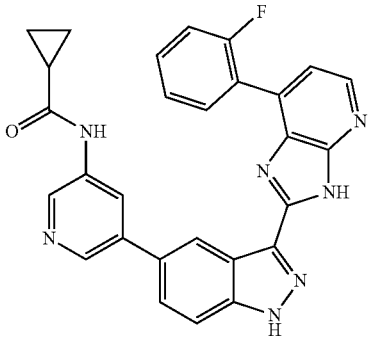
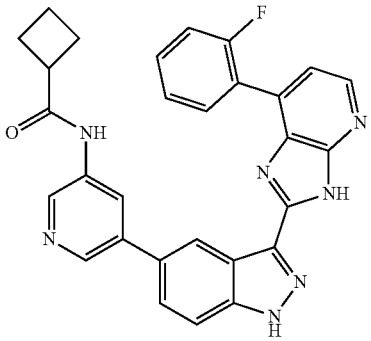
69	
70	
71	
72	

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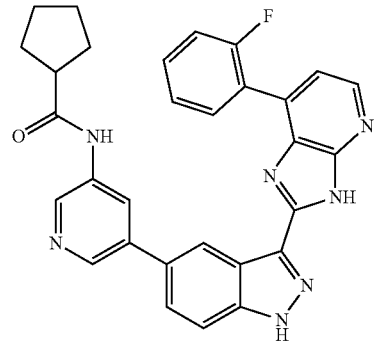
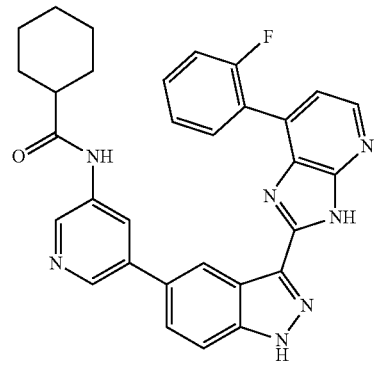
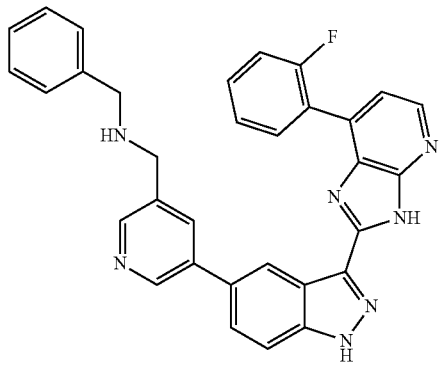
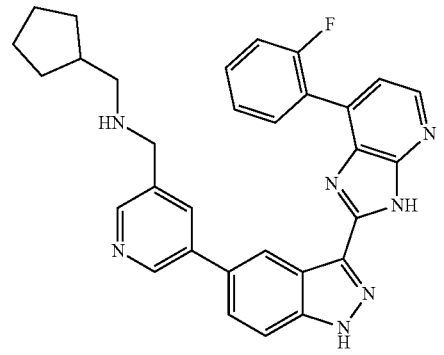
73	
74	
75	
76	

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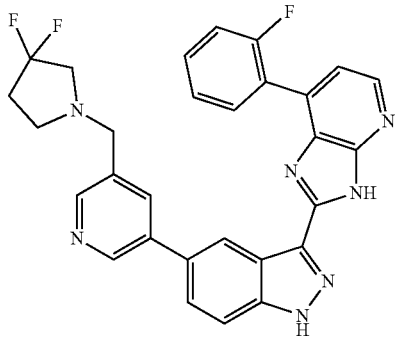
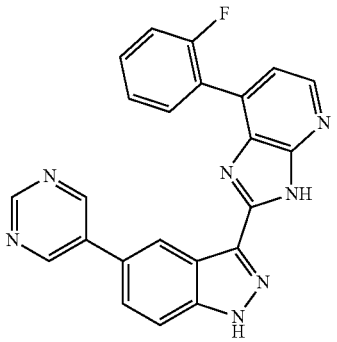
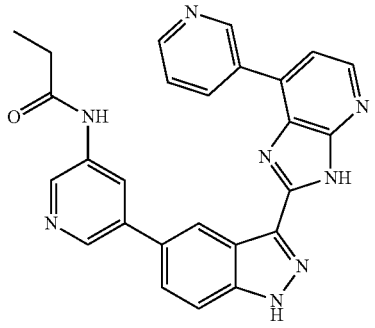
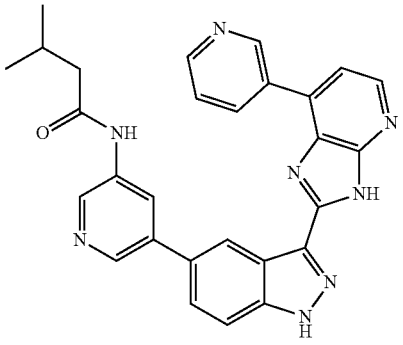
77	
78	
79	
80	

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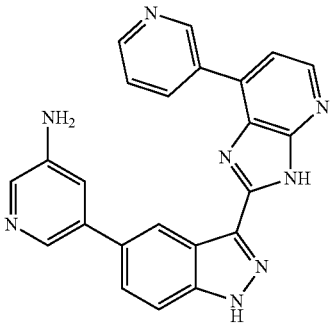
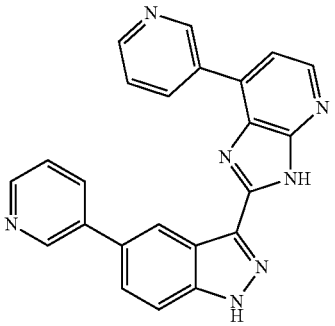
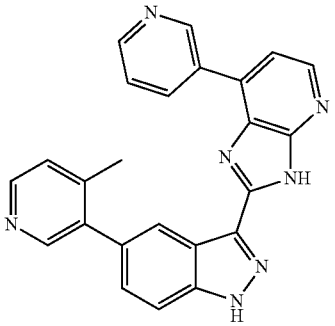
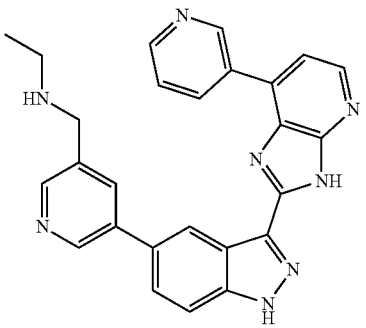
81	
82	
83	
84	

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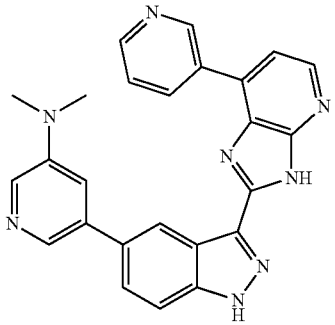
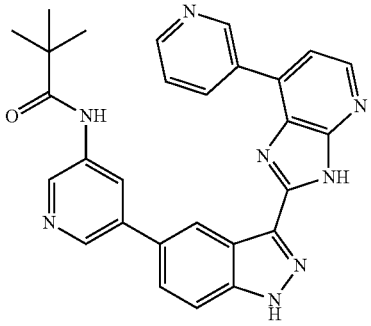
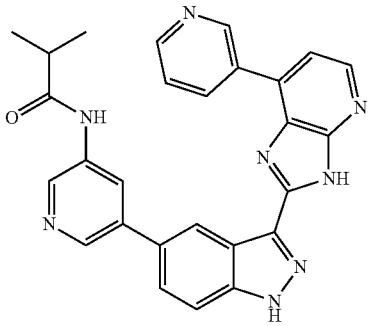
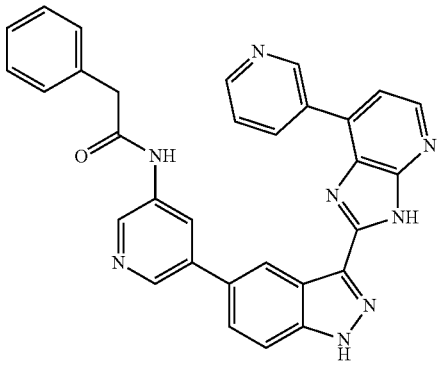
85	
86	
87	
88	

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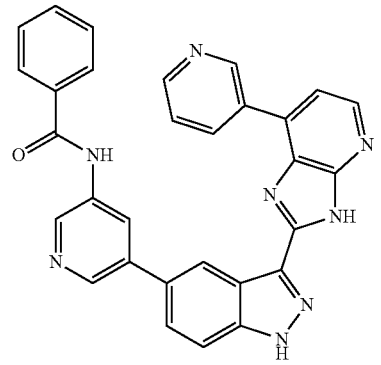
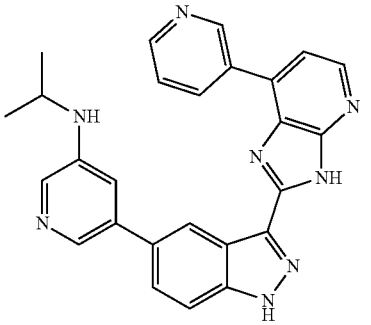
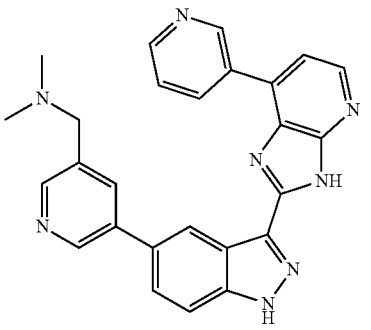
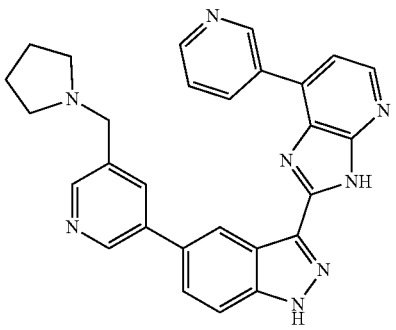
89	
90	
91	
92	

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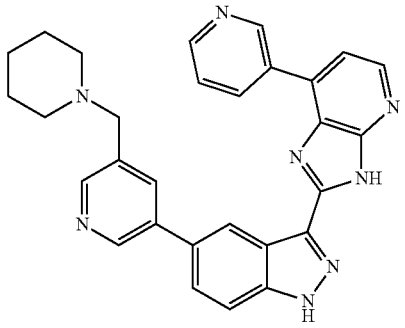
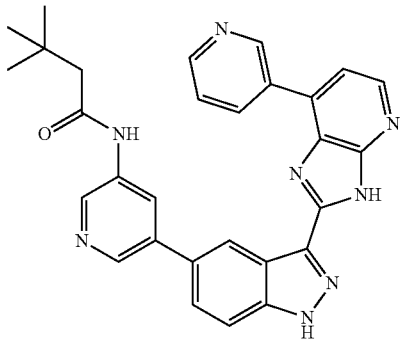
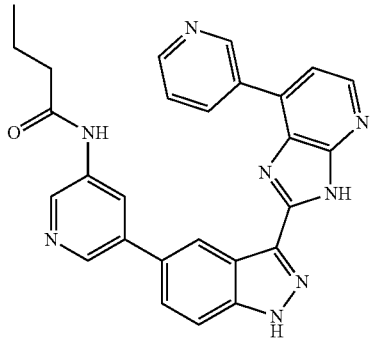
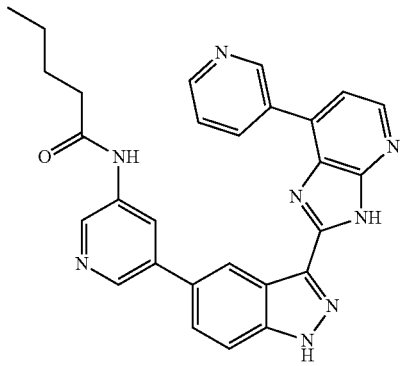
93	
94	
95	
96	

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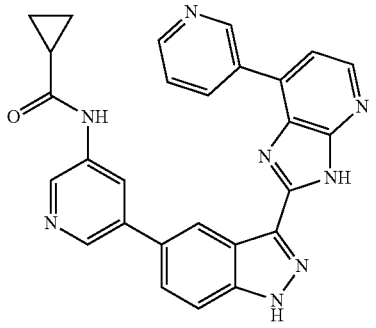
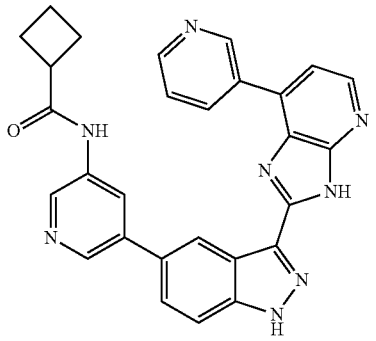
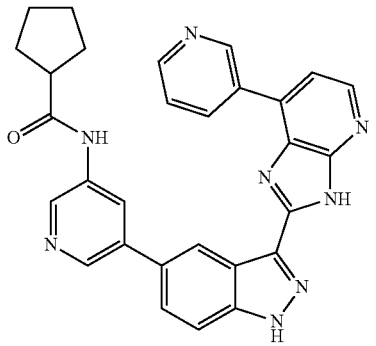
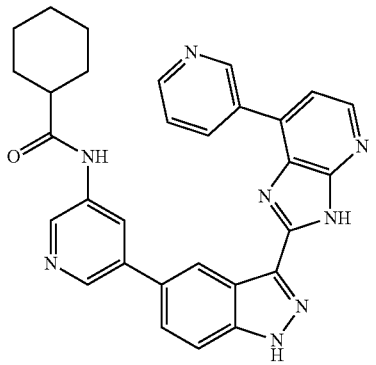
97	
98	
99	
100	

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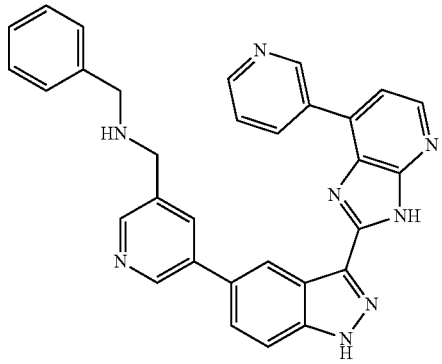
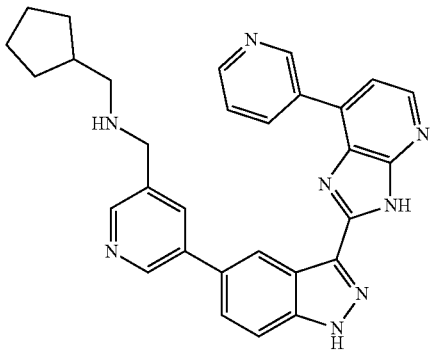
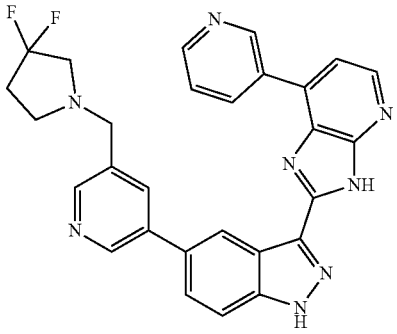
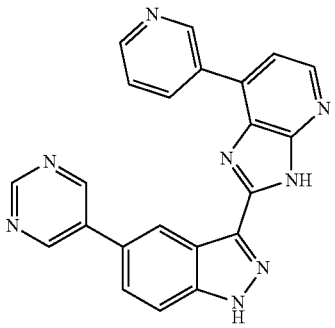
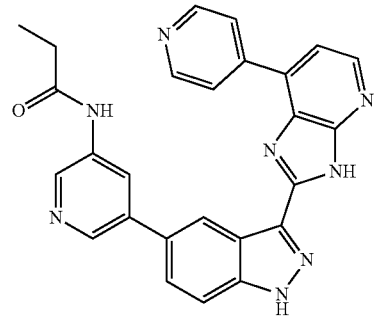
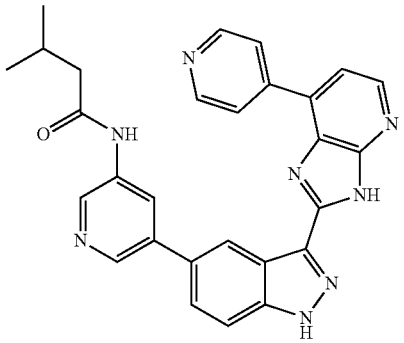
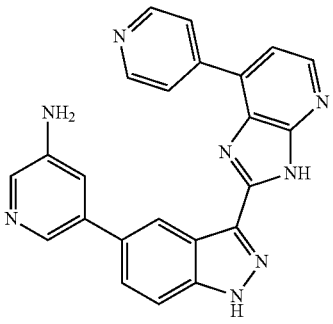
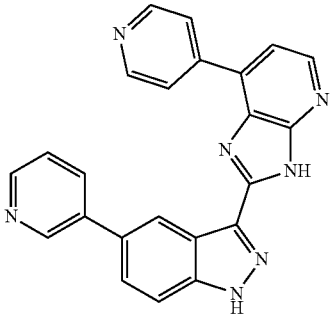
101	
102	
103	
104	

TABLE 1-continued

105	
106	
107	
108	

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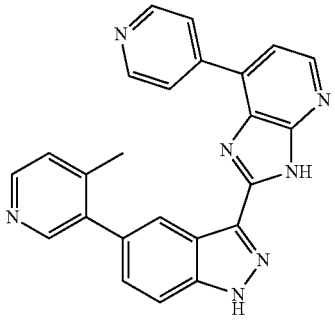
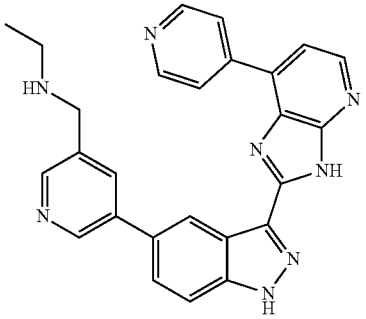
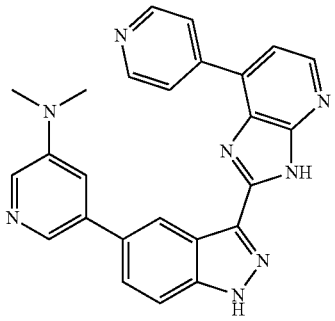
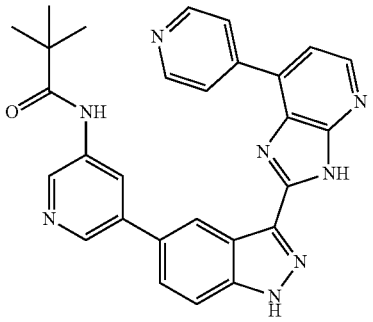
109	
110	
111	
112	

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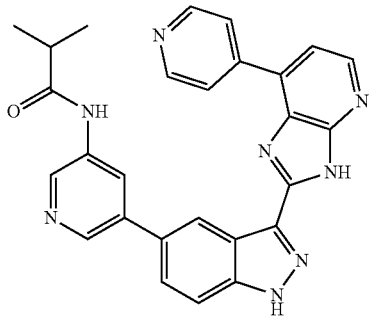
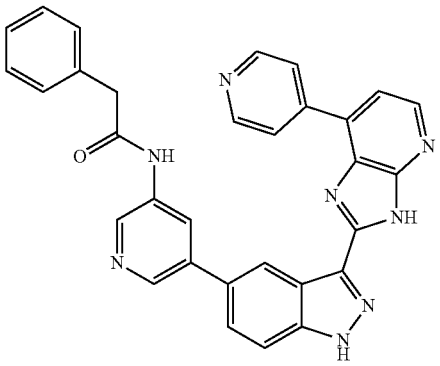
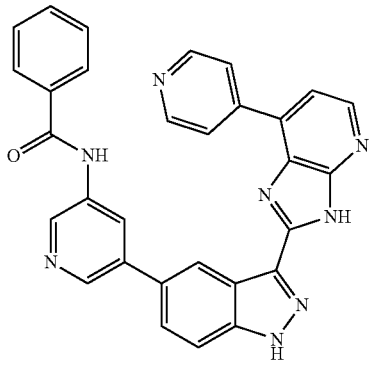
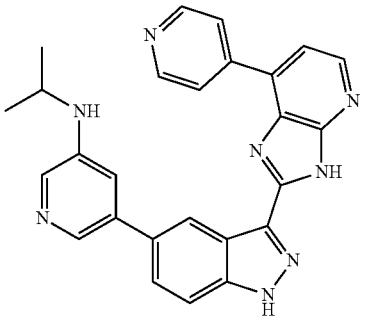
113	
114	
115	
116	

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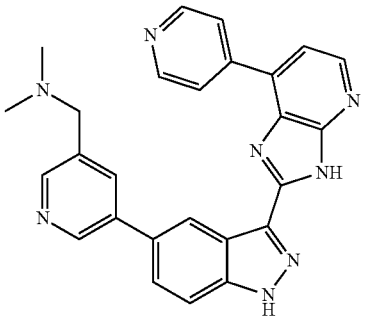
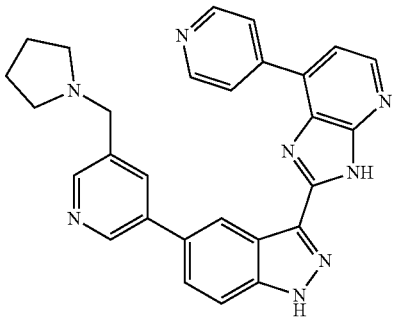
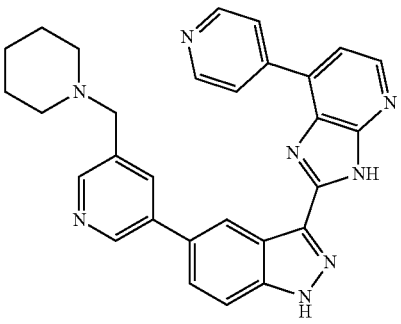
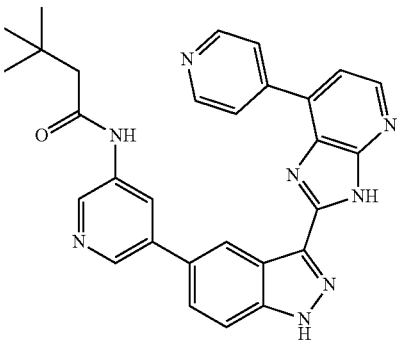
117	
118	
119	
120	

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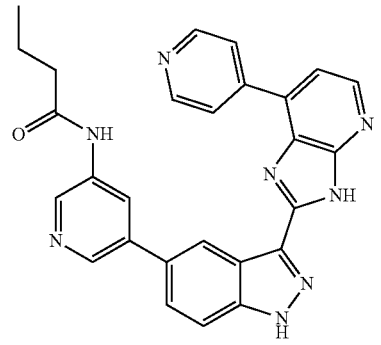
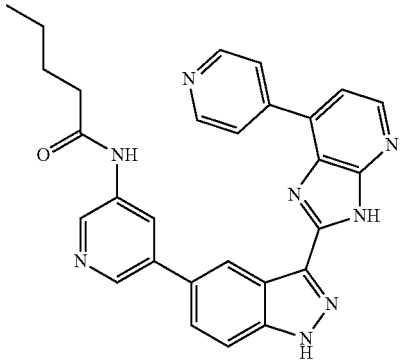
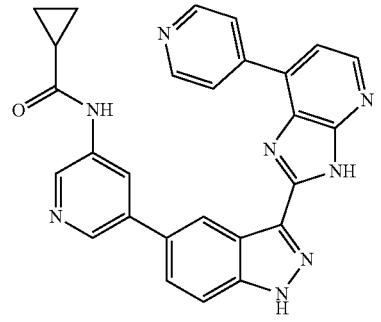
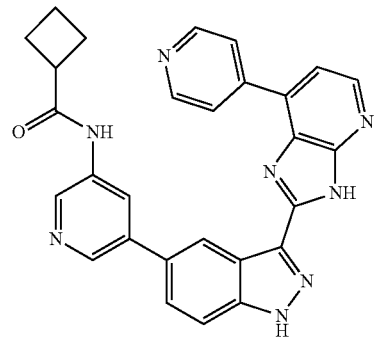
121	
122	
123	
124	

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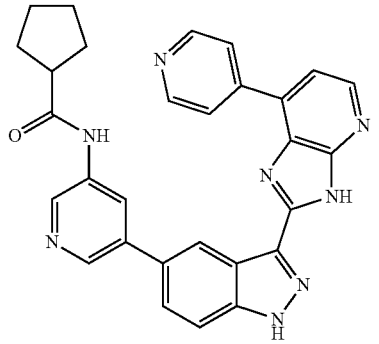
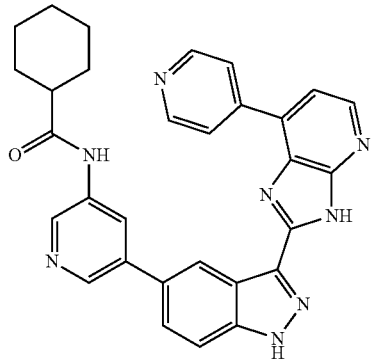
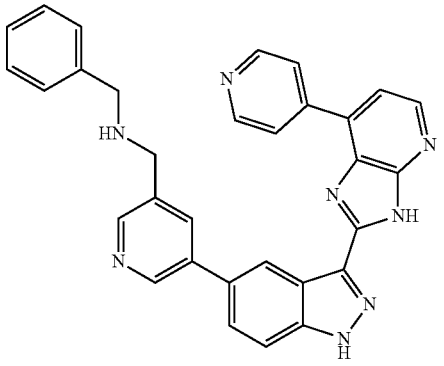
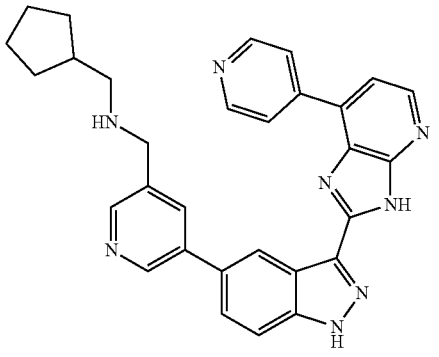
125	
126	
127	
128	

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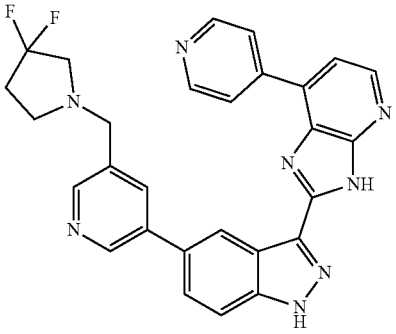
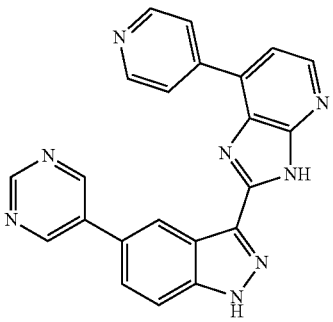
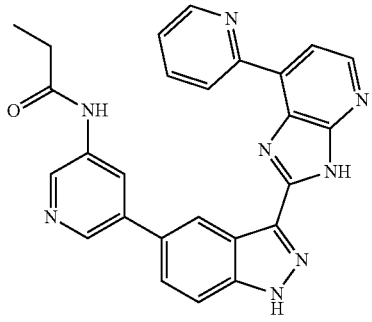
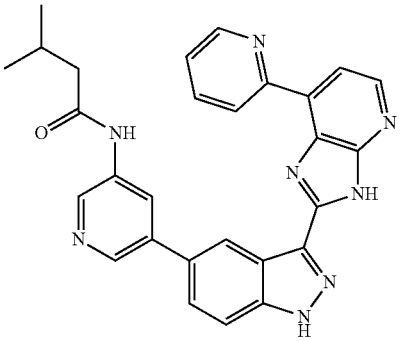
129	
130	
131	
132	

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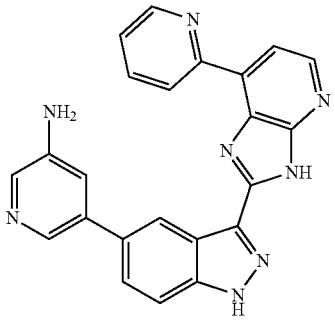
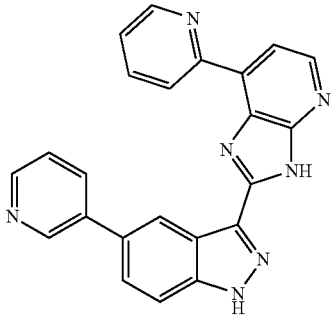
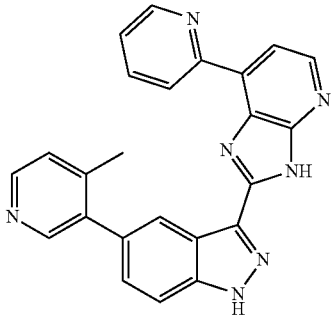
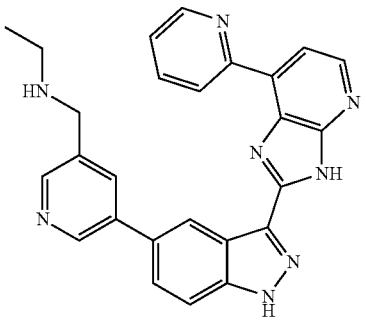
133	
134	
135	
136	

TABLE 1-continued

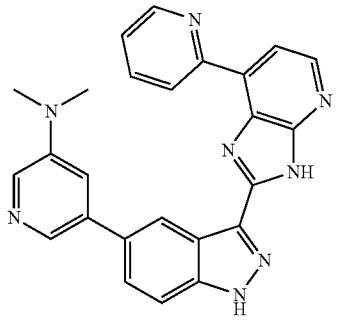
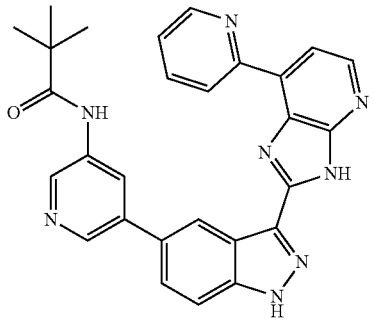
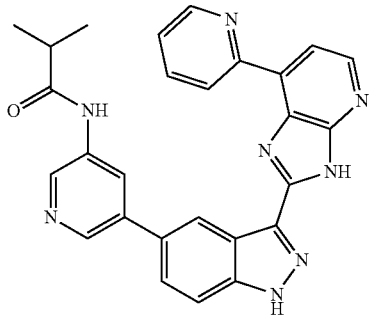
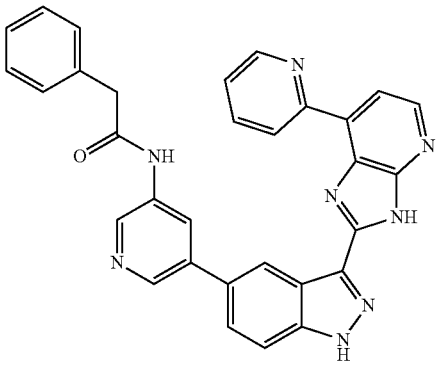
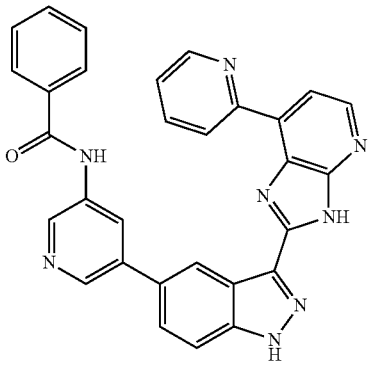
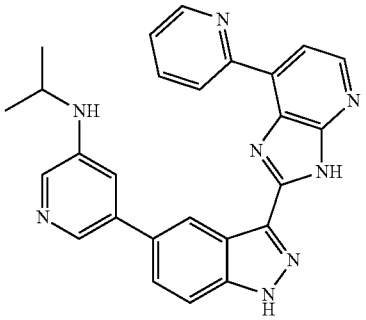
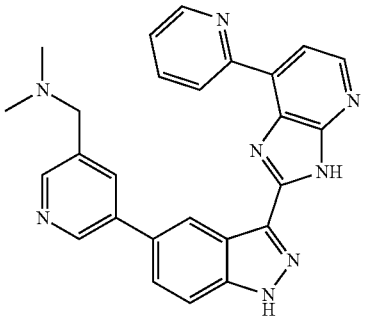
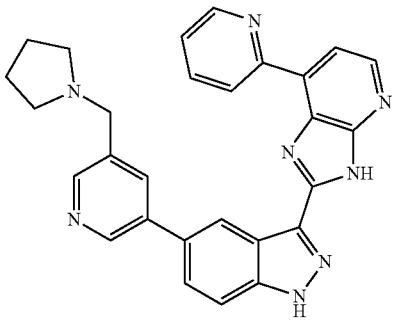
137	
138	
139	
140	

TABLE 1-continued

141	
142	
143	
144	

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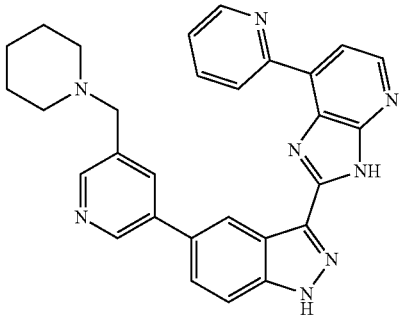
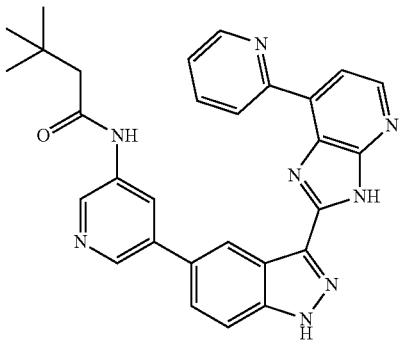
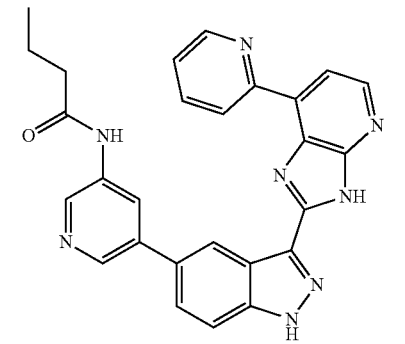
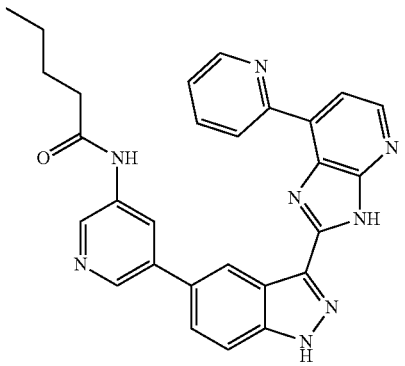
145	
146	
147	
148	

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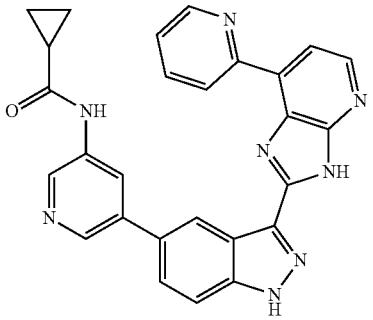
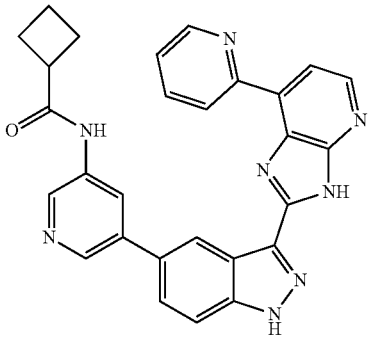
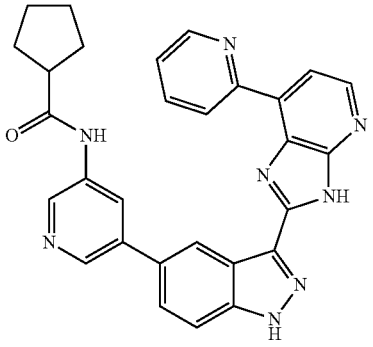
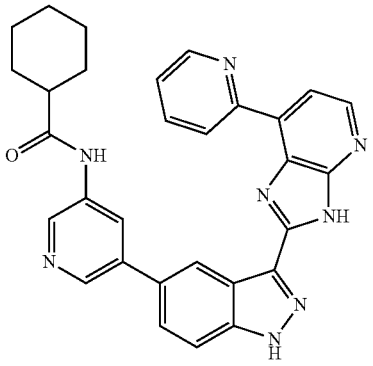
149	
150	
151	
152	

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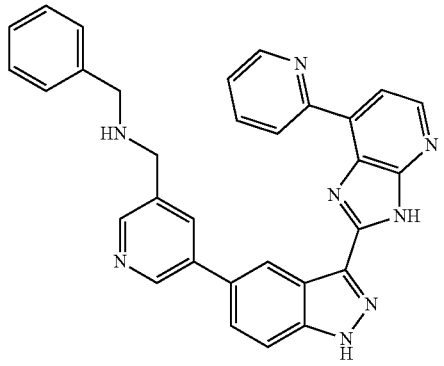
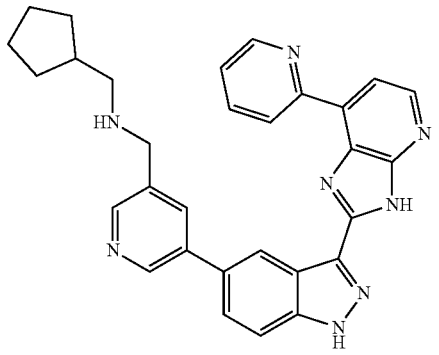
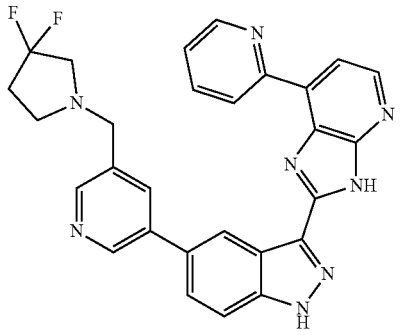
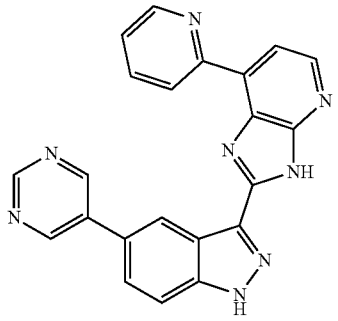
153	
154	
155	
156	

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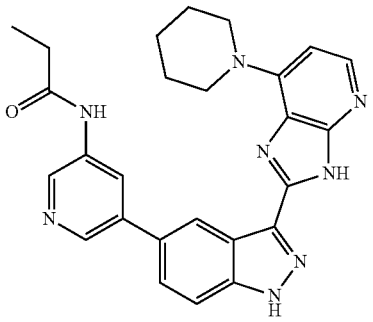
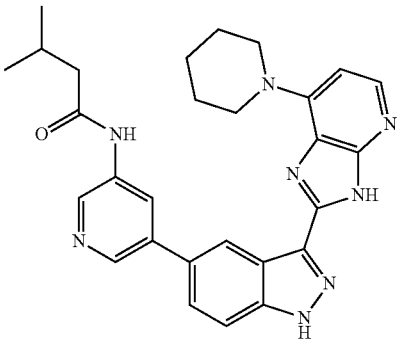
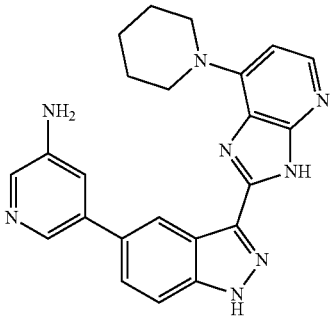
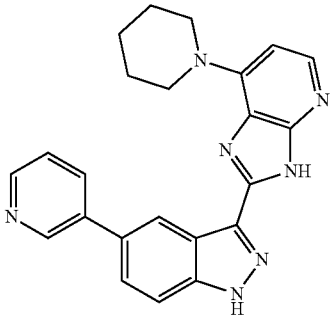
157	
158	
159	
160	

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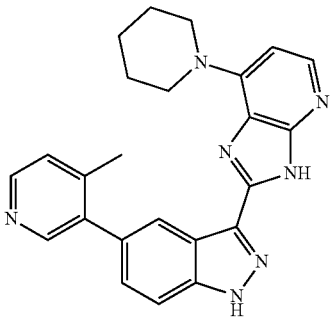
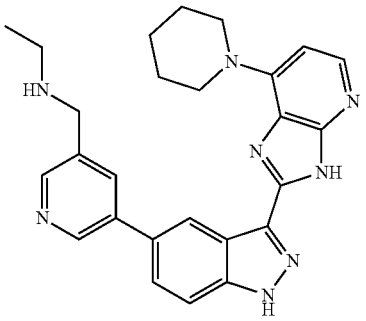
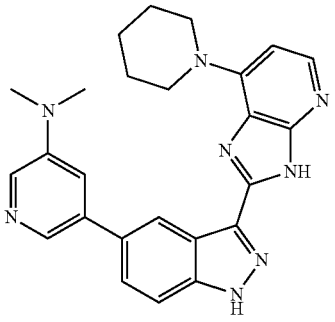
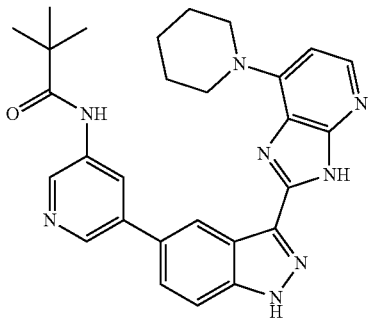
161	
162	
163	
164	

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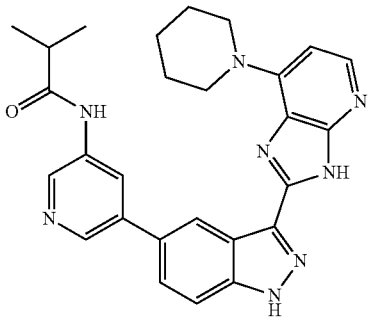
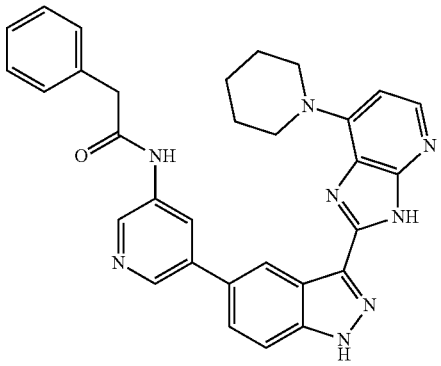
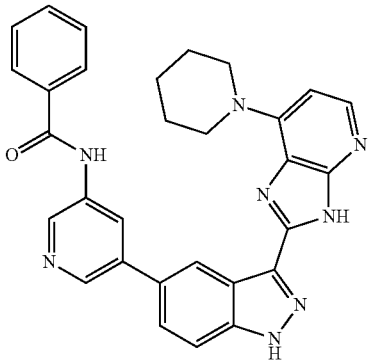
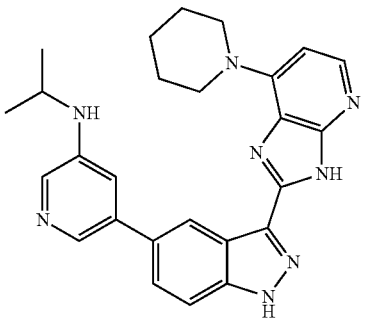
165	
166	
167	
168	

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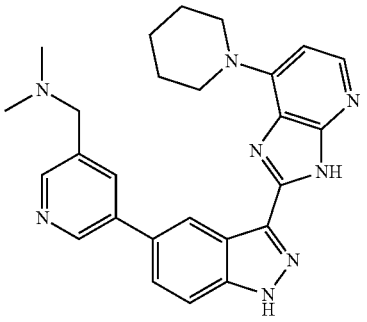
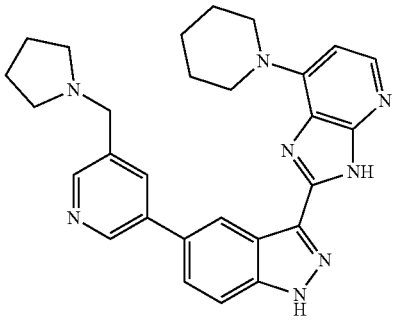
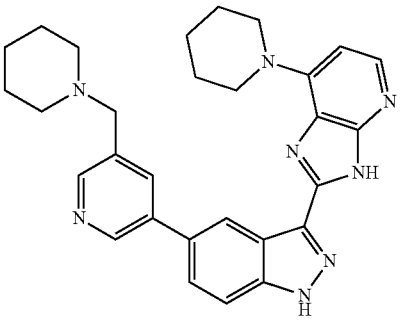
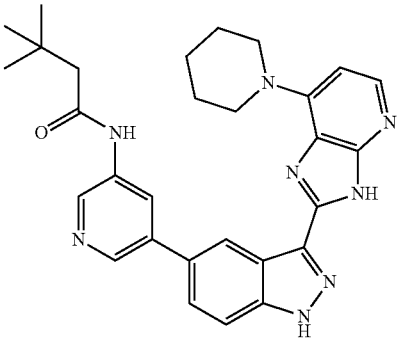
169	
170	
171	
172	

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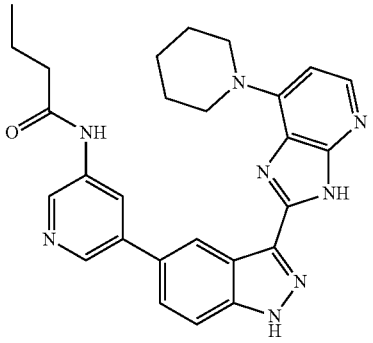
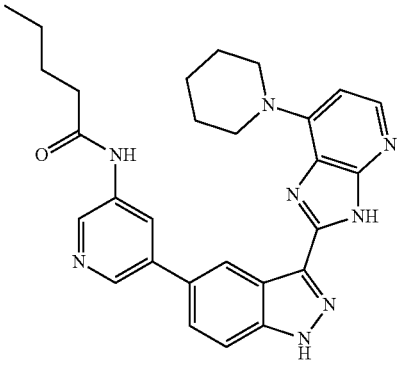
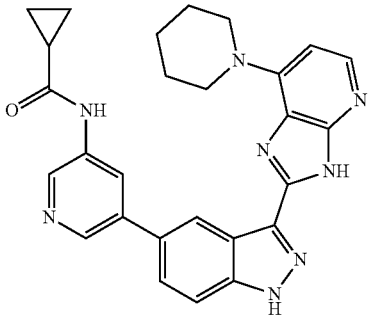
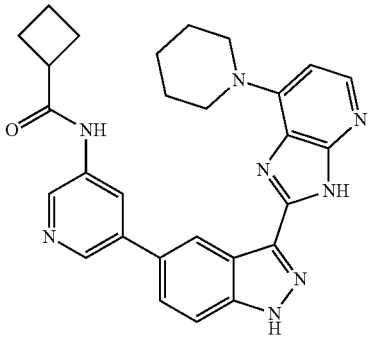
173	
174	
175	
176	

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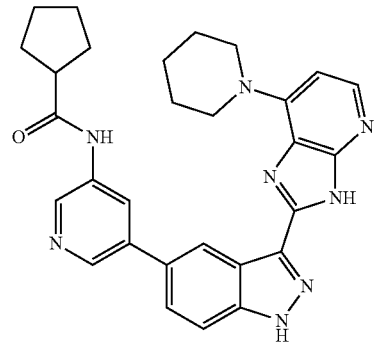
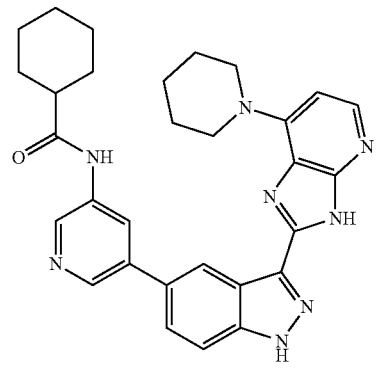
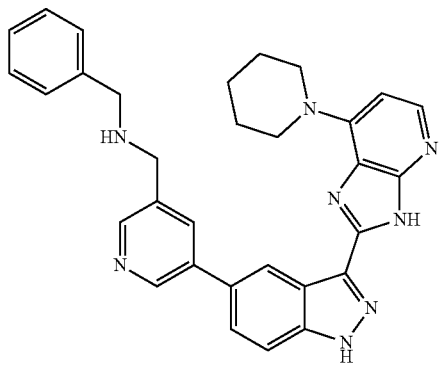
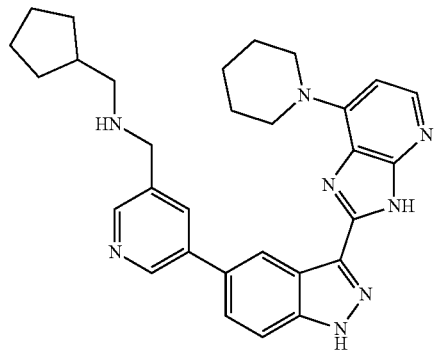
177	
178	
179	
180	

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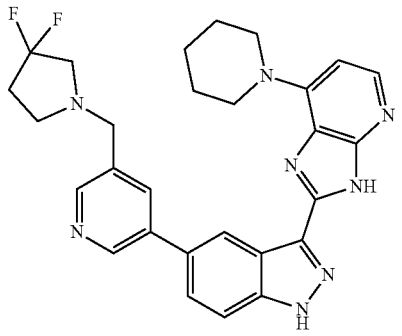
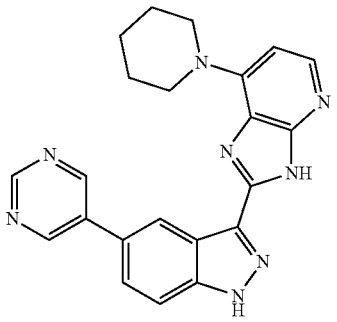
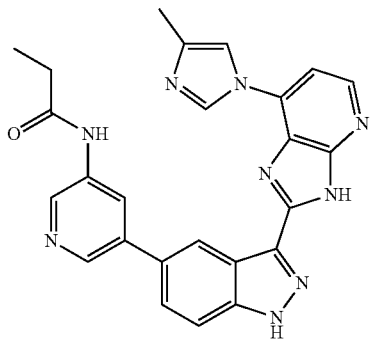
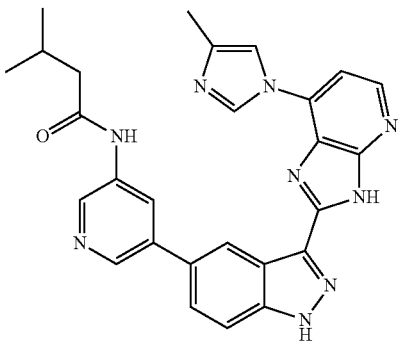
181	
182	
183	
184	

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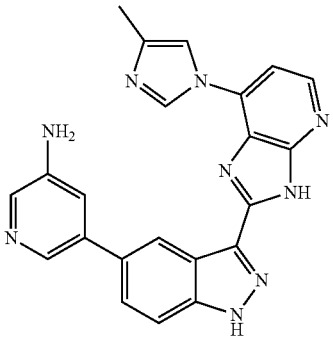
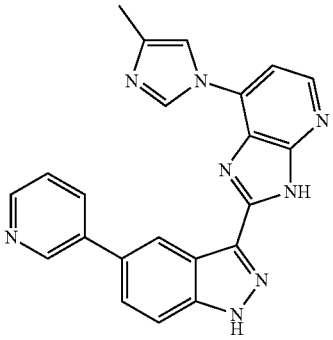
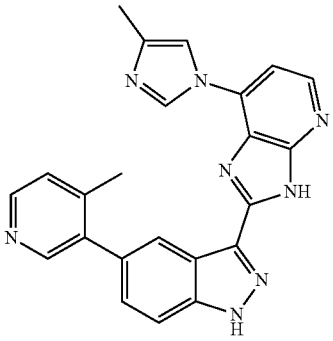
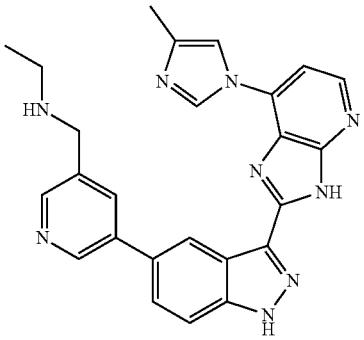
185	
186	
187	
188	

TABLE 1-continued

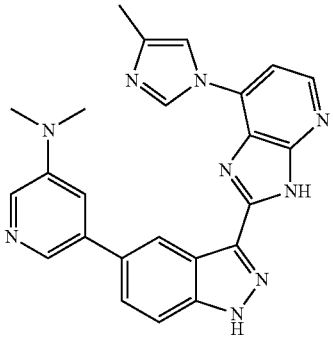
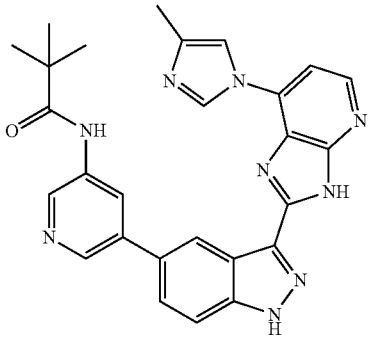
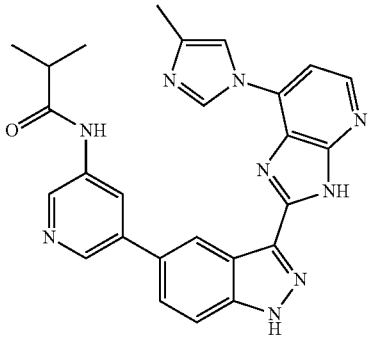
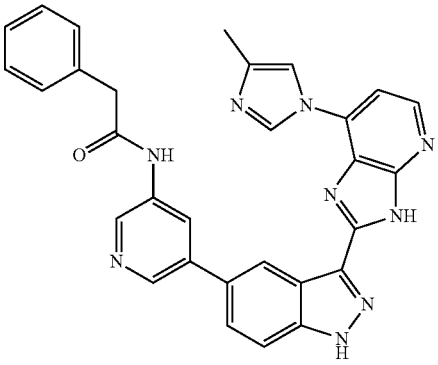
189	
190	
191	
192	

TABLE 1-continued

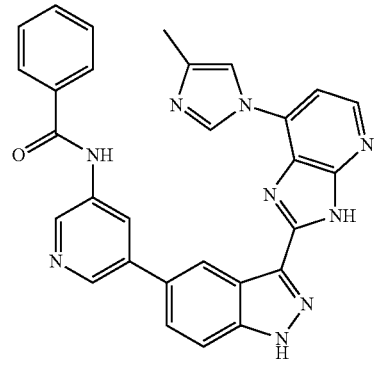
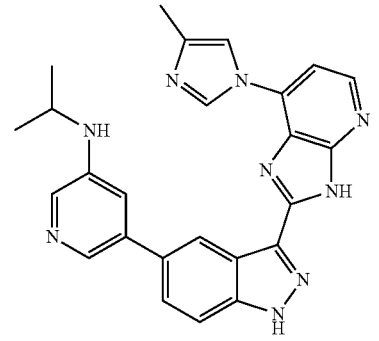
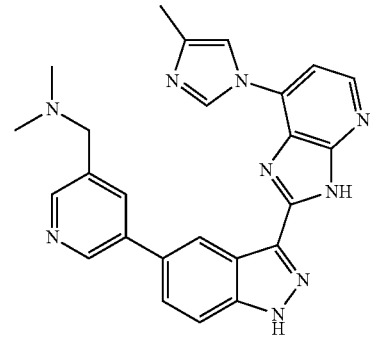
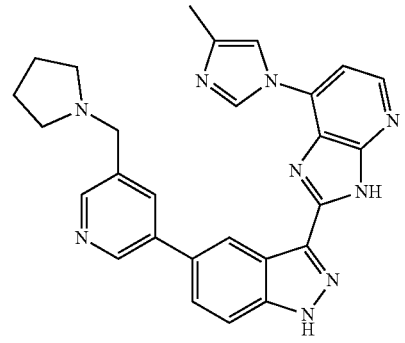
193	
194	
195	
196	

TABLE 1-continued

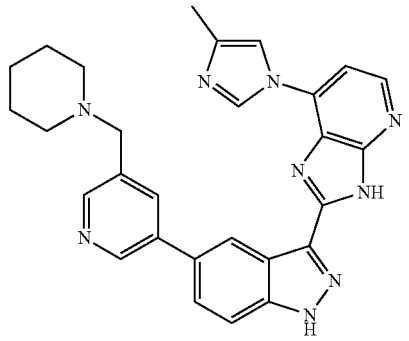
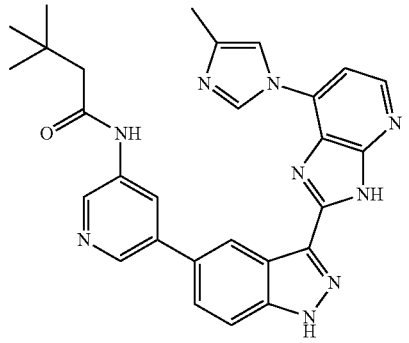
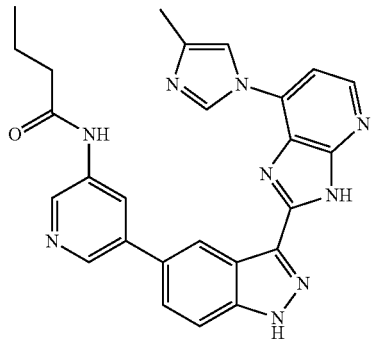
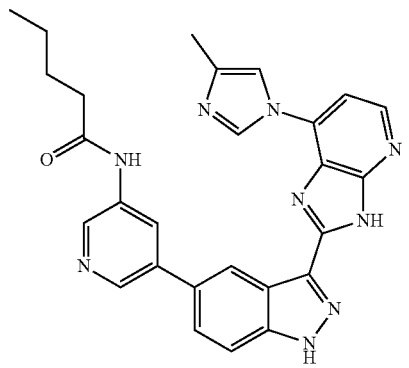
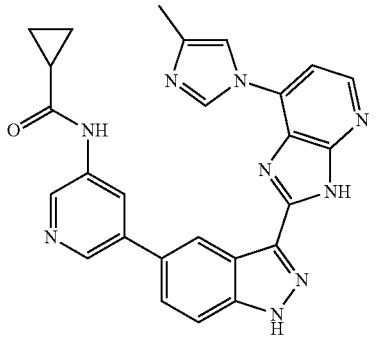
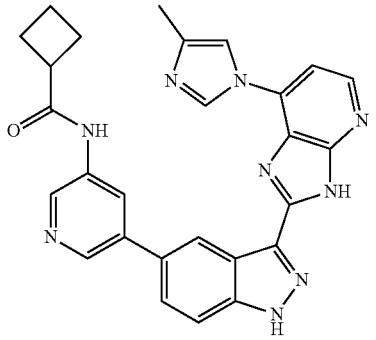
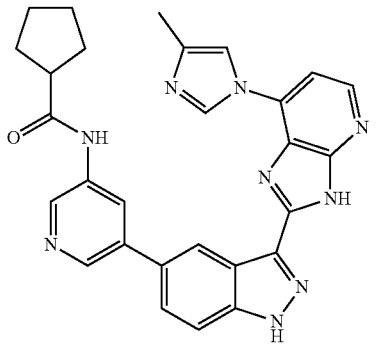
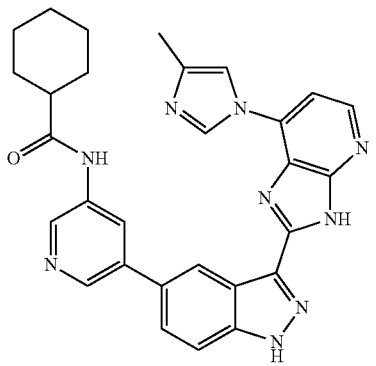
197	
198	
199	
200	

TABLE 1-continued

201	
202	
203	
204	

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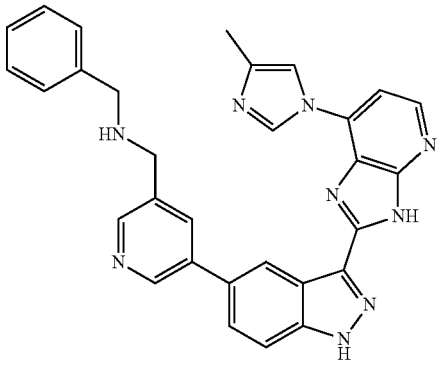
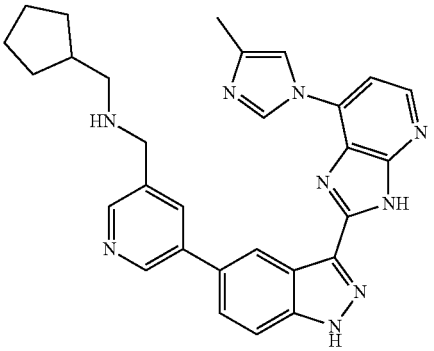
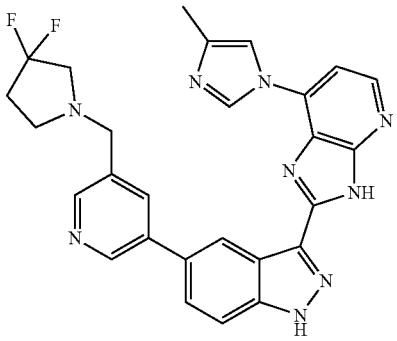
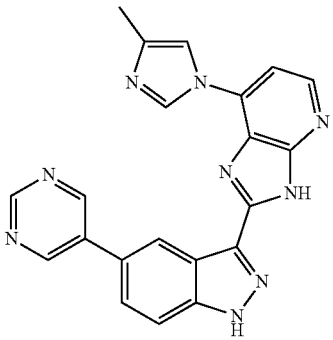
205	
206	
207	
208	

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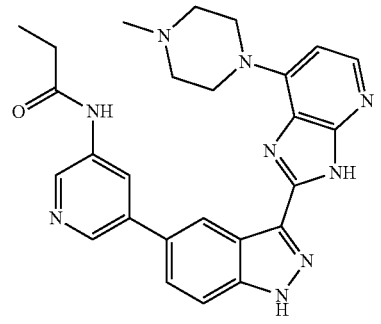
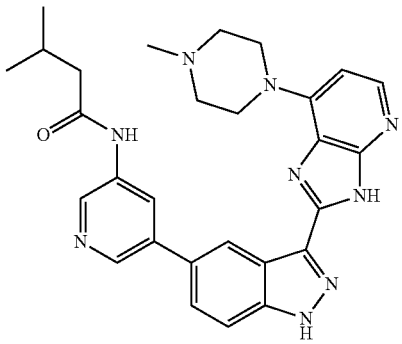
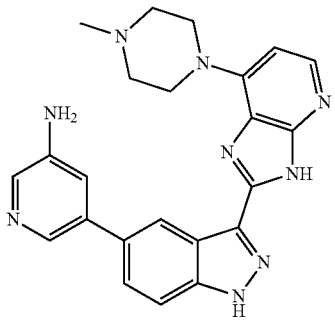
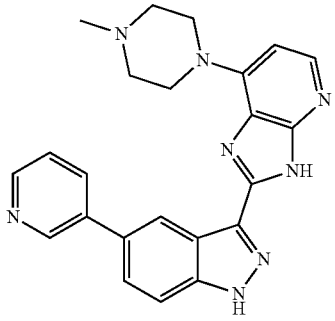
209	
210	
211	
212	

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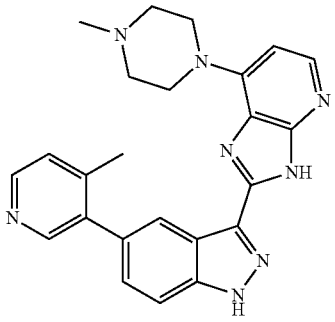
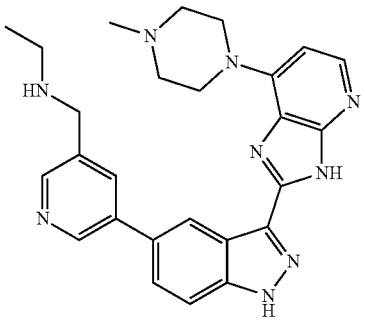
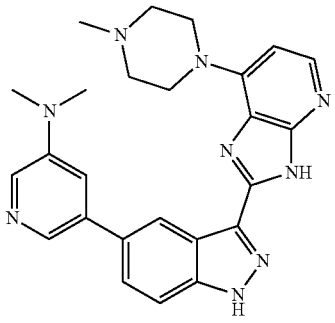
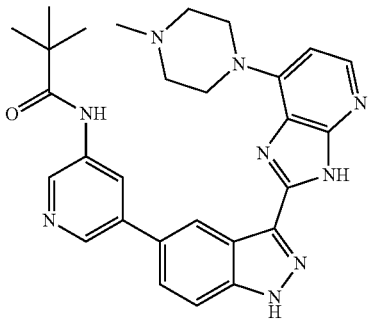
213	
214	
215	
216	

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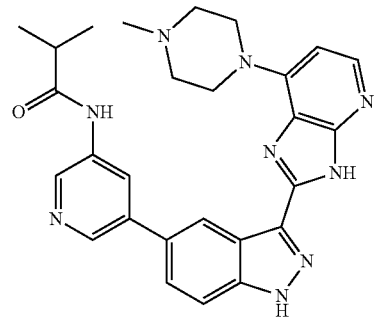
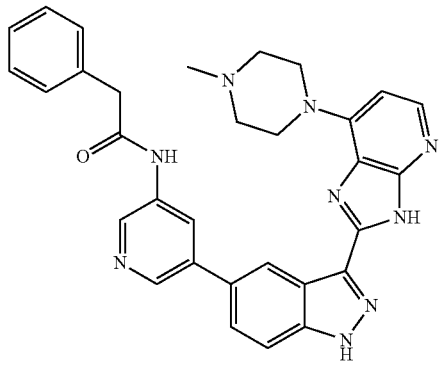
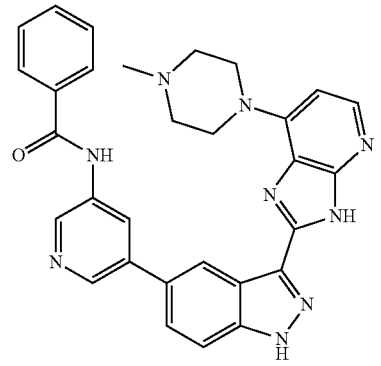
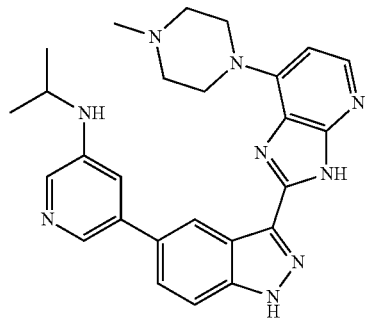
217	
218	
219	
220	

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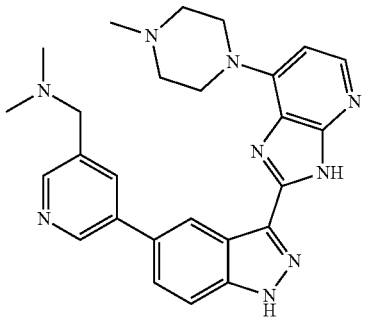
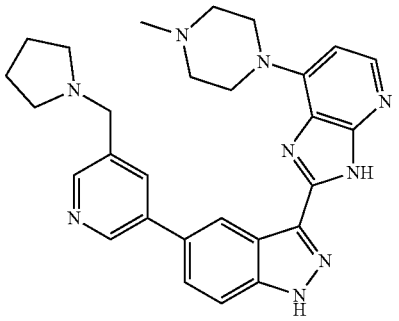
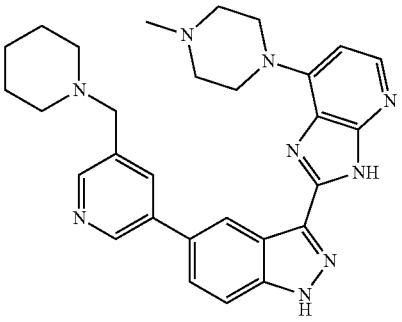
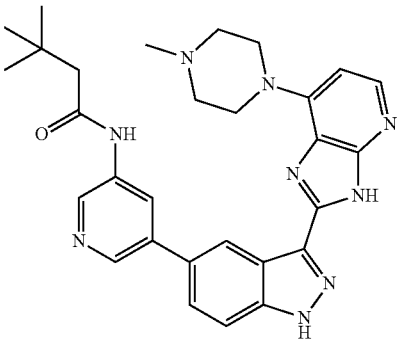
221	
222	
223	
224	

TABLE 1-continued

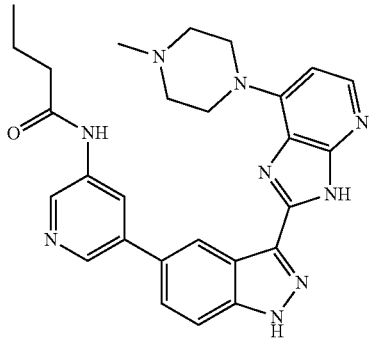
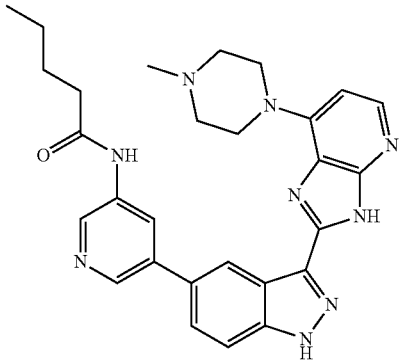
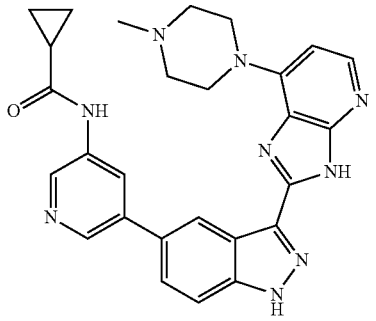
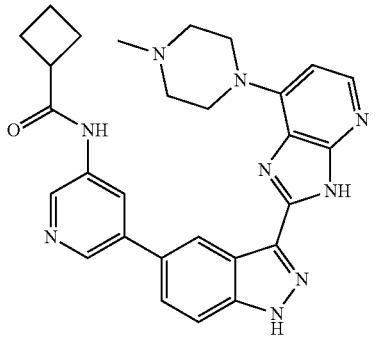
225	
226	
227	
228	

TABLE 1-continued

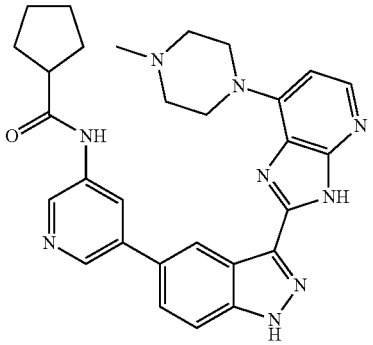
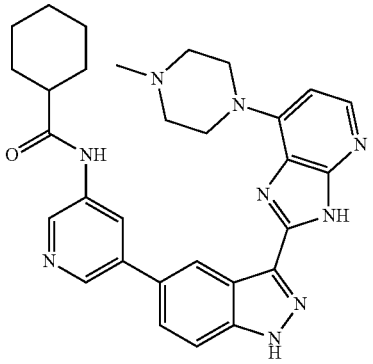
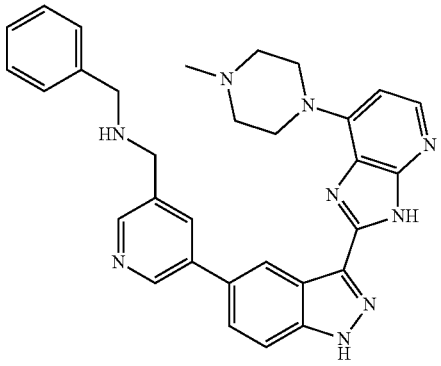
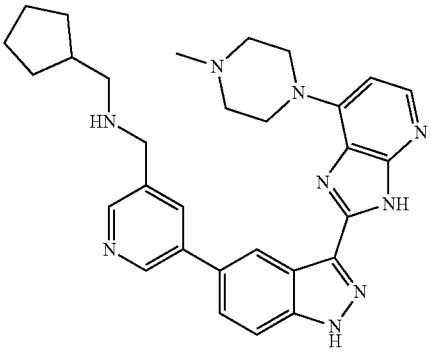
229	
230	
231	
232	

TABLE 1-continued

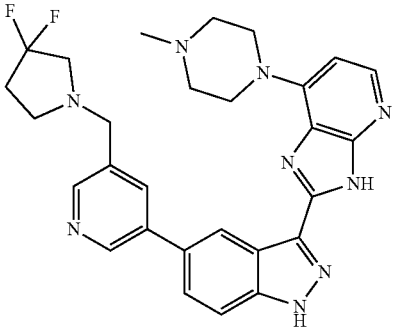
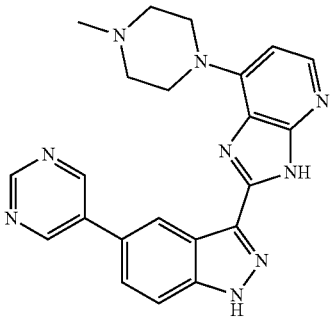
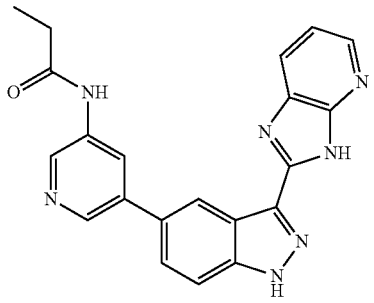
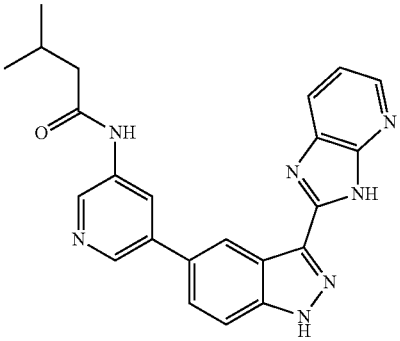
233	
234	
235	
236	

TABLE 1-continued

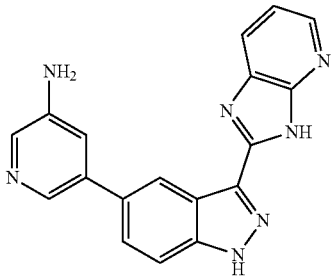
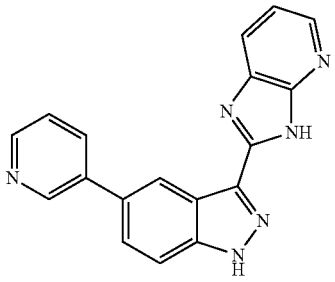
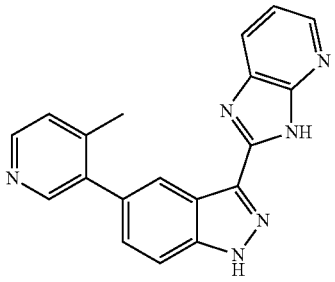
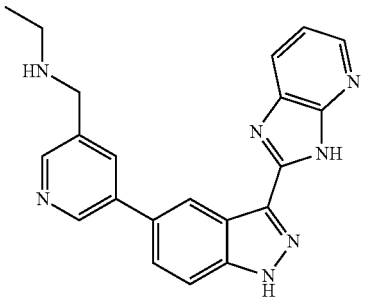
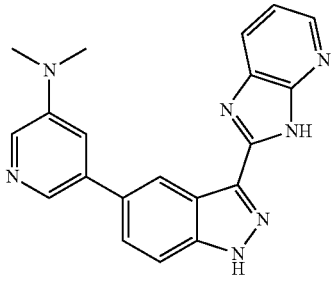
237	
238	
239	
240	
241	

TABLE 1-continued

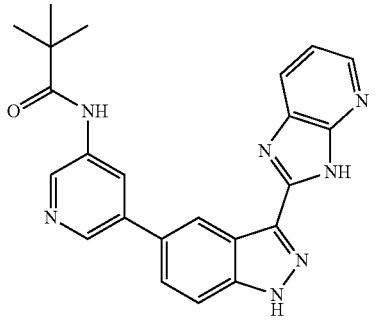
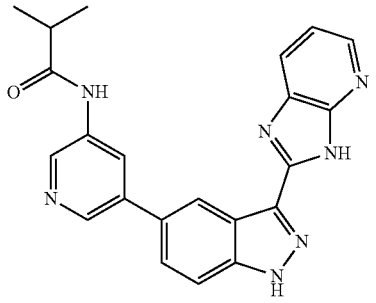
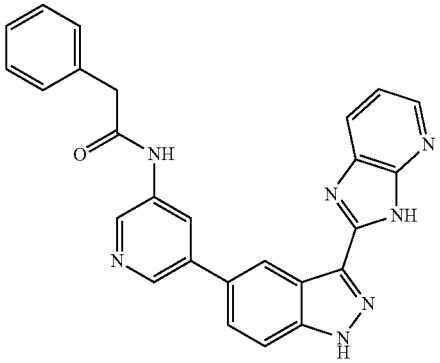
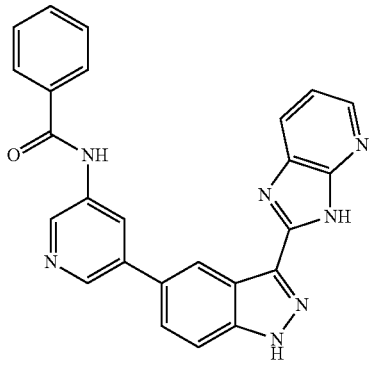
242	
243	
244	
245	

TABLE 1-continued

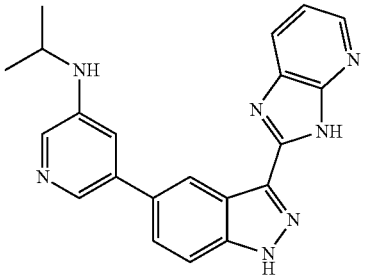
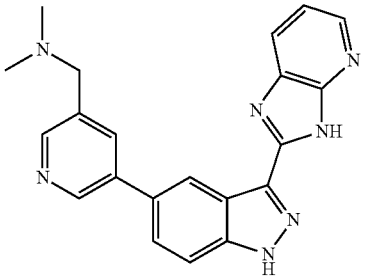
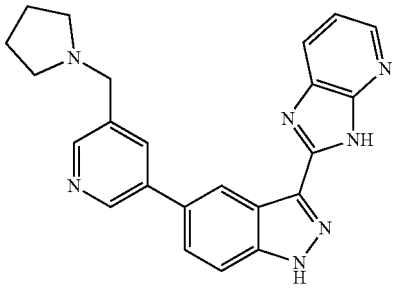
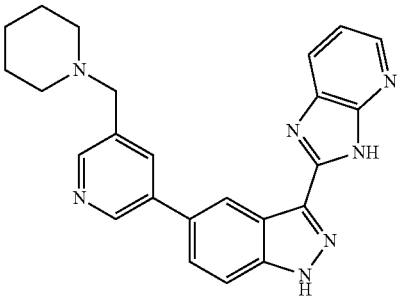
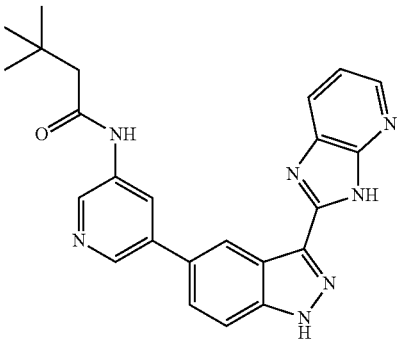
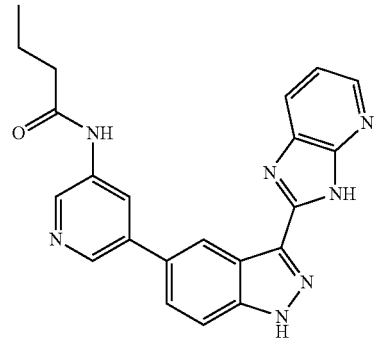
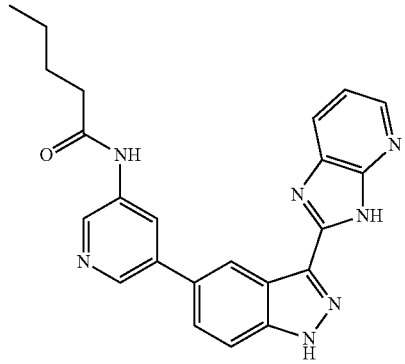
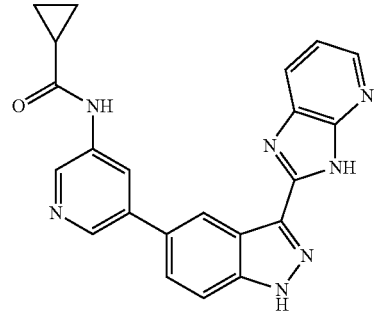
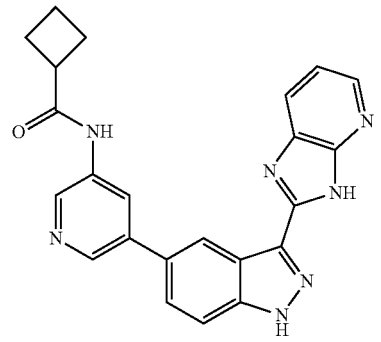
246	
247	
248	
249	
250	

TABLE 1-continued

251	
252	
253	
254	

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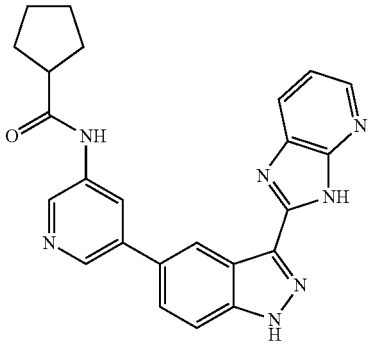
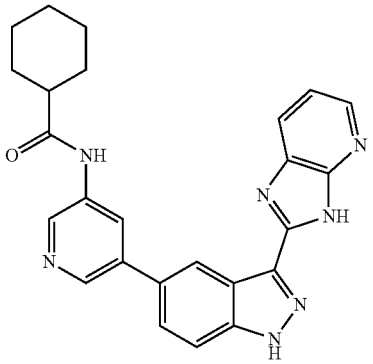
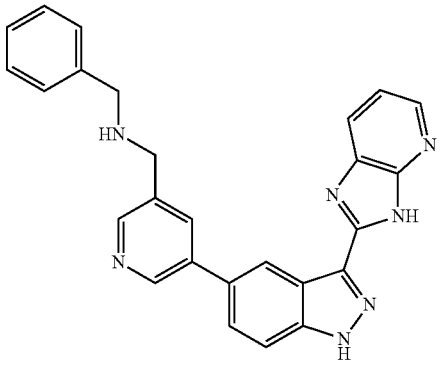
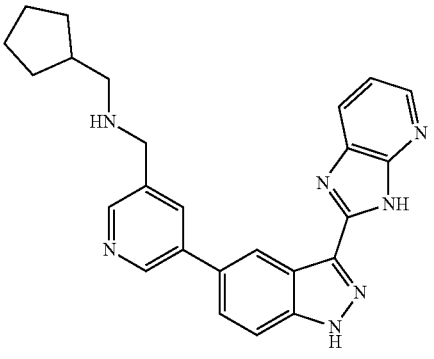
255	
256	
257	
258	

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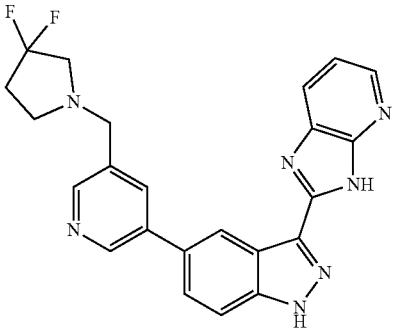
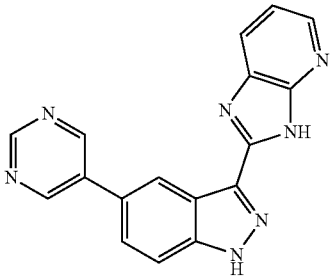
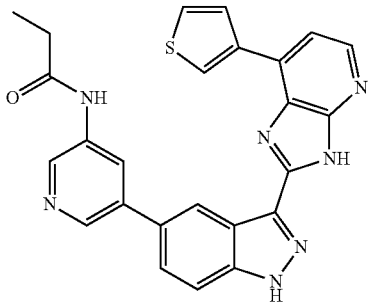
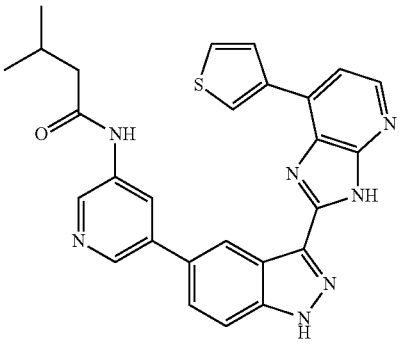
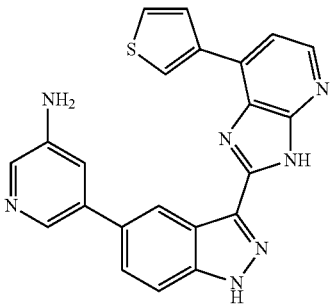
259	
260	
261	
262	
263	

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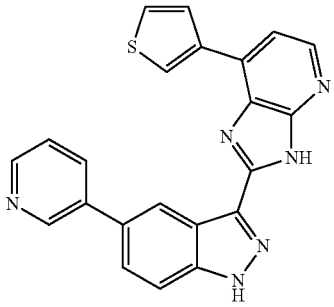
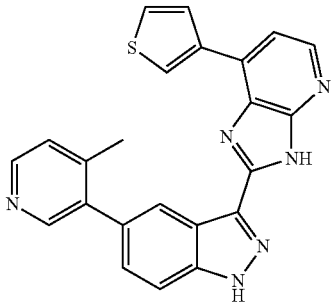
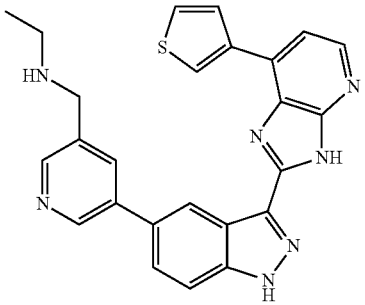
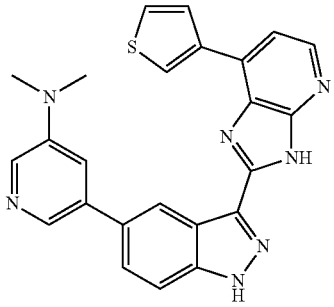
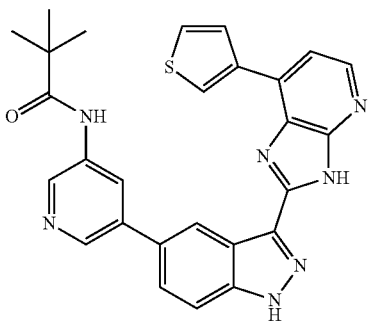
264	
265	
266	
267	
268	

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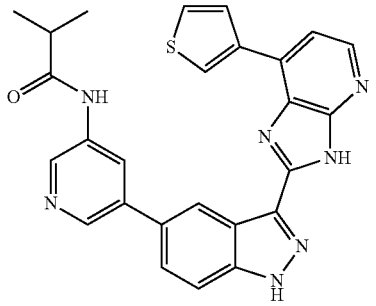
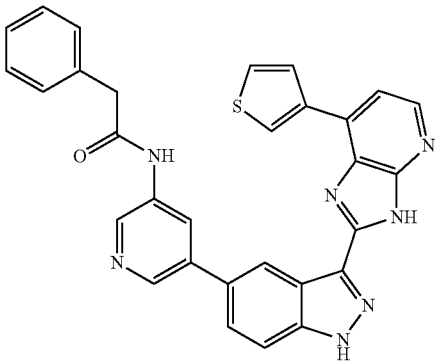
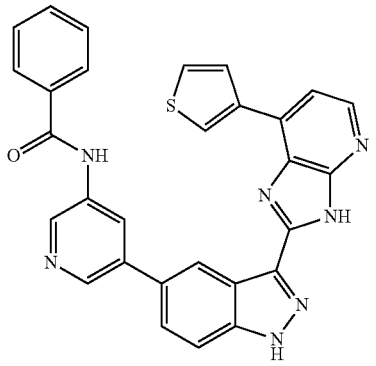
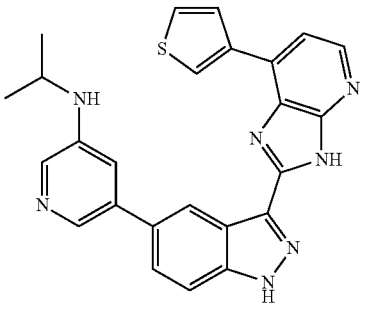
269	
270	
271	
272	

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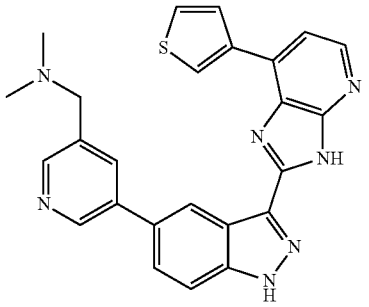
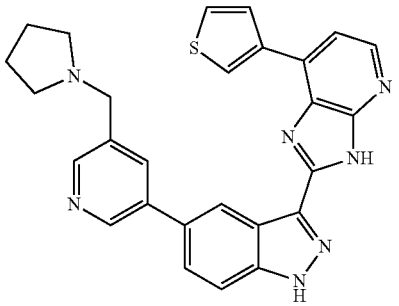
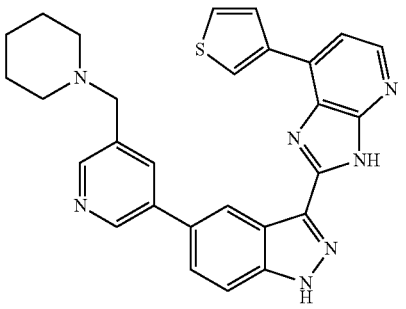
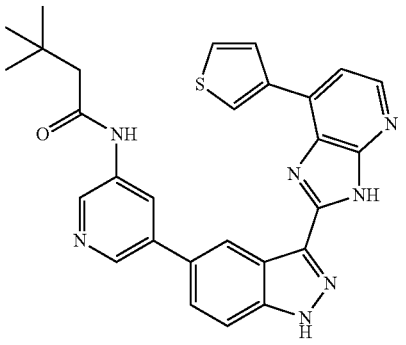
273	
274	
275	
276	

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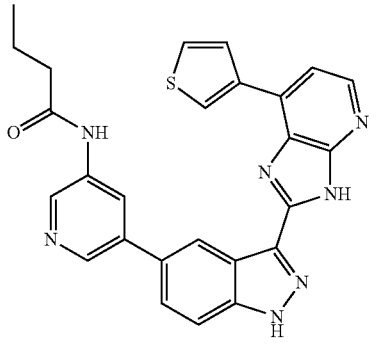

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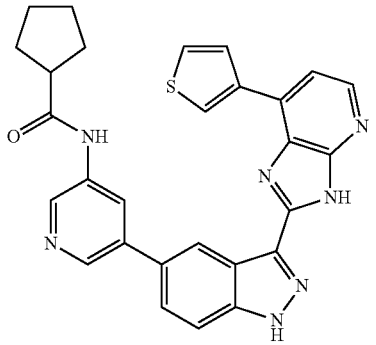

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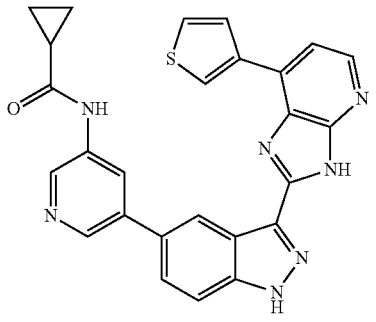

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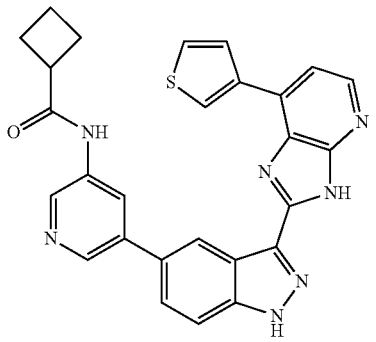

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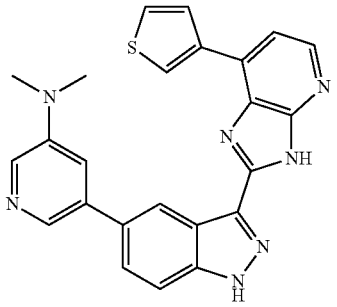

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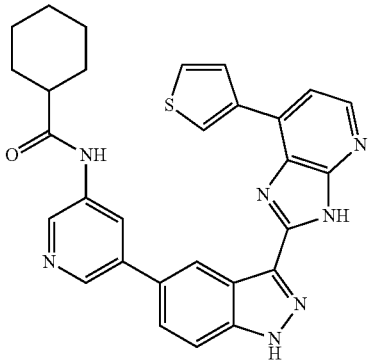

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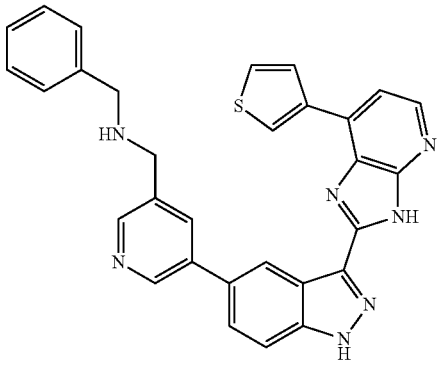

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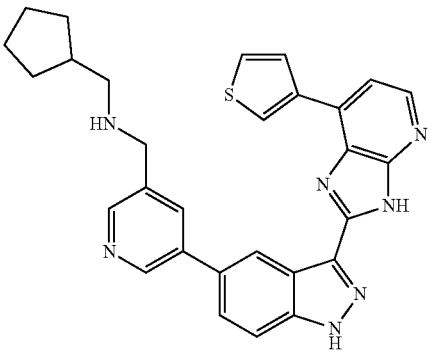

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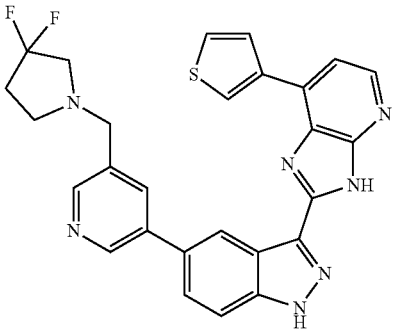
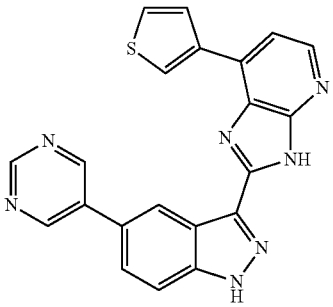
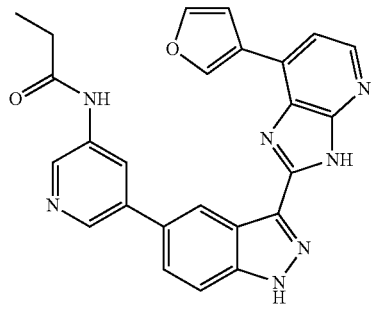
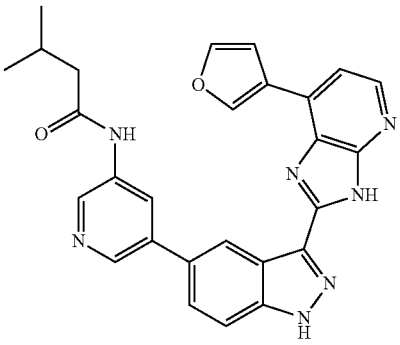
285	
286	
287	
288	

TABLE 1-continued

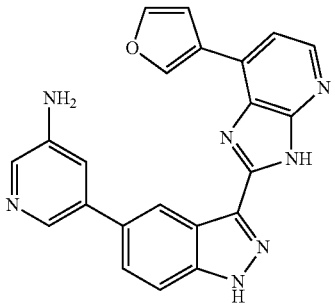
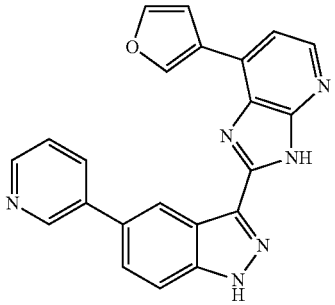
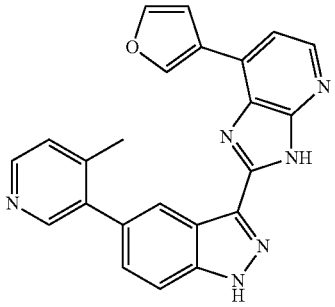
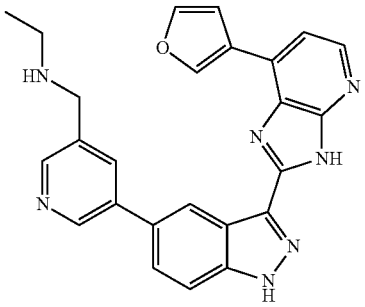
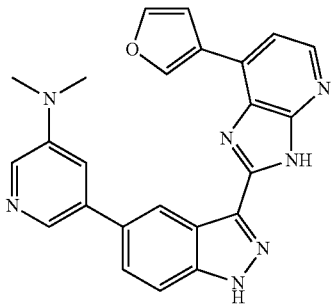
289	
290	
291	
292	
293	

TABLE 1-continued

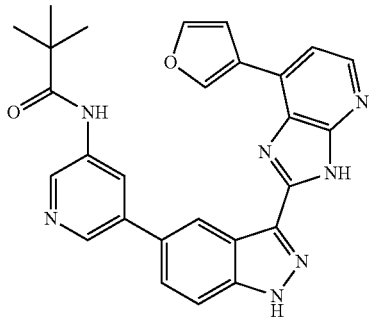
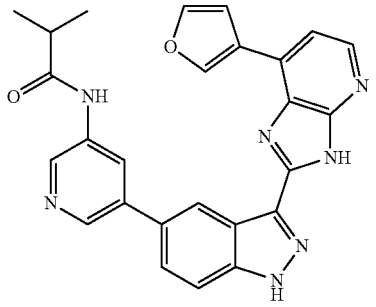
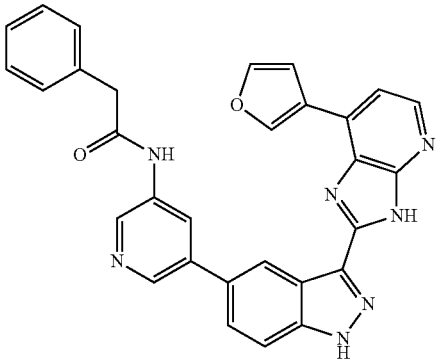
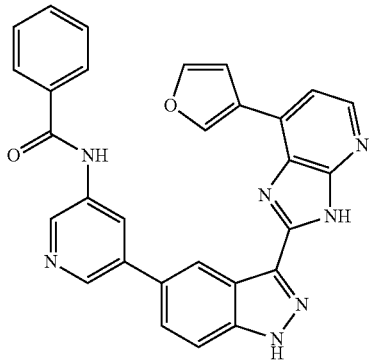
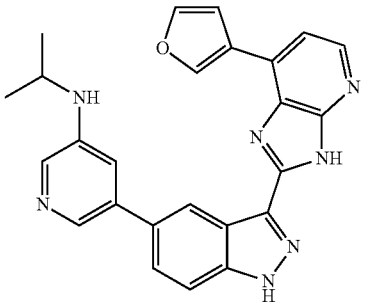
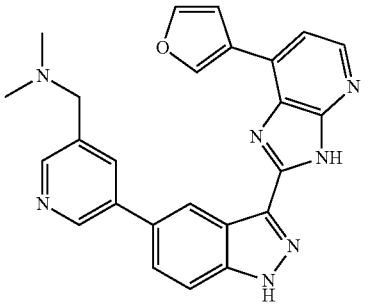
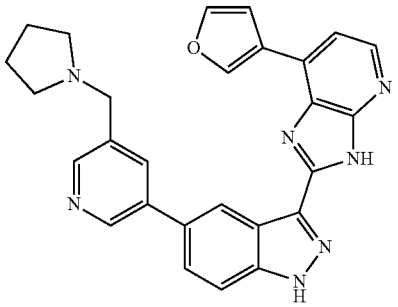
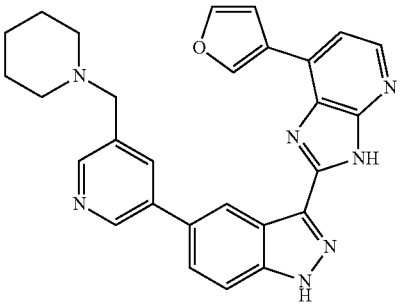
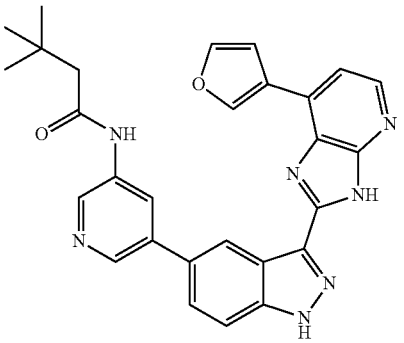
294	
295	
296	
297	

TABLE 1-continued

298	
299	
300	
301	
302	

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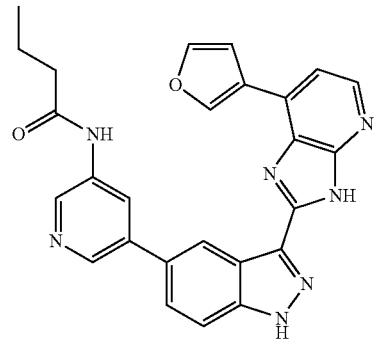
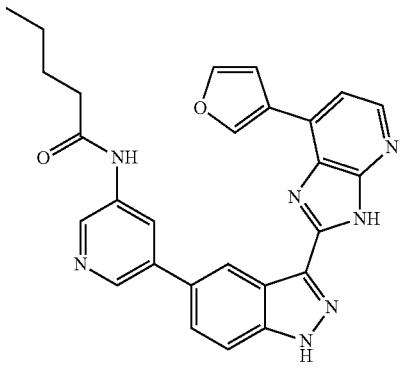
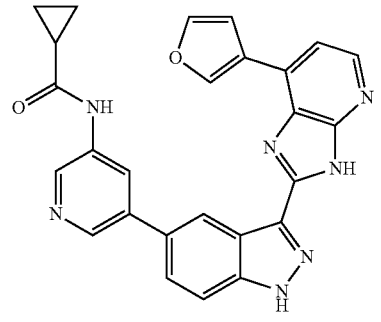
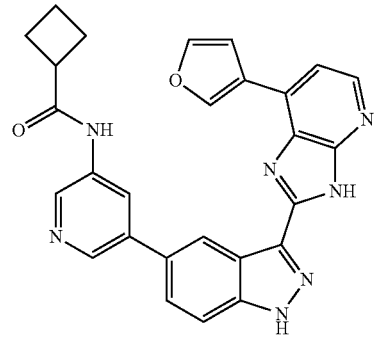
303	
304	
305	
306	

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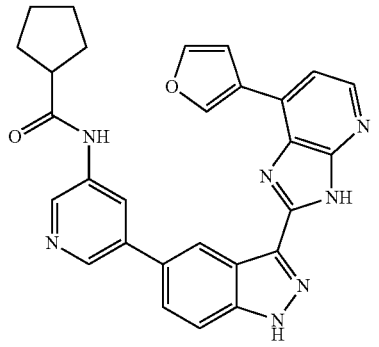
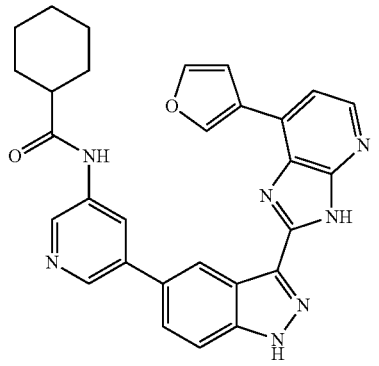
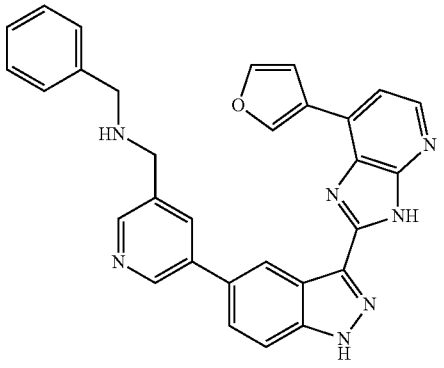
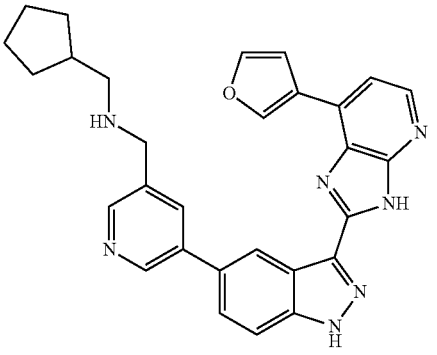
307	
308	
309	
310	

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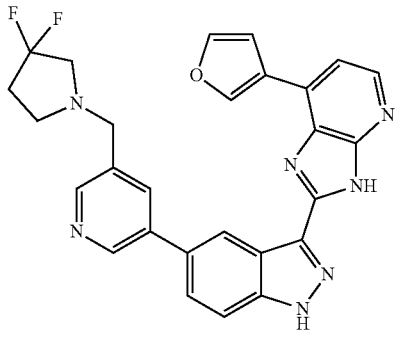
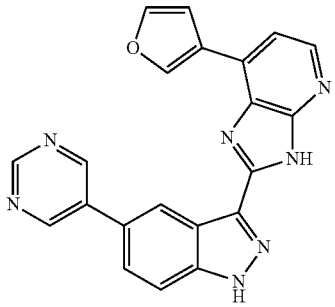
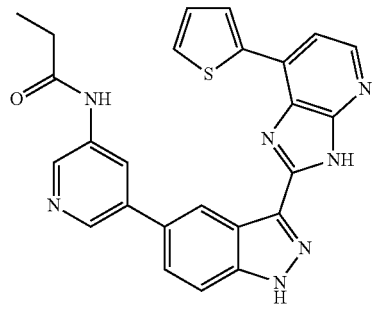
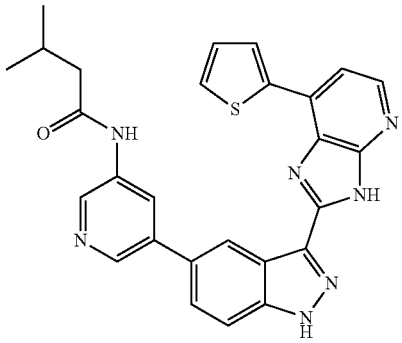
311	
312	
313	
314	

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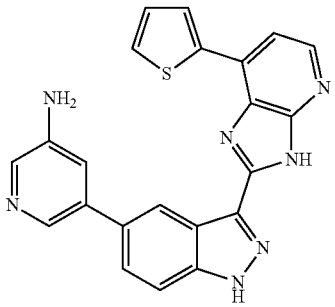
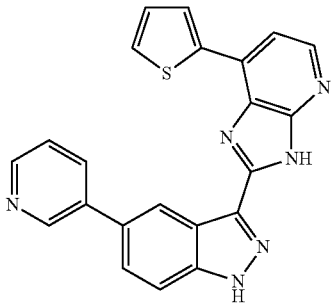
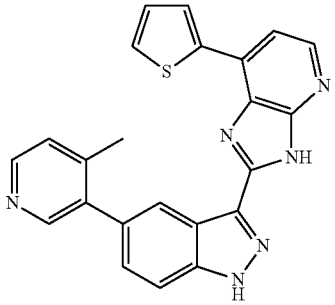
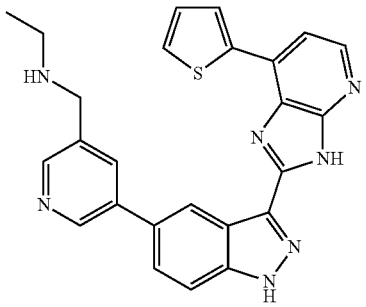
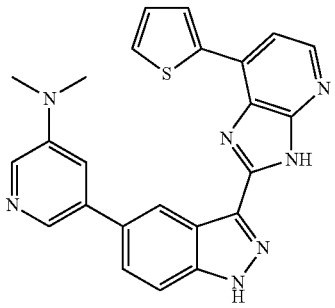
315	
316	
317	
318	
319	

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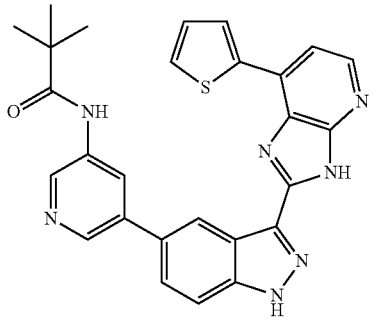
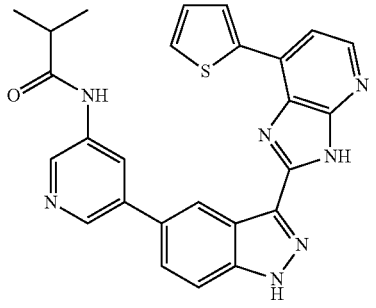
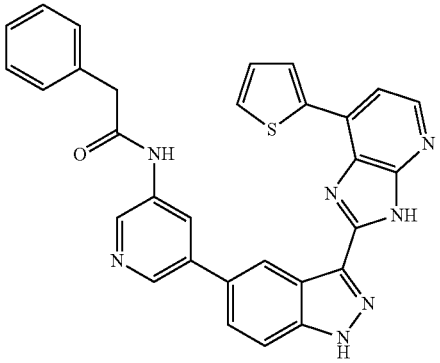
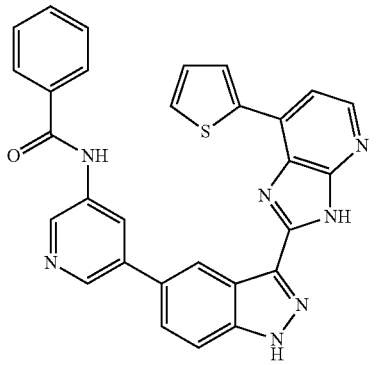
320	
321	
322	
323	

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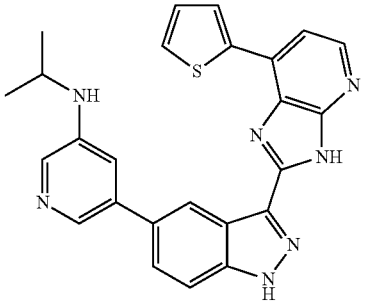
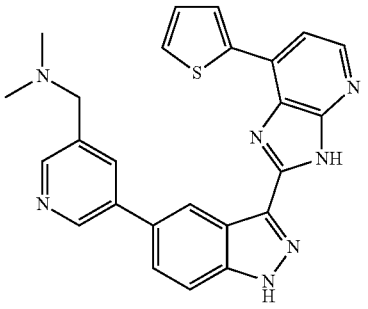
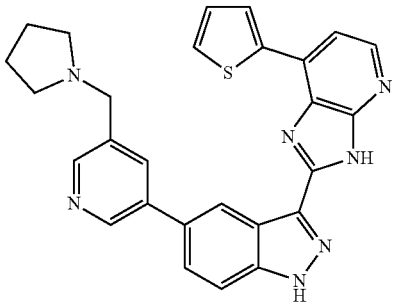
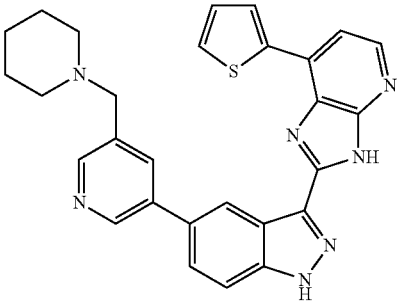
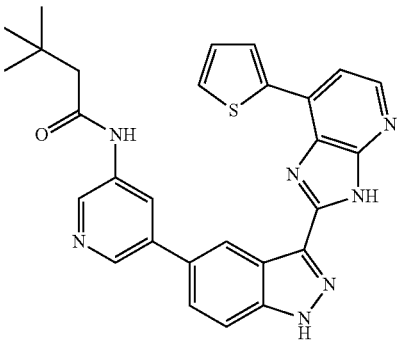
324	
325	
326	
327	
328	

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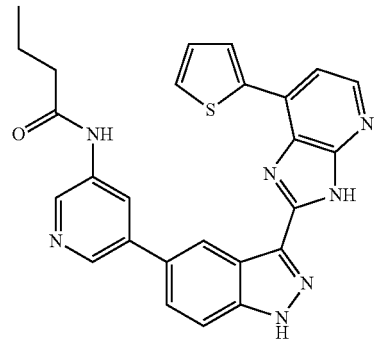
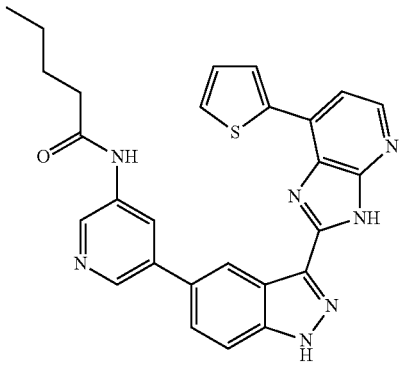
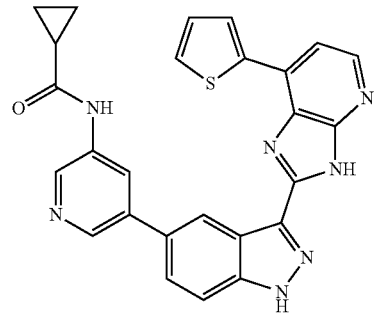
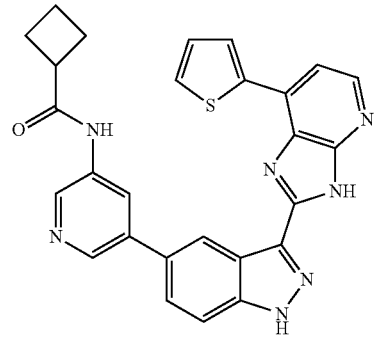
329	
330	
331	
332	

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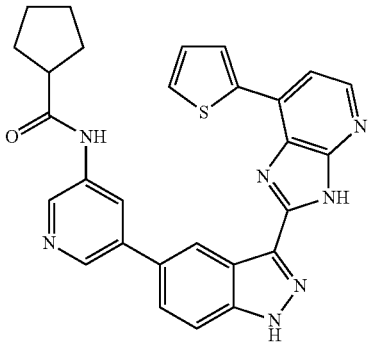
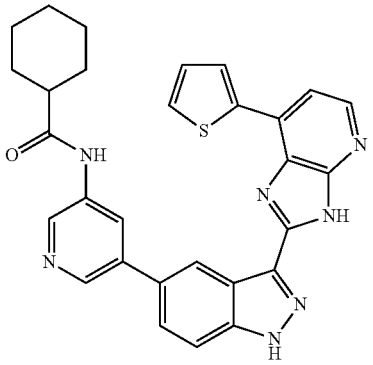
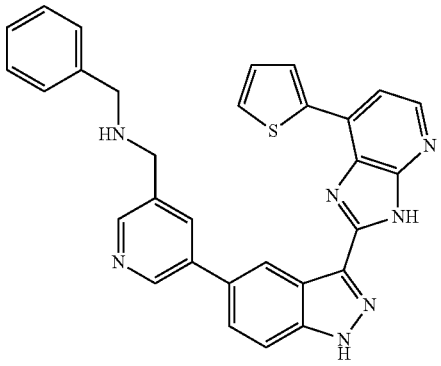
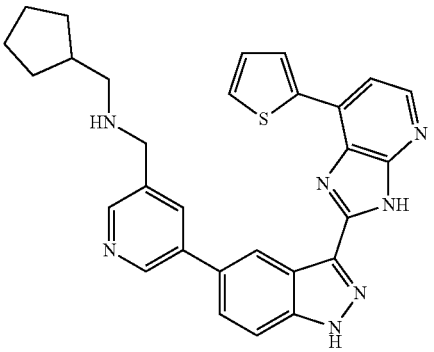
333	
334	
335	
336	

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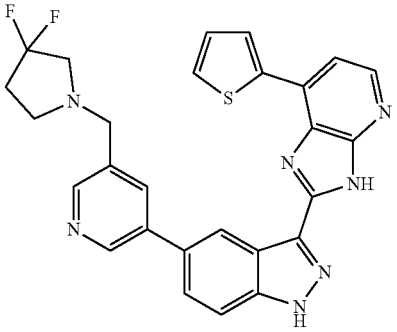
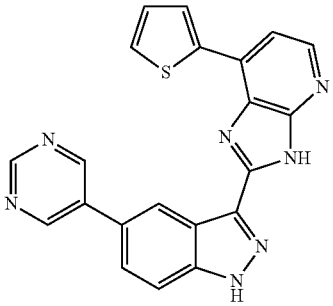
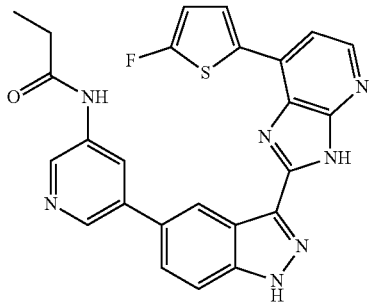
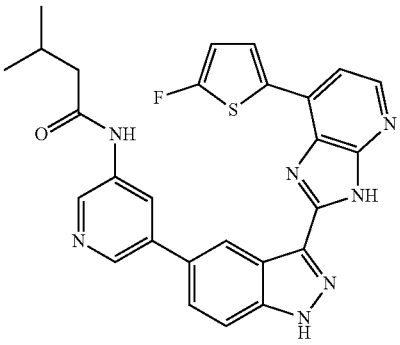
337	
338	
339	
340	

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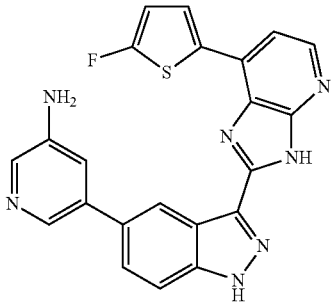
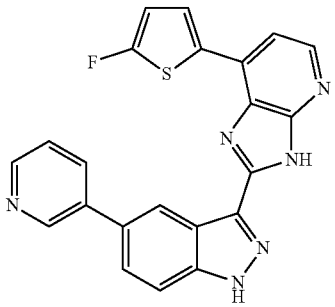
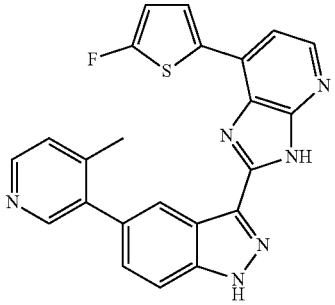
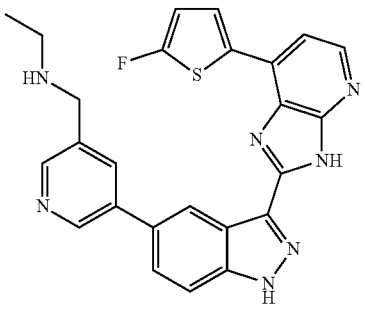
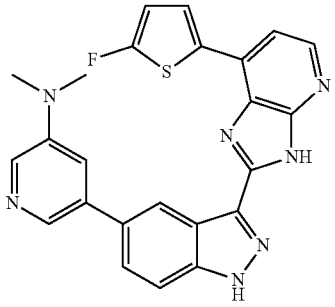
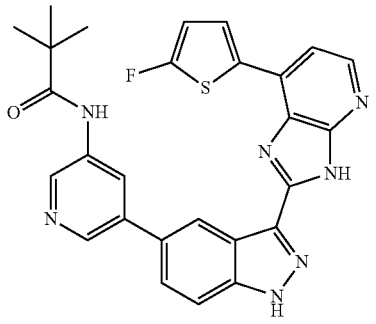
341	
342	
343	
344	
345	

TABLE 1-continued

346



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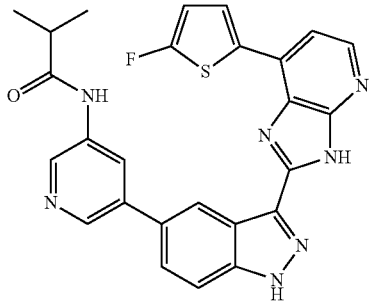

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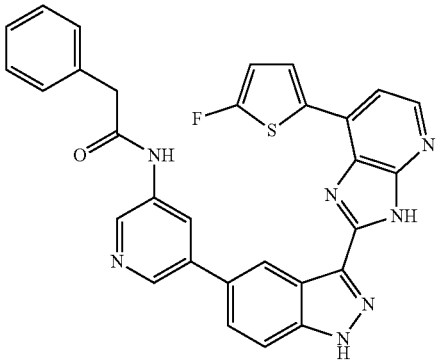

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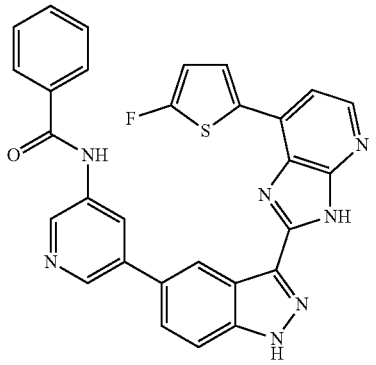

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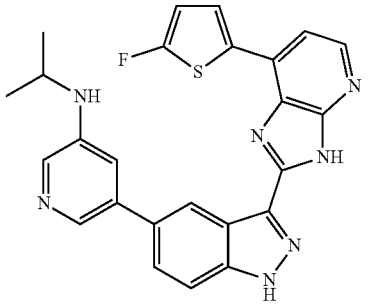

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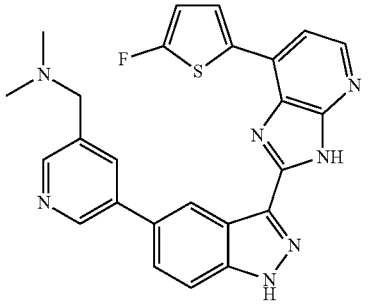

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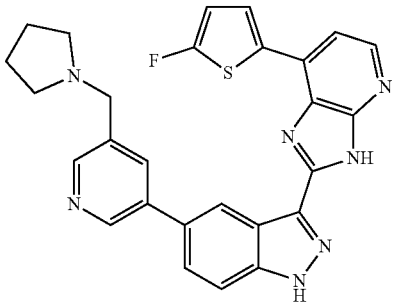

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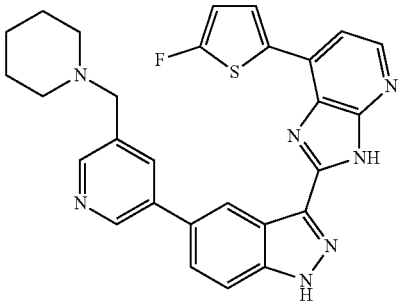

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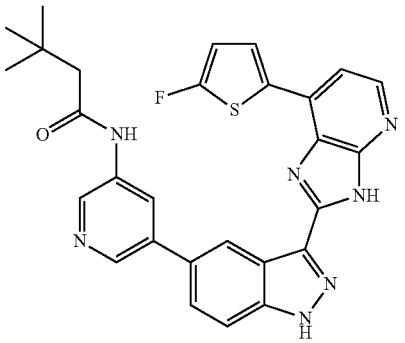

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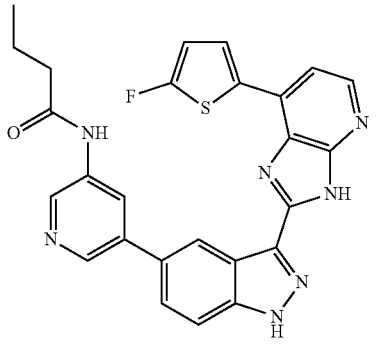
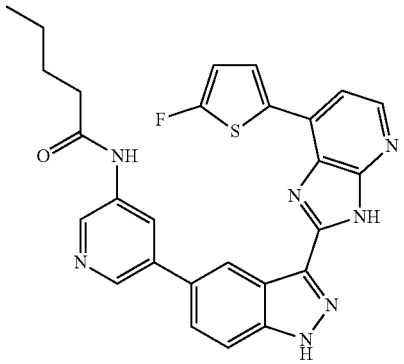
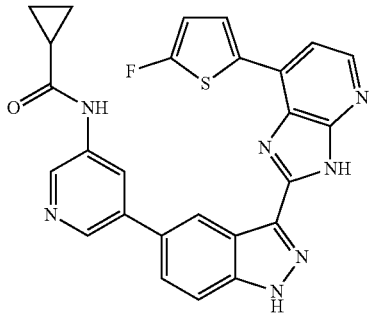
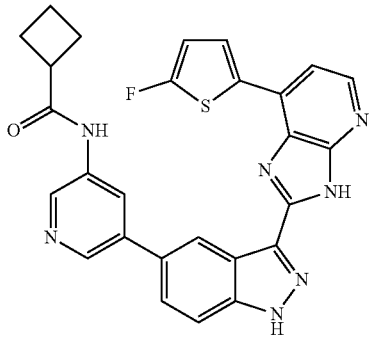
355	
356	
357	
358	

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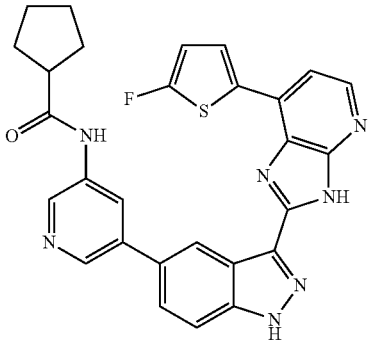
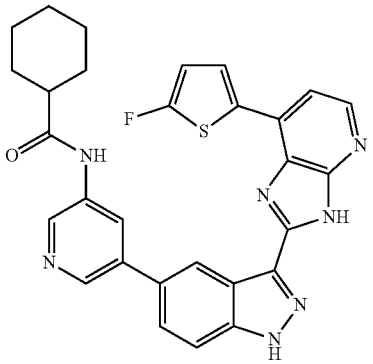
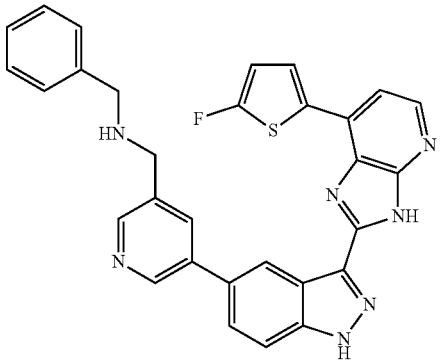
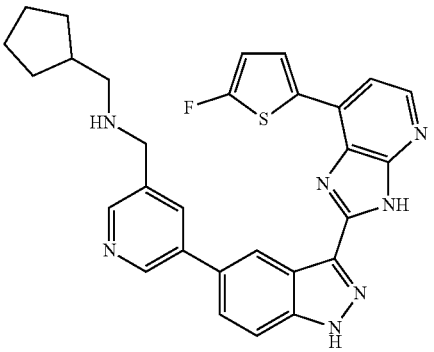
359	
360	
361	
362	

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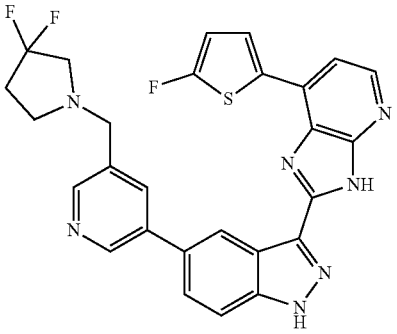
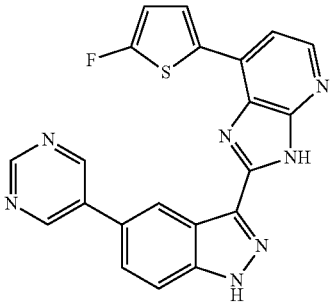
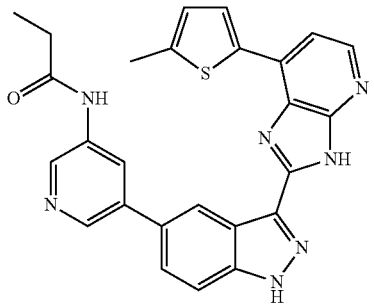
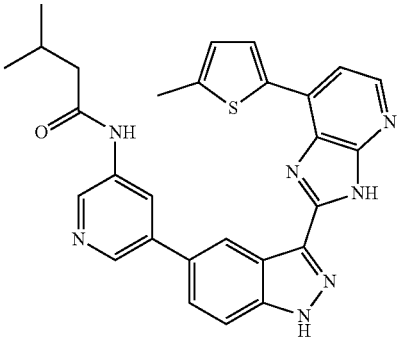
363	
364	
365	
366	

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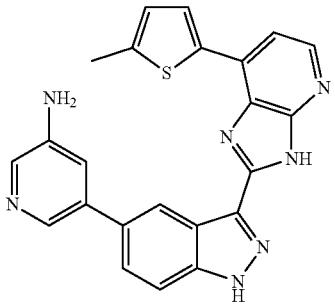
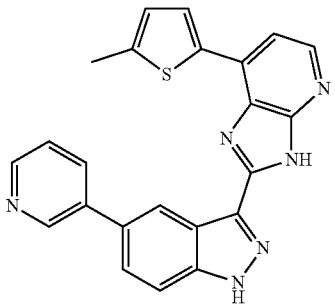
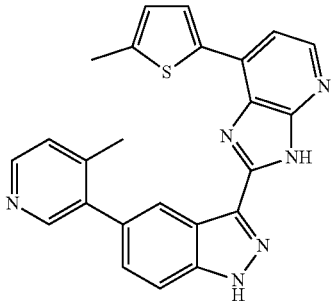
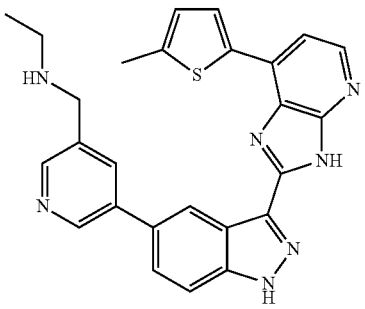
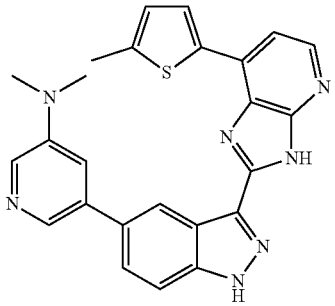
367	
368	
369	
370	
371	

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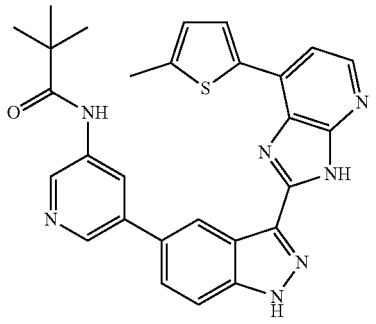
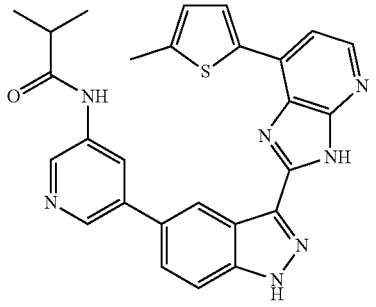
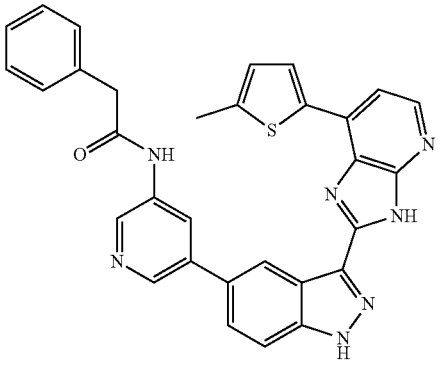
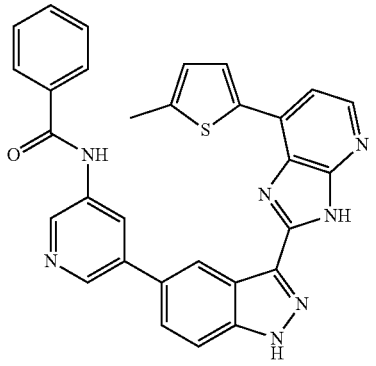
372	
373	
374	
375	

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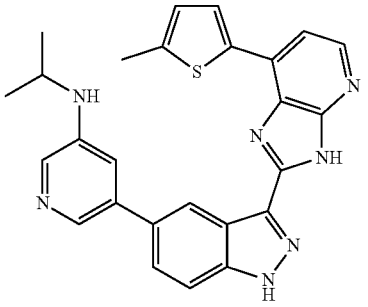
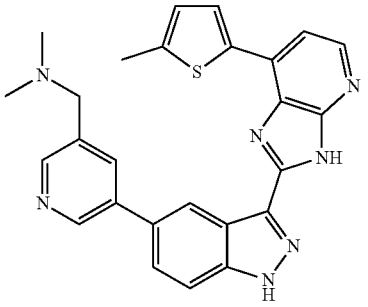
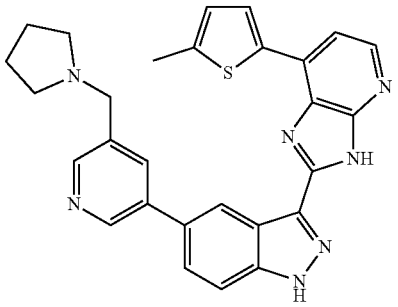
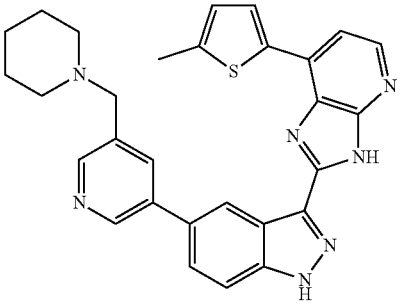
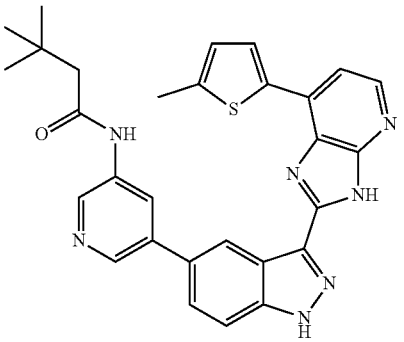
376	
377	
378	
379	
380	

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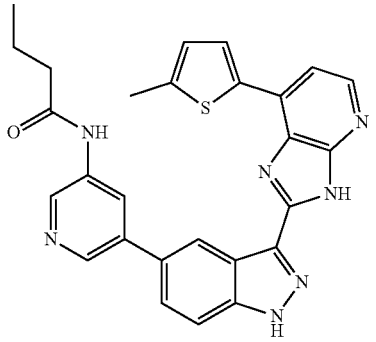
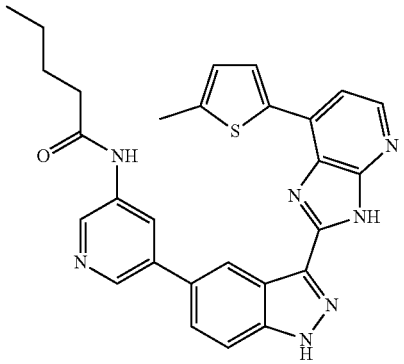
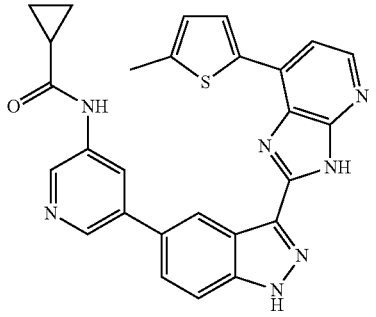
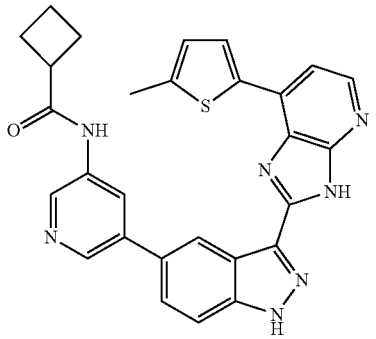
381	
382	
383	
384	

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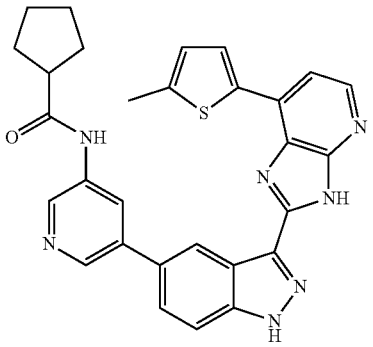
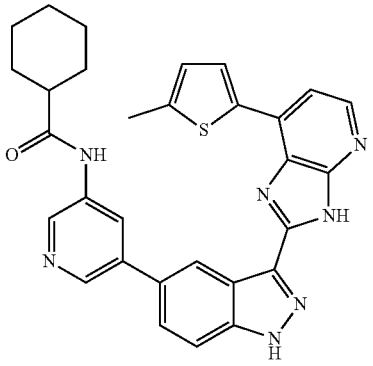
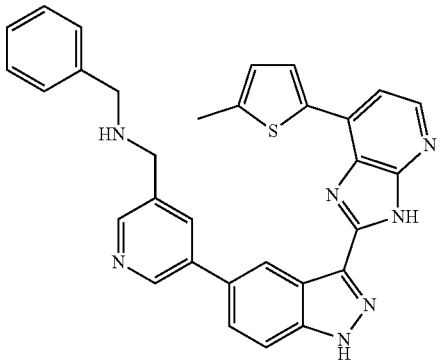
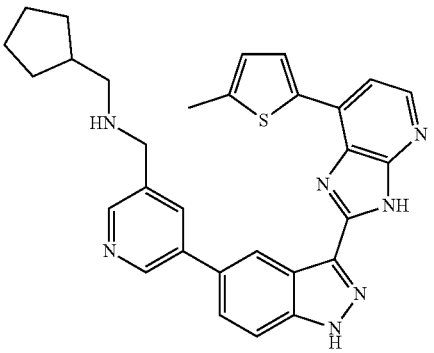
385	
386	
387	
388	

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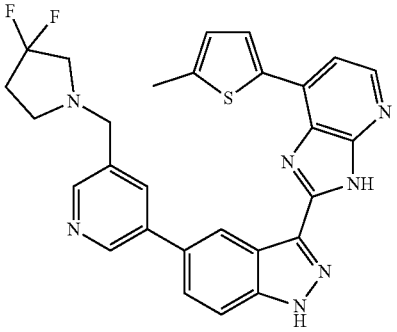
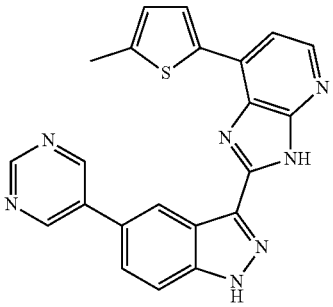
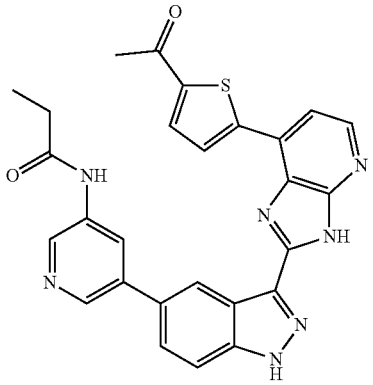
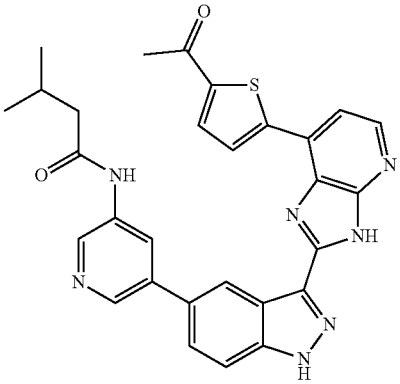
389	
390	
391	
392	

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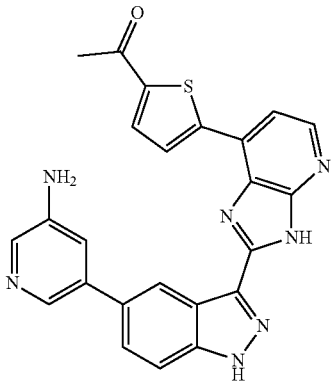
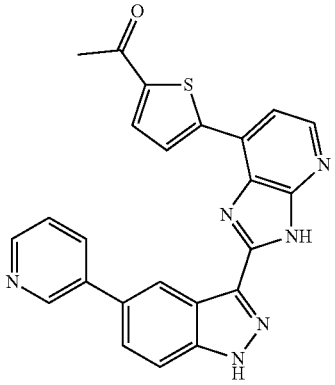
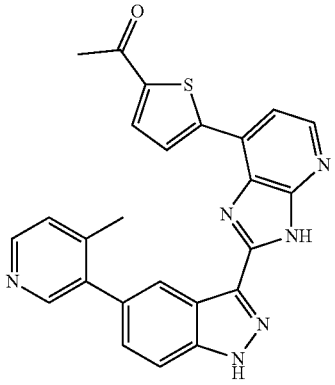
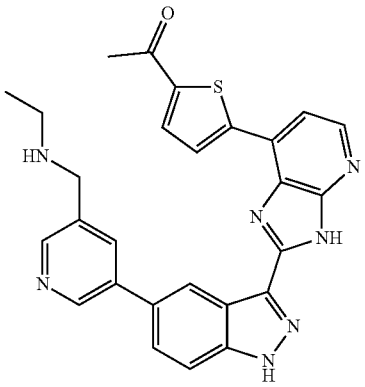
393	
394	
395	
396	

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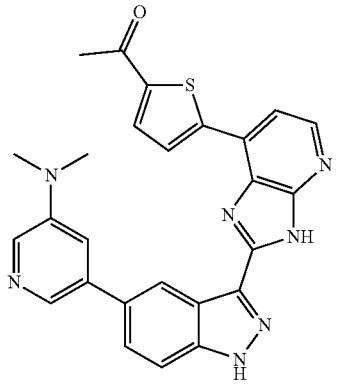
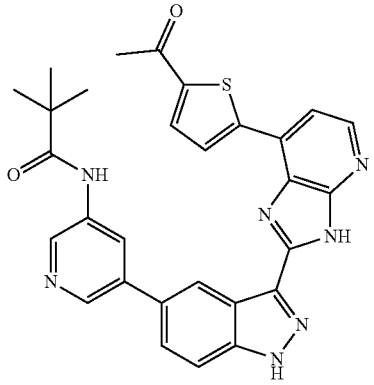
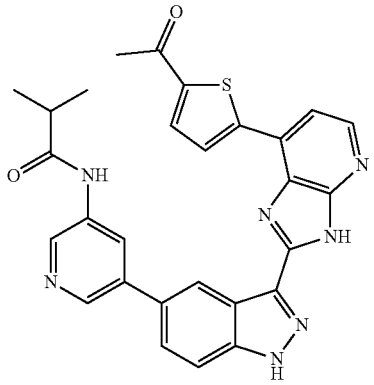
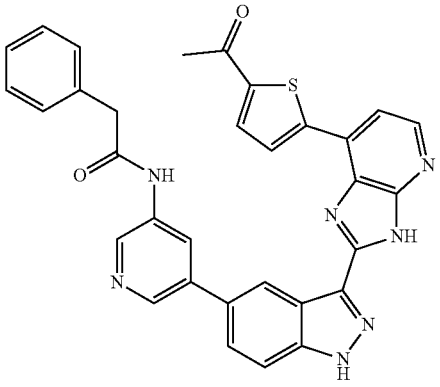
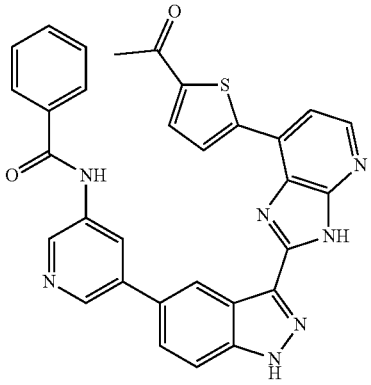
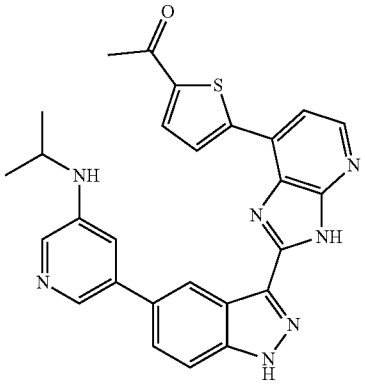
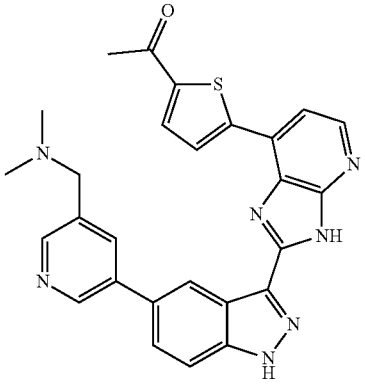
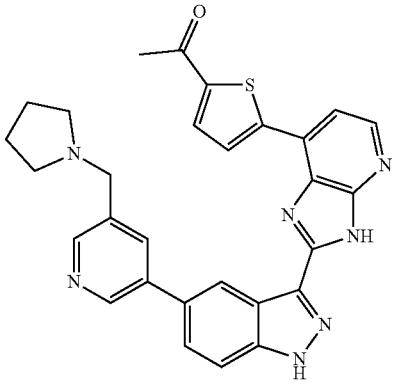
397	
398	
399	
400	

TABLE 1-continued

401	
402	
403	
404	

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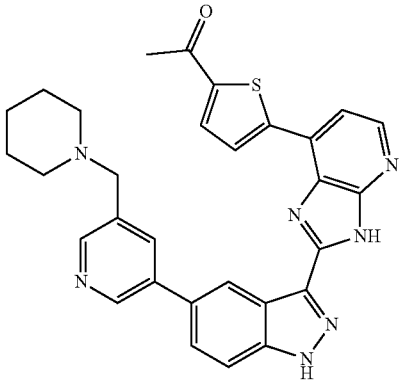
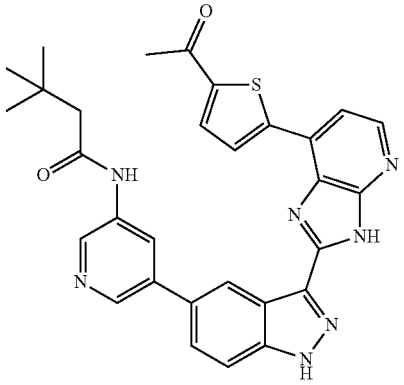
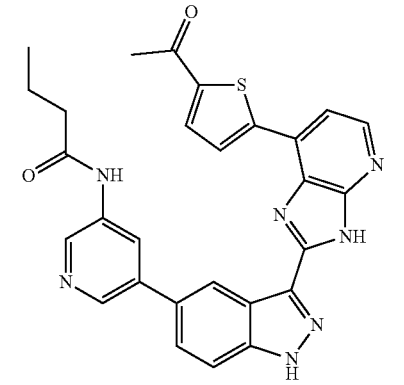
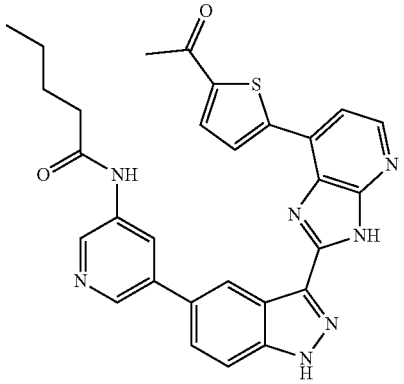
405	
406	
407	
408	

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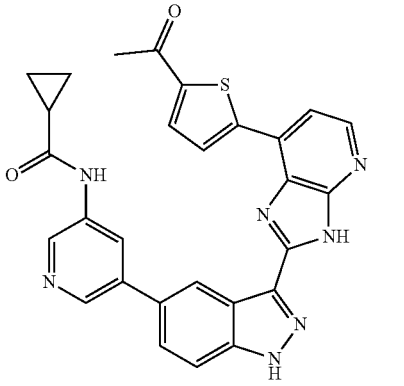
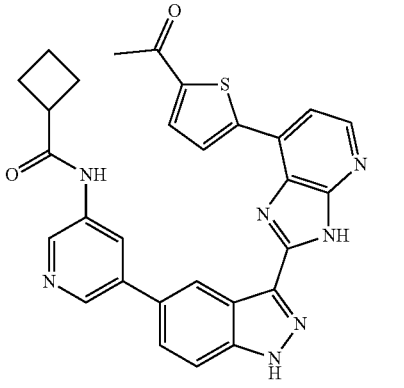
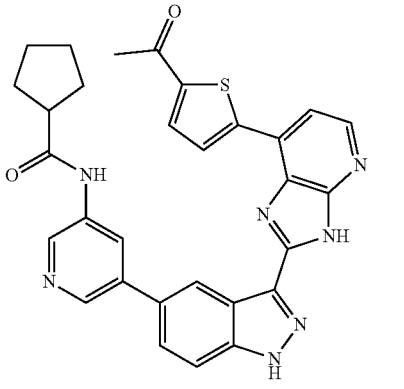
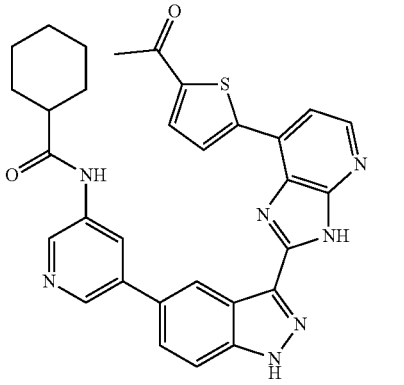
409	
410	
411	
412	

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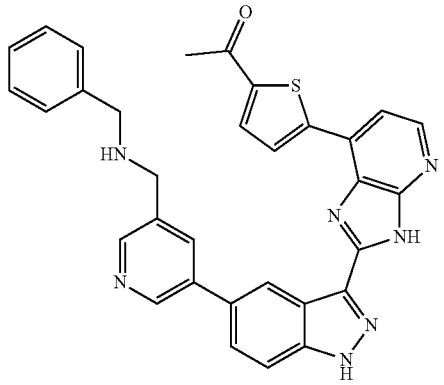
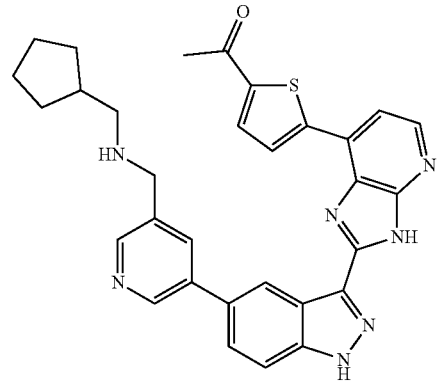
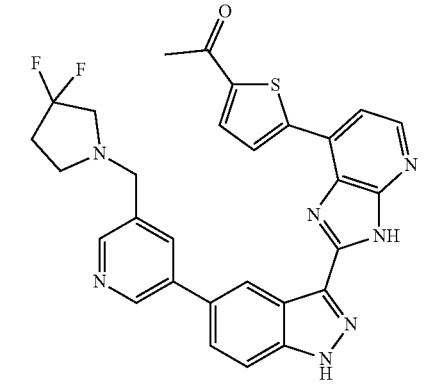
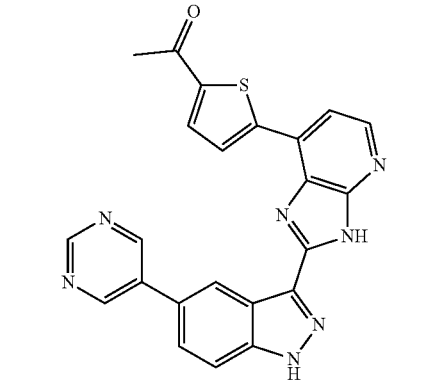
413	
414	
415	
416	

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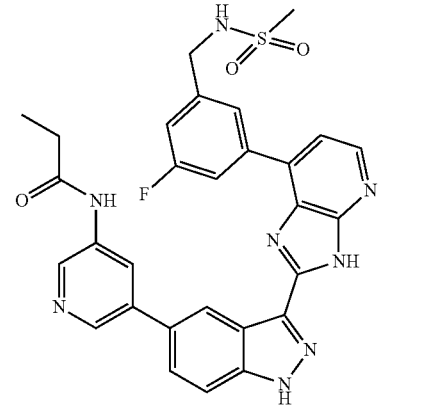
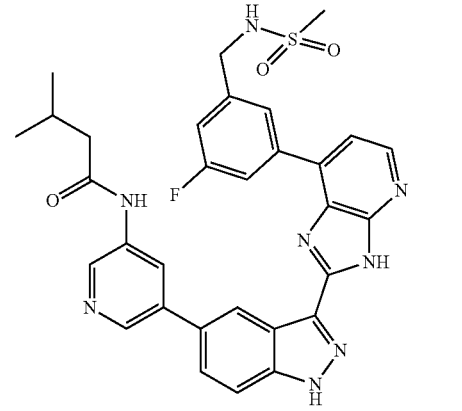
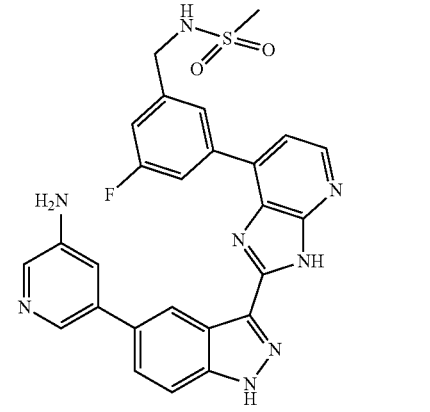
417	
418	
419	

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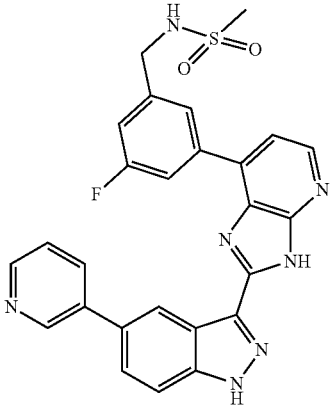
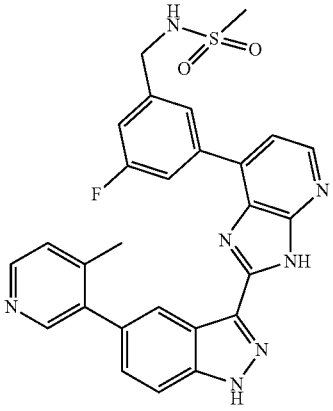
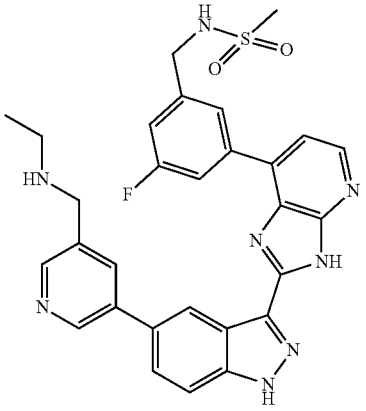
420	
421	
422	

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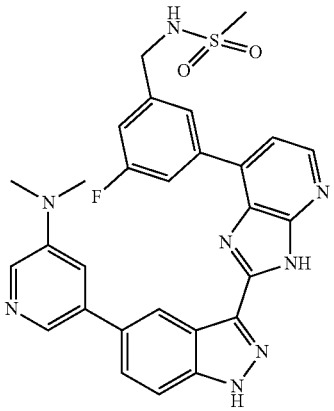
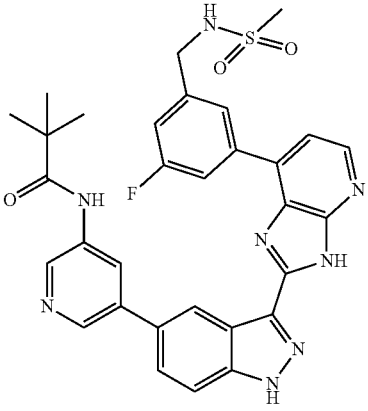
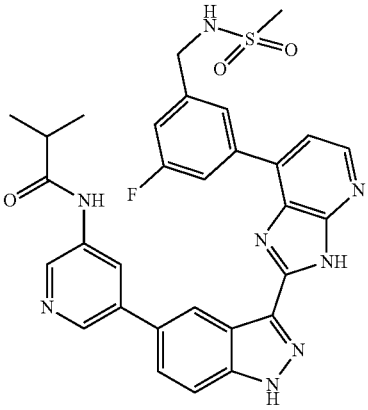
423	
424	
425	

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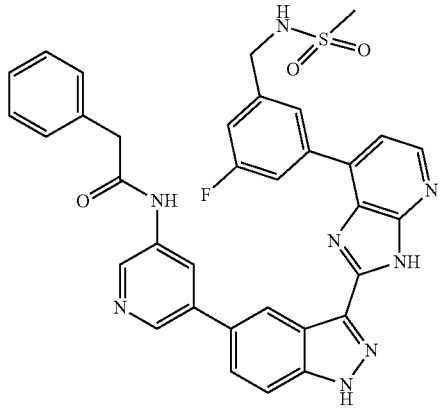
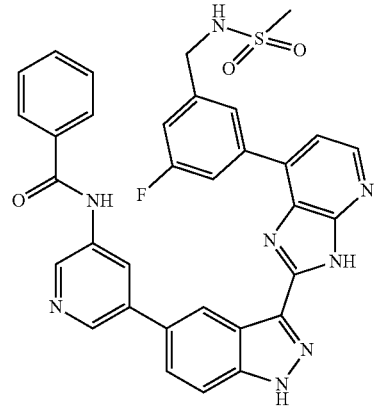
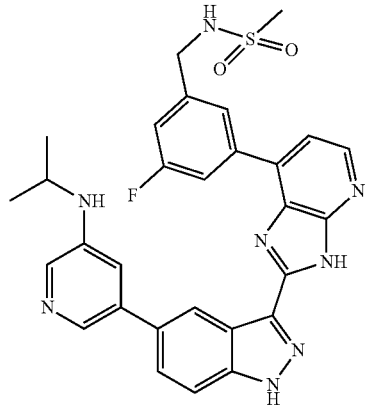
426	
427	
428	

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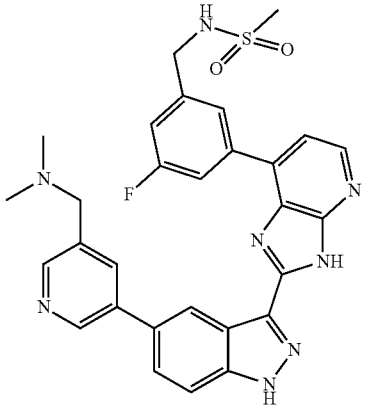
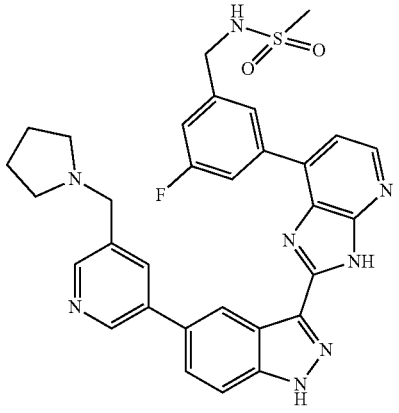
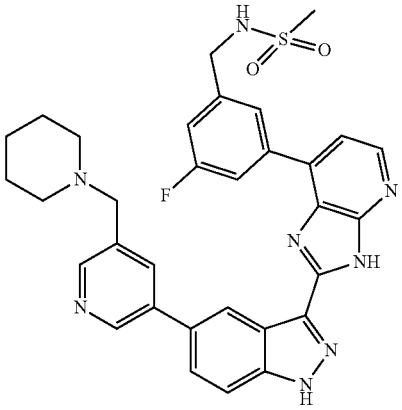
429	
430	
431	

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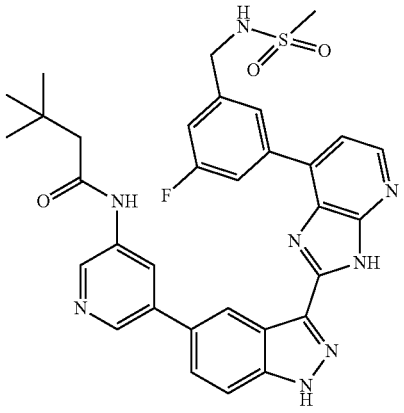
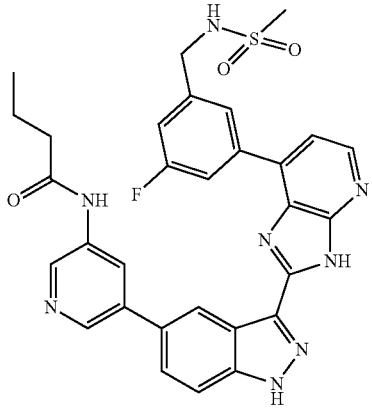
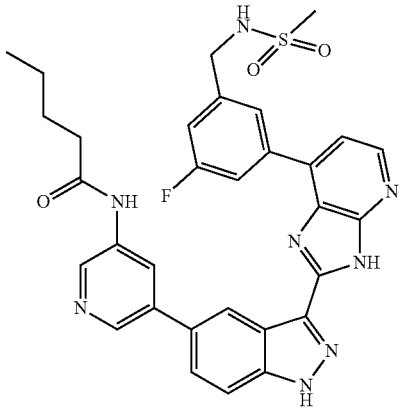
432	
433	
434	

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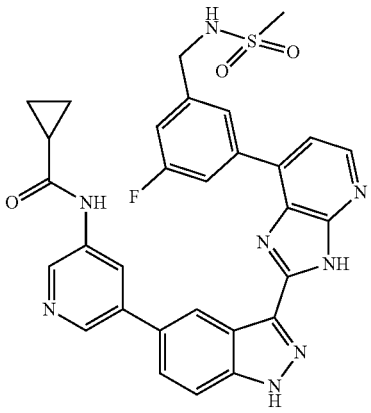
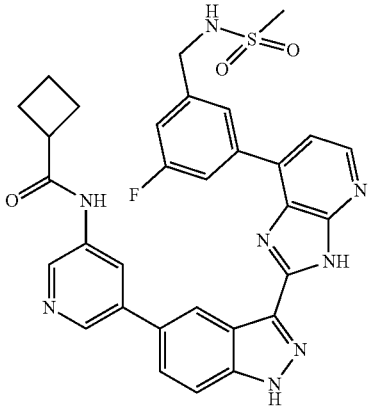
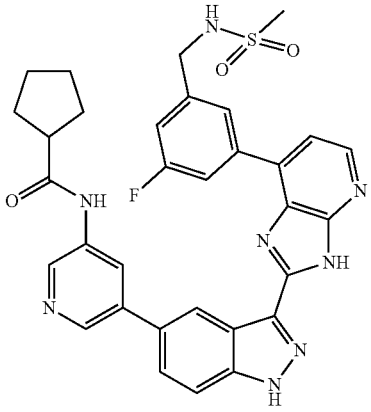
435	
436	
437	

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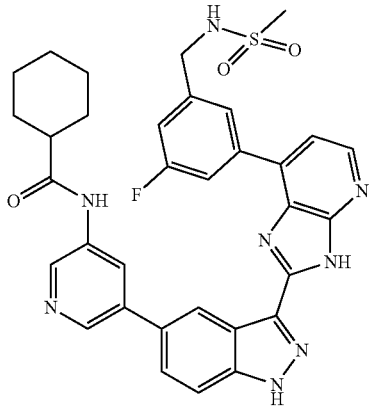
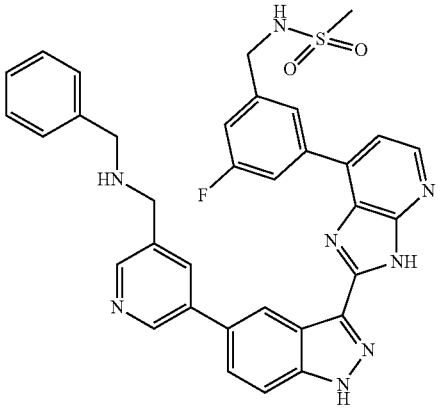
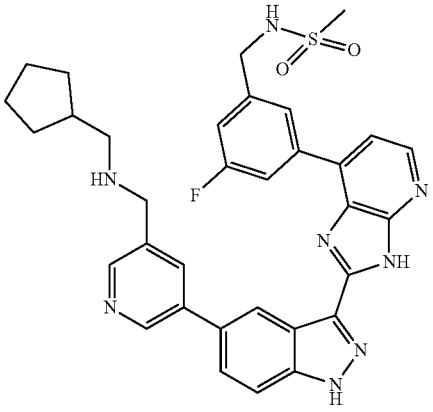
438	
439	
440	

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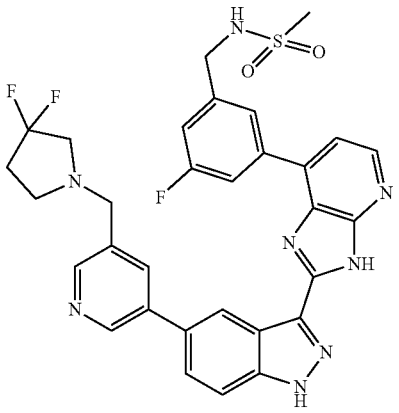
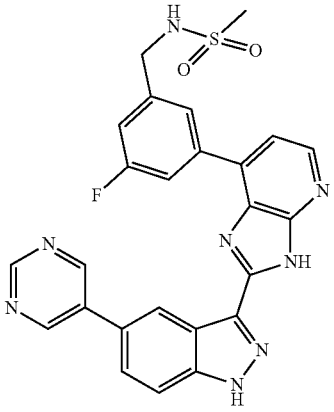
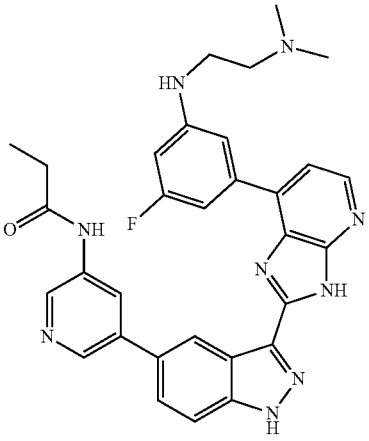
441	
442	
443	

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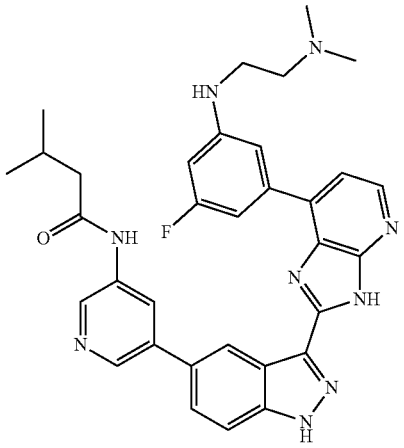
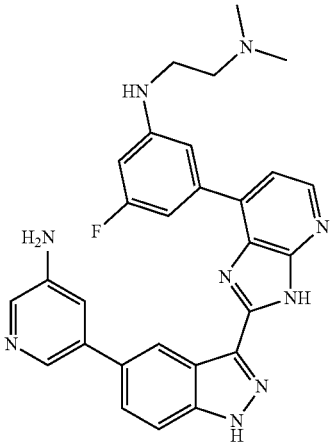
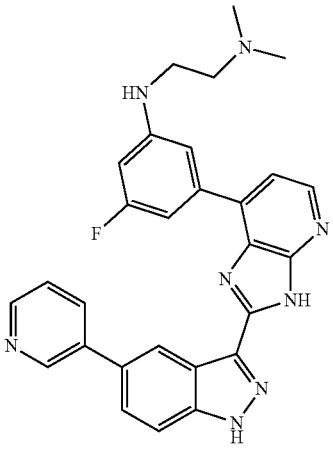
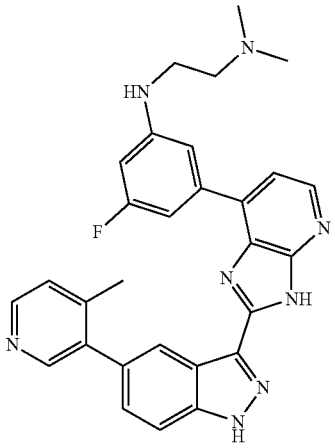
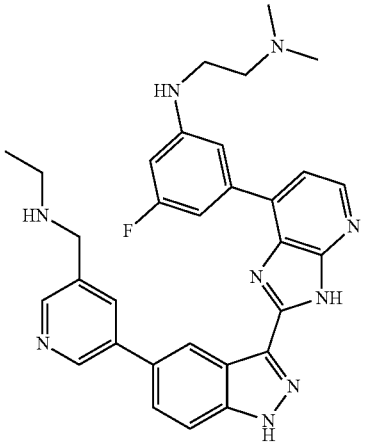
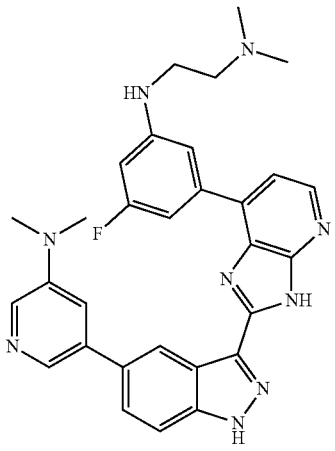
444	
445	
446	

TABLE 1-continued

447	
448	
449	

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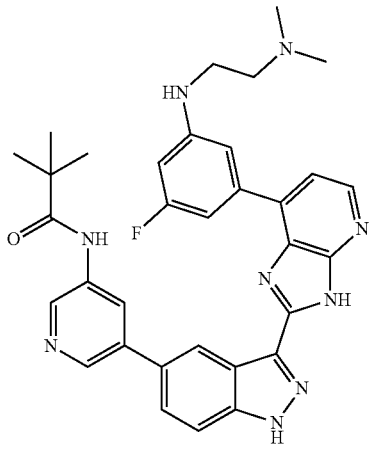
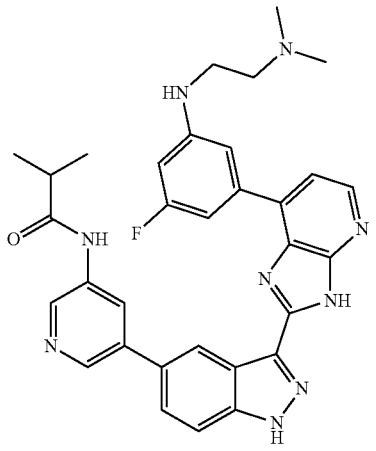
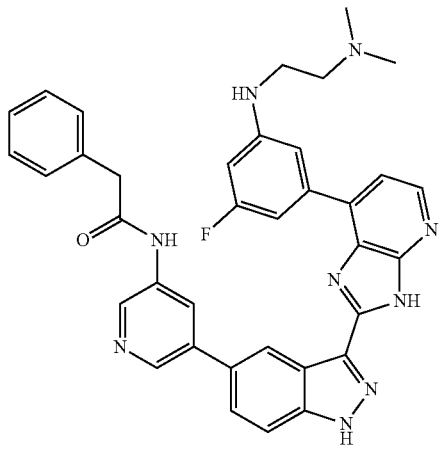
450	
451	
452	

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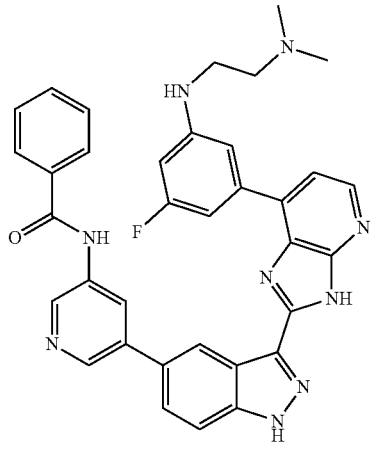
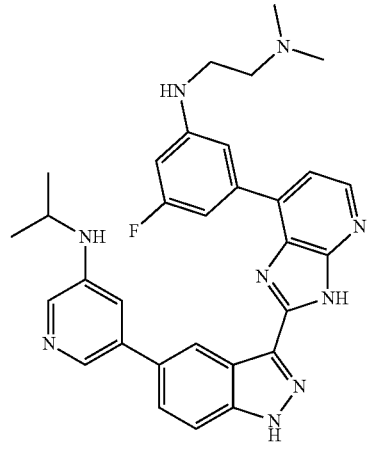
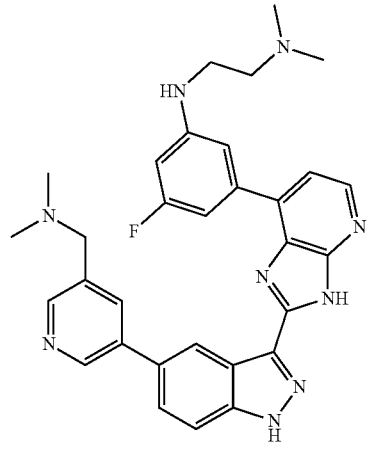
453	
454	
455	

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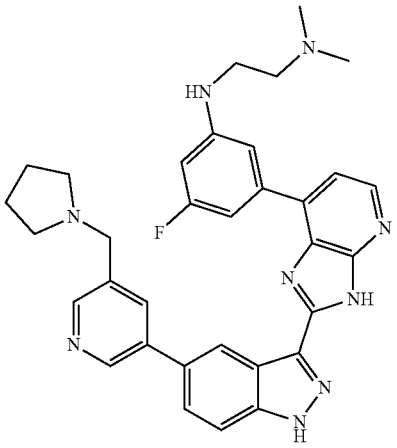
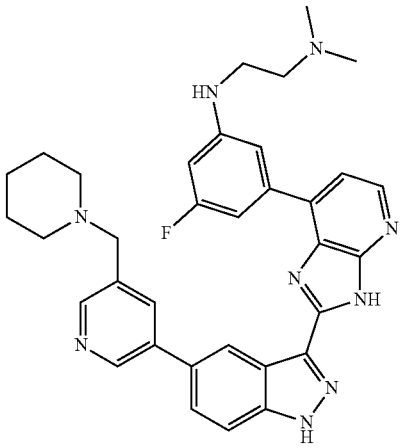
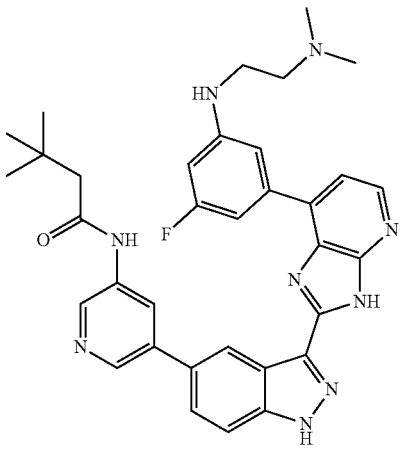
456	
457	
458	

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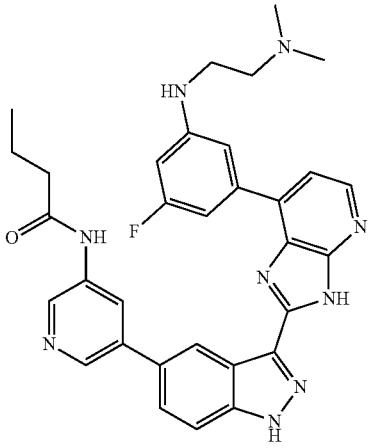
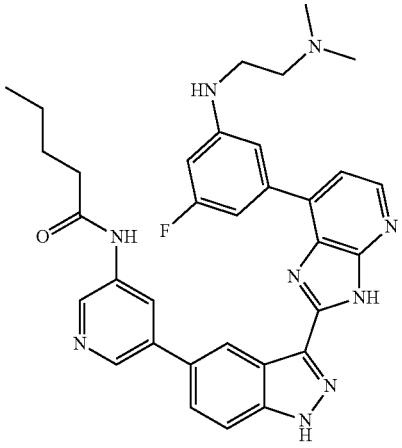
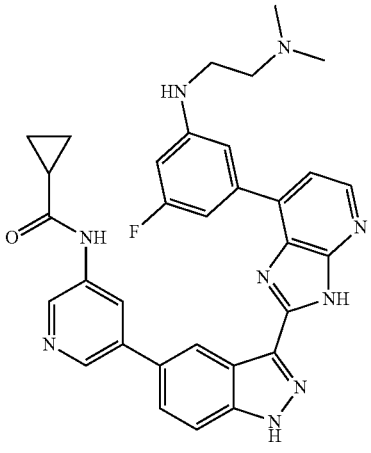
459	
460	
461	

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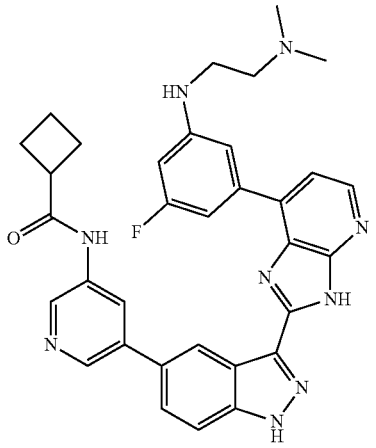
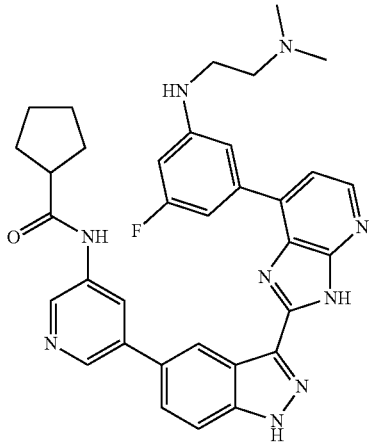
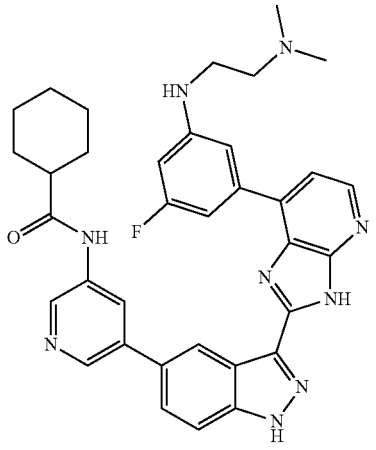
462	
463	
464	

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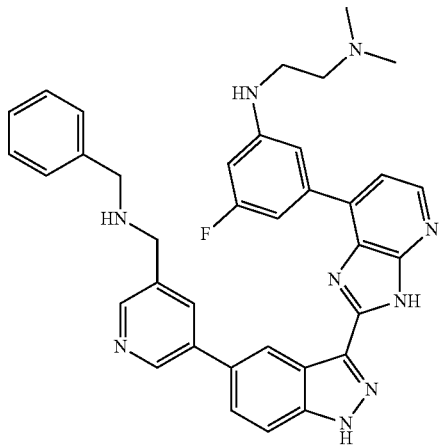
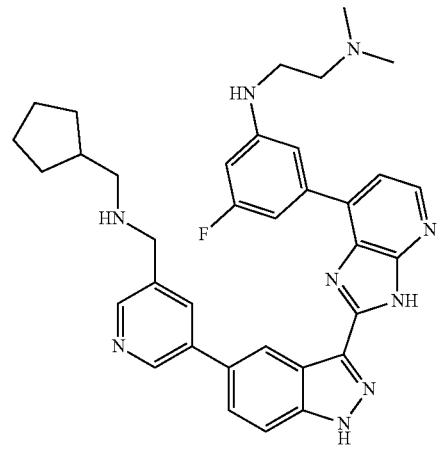
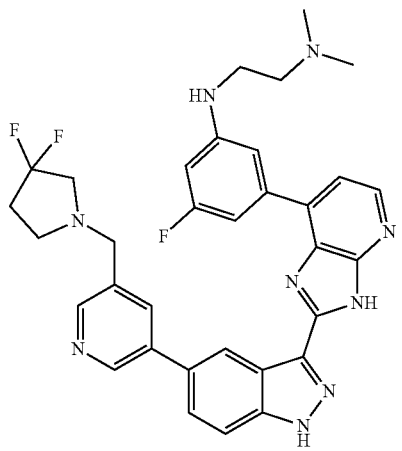
465	
466	
467	

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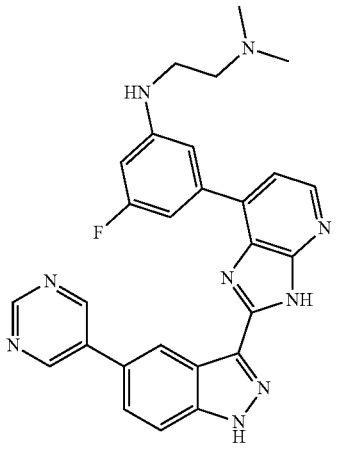
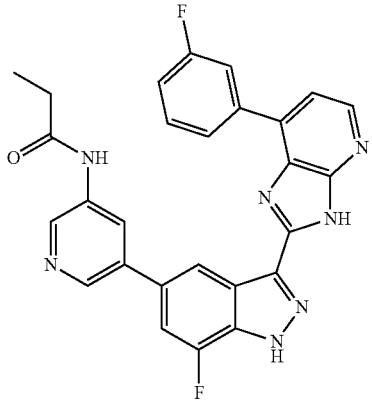
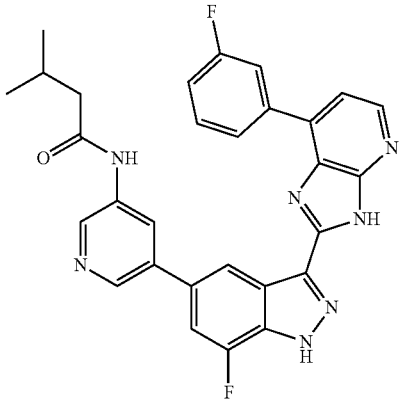
468	
469	
470	

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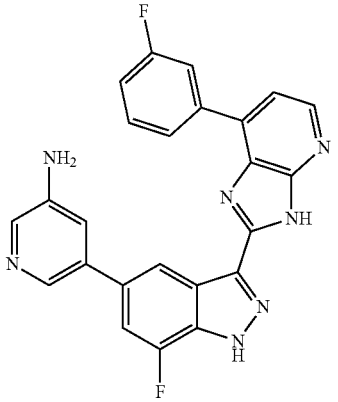
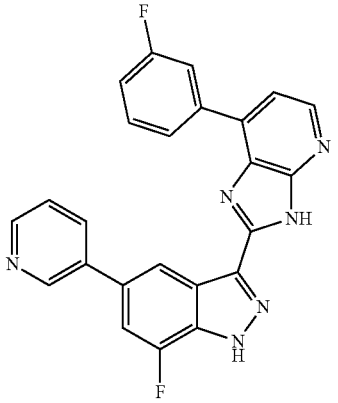
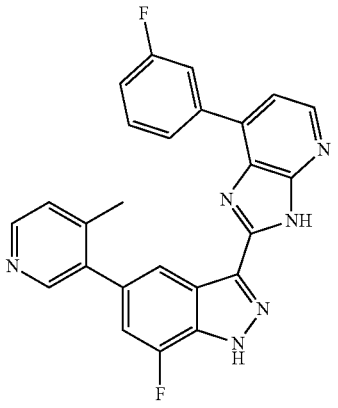
471	
472	
473	

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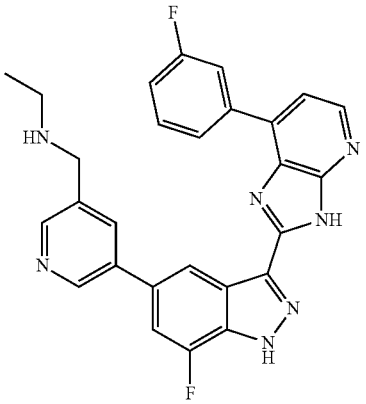
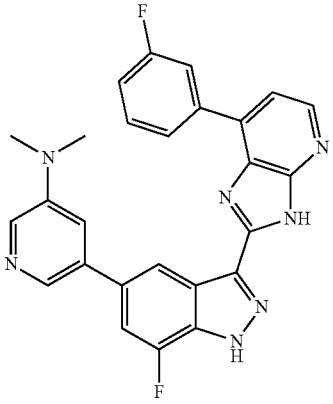
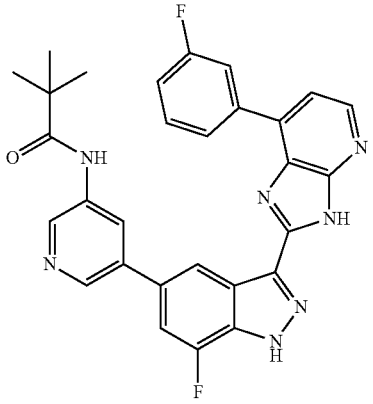
474	
475	
476	

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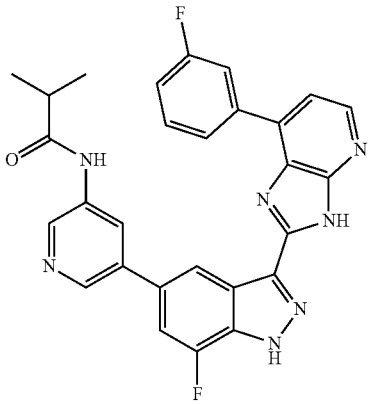
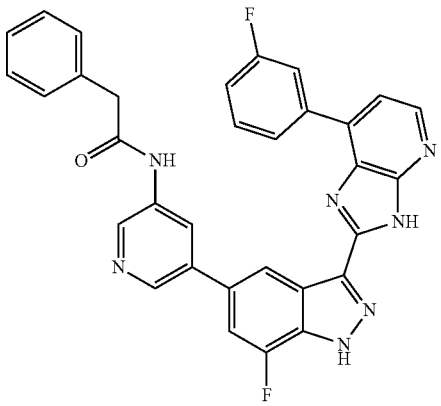
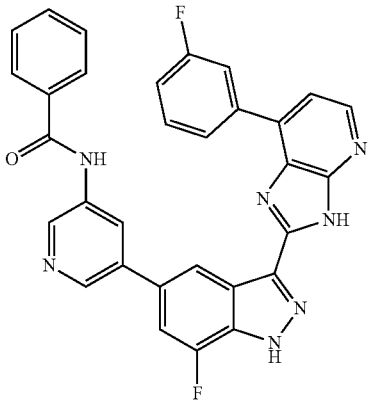
477	
478	
479	

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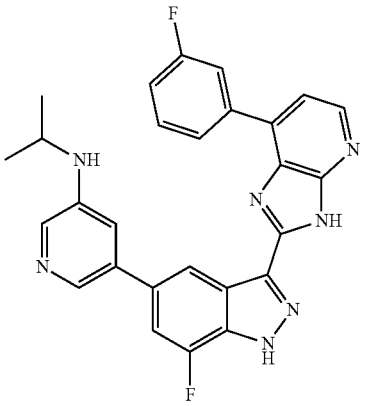
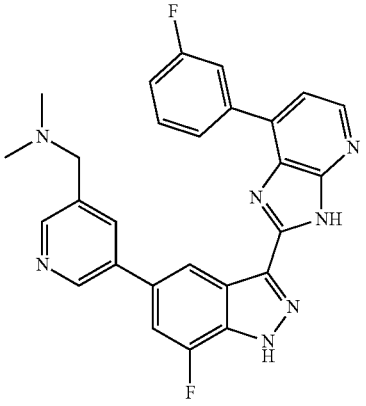
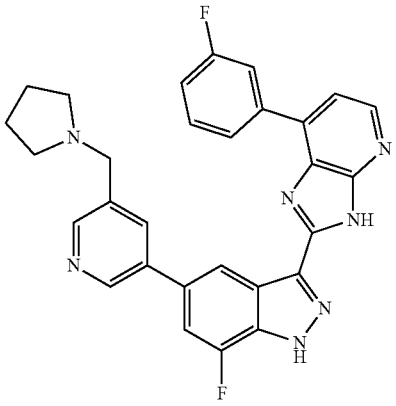
480	
481	
482	

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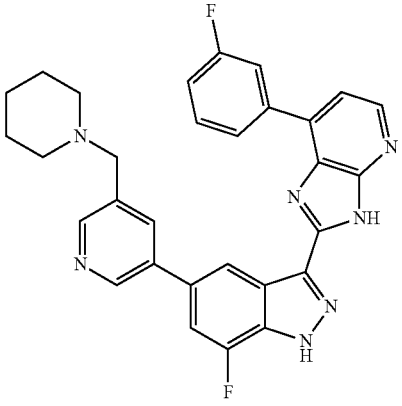
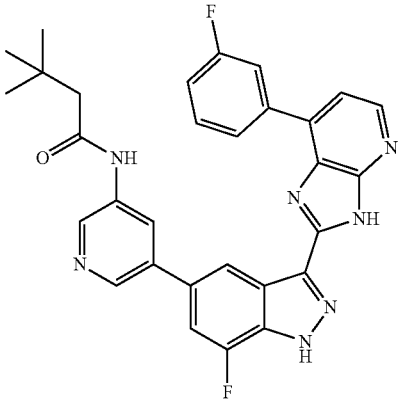
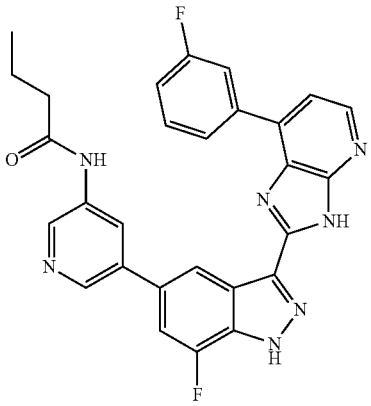
483	
484	
485	

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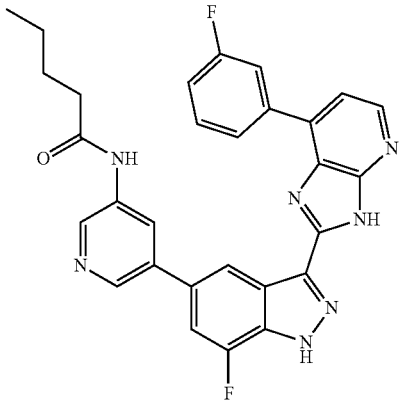
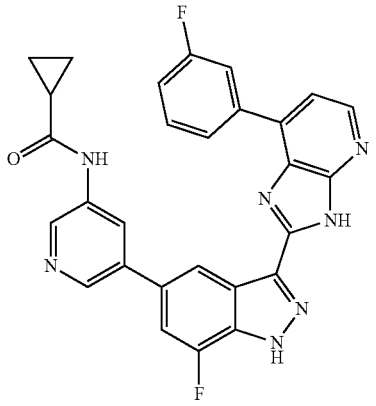
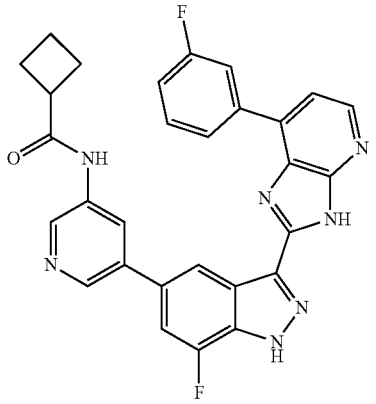
486	
487	
488	

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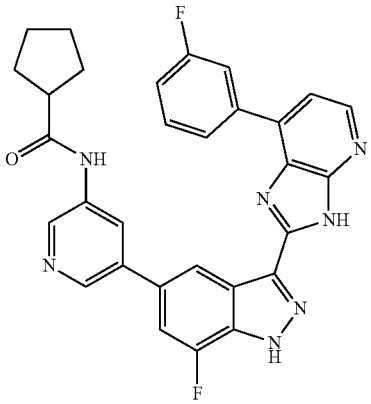
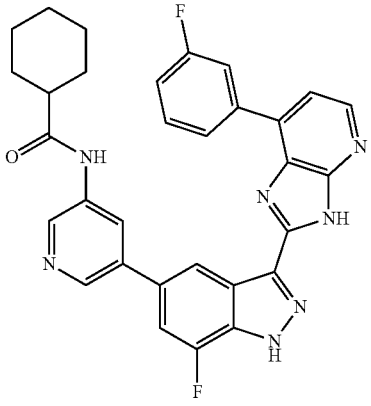
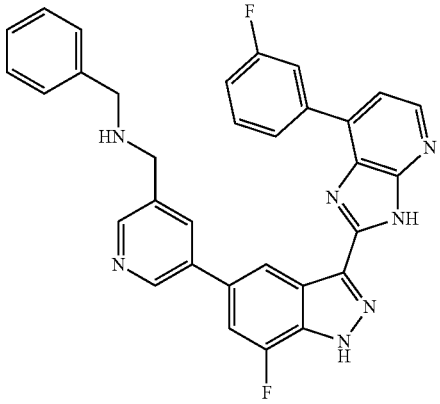
489	
490	
491	

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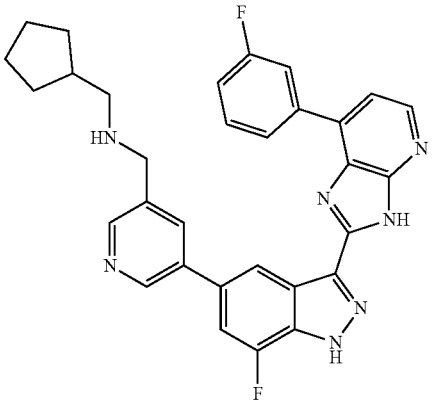
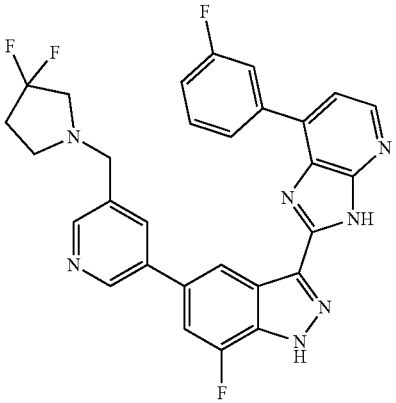
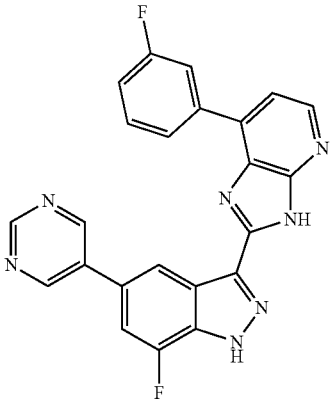
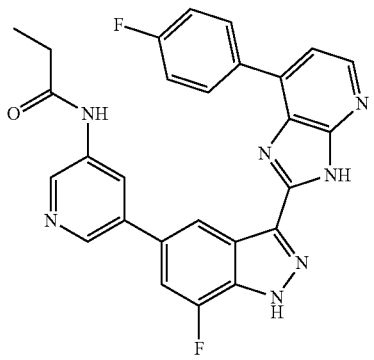
492	
493	
494	
495	

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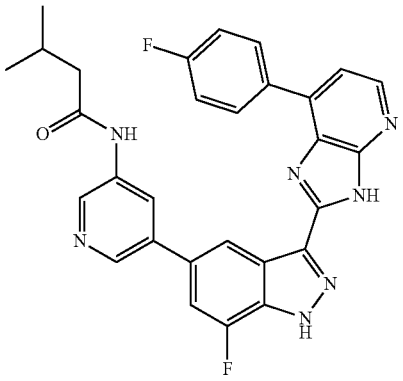
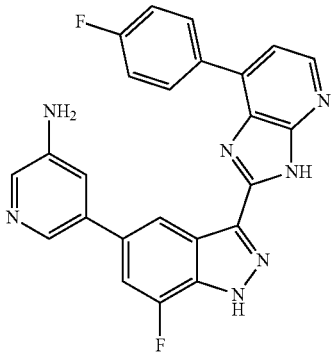
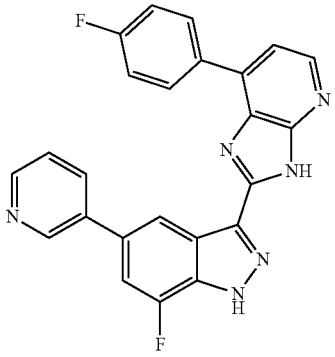
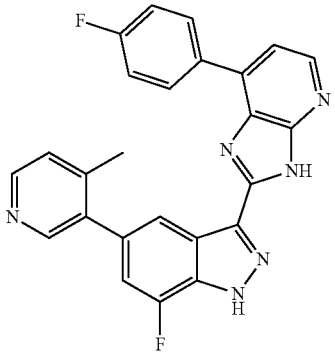
496	
497	
498	
499	

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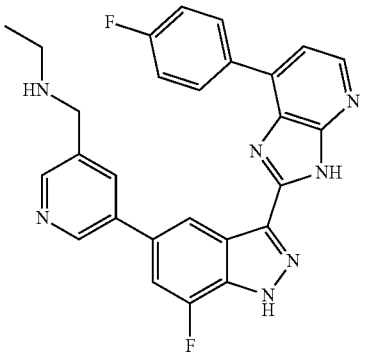
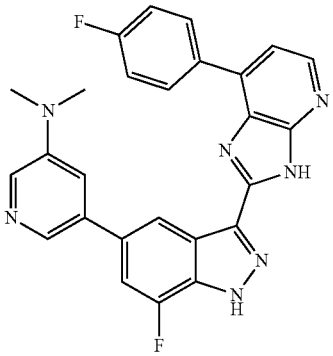
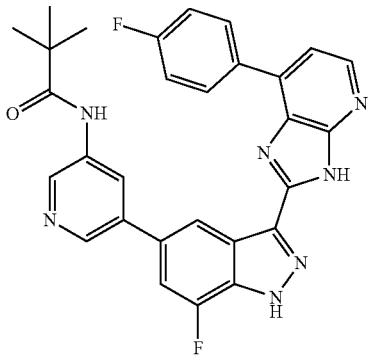
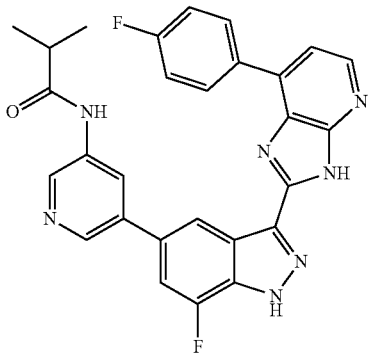
500	
501	
502	
503	

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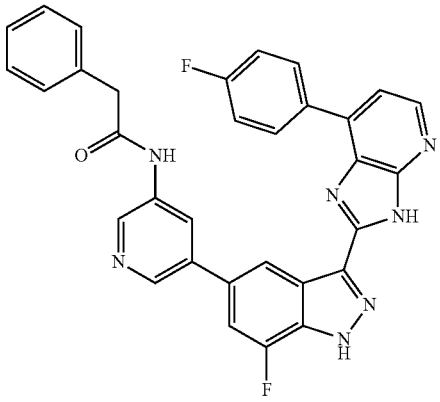
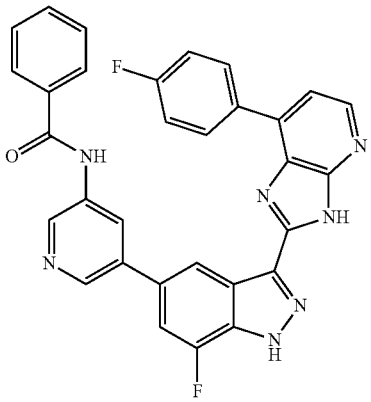
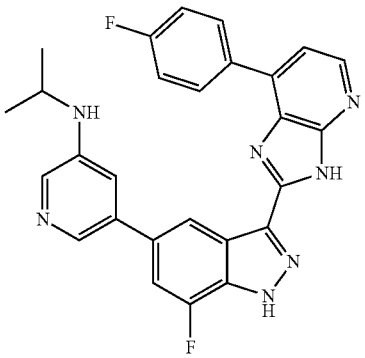
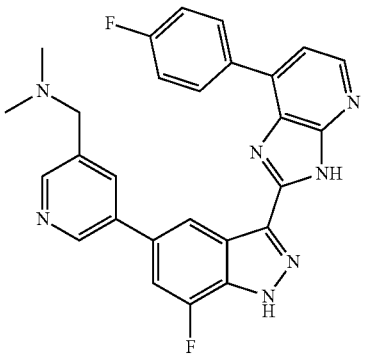
504	
505	
506	
507	

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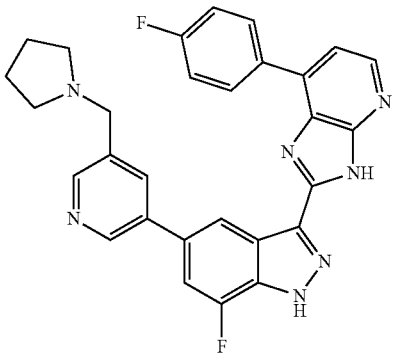
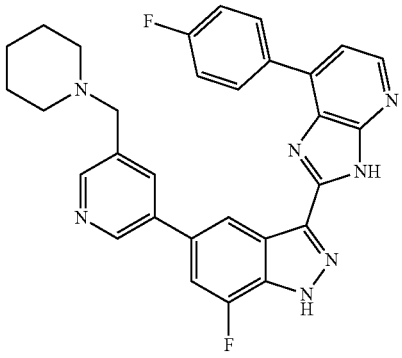
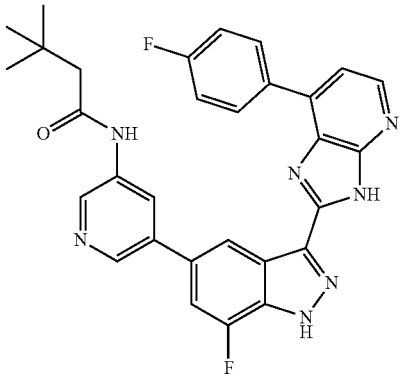
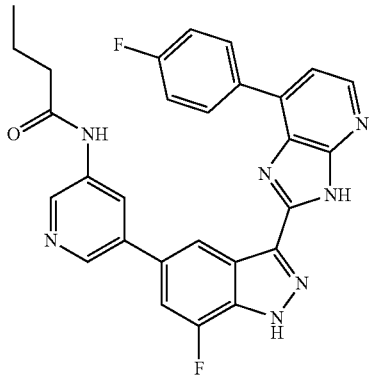
508	
509	
510	
511	

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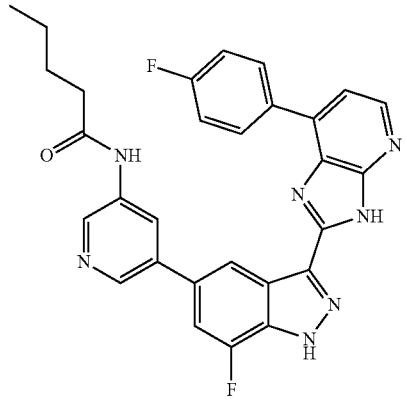
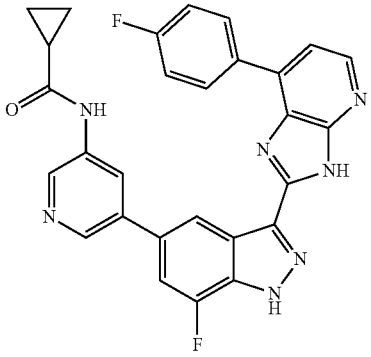
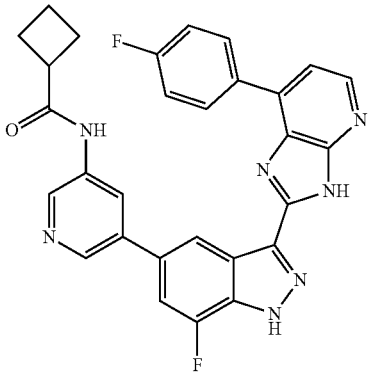
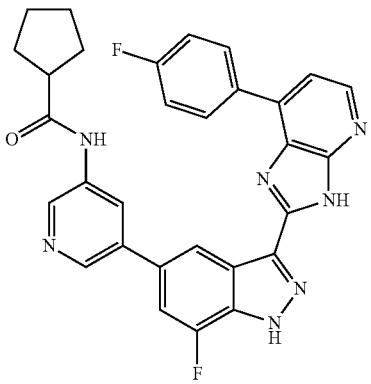
512	
513	
514	
515	

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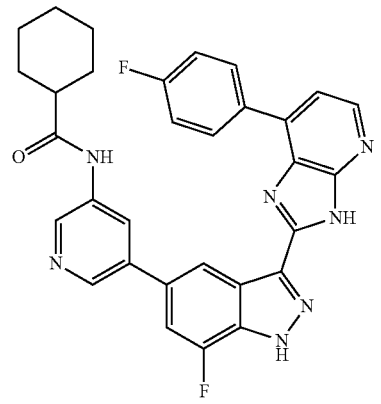
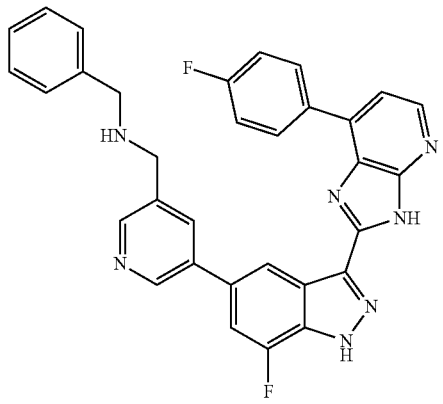
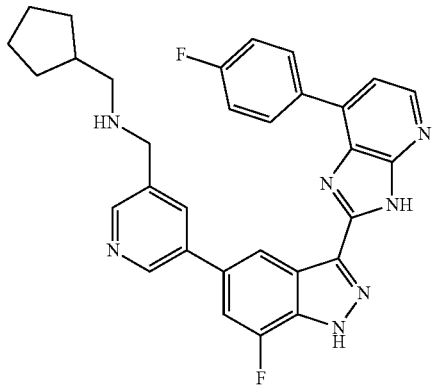
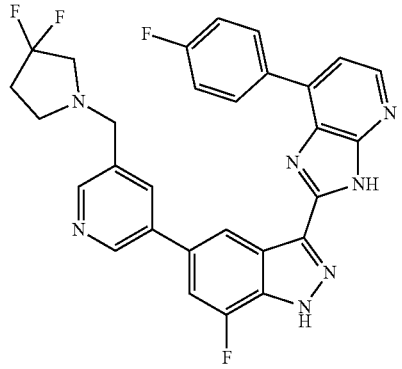
516	
517	
518	
519	

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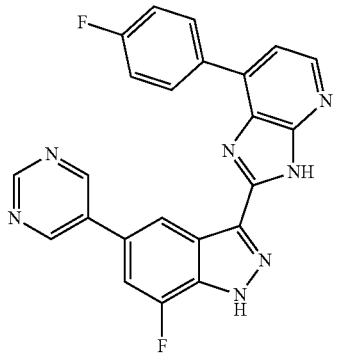
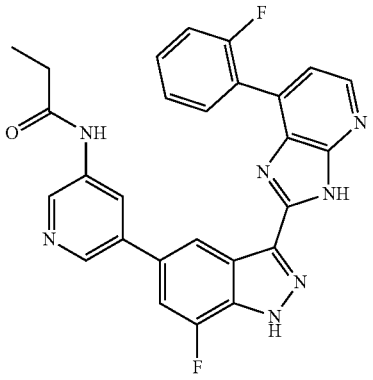
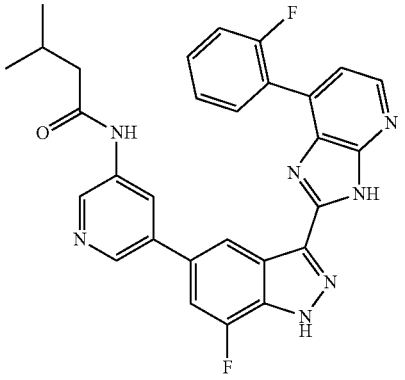
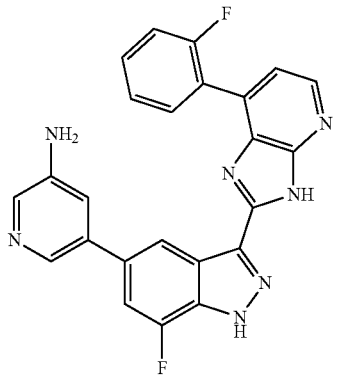
520	
521	
522	
523	

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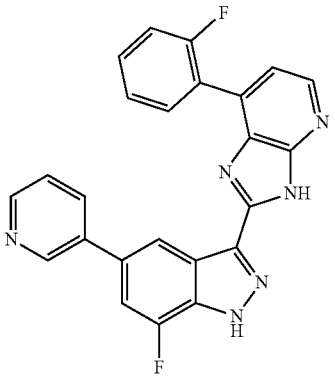
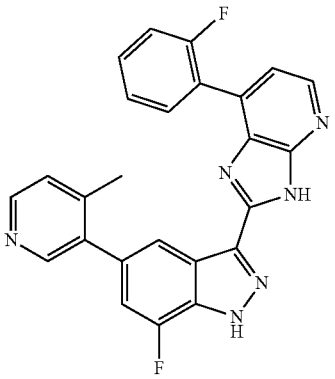
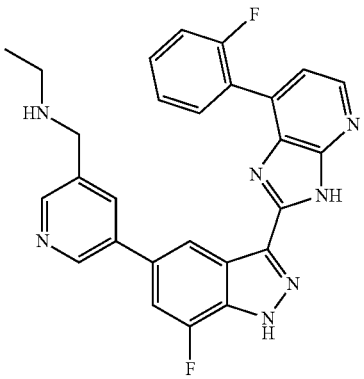
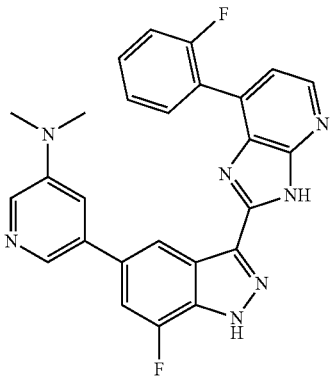
524	
525	
526	
527	

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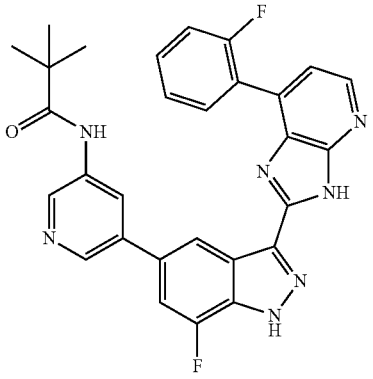
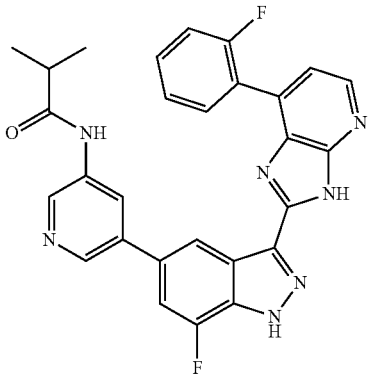
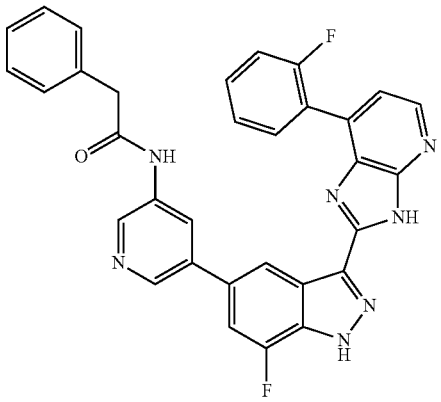
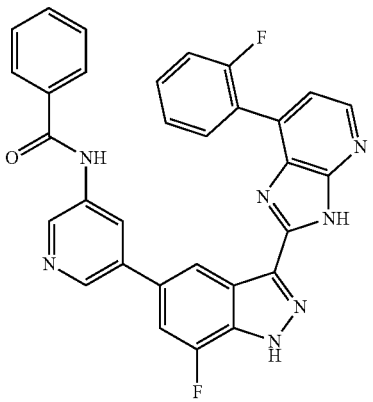
528	
529	
530	
531	

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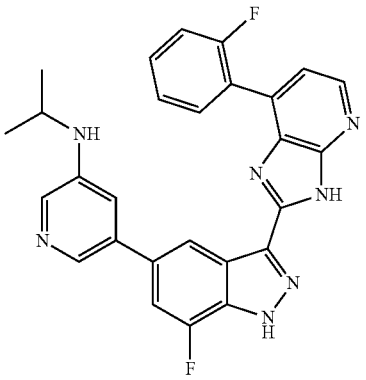
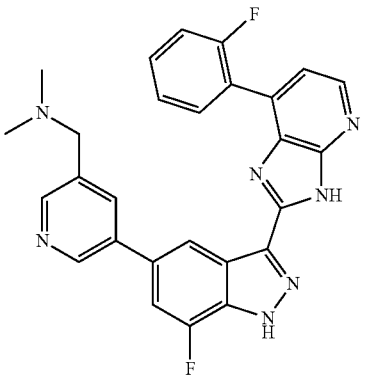
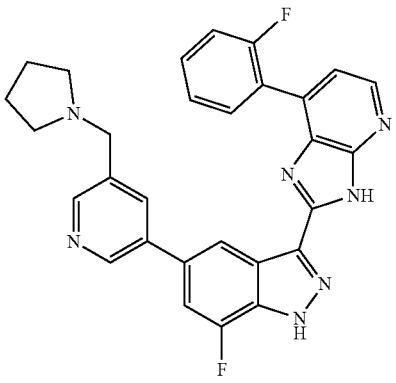
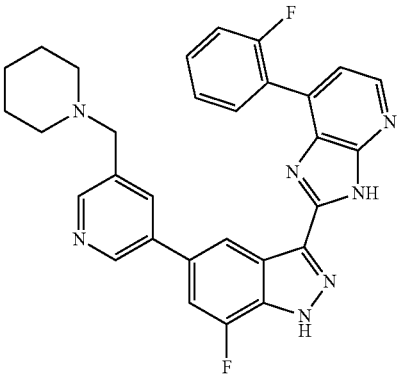
532	
533	
534	
535	

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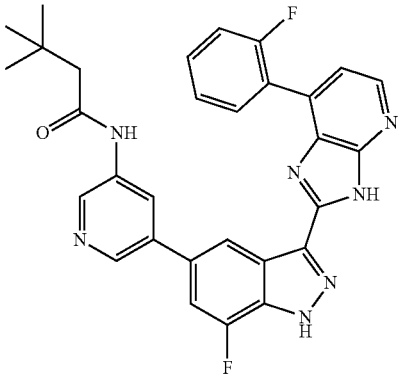
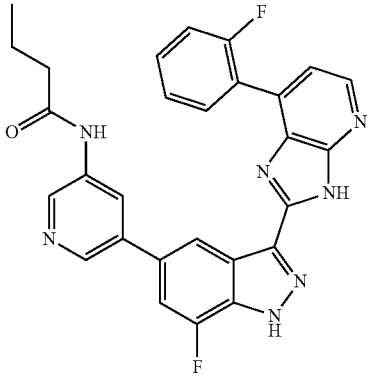
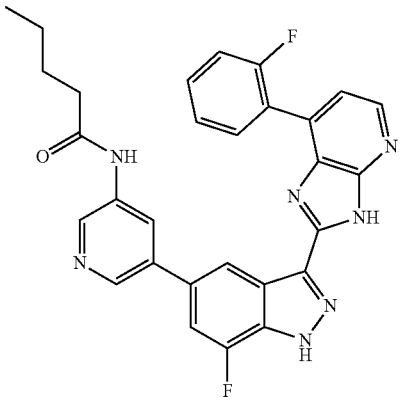
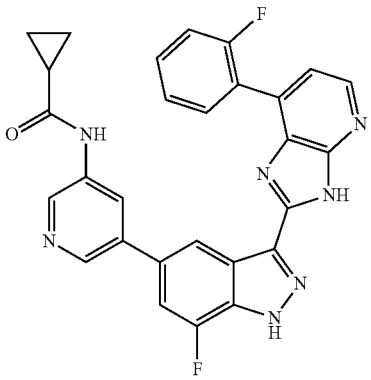
536	
537	
538	
539	

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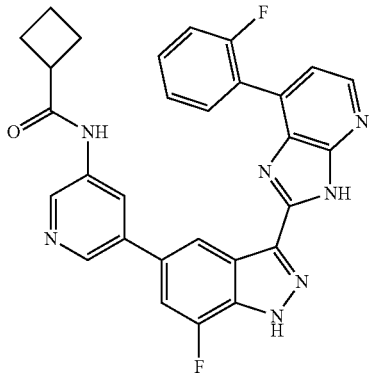
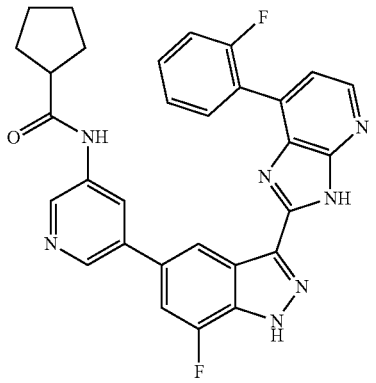
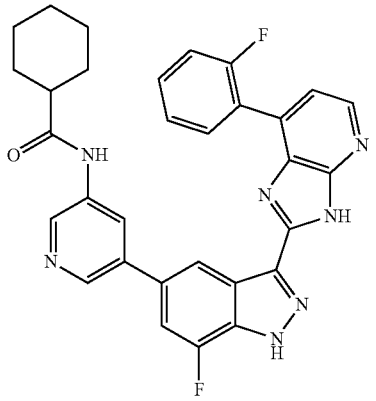
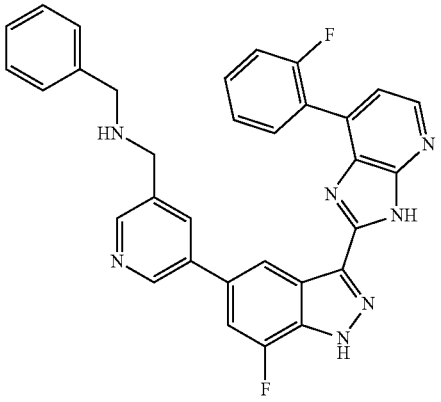
540	
541	
542	
543	

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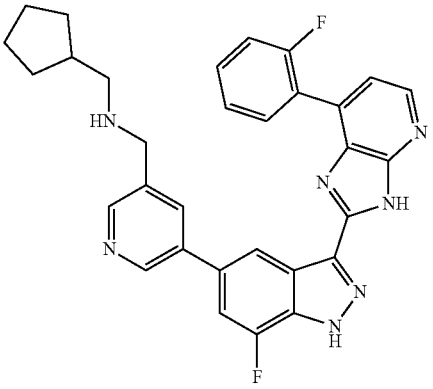
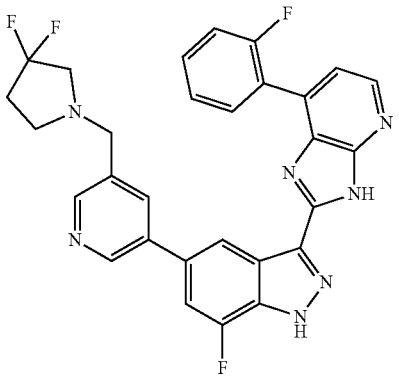
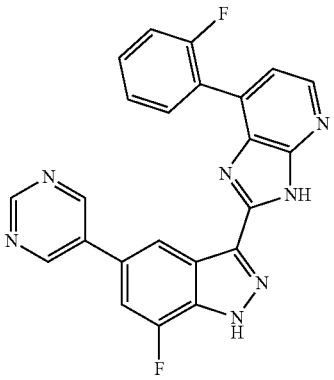
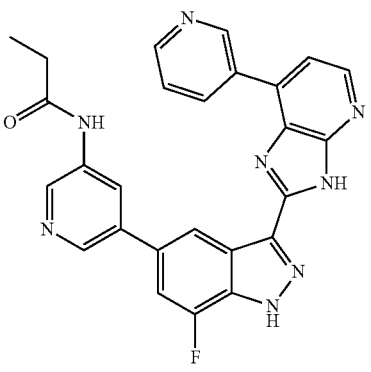
544	
545	
546	
547	

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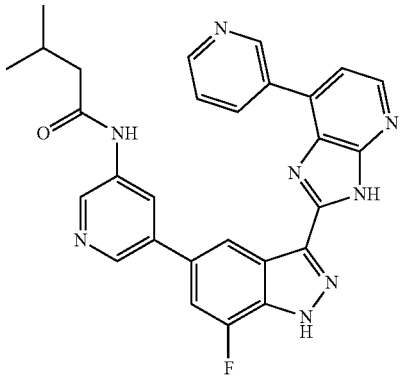
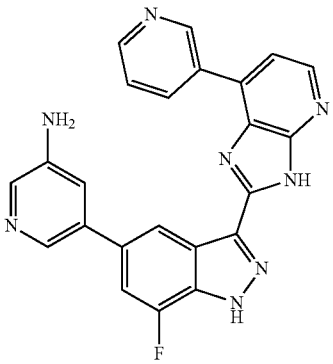
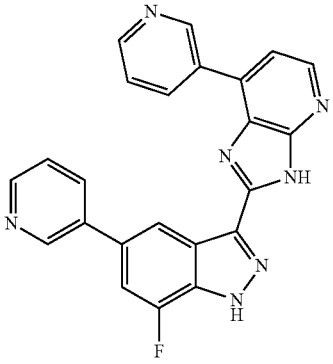
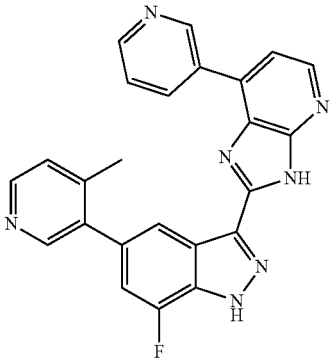
548	
549	
550	
551	

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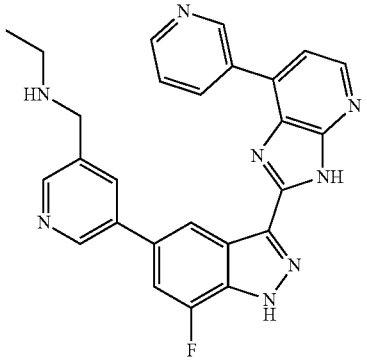
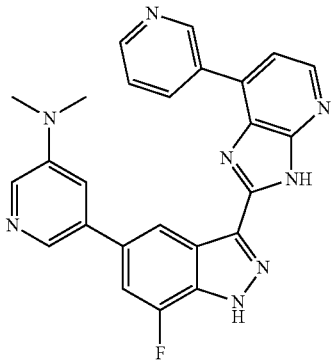
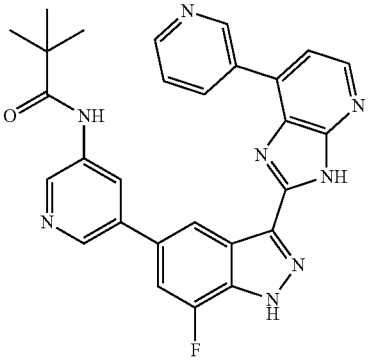
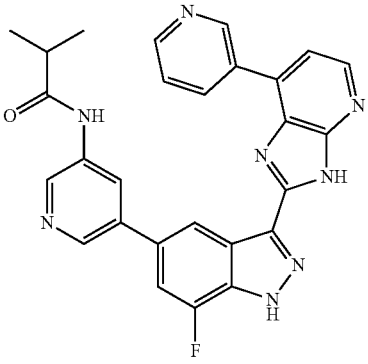
552	
553	
554	
555	

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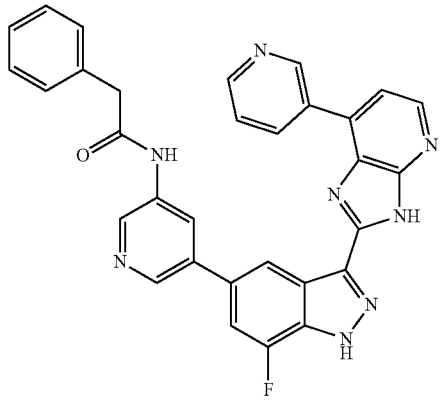
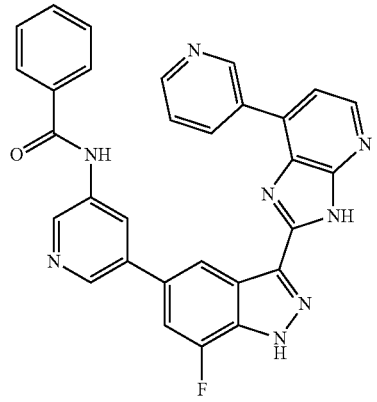
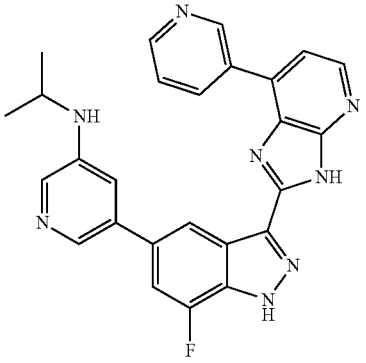
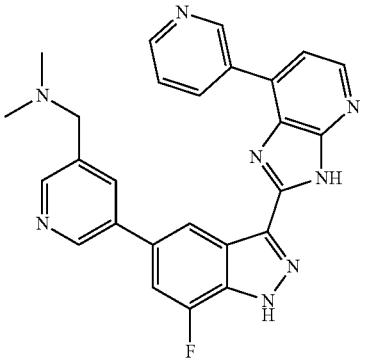
556	
557	
558	
559	

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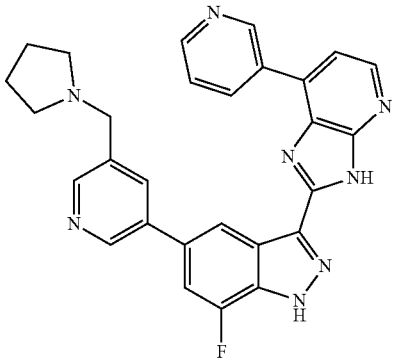
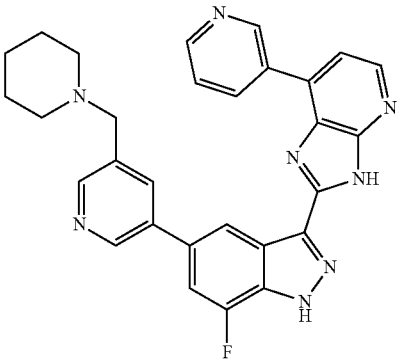
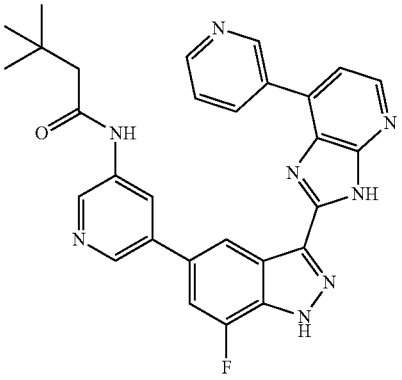
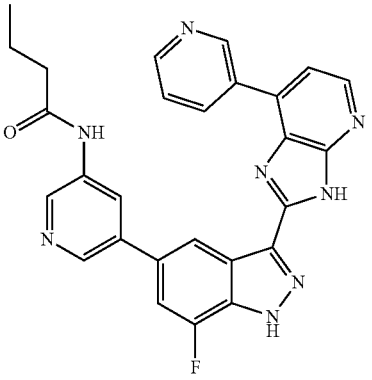
560	
561	
562	
563	

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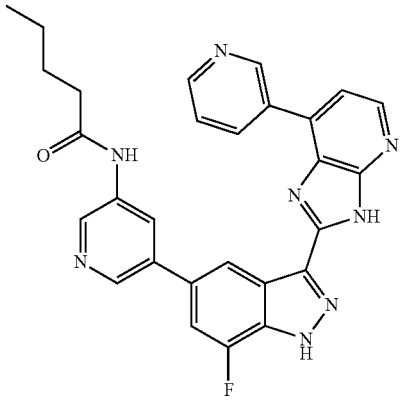
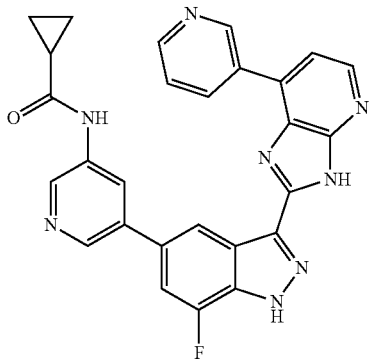
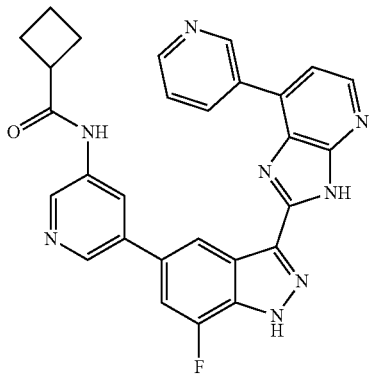
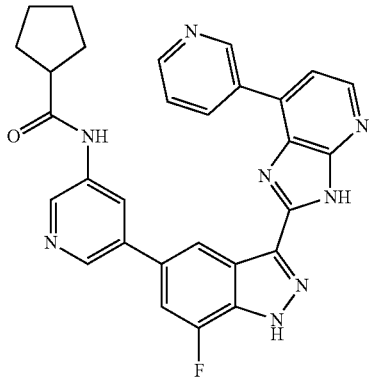
564	
565	
566	
567	

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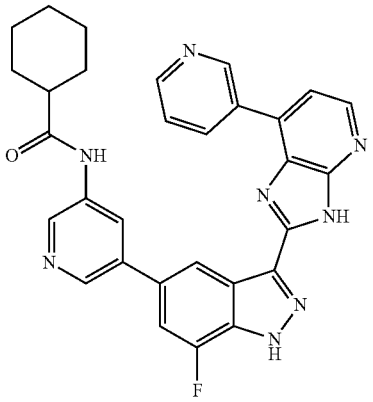
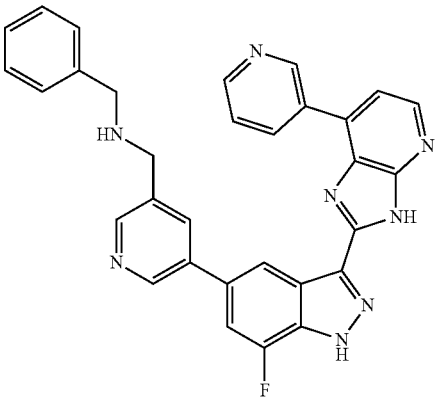
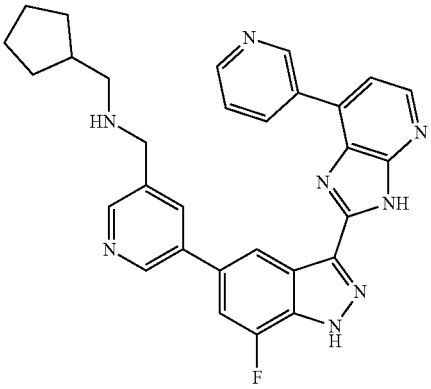
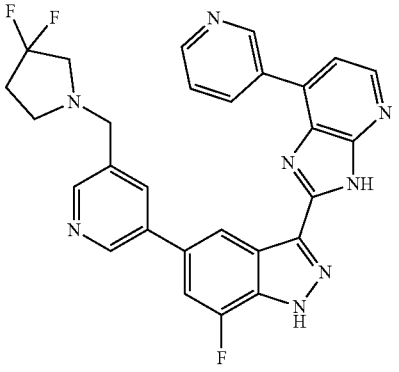
568	
569	
570	
571	

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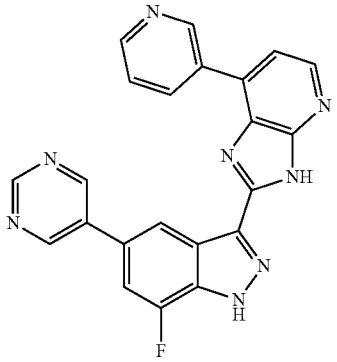
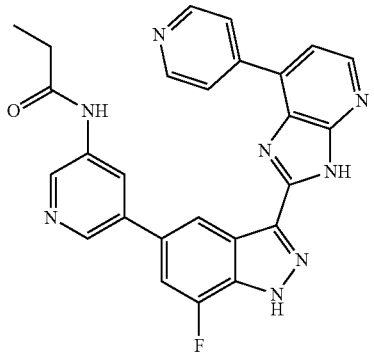
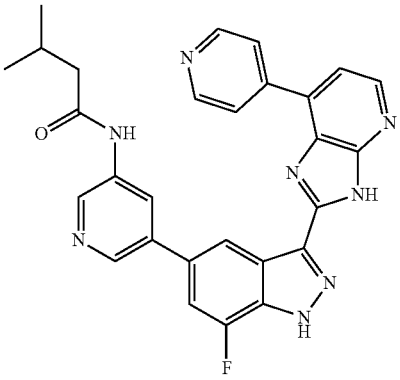
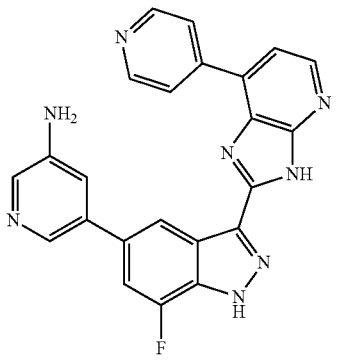
572	
573	
574	
575	

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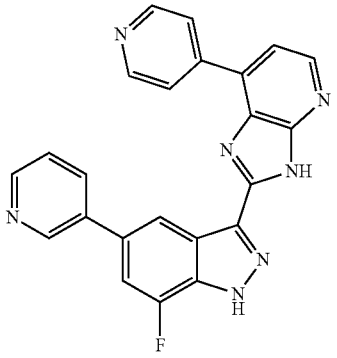
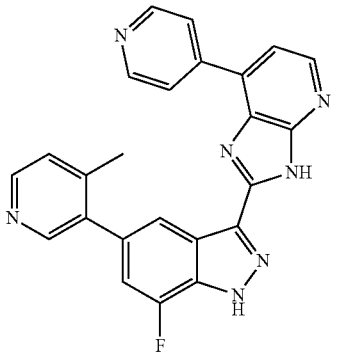
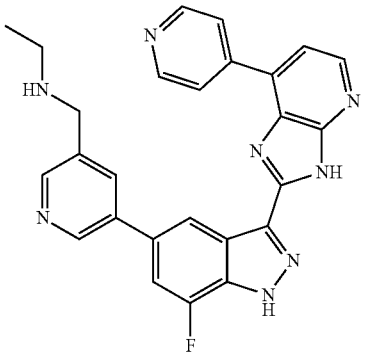
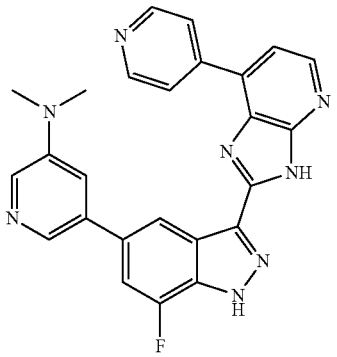
576	
577	
578	
579	

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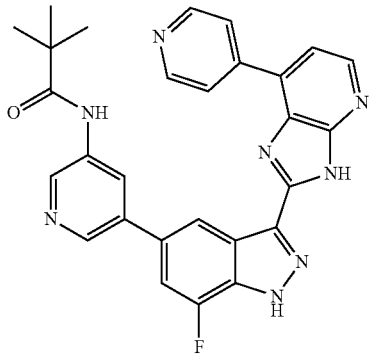
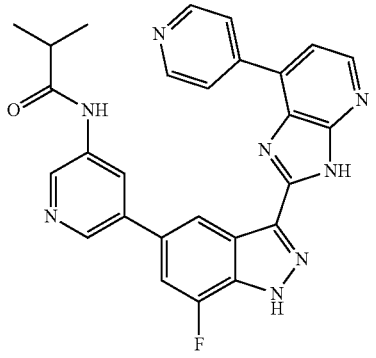
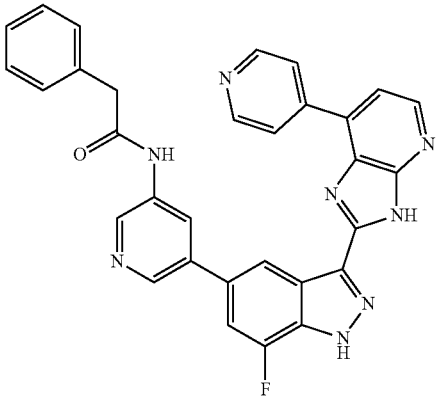
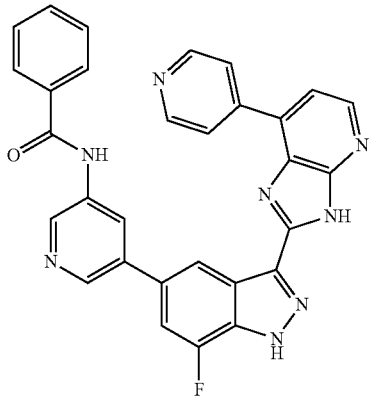
580	
581	
582	
583	

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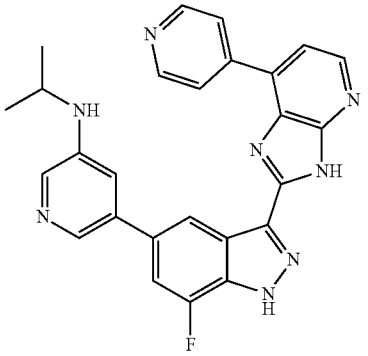
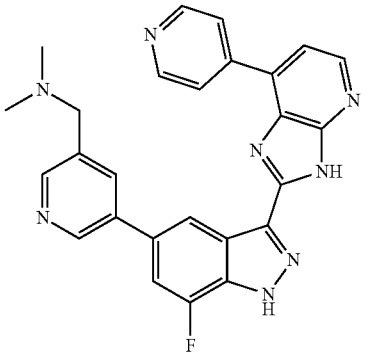
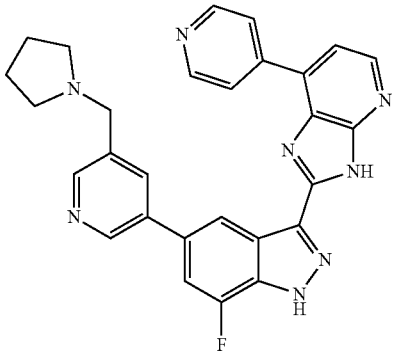
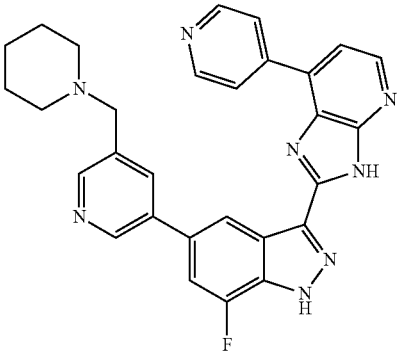
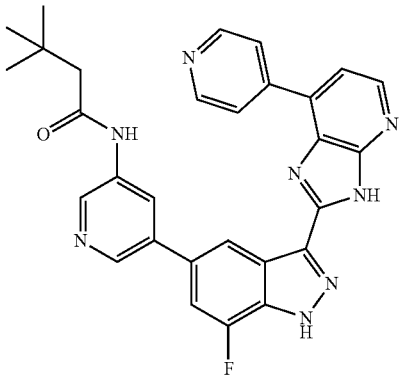
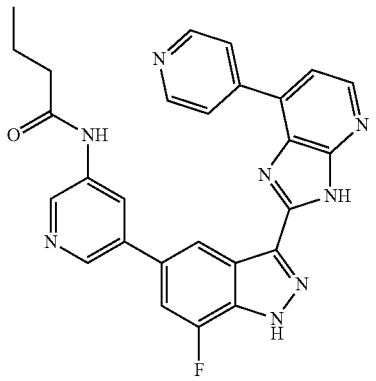
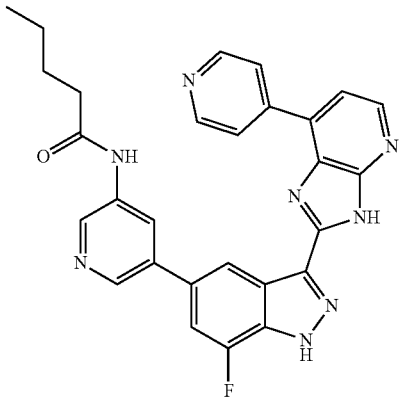
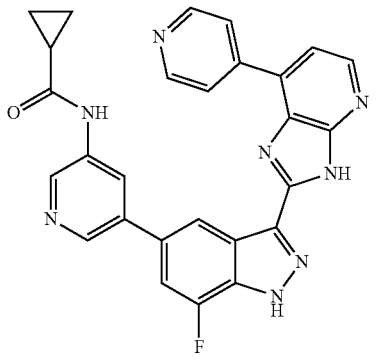
584	
585	
586	
587	

TABLE 1-continued

588	
589	
590	
591	

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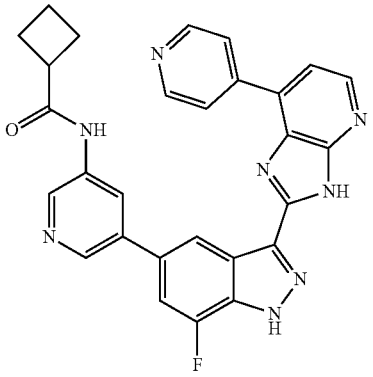
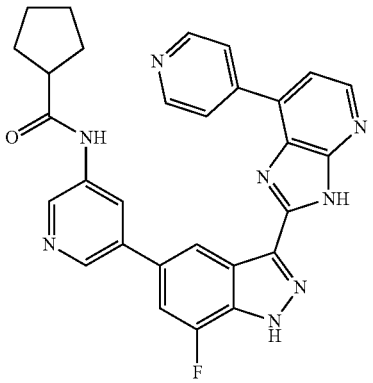
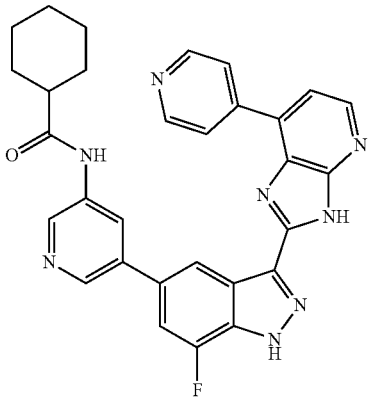
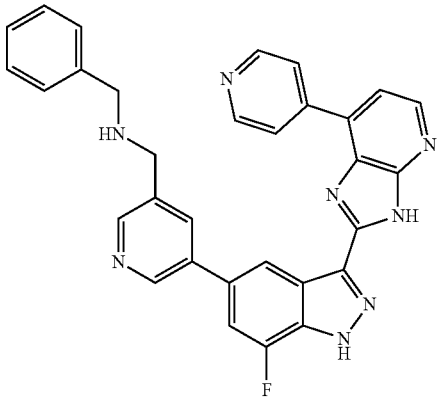
592	
593	
594	
595	

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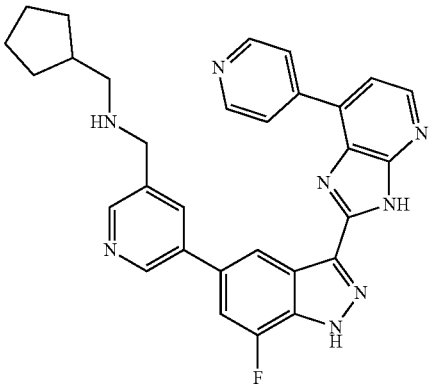
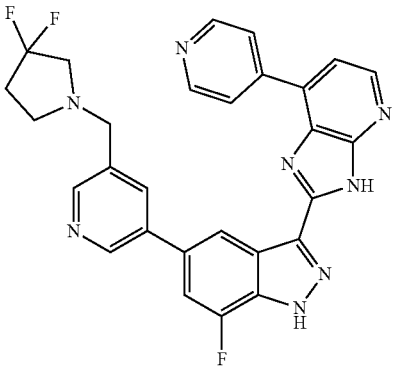
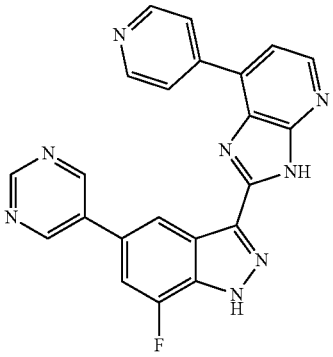
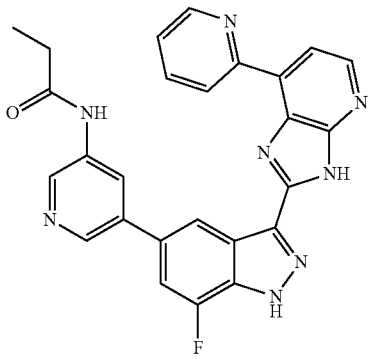
596	
597	
598	
599	

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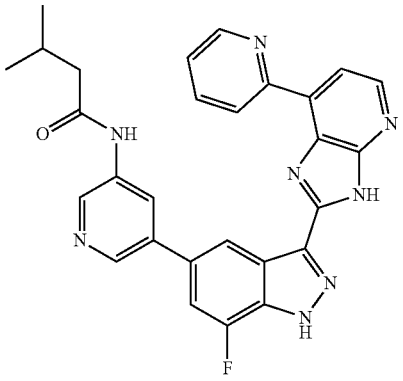
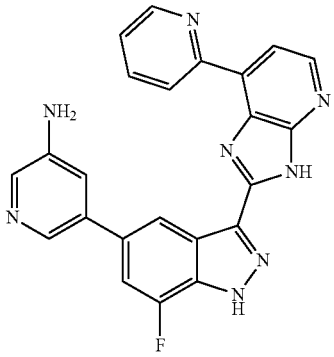
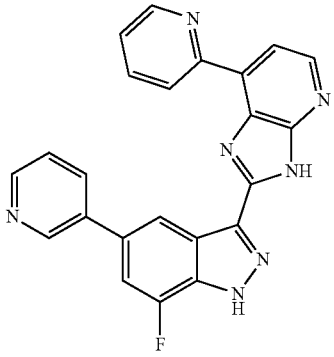
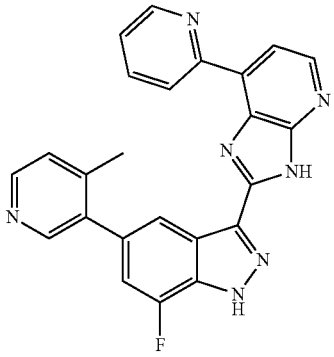
600	
601	
602	
603	

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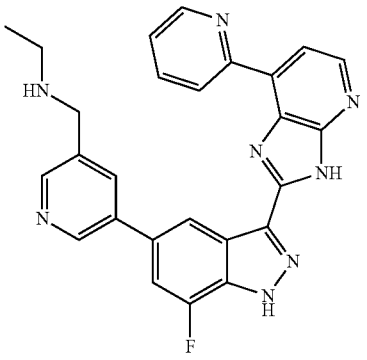
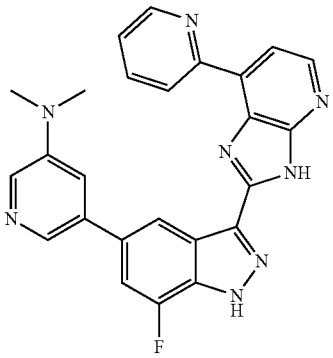
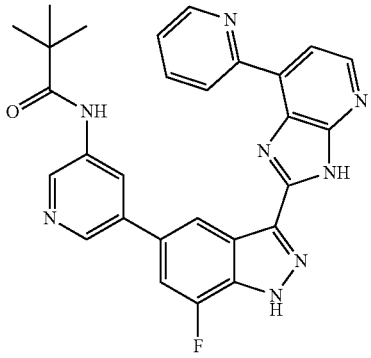
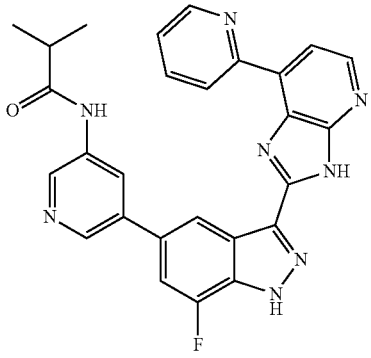
604	
605	
606	
607	

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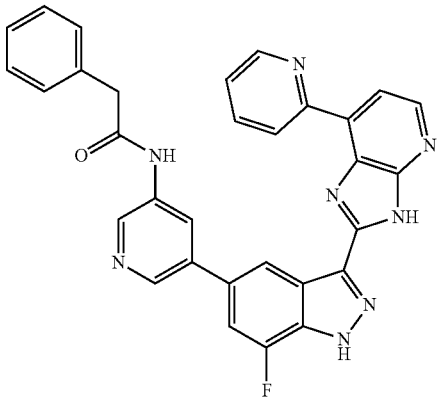
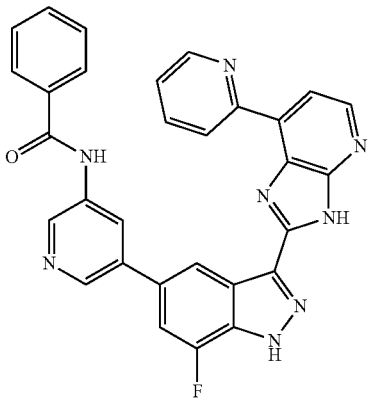
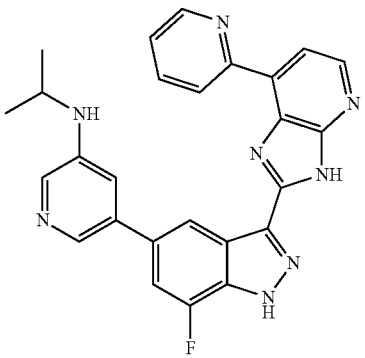
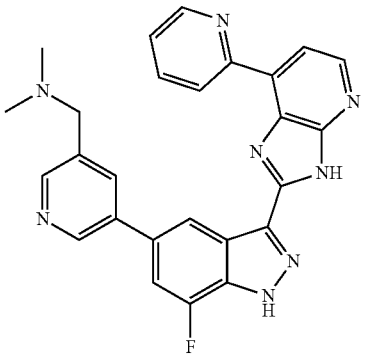
608	
609	
610	
611	

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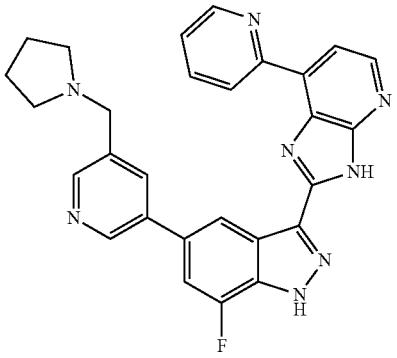
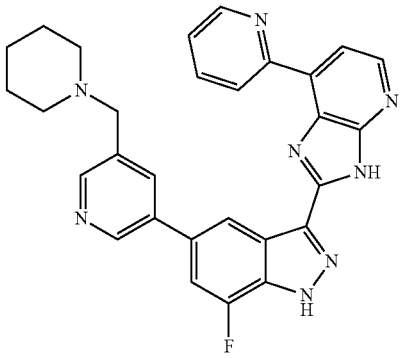
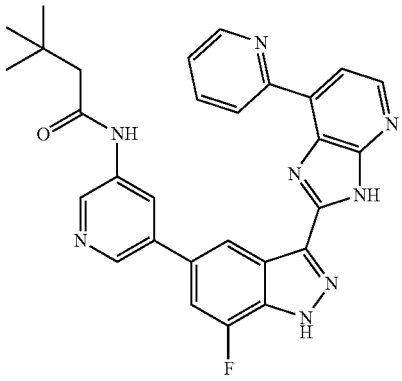
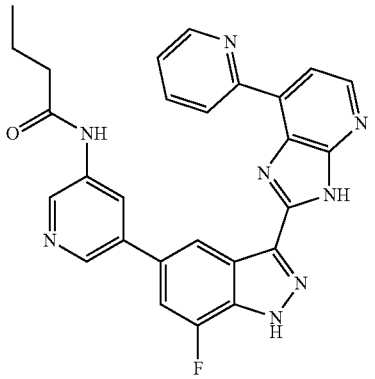
612	
613	
614	
615	

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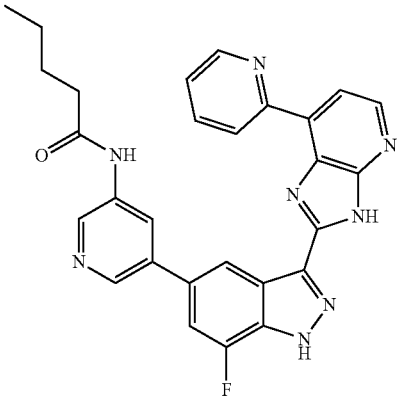
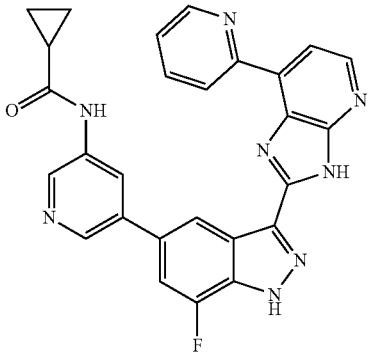
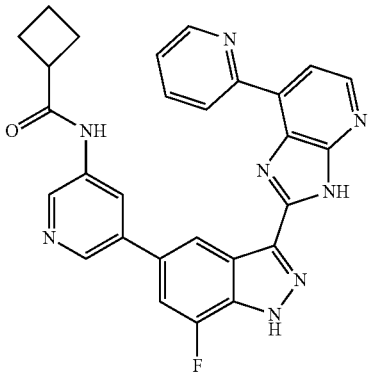
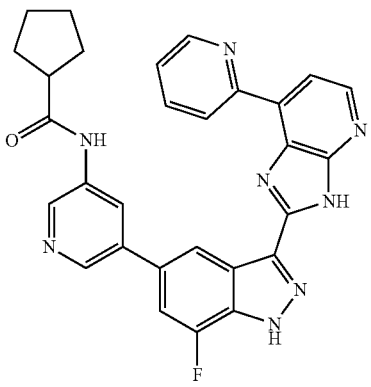
616	
617	
618	
619	

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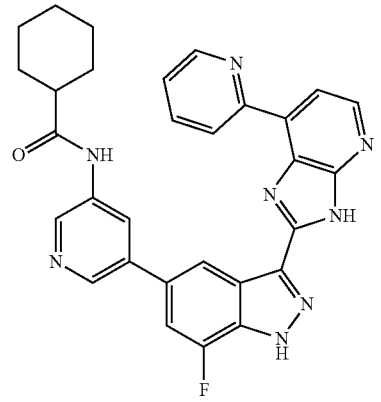

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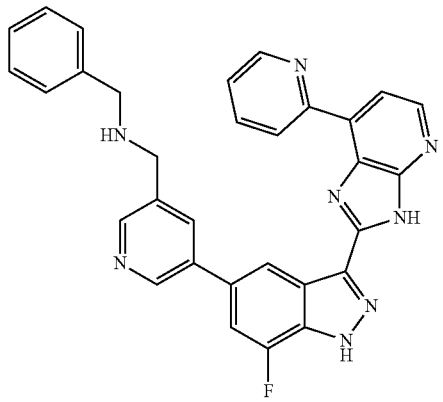

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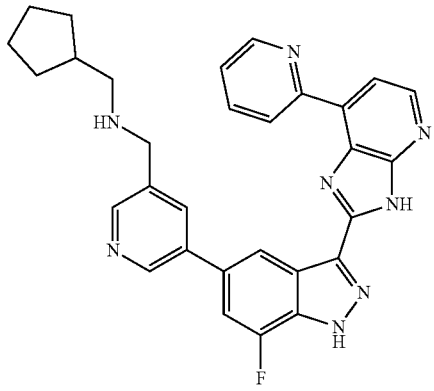

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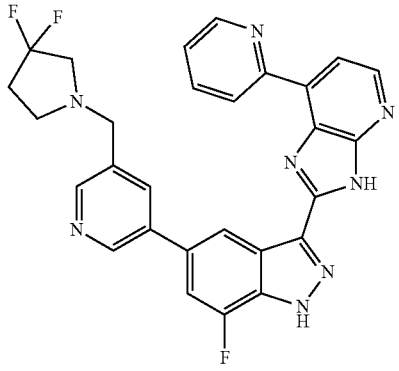

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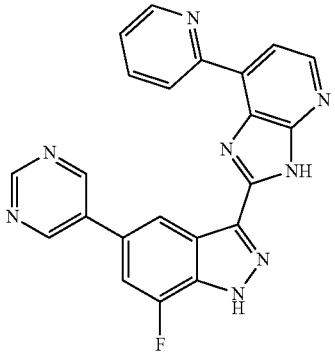

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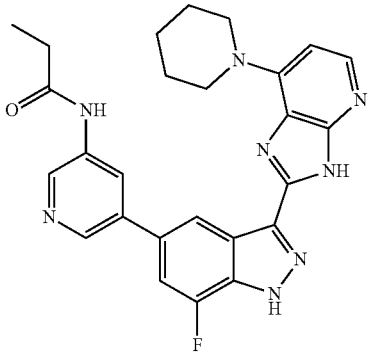

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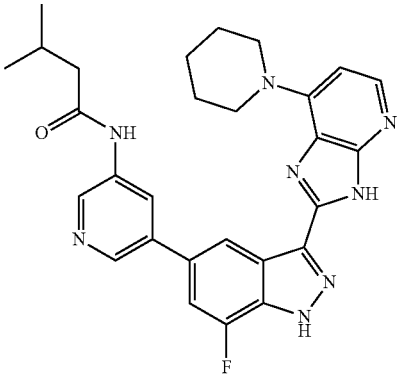

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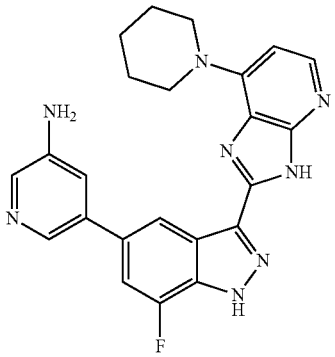

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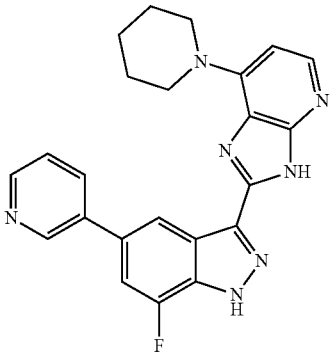
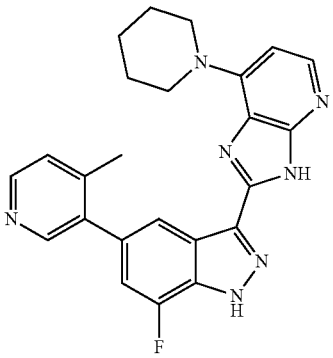
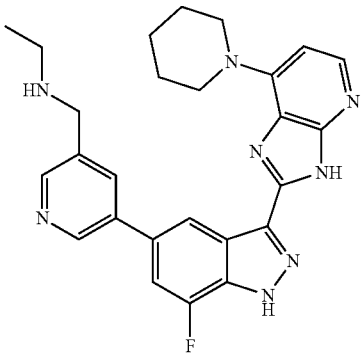
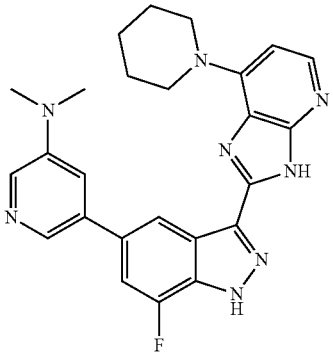
628	
629	
630	
631	

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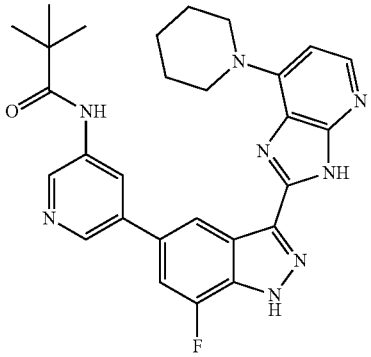
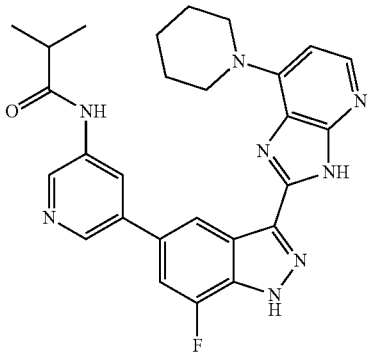
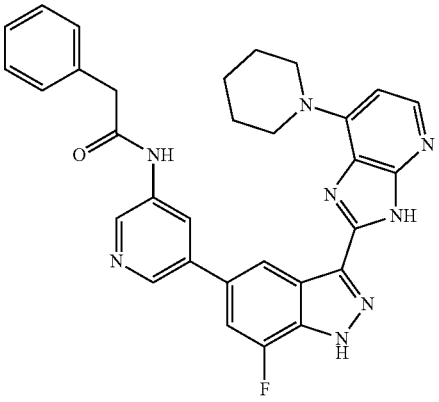
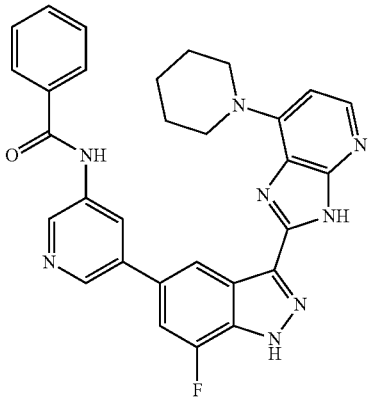
632	
633	
634	
635	

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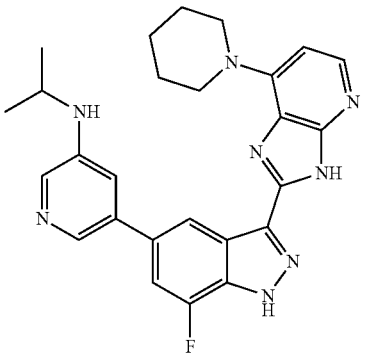
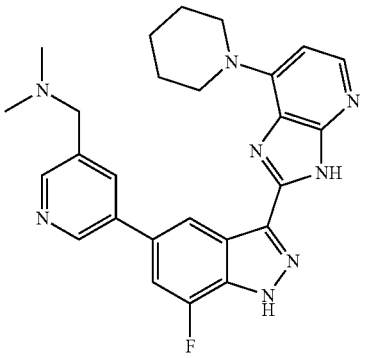
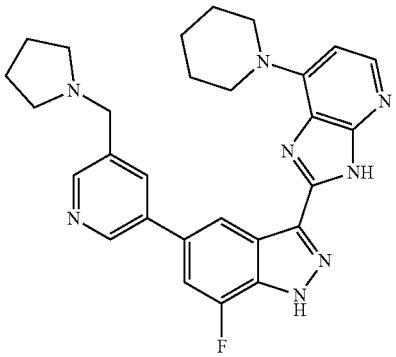
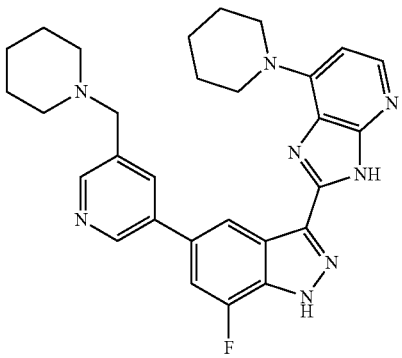
636	
637	
638	
639	

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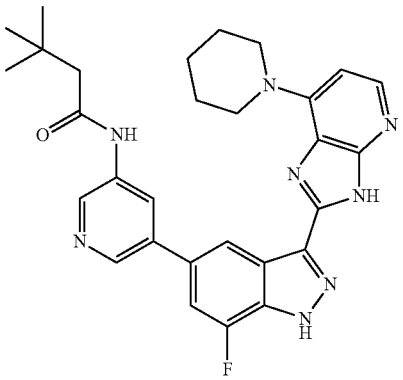
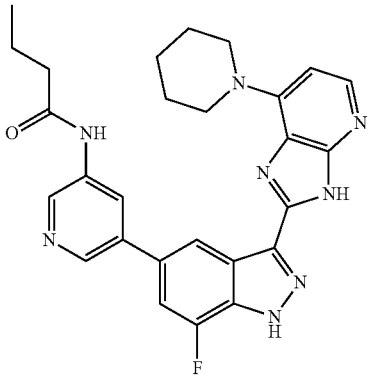
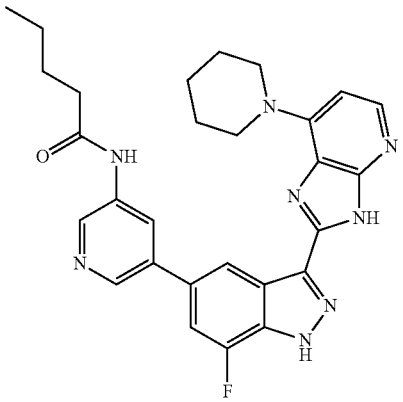
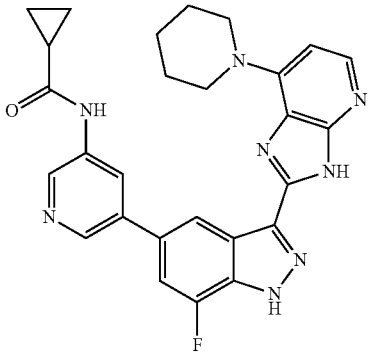
640	
641	
642	
643	

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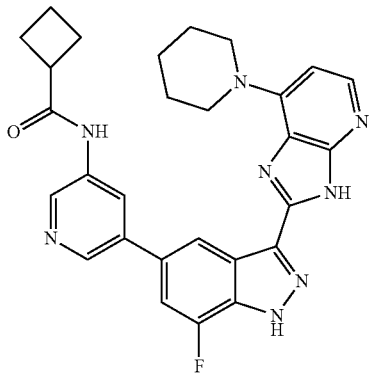

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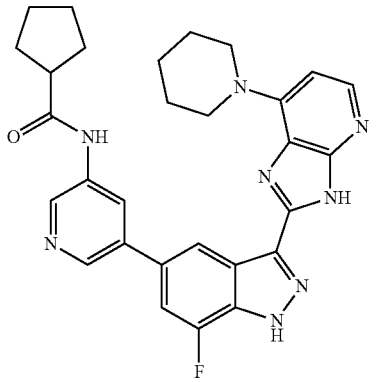

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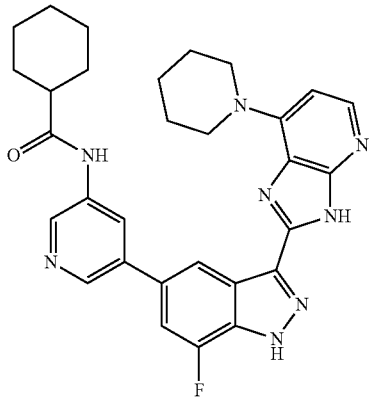

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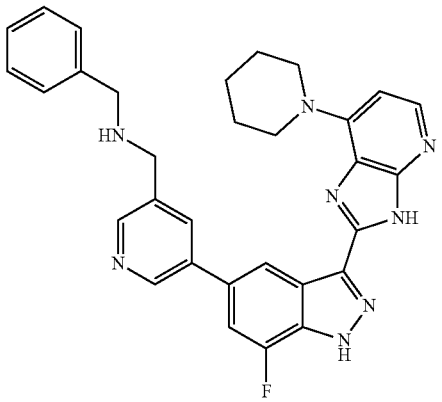

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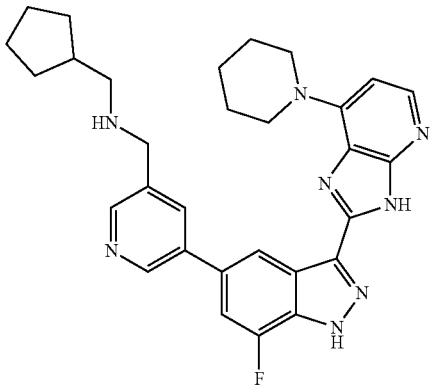

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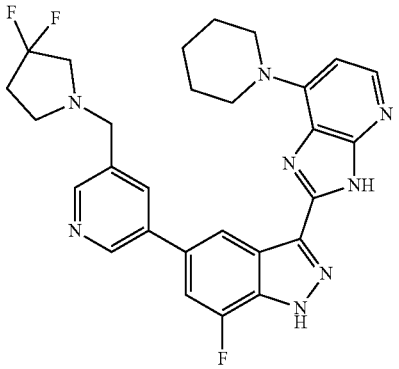

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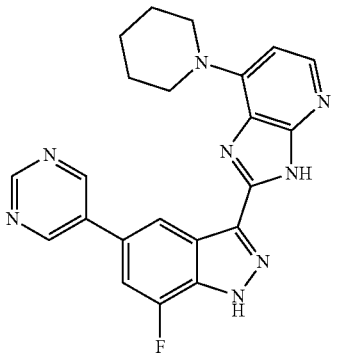

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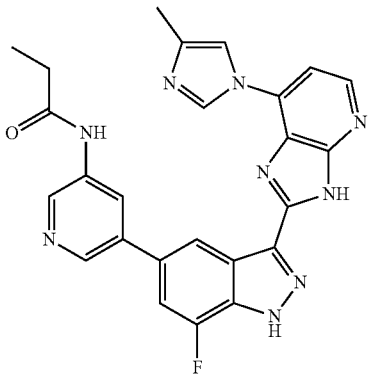

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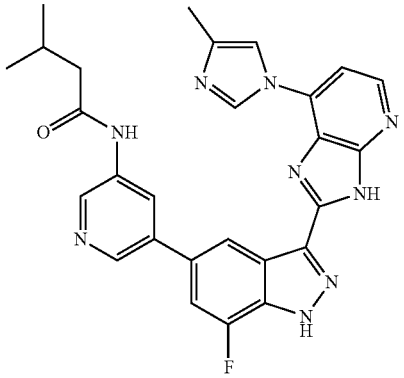
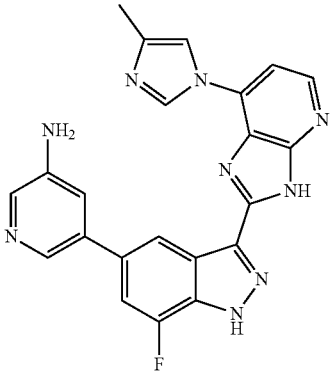
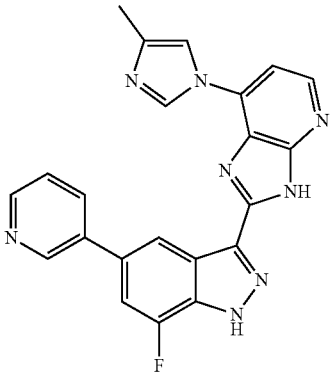
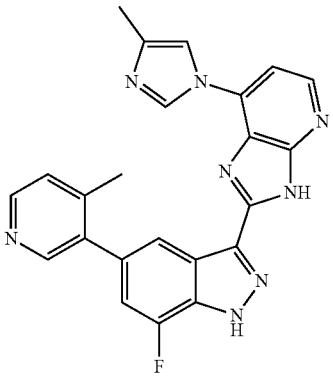
652	
653	
654	
655	

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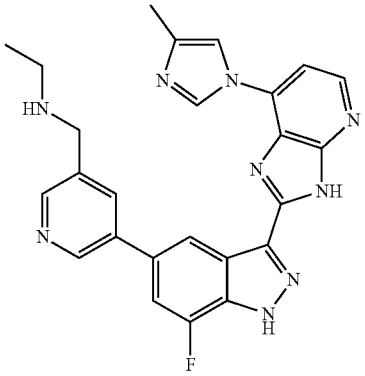
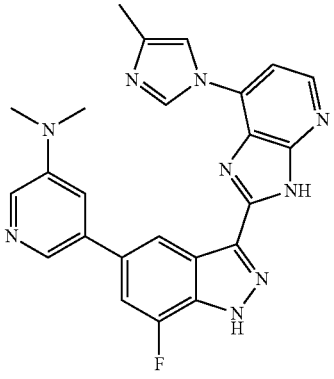
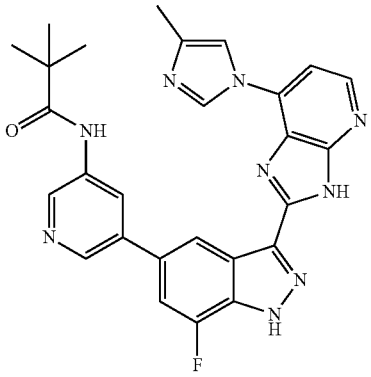
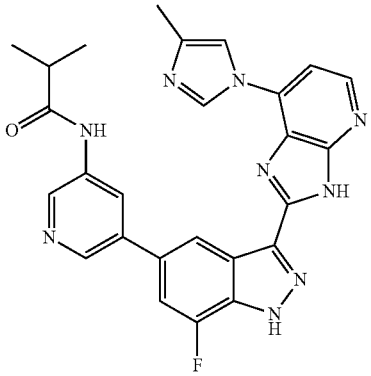
656	
657	
658	
659	

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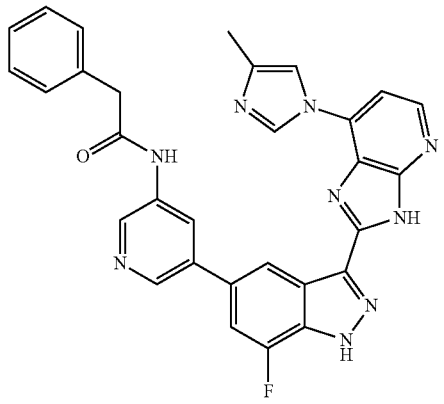
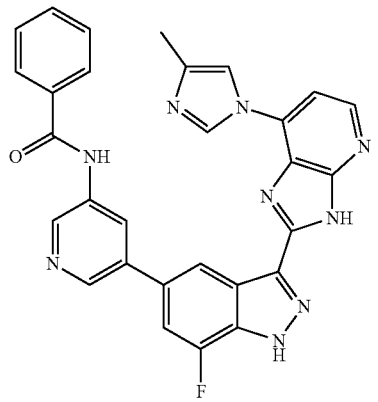
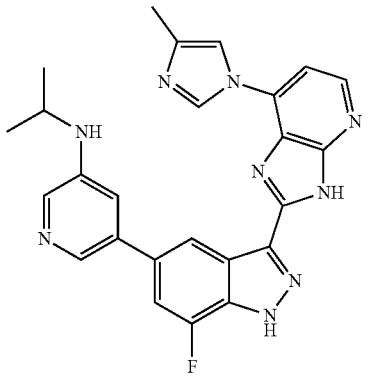
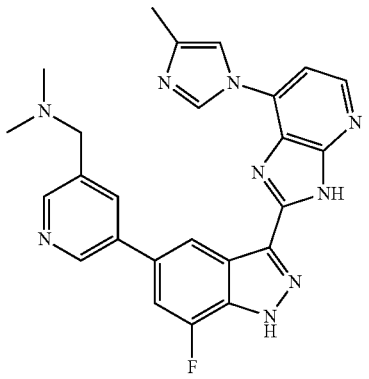
660	
661	
662	
663	

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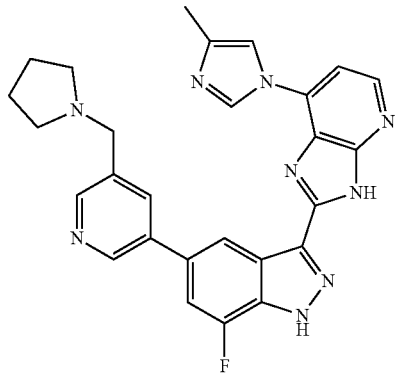
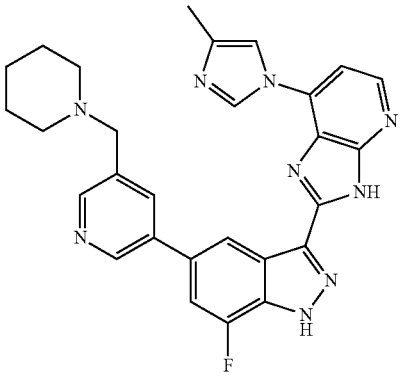
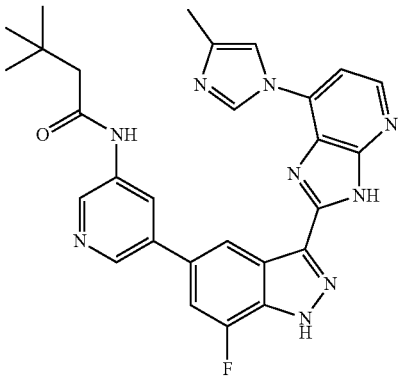
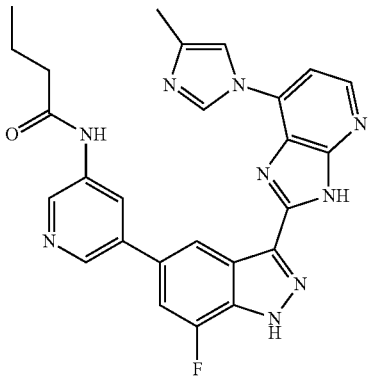
664	
665	
666	
667	

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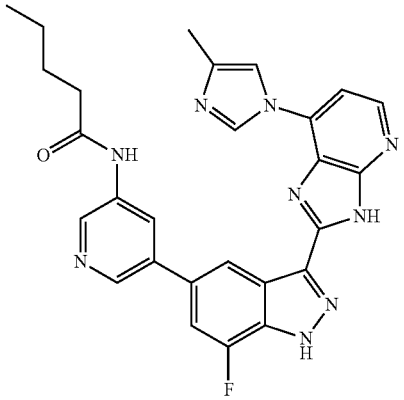

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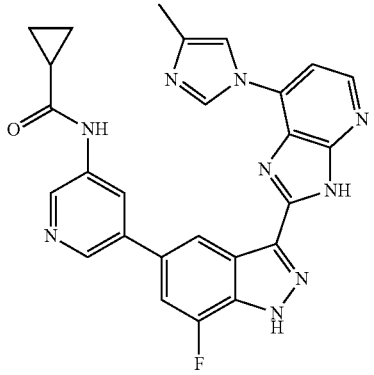

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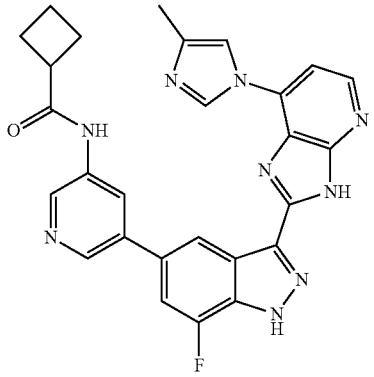

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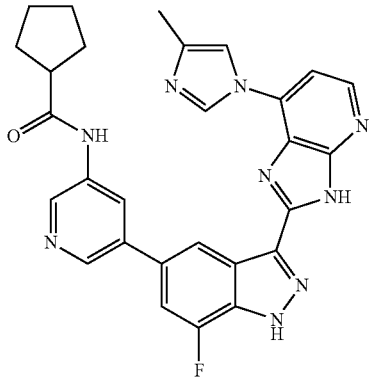

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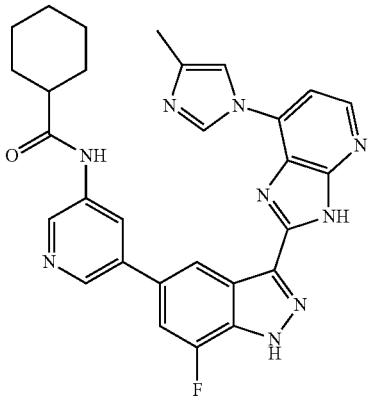

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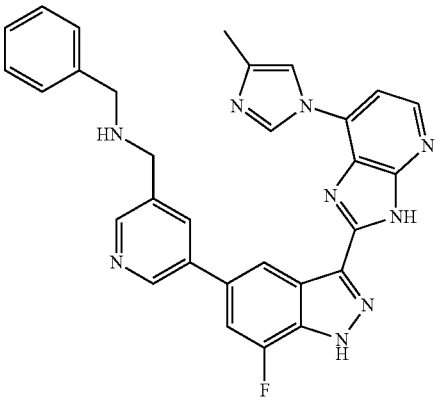

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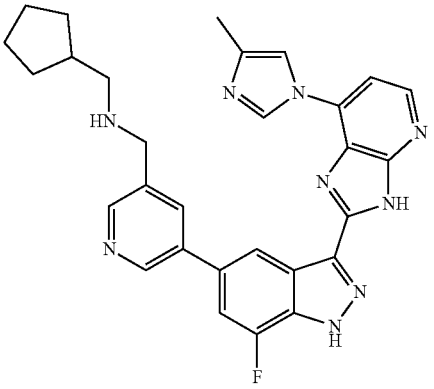

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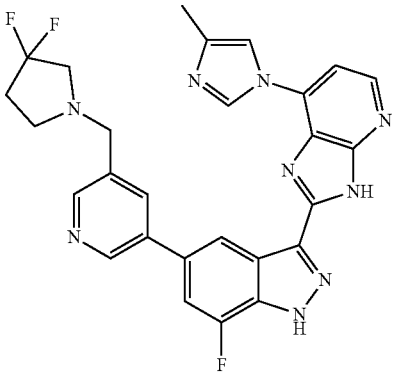

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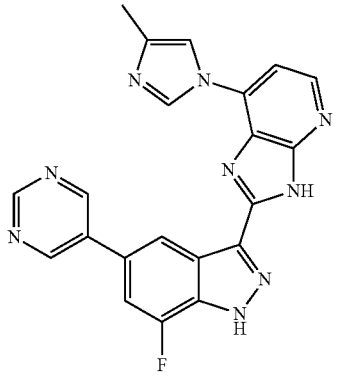
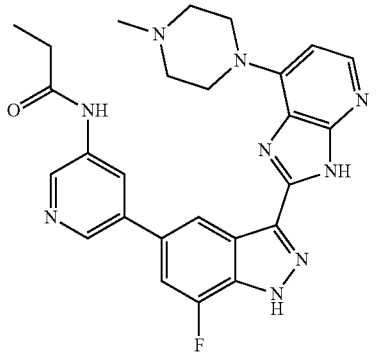
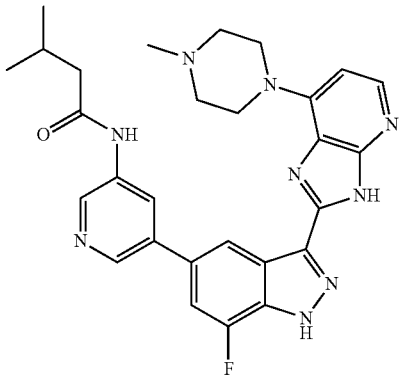
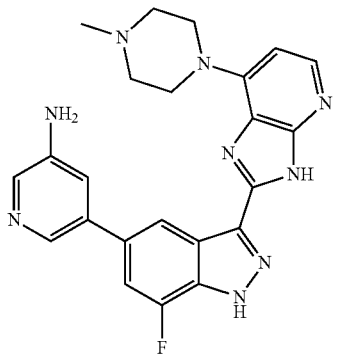
676	
677	
678	
679	

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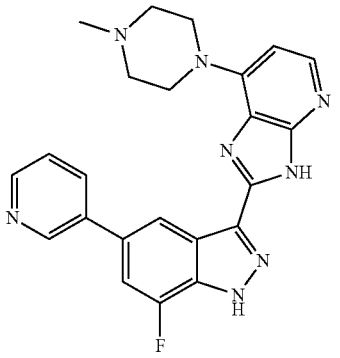
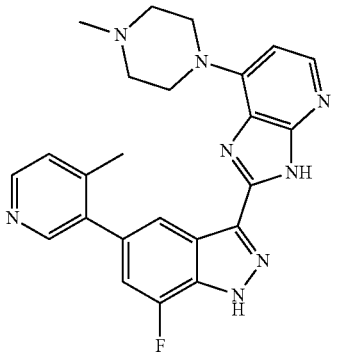
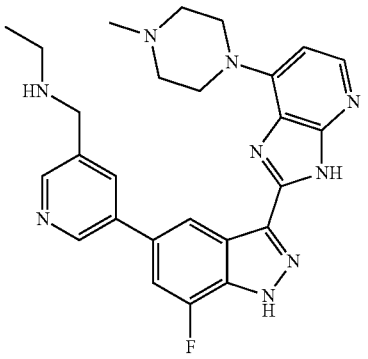
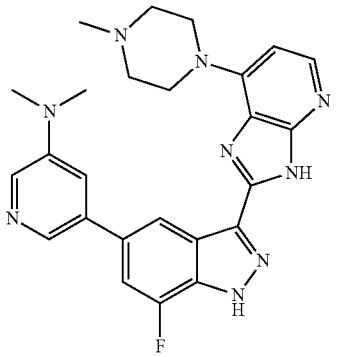
680	
681	
682	
683	

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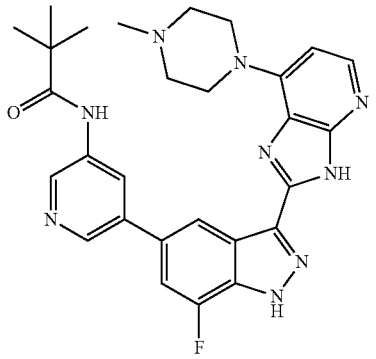
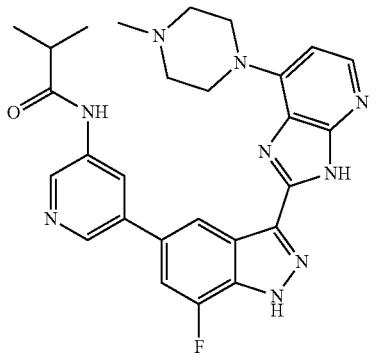
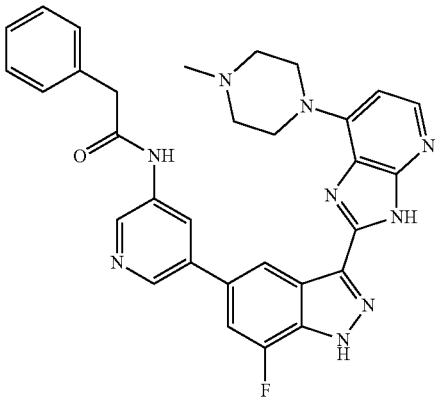
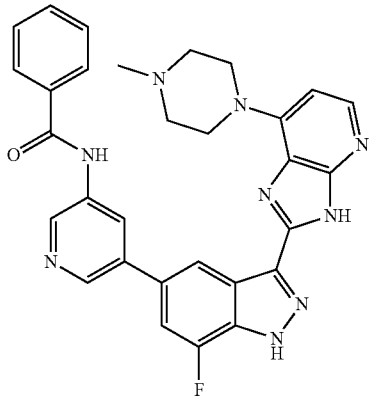
684	
685	
686	
687	

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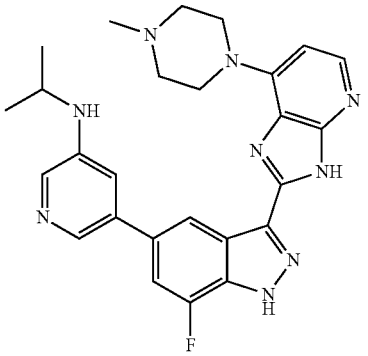
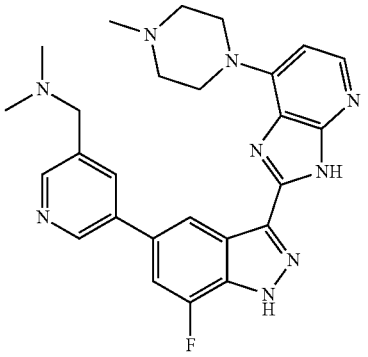
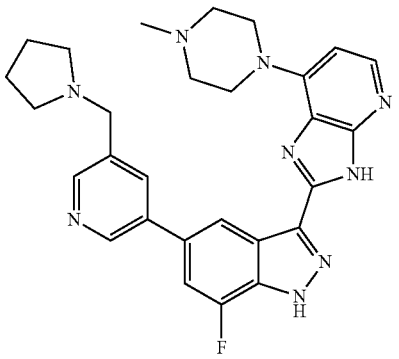
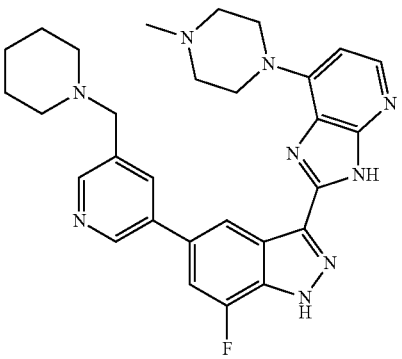
688	
689	
690	
691	

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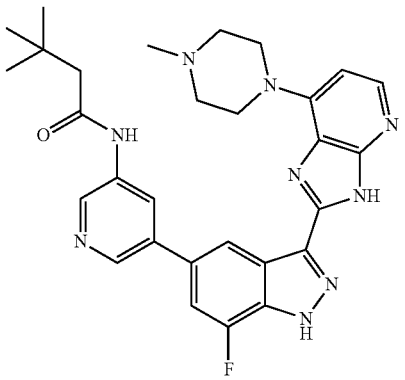
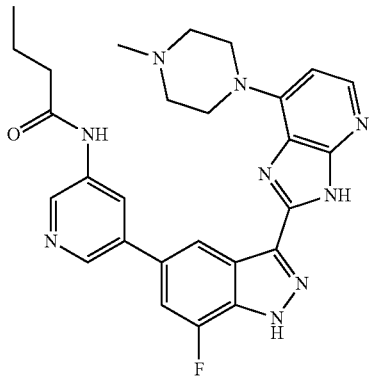
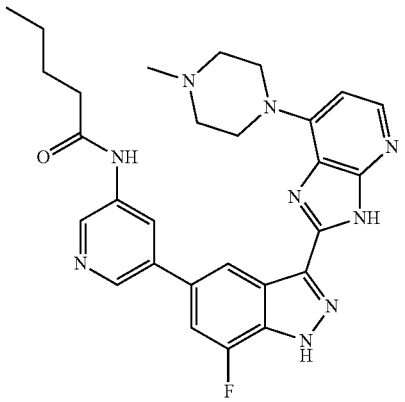
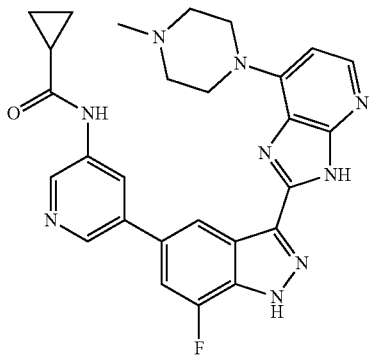
692	
693	
694	
695	

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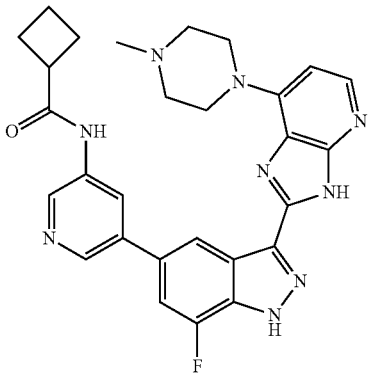
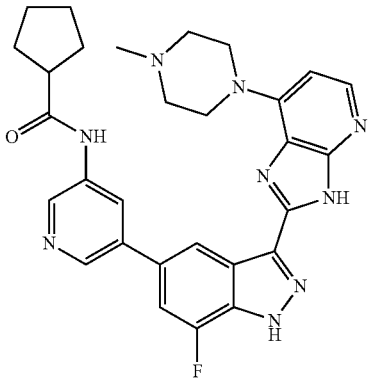
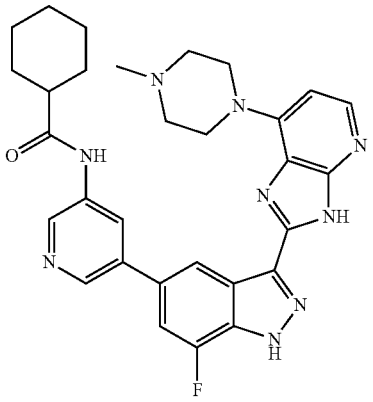
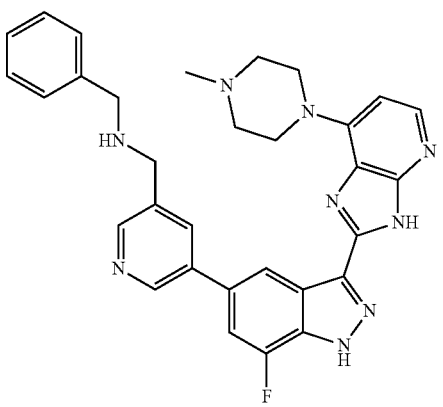
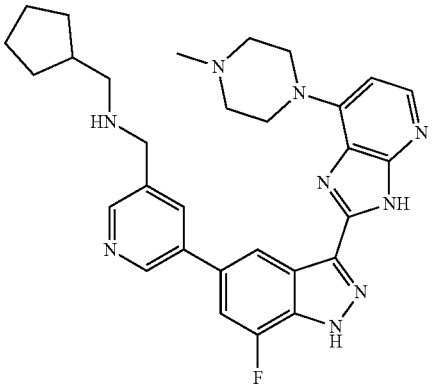
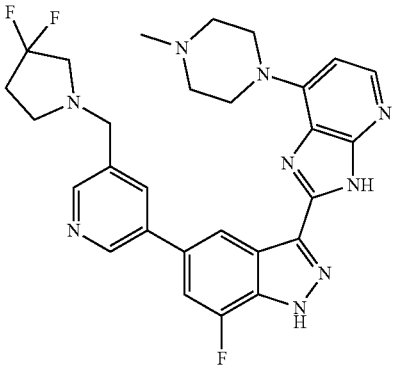
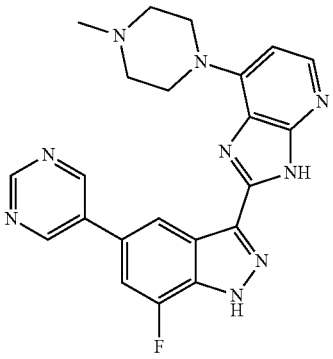
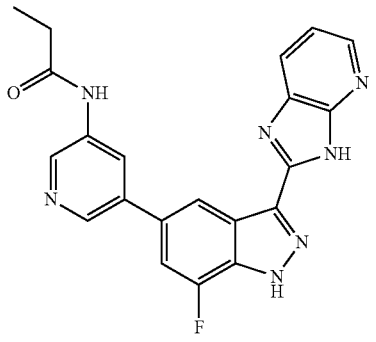
696	
697	
698	
699	

TABLE 1-continued

700	
701	
702	
703	

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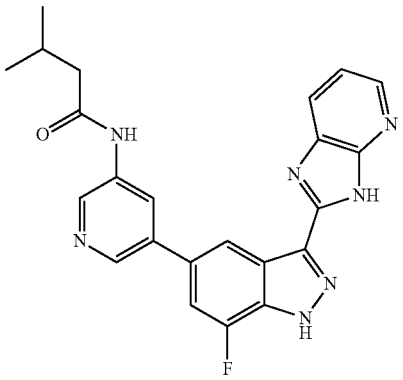
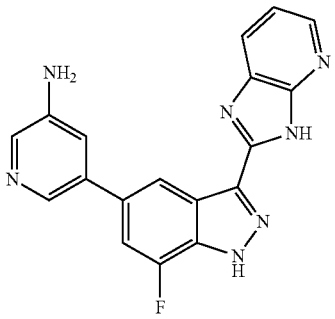
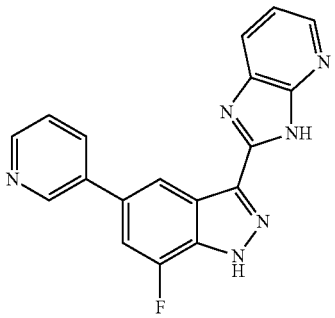
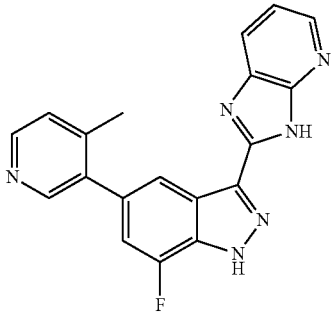
704	
705	
706	
707	

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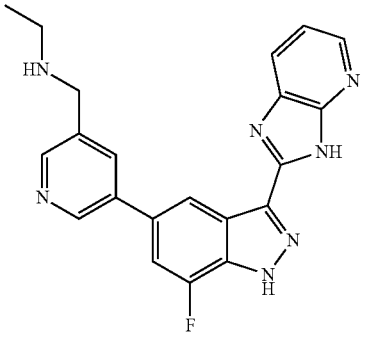
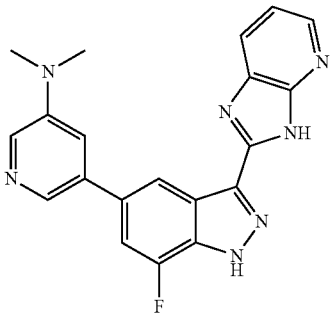
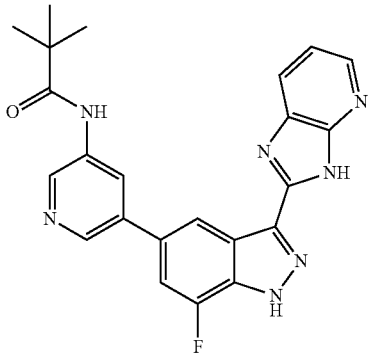
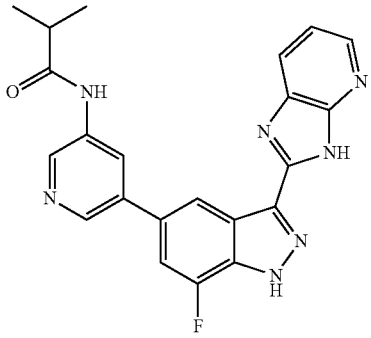
708	
709	
710	
711	

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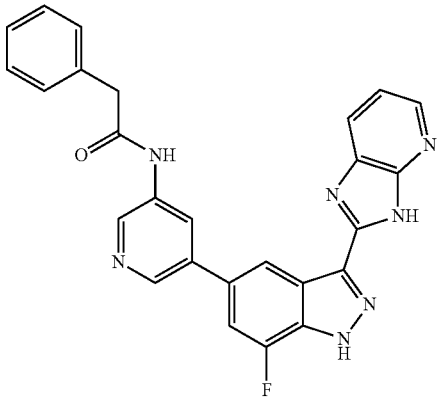
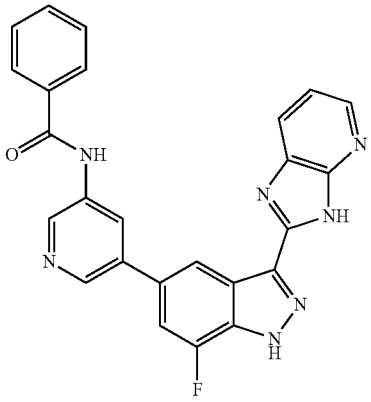
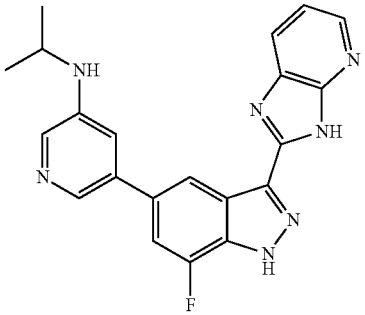
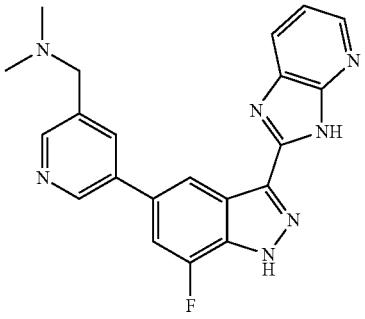
712	
713	
714	
715	

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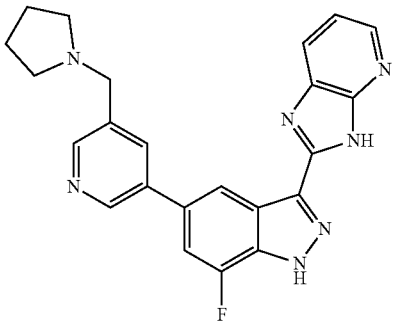
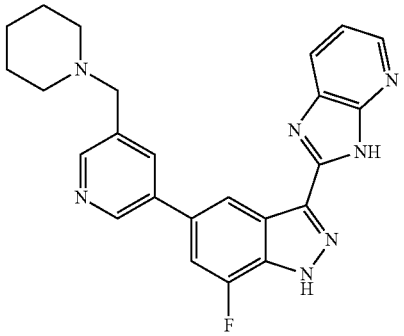
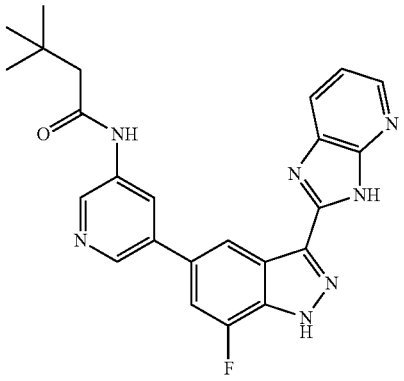
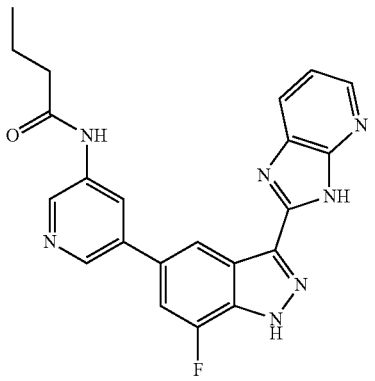
716	
717	
718	
719	

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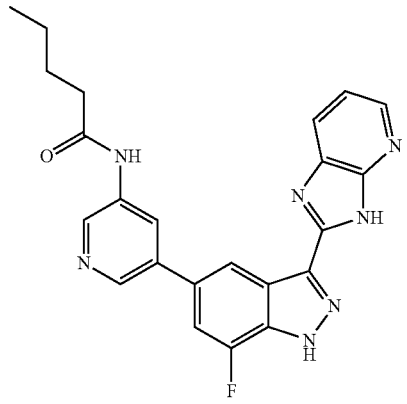
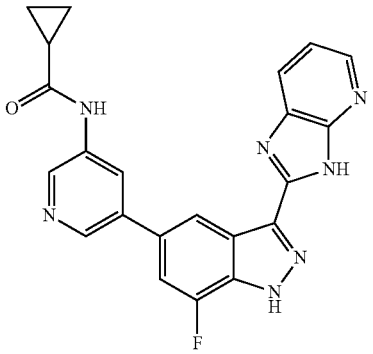
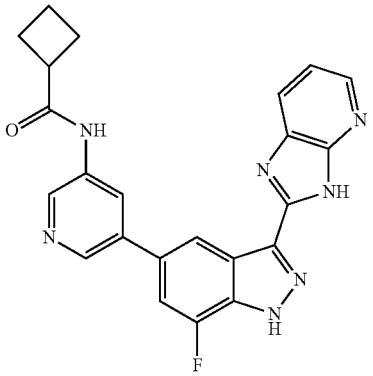
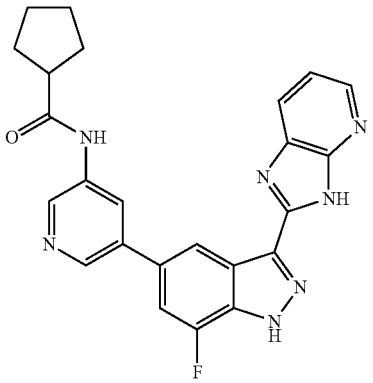
720	
721	
722	
723	

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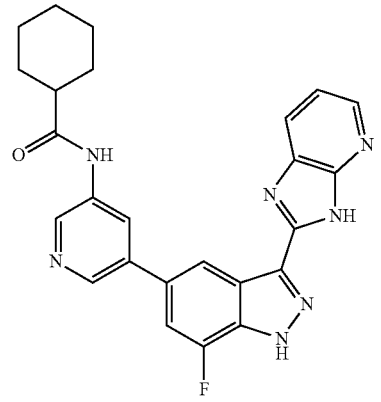
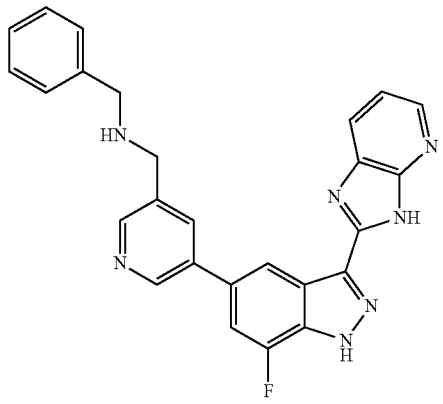
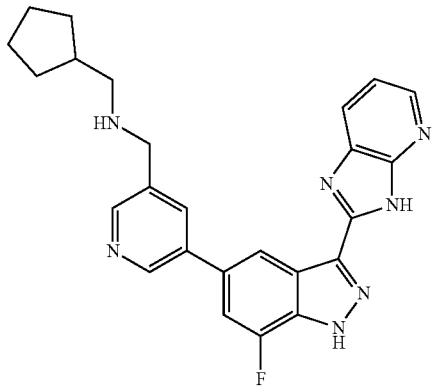
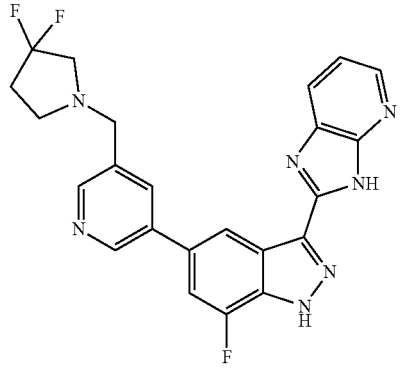
724	
725	
726	
727	

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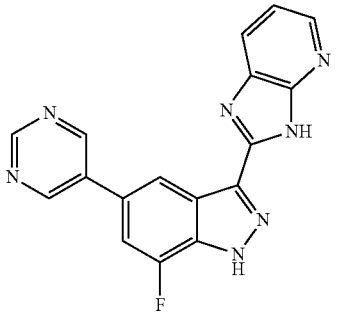
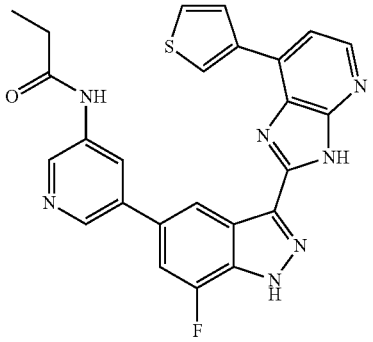
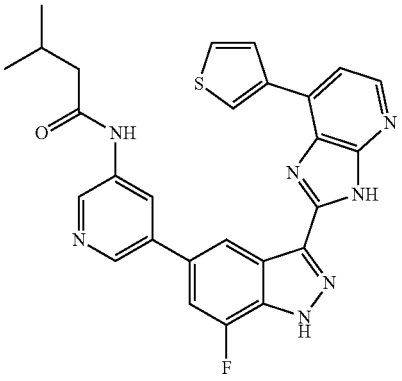
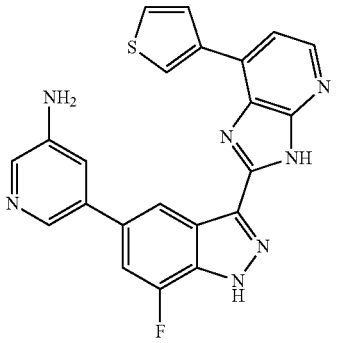
728	
729	
730	
731	

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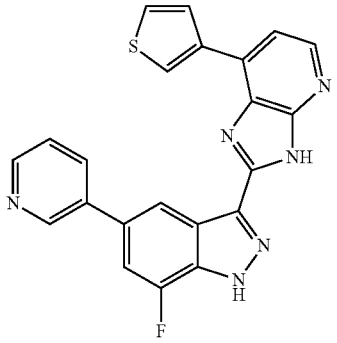
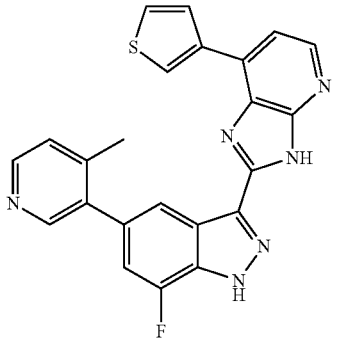
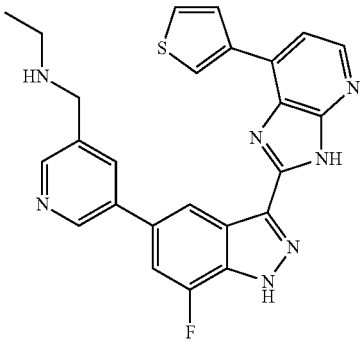
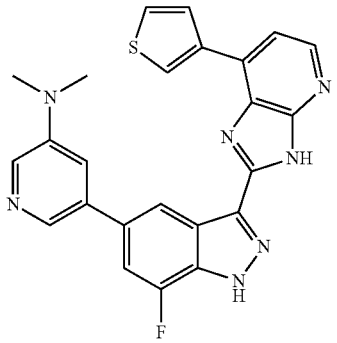
732	
733	
734	
735	

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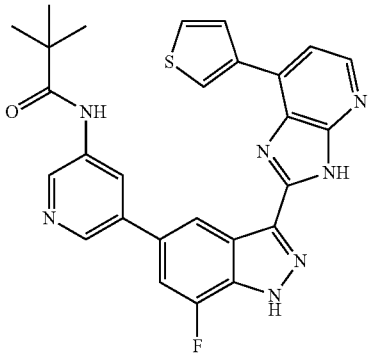
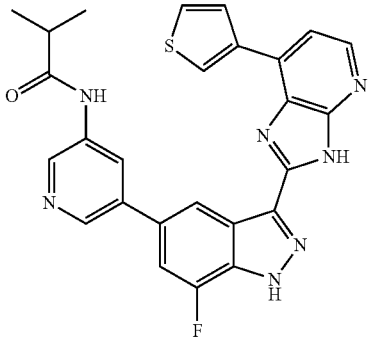
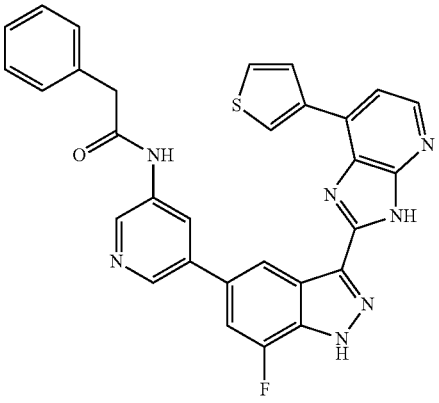
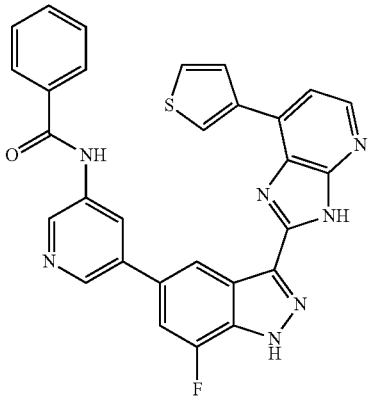
736	
737	
738	
739	

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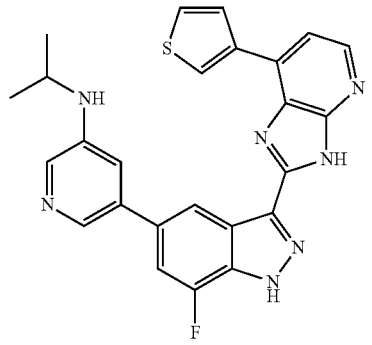

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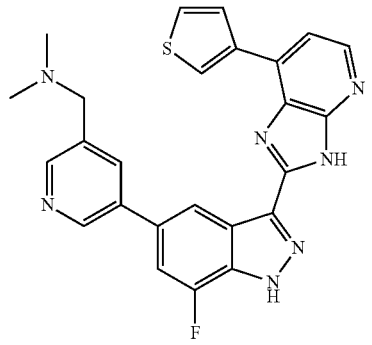

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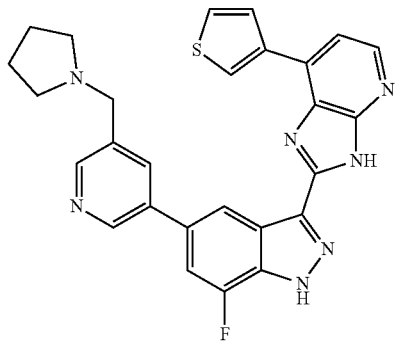

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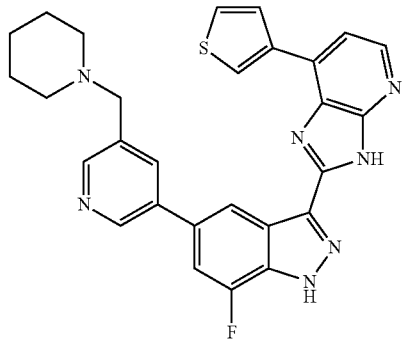

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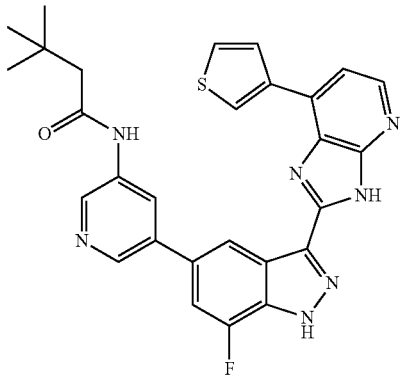

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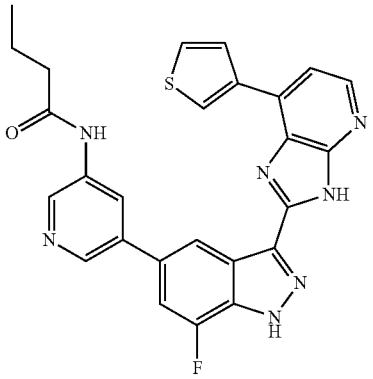

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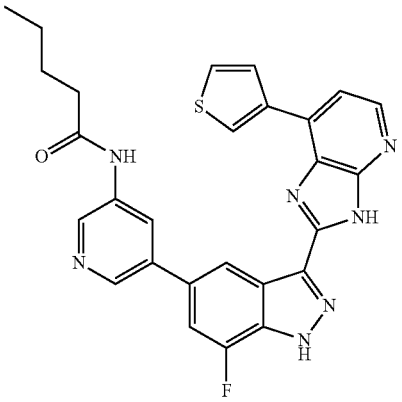

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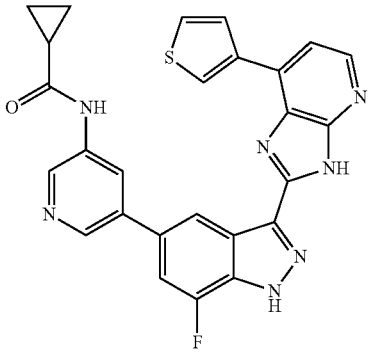

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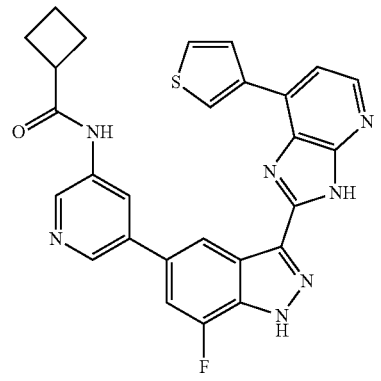

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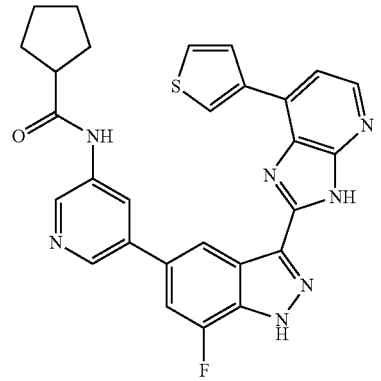

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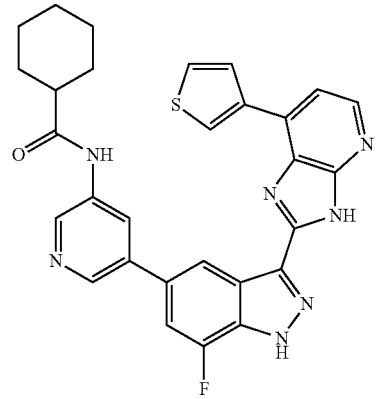

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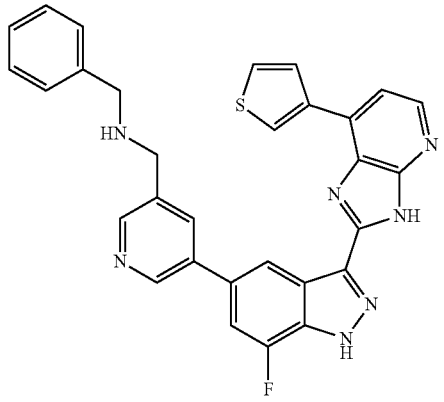

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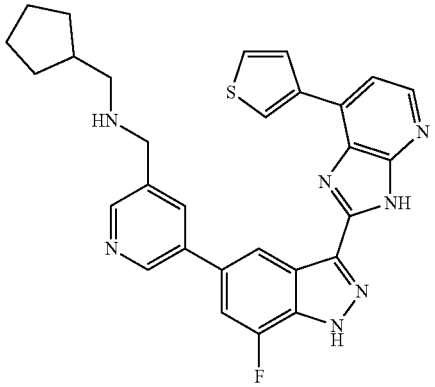

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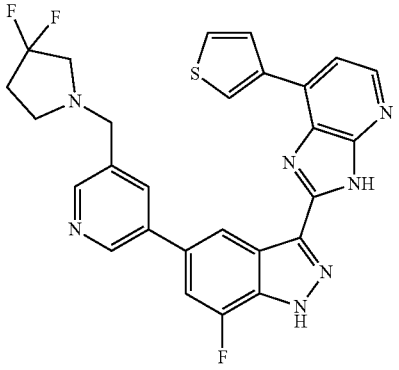

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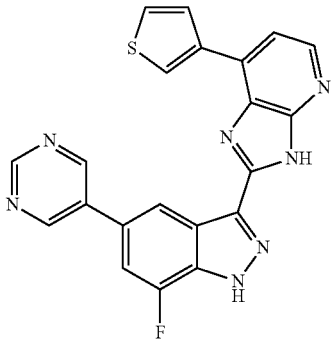

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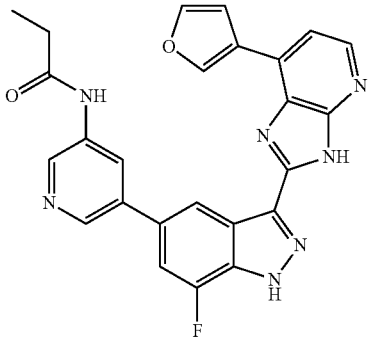

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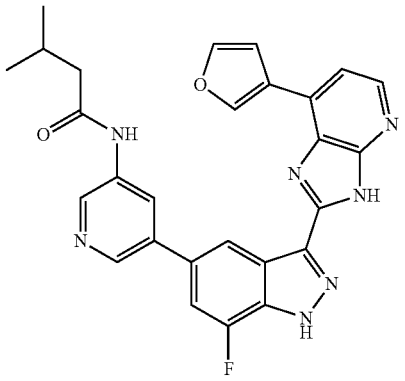
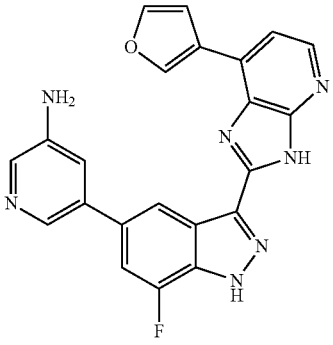
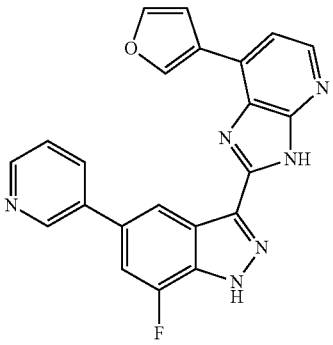
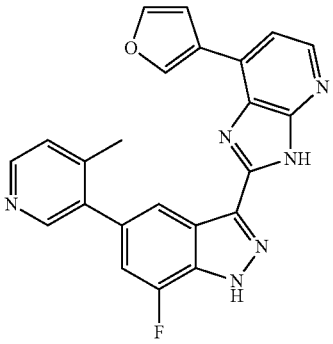
756	
757	
758	
759	

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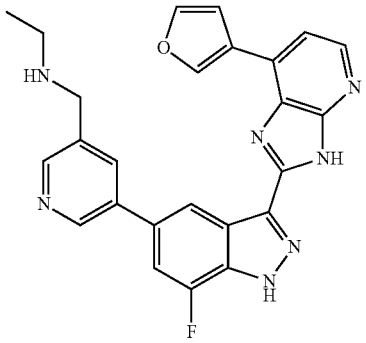
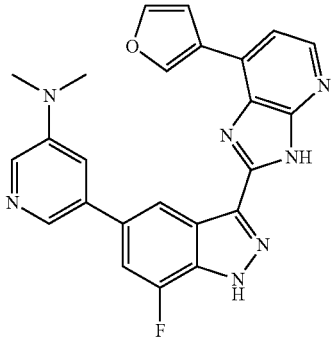
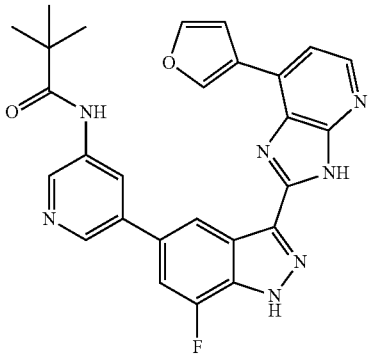
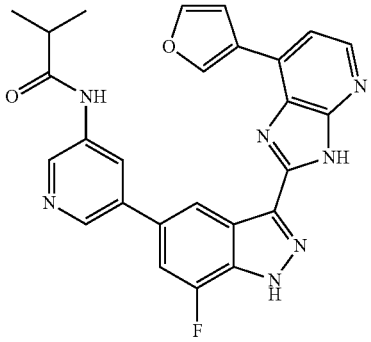
760	
761	
762	
763	

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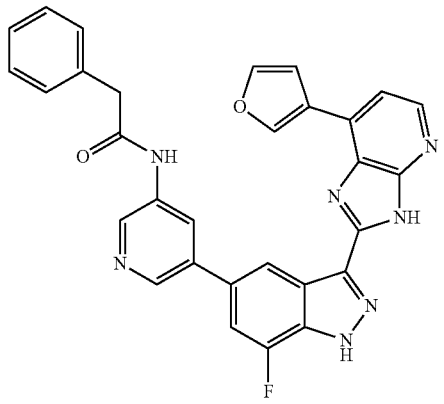

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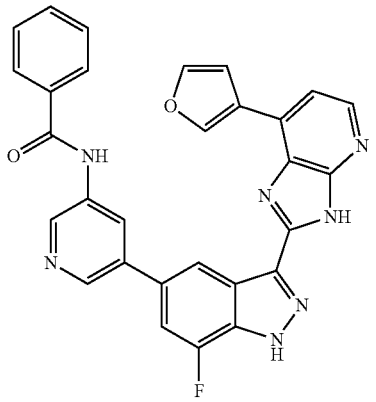

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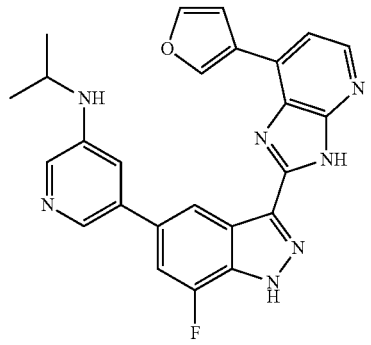

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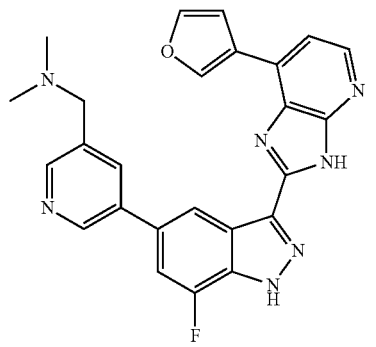

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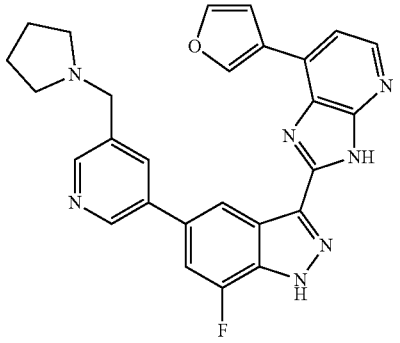

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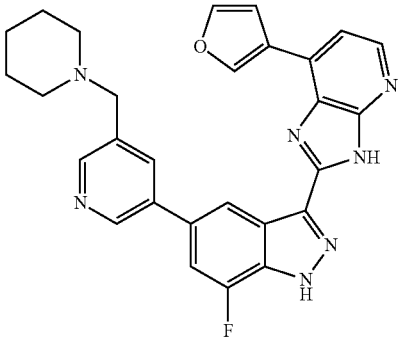

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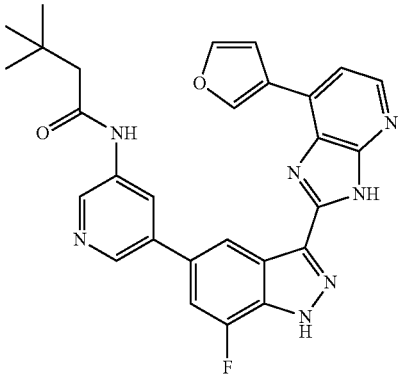

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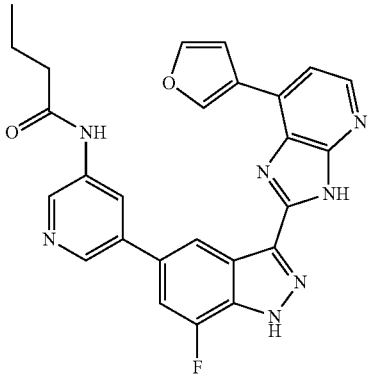

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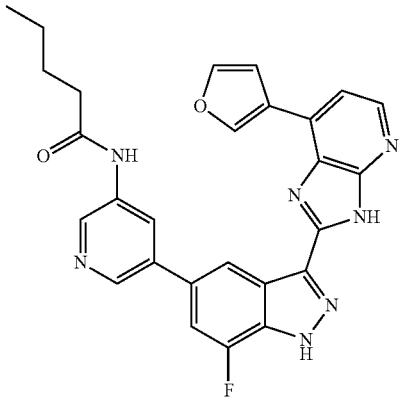
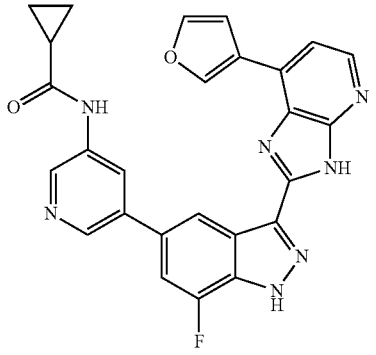
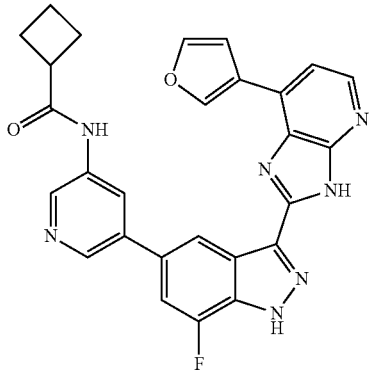
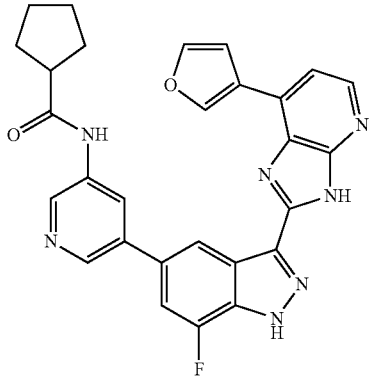
772	
773	
774	
775	

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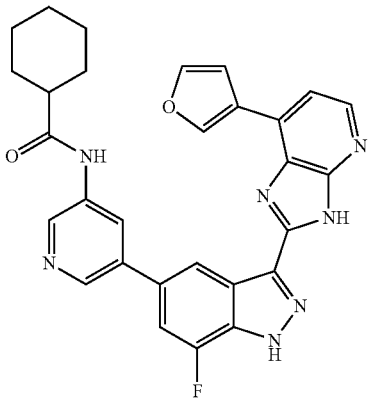
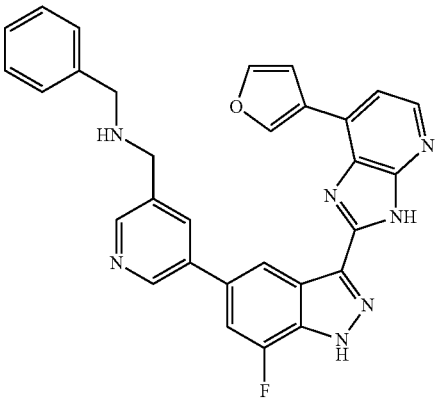
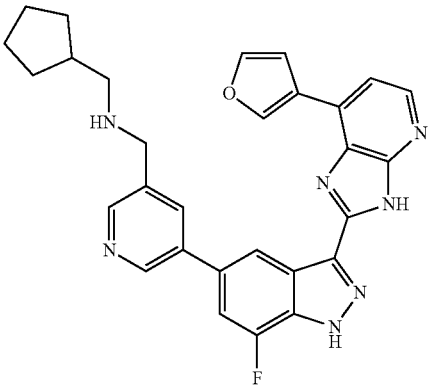
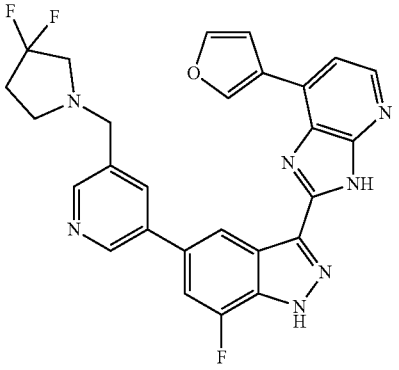
776	
777	
778	
779	

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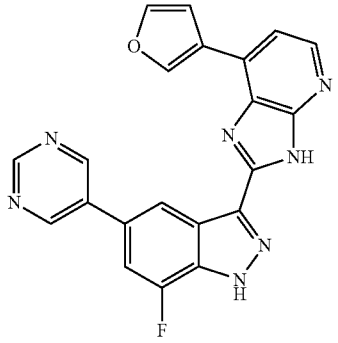
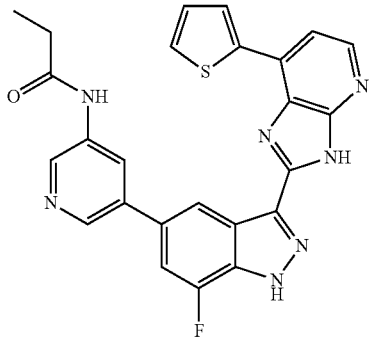
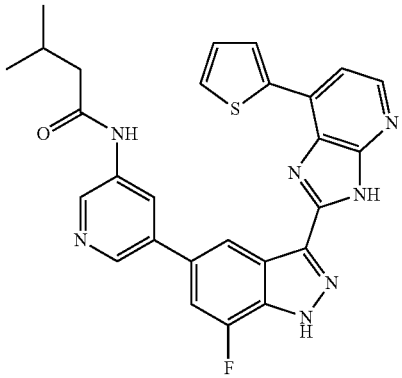
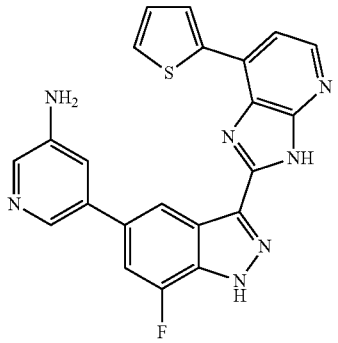
780	
781	
782	
783	

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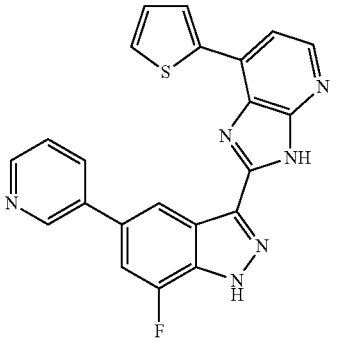
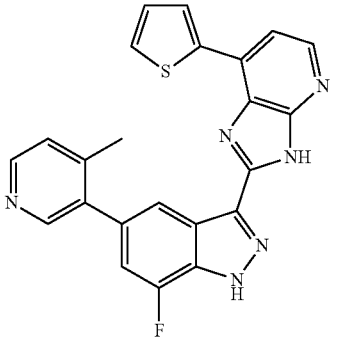
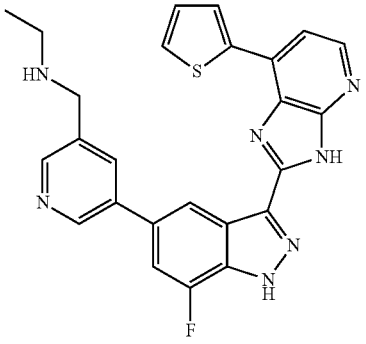
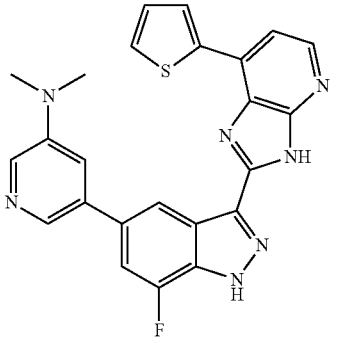
784	
785	
786	
787	

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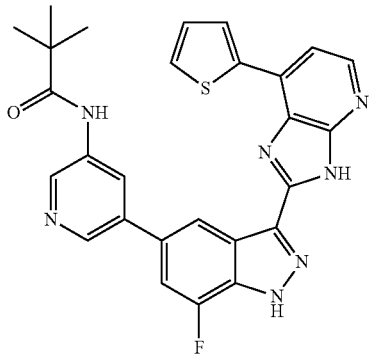

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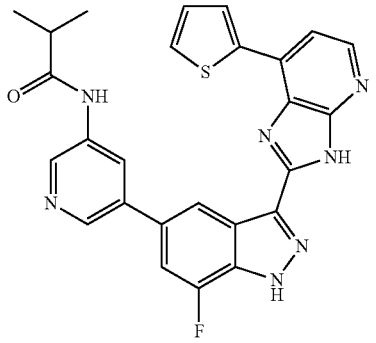

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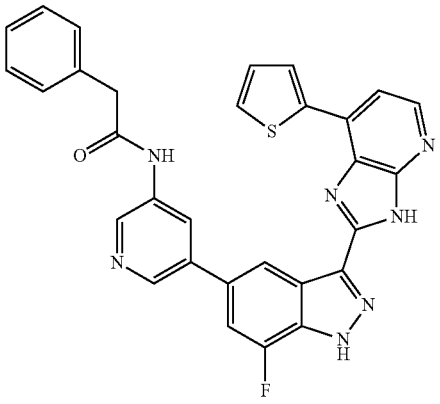

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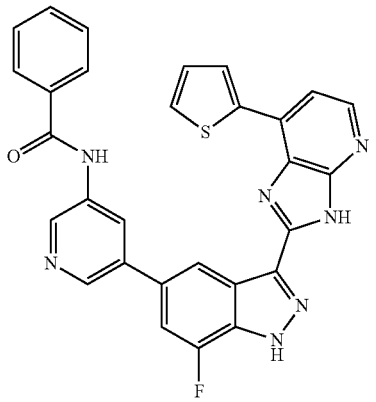

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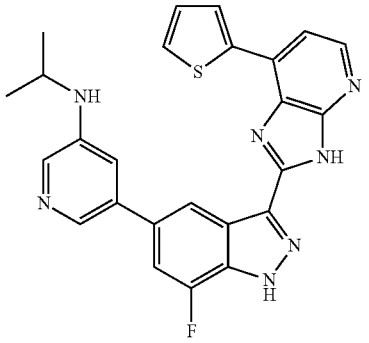

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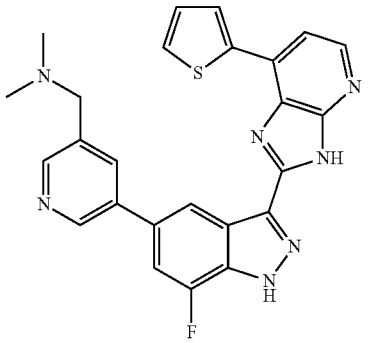

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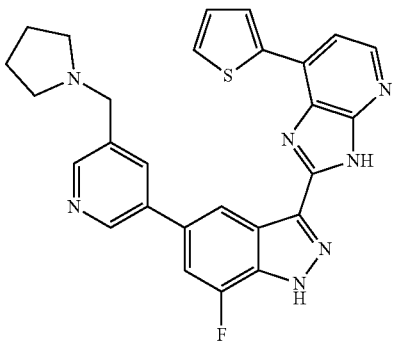

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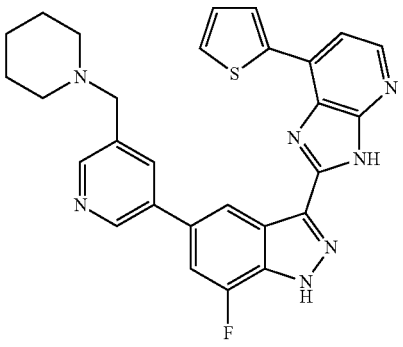

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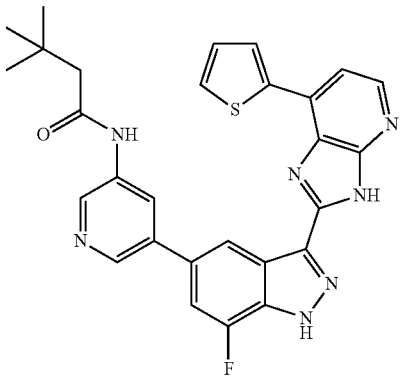
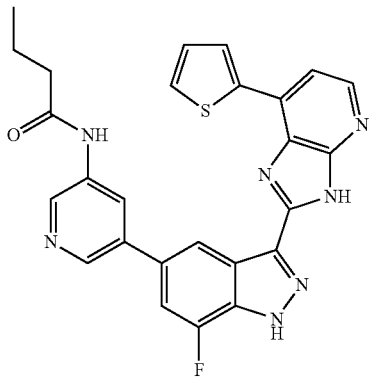
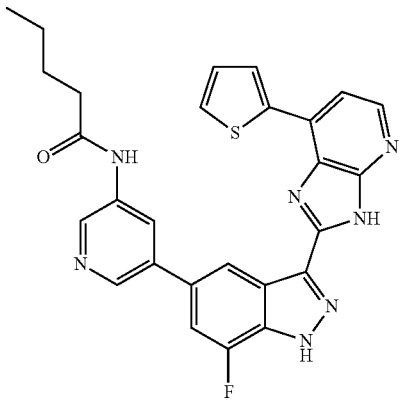
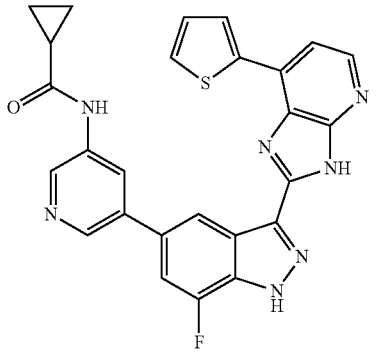
796	
797	
798	
799	

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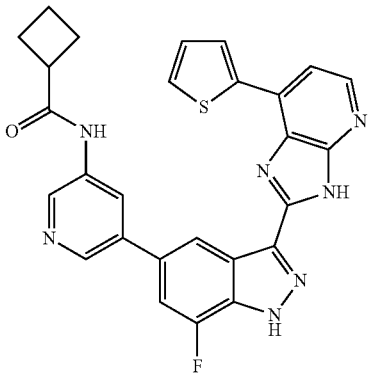
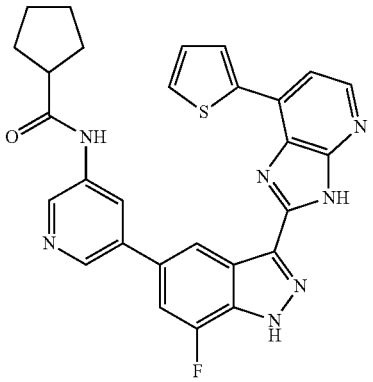
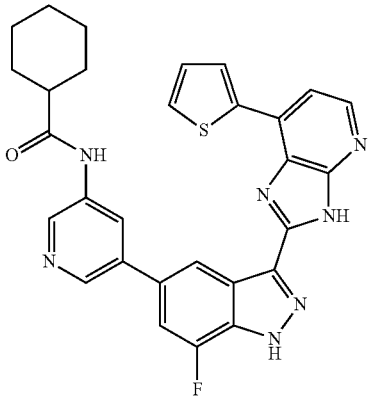
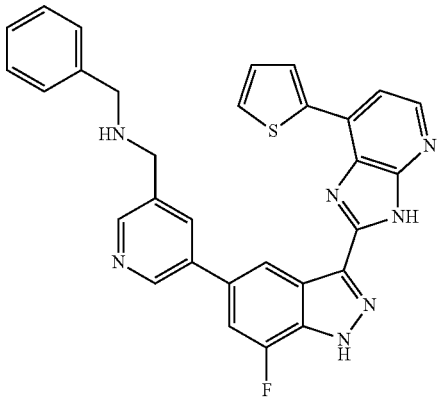
800	
801	
802	
803	

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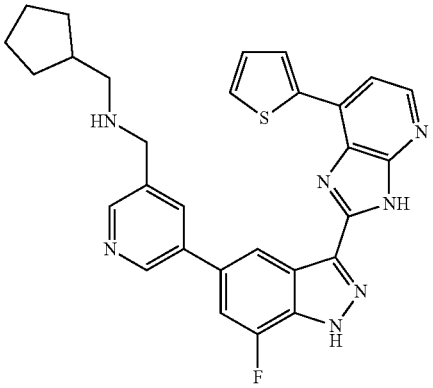
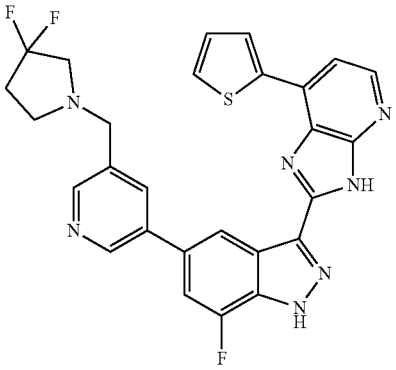
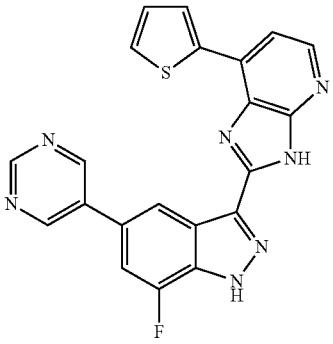
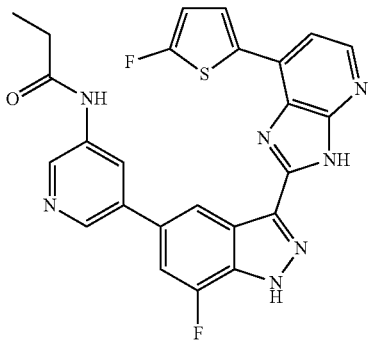
804	
805	
806	
807	

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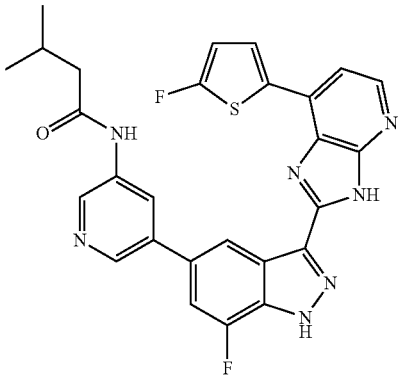
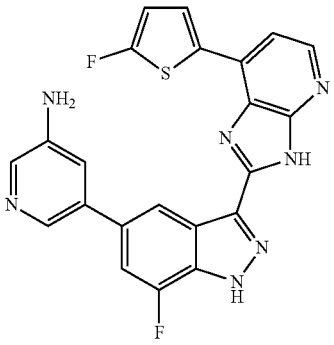
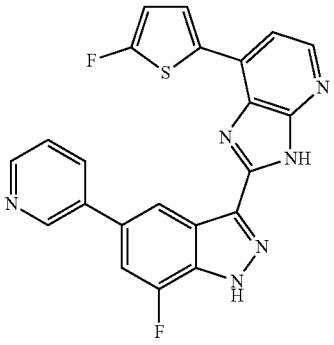
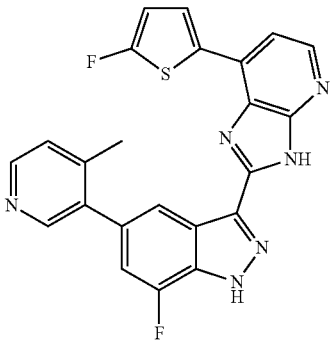
808	
809	
810	
811	

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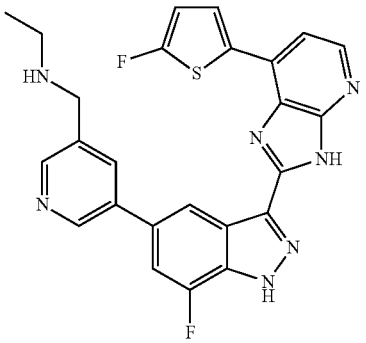
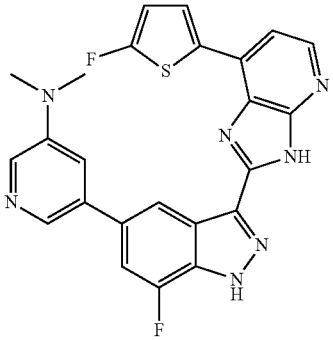
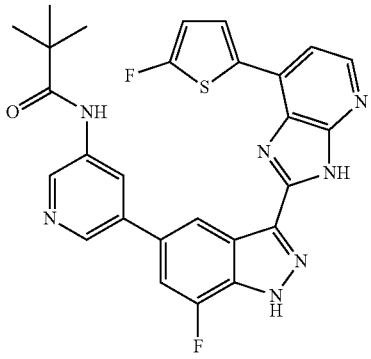
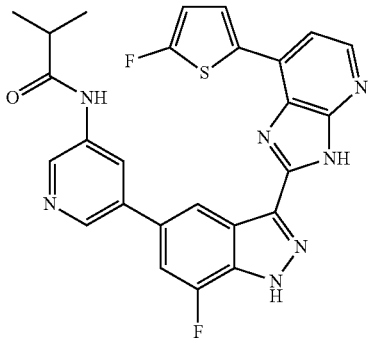
812	
813	
814	
815	

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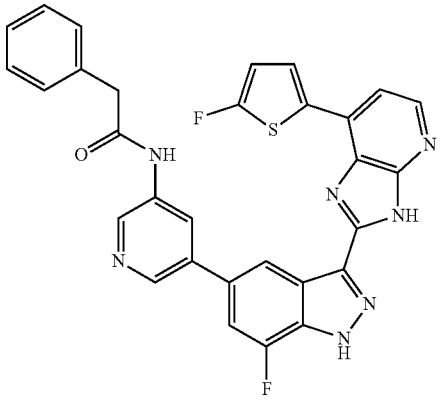
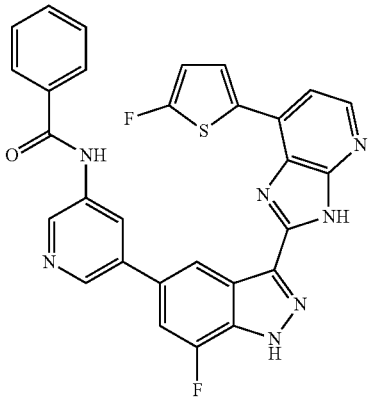
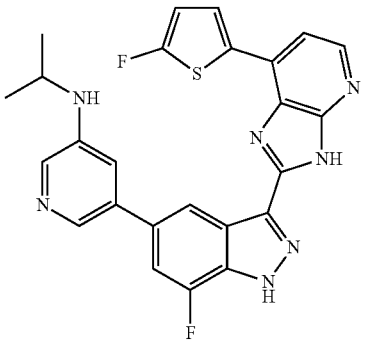
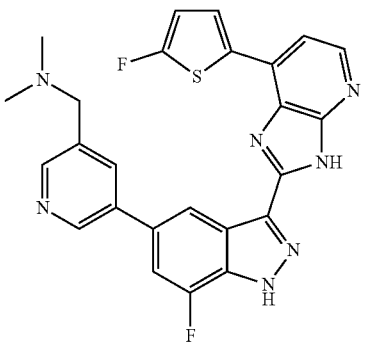
816	
817	
818	
819	

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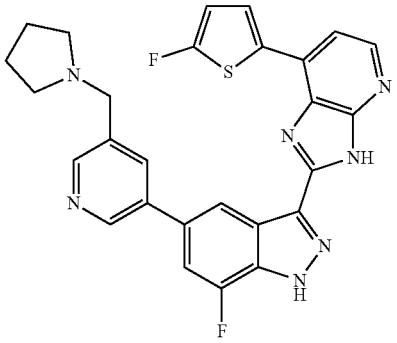
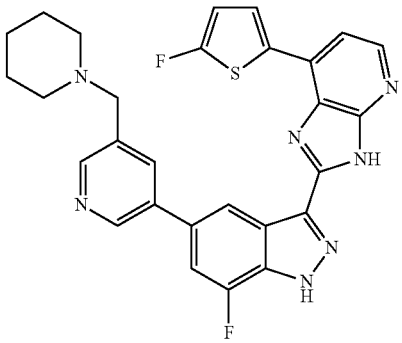
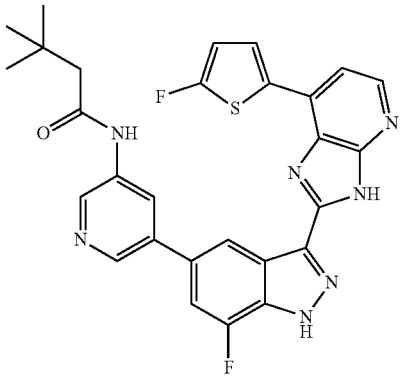
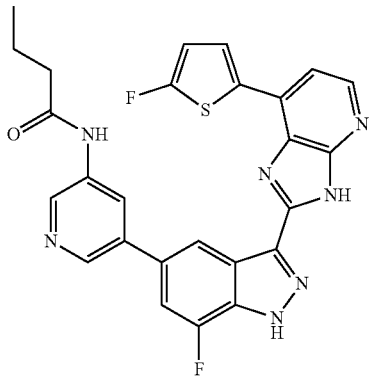
820	
821	
822	
823	

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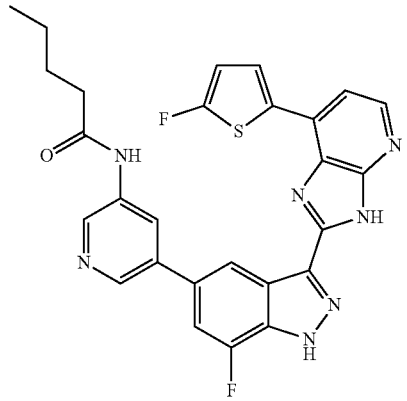
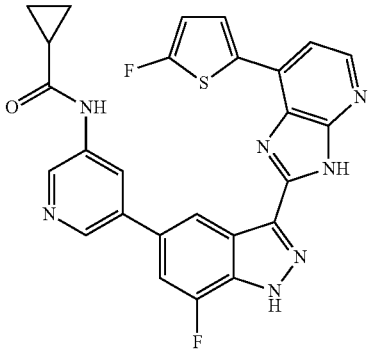
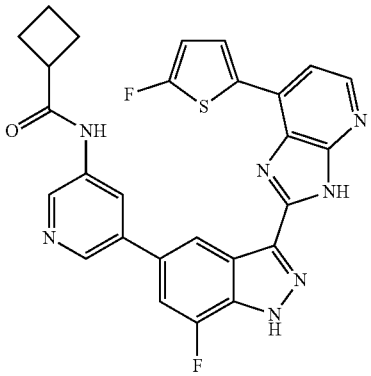
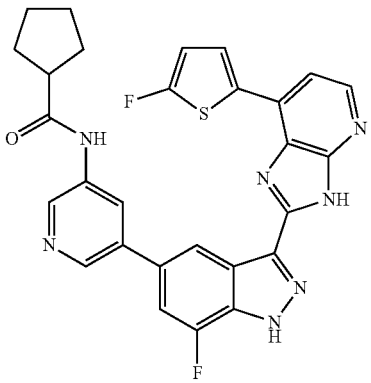
824	
825	
826	
827	

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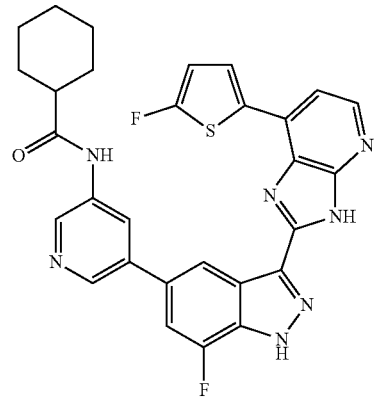

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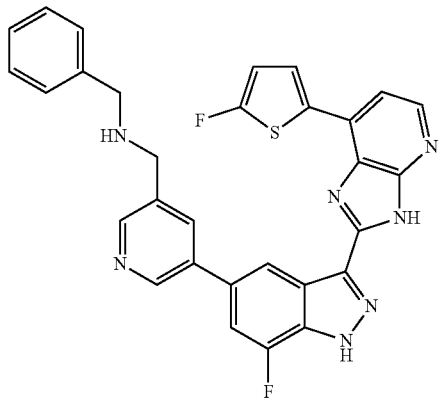

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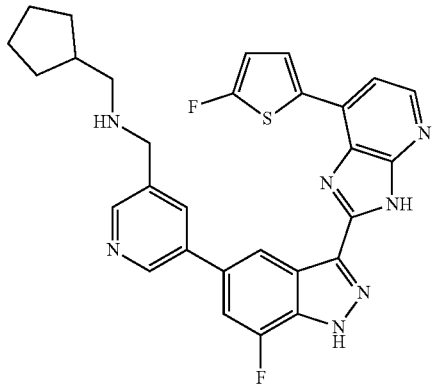

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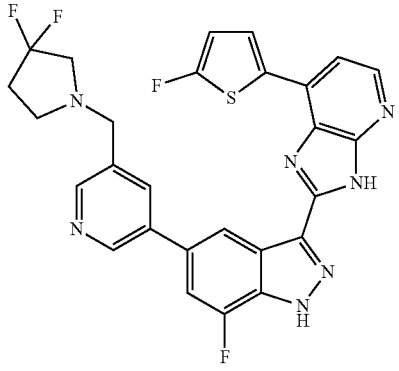

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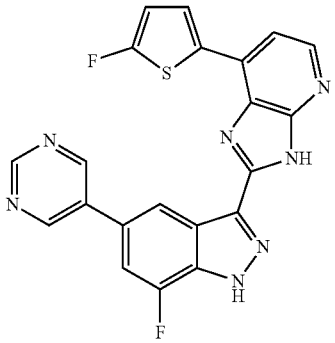

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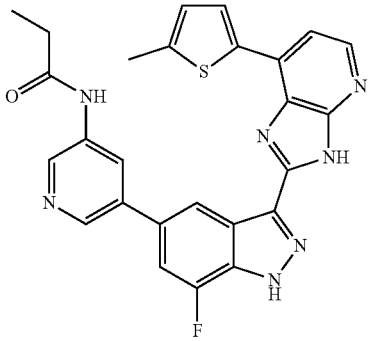

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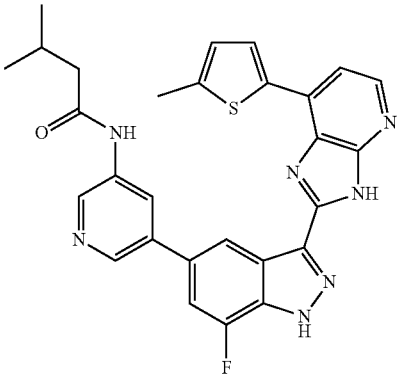

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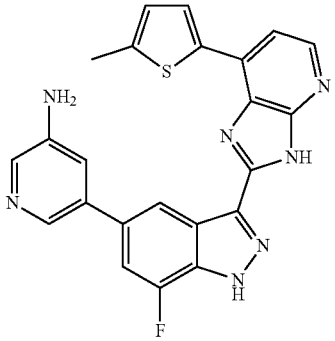

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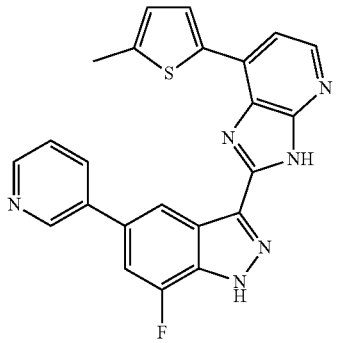

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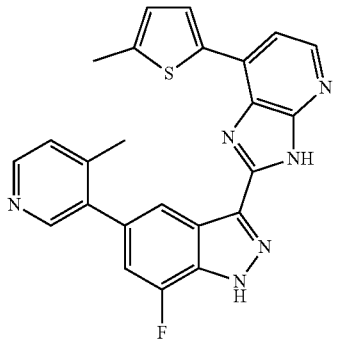

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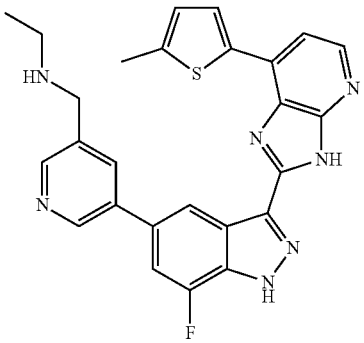

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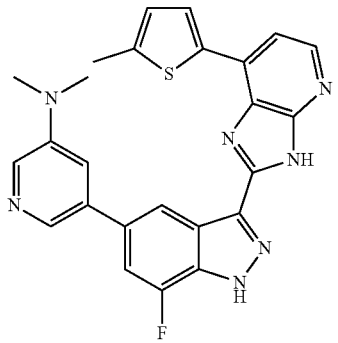

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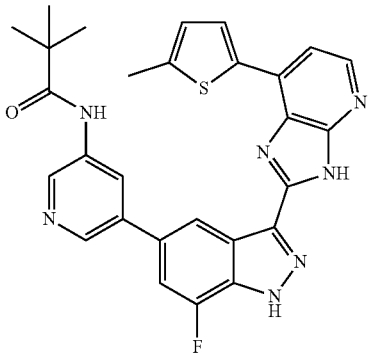

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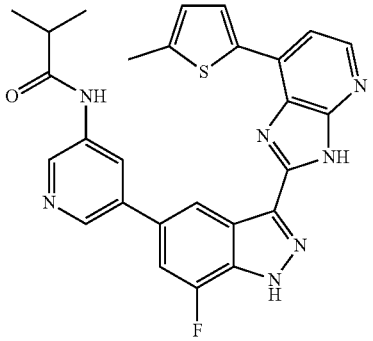

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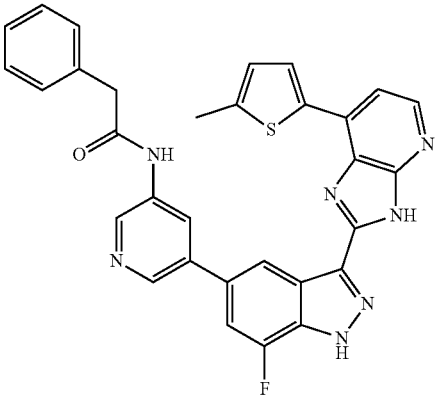

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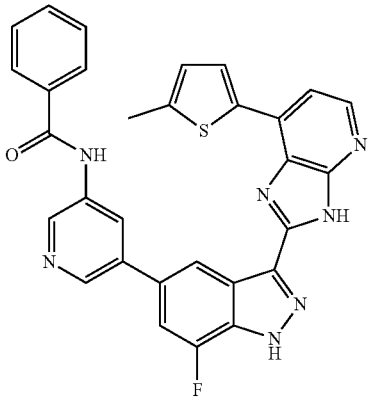

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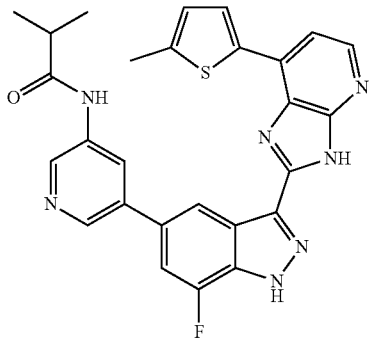
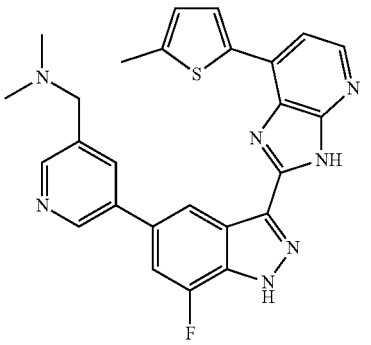
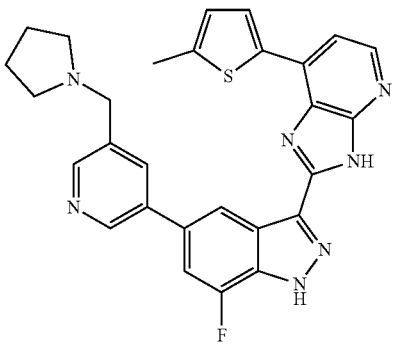
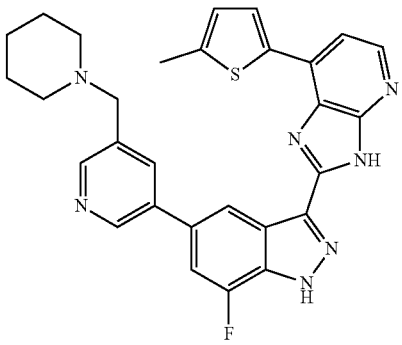
844	
845	
846	
847	

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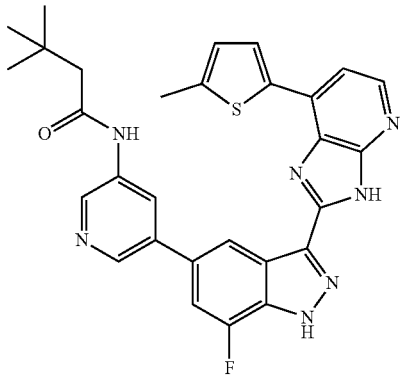
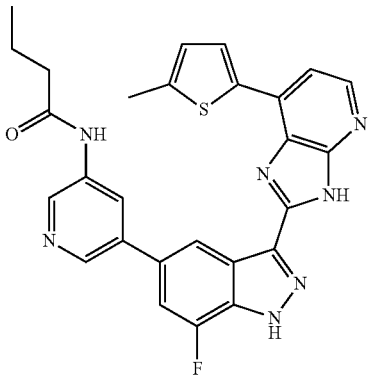
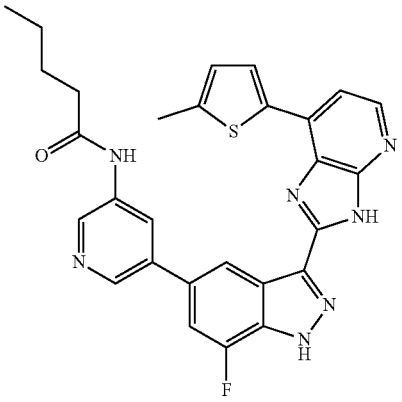
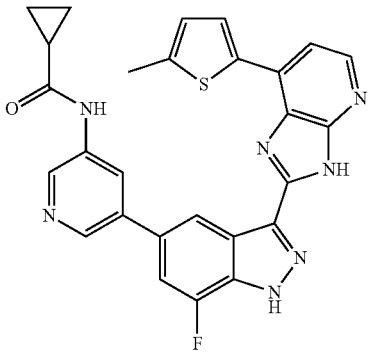
848	
849	
850	
851	

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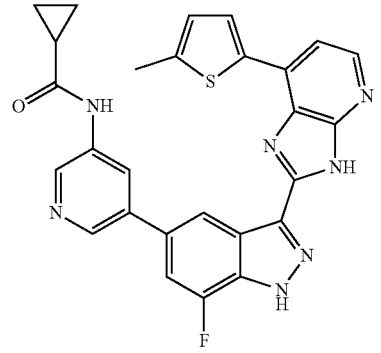

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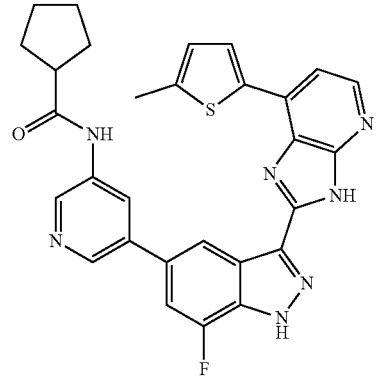

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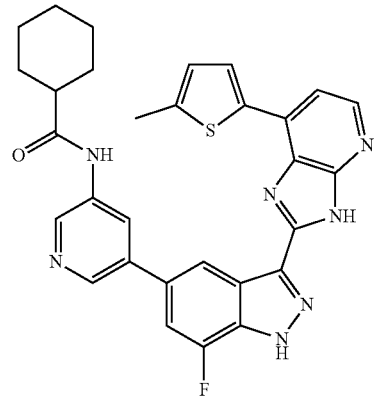

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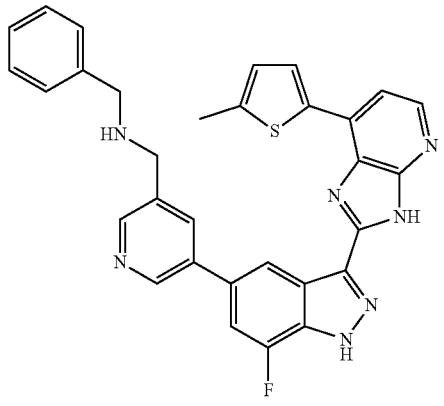

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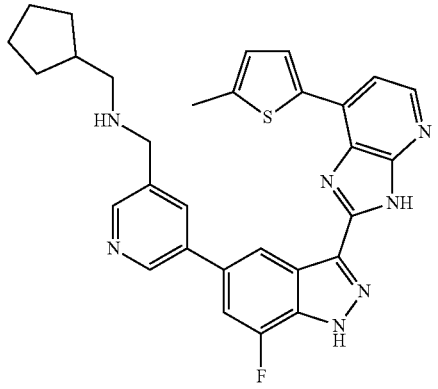

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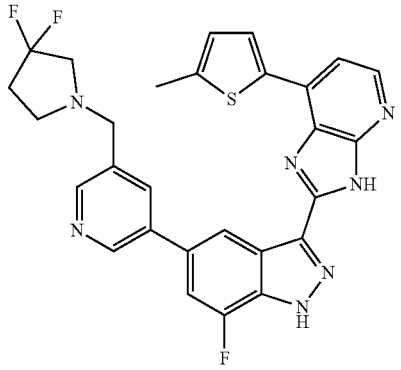

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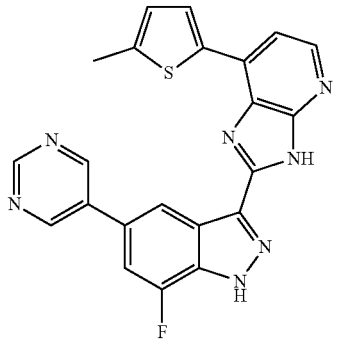

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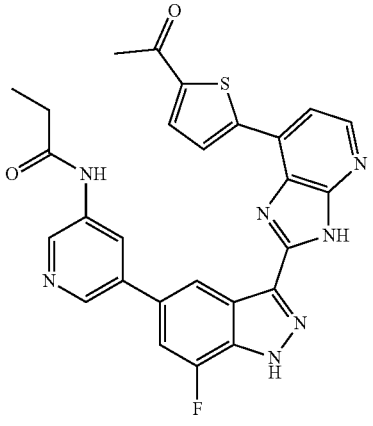

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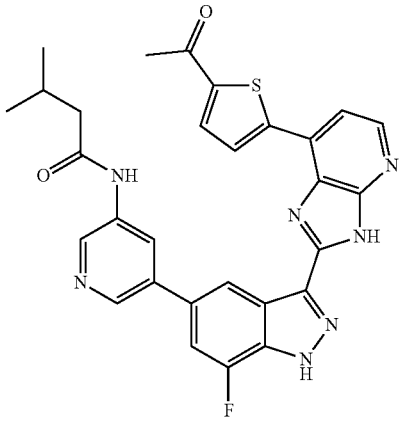
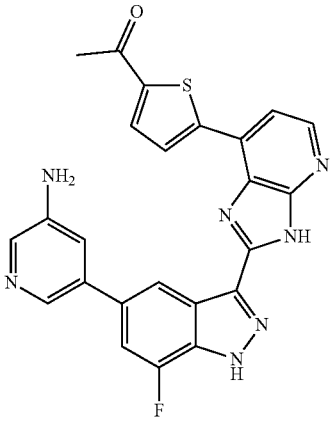
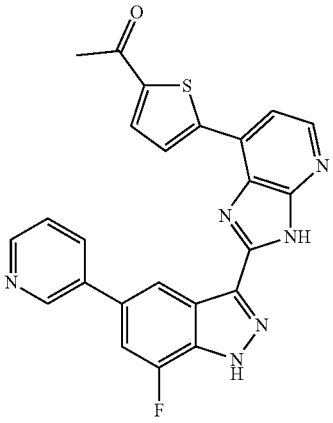
860	
861	
862	

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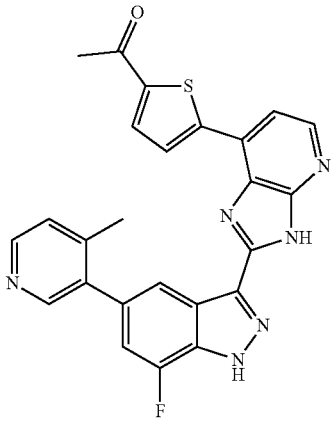
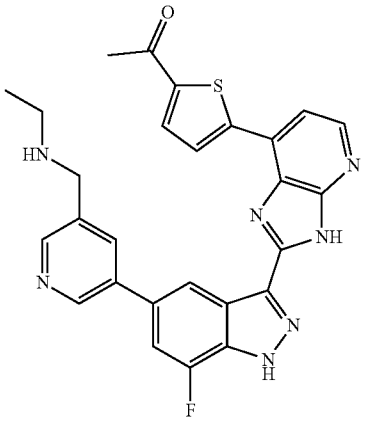
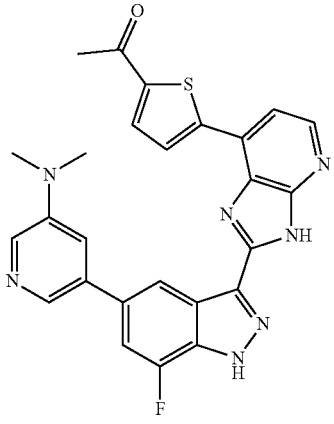
863	
864	
865	

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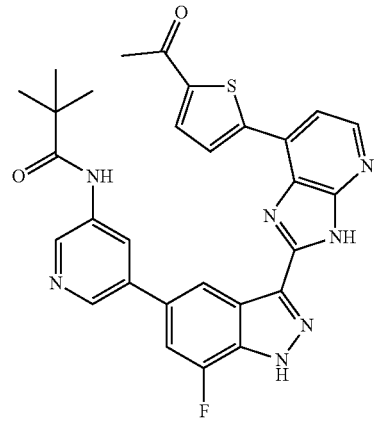
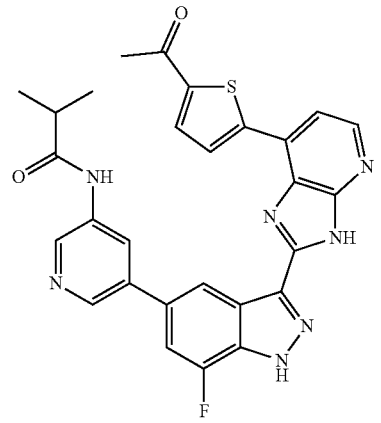
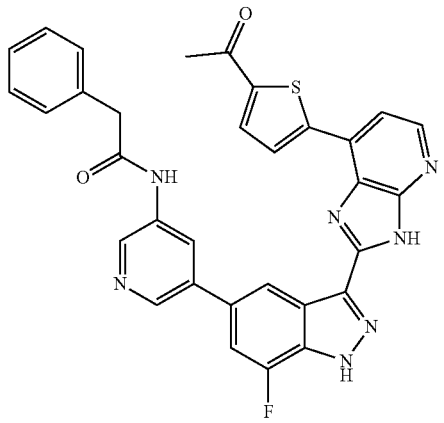
866	
867	
868	

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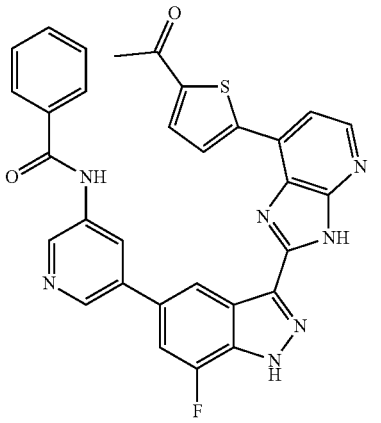
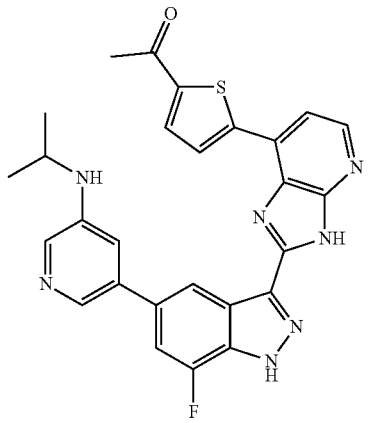
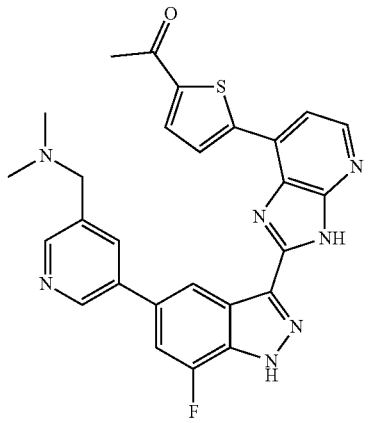
869	
870	
871	

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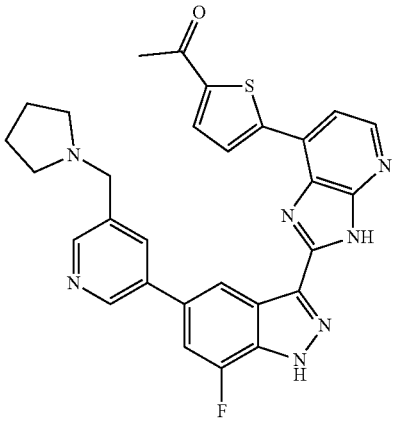
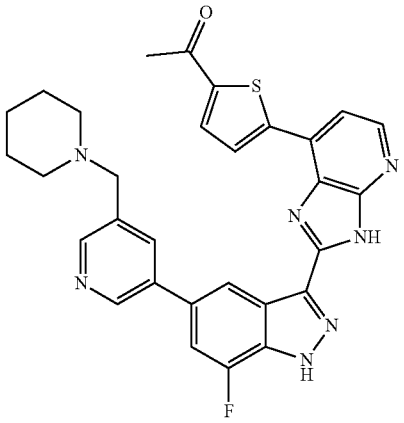
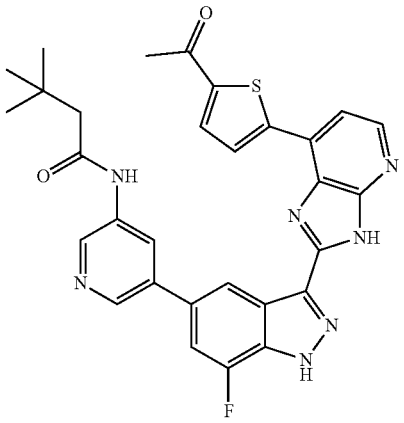
872	
873	
874	

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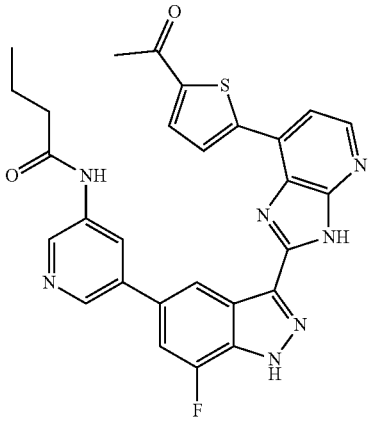
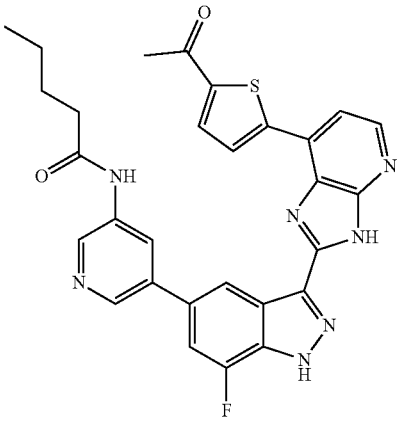
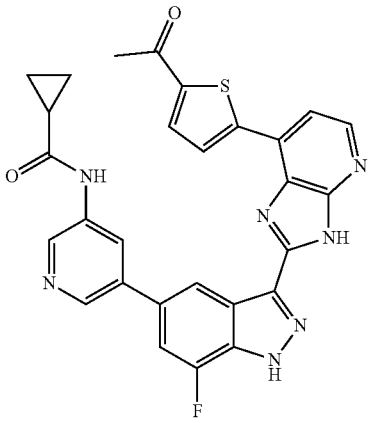
875	
876	
877	

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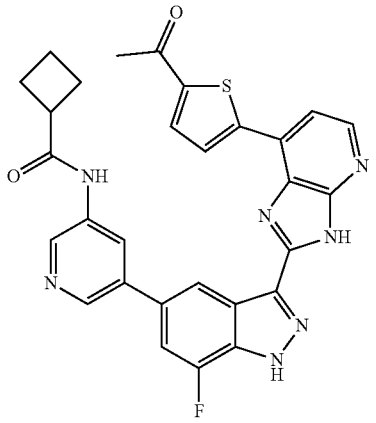
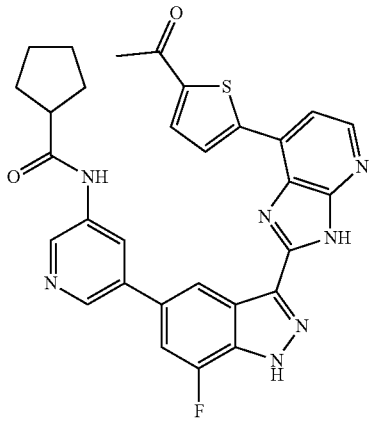
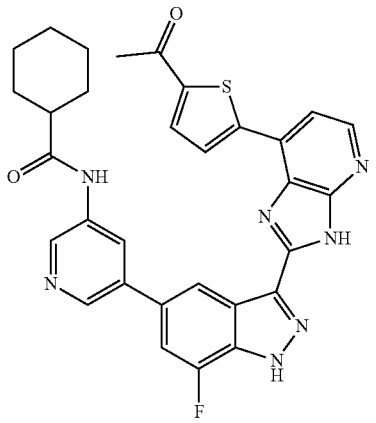
878	
879	
880	

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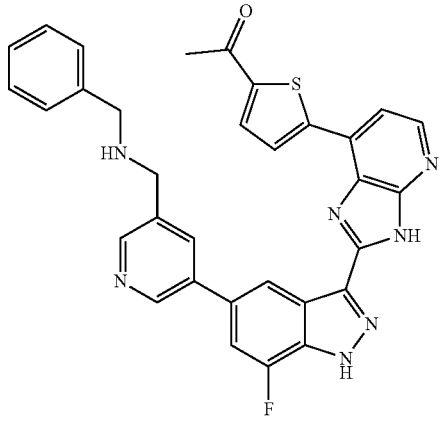
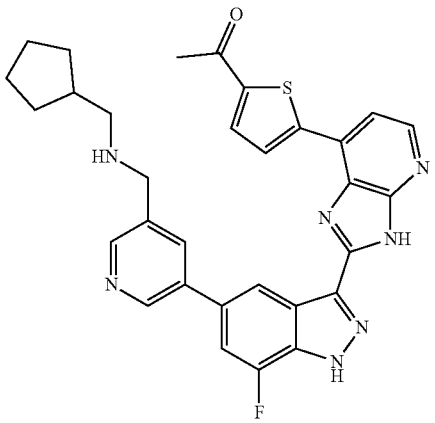
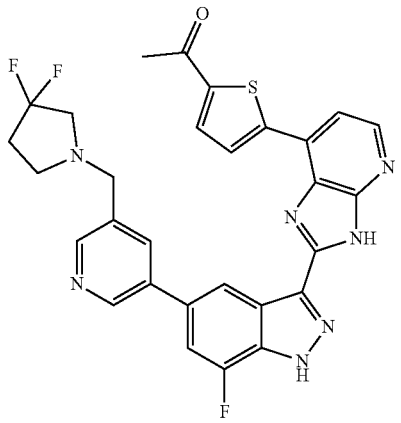
881	
882	
883	

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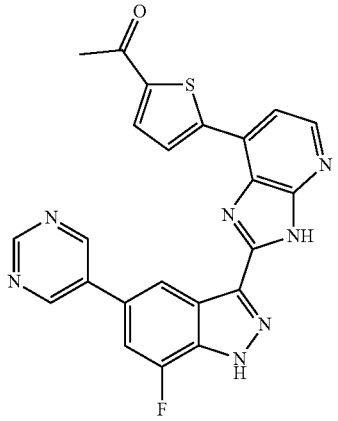
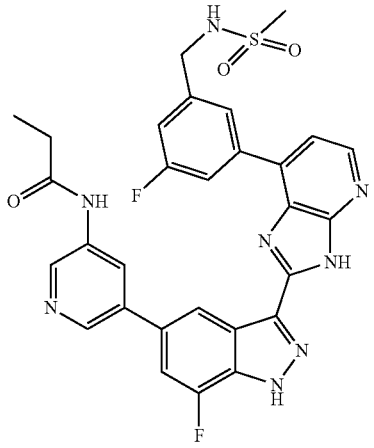
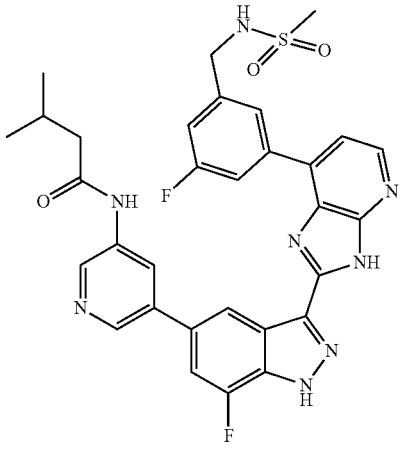
884	
885	
886	

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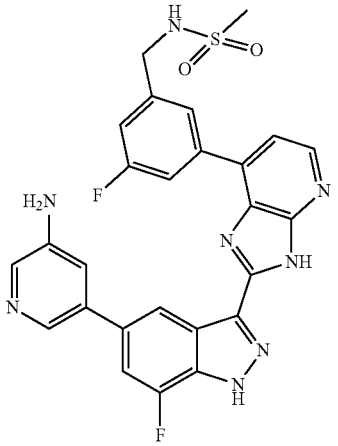
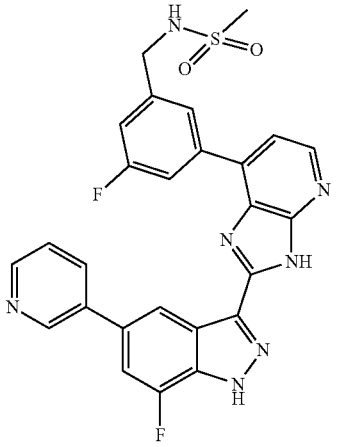
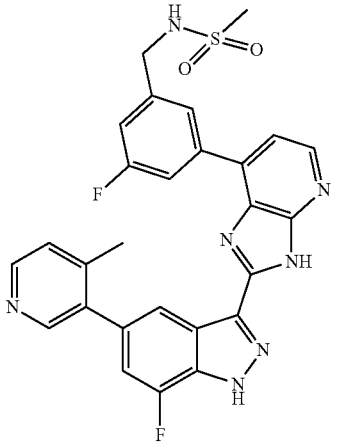
887	
888	
889	

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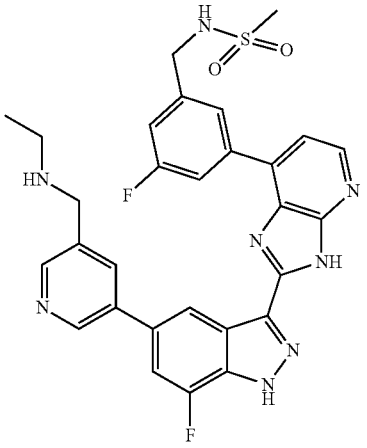
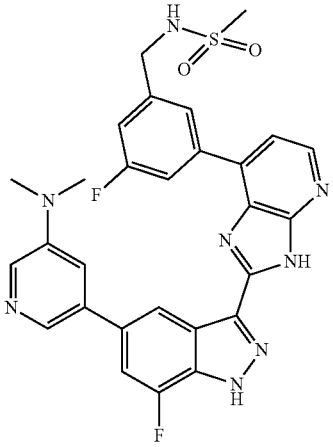
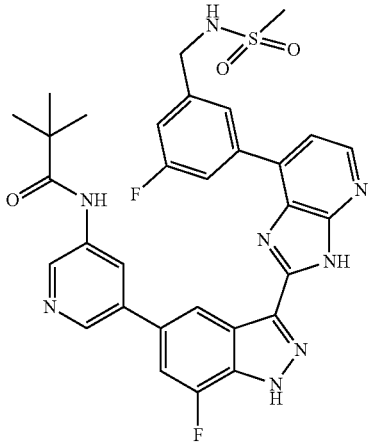
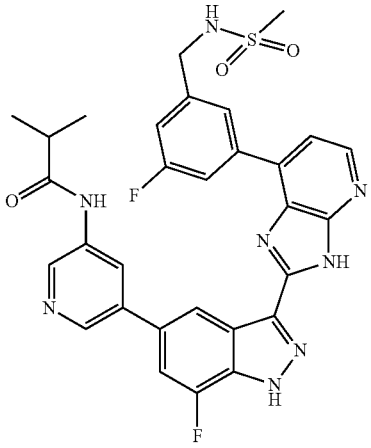
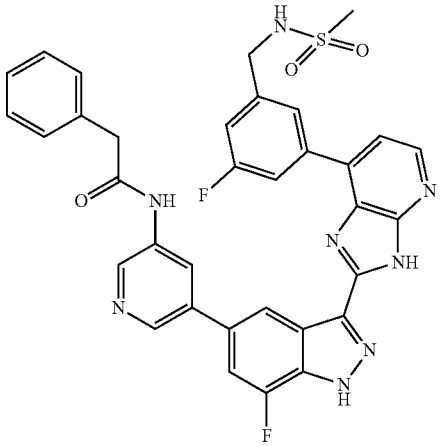
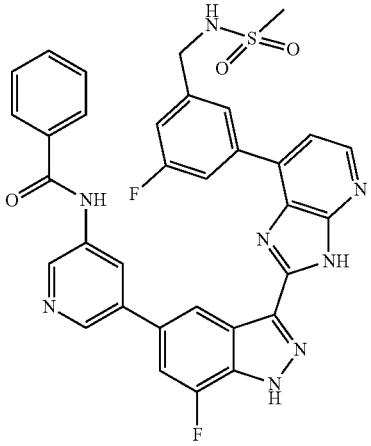
890	
891	
892	

TABLE 1-continued

893	
894	
895	

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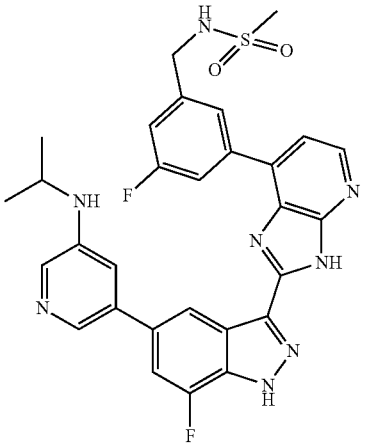
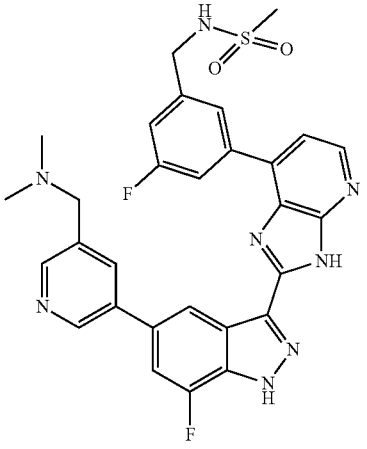
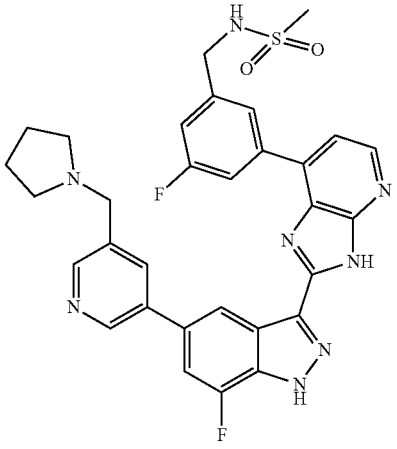
896	
897	
898	

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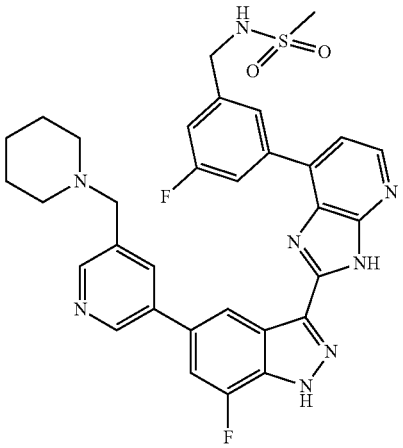
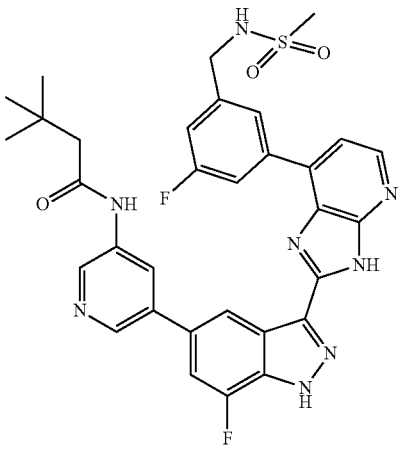
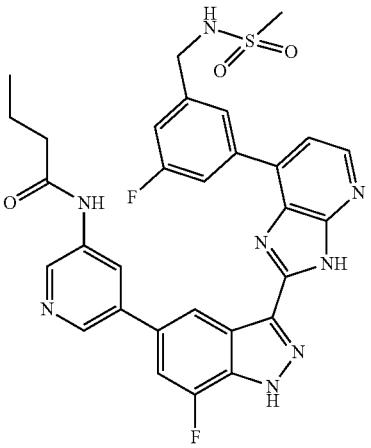
899	
900	
901	

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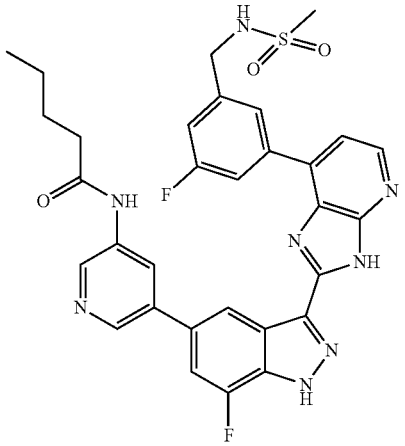
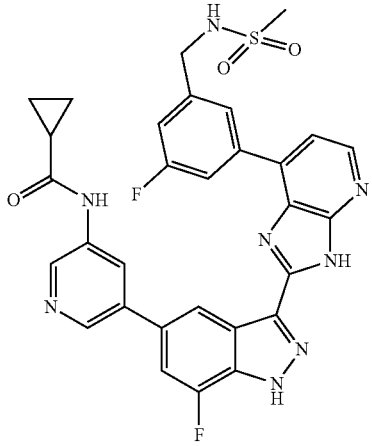
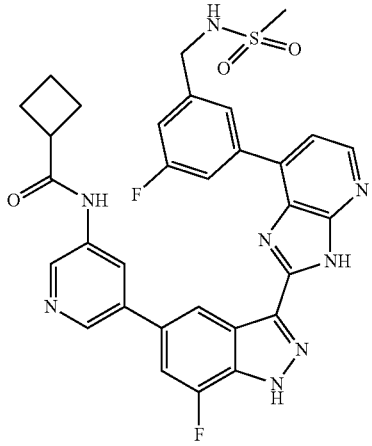
902	
903	
904	

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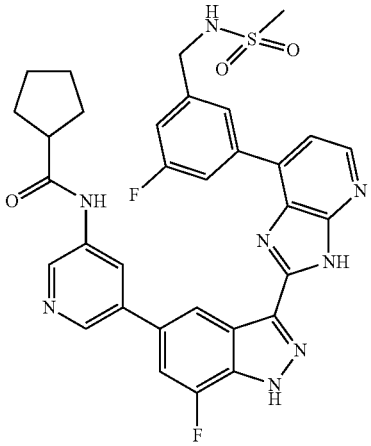
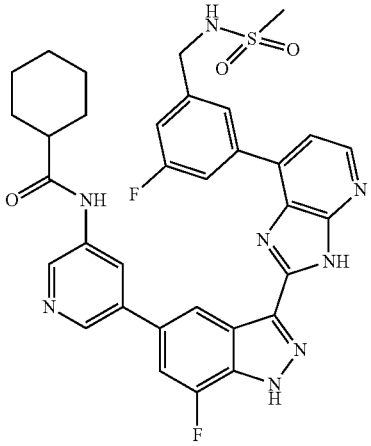
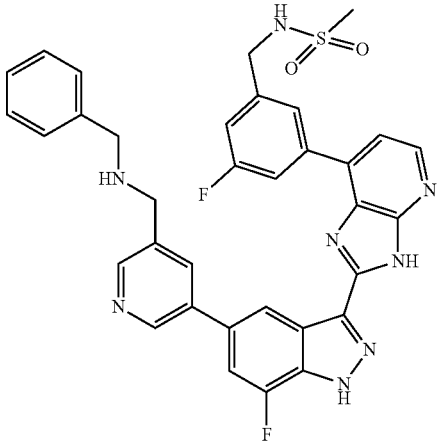
905	
906	
907	

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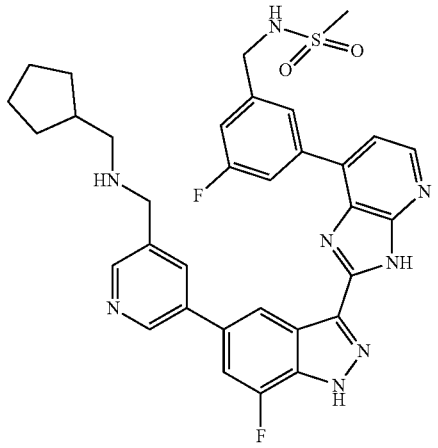
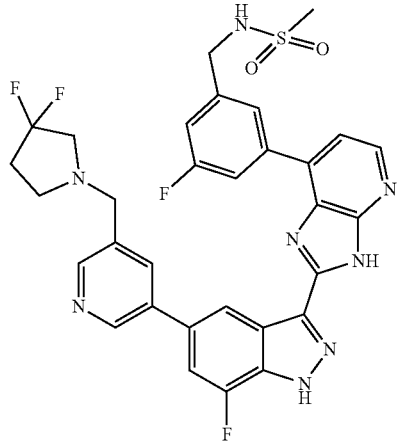
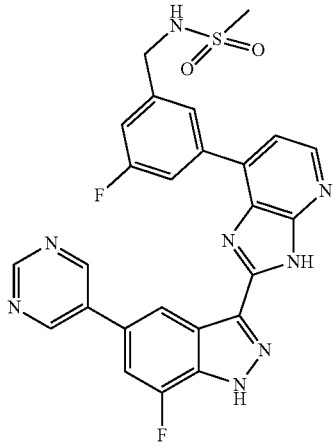
908	
909	
910	

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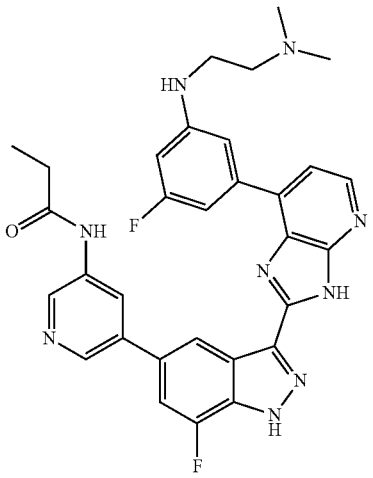
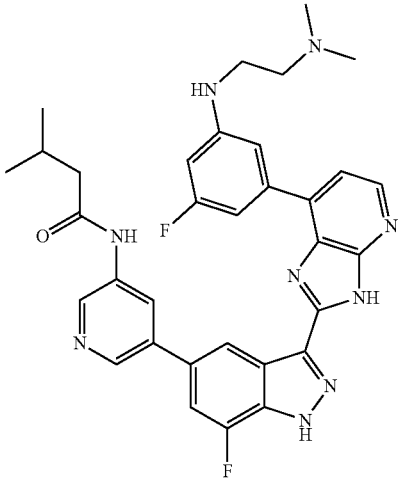
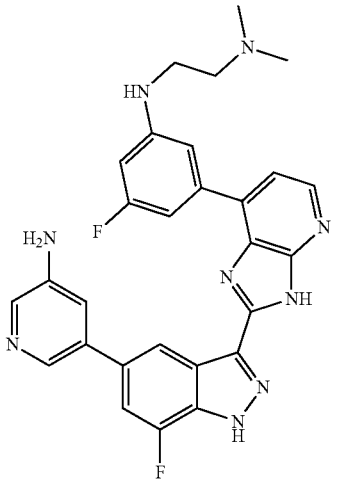
911	
912	
913	

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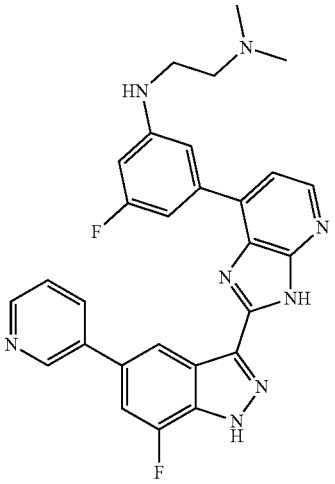

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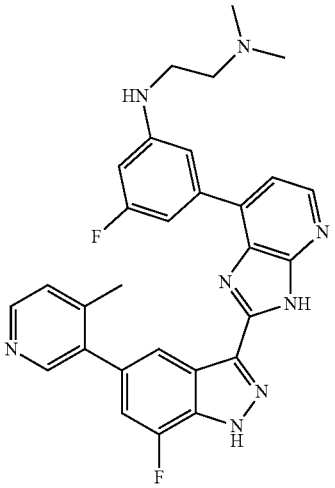

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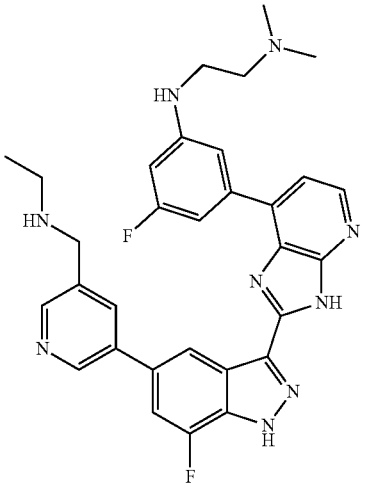

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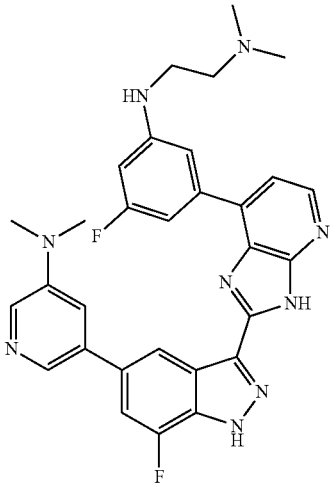

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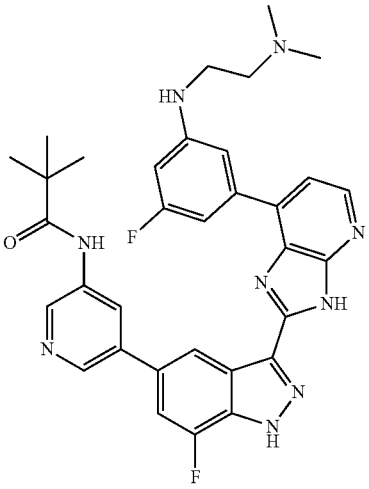

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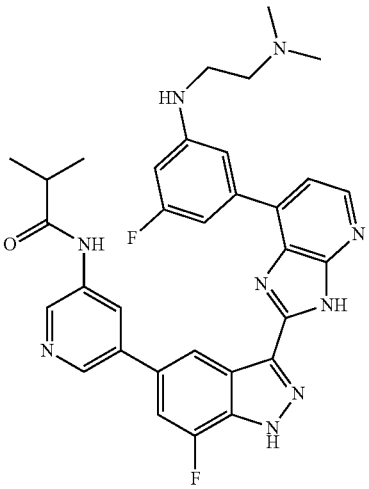

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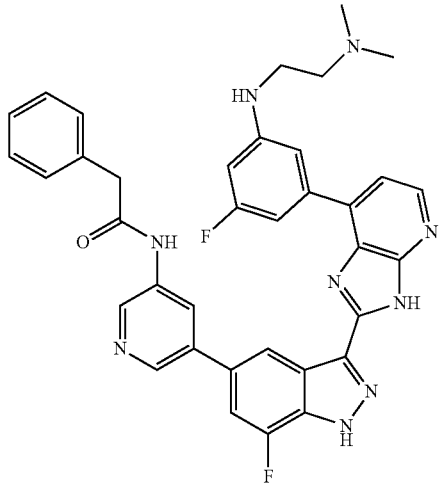
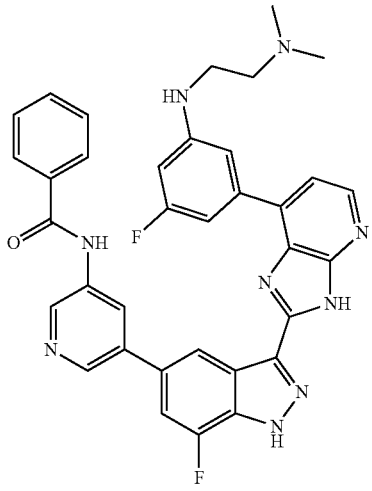
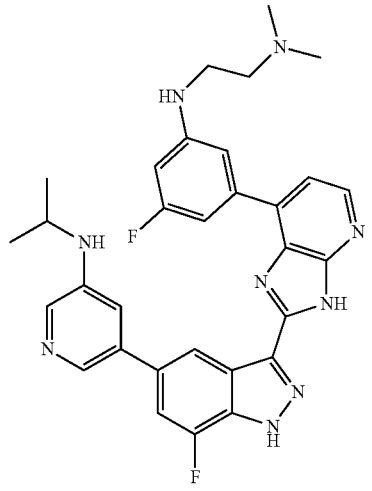
920	
921	
922	

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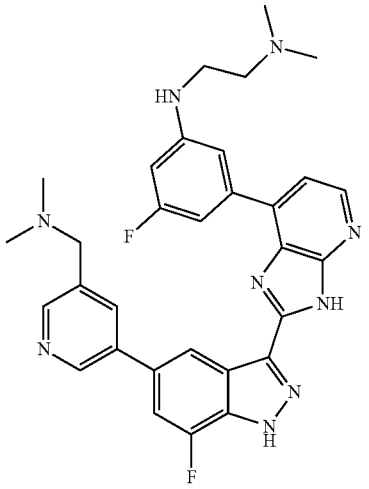
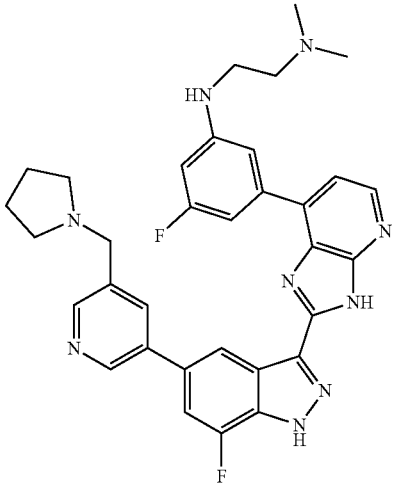
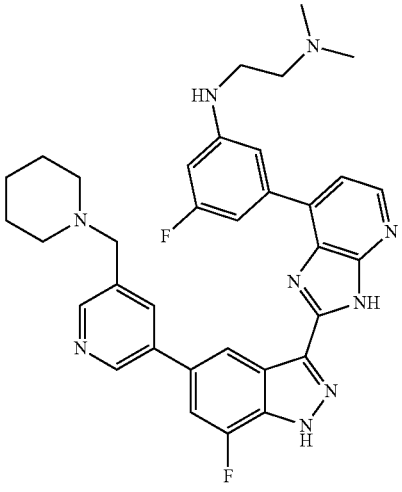
923	
924	
925	

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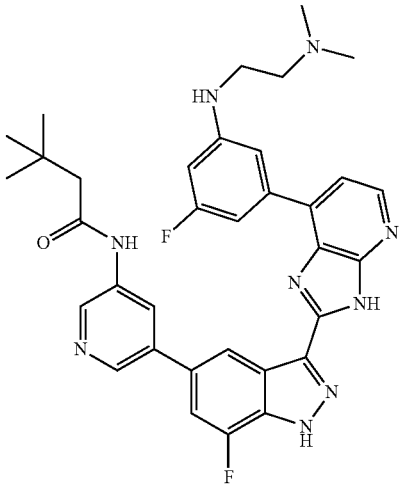

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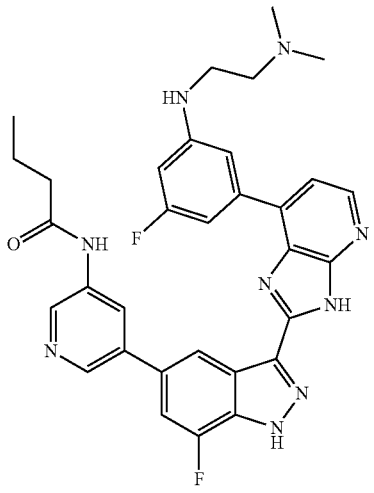

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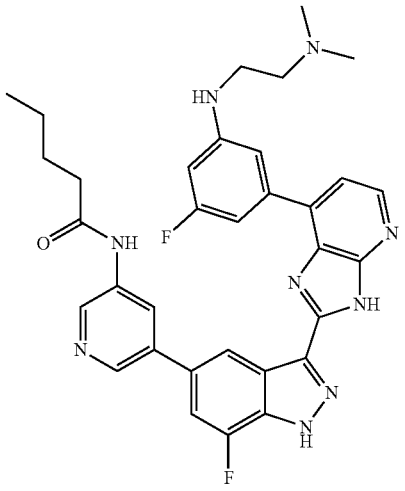

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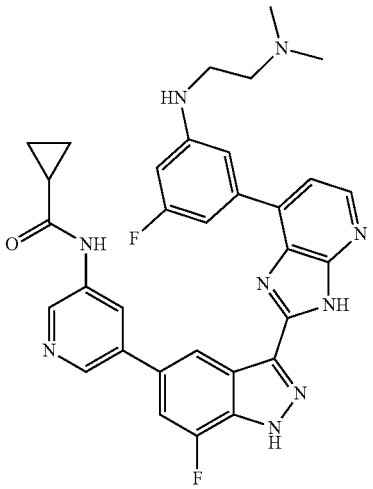

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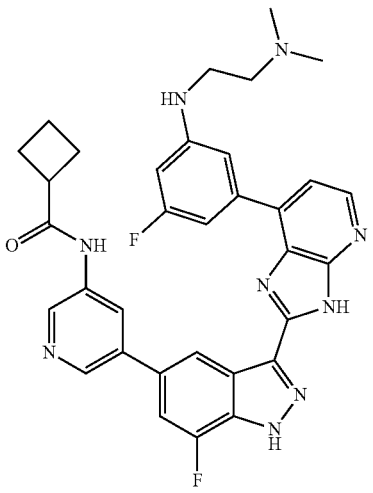

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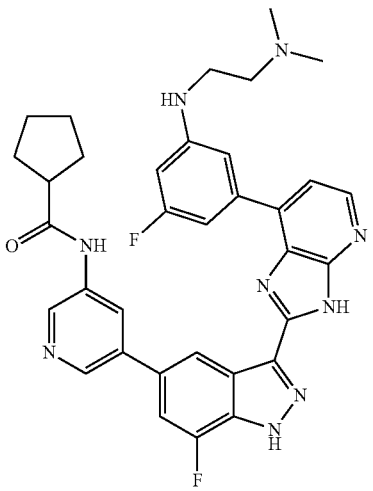

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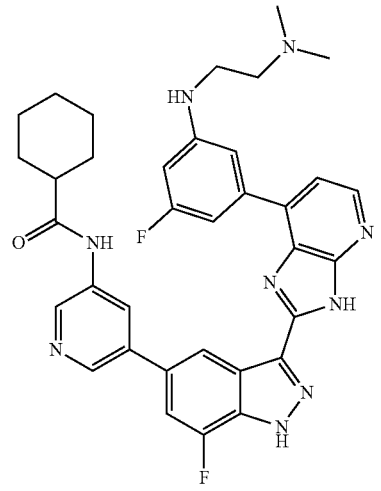
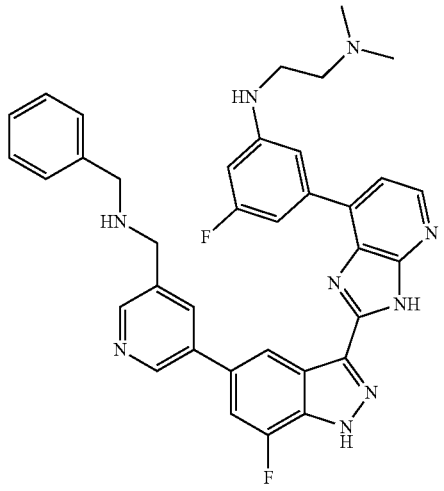
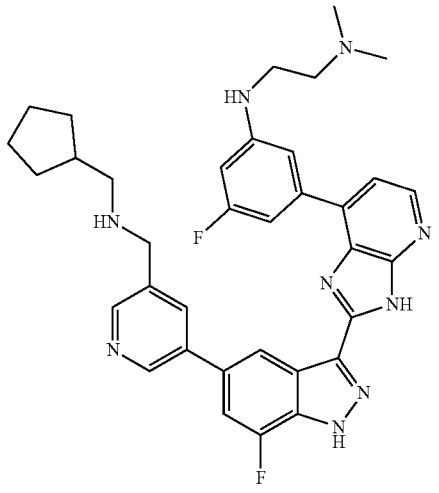
932	
933	
934	

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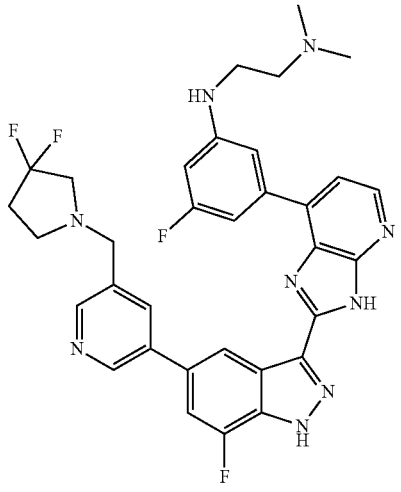
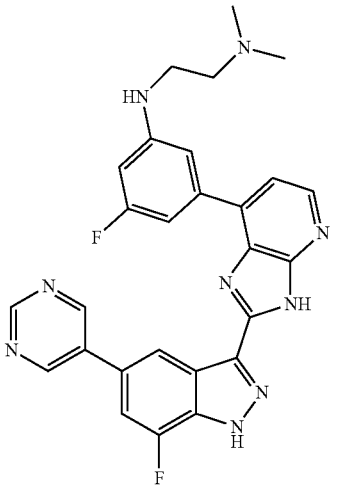
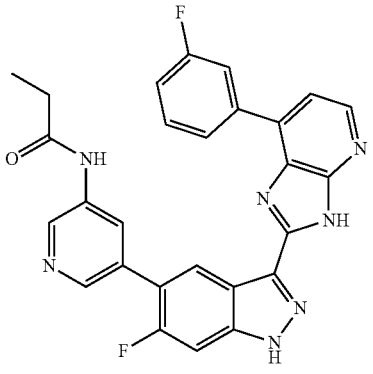
935	
936	
937	

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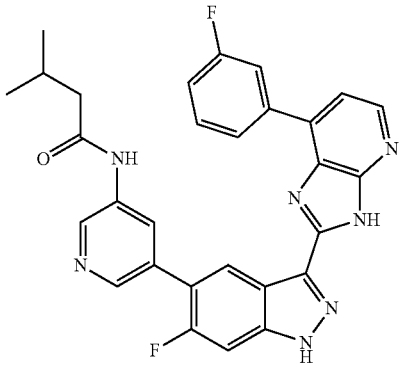
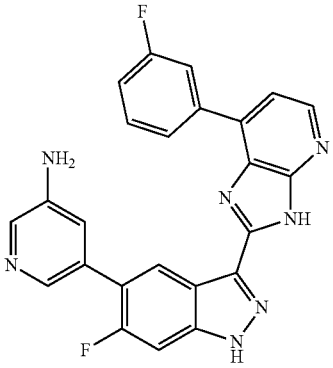
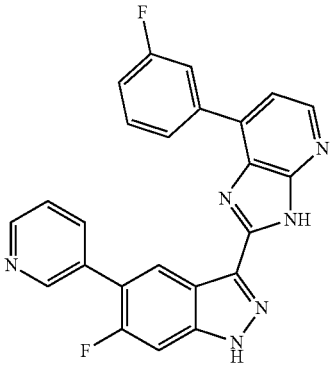
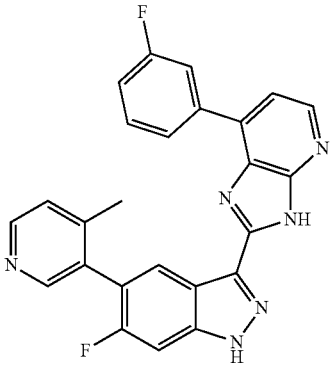
938	
939	
940	
941	

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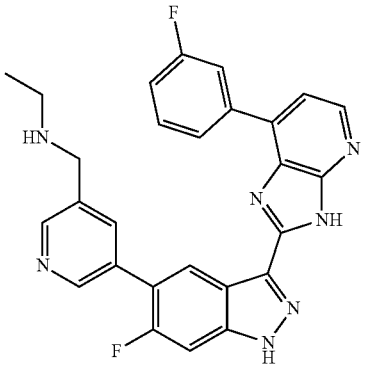
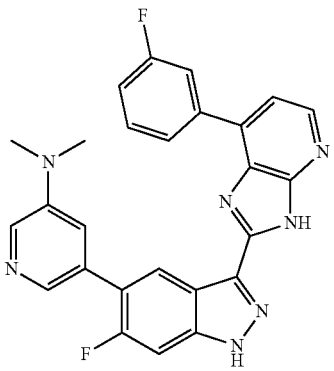
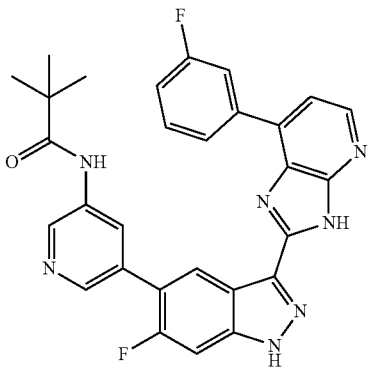
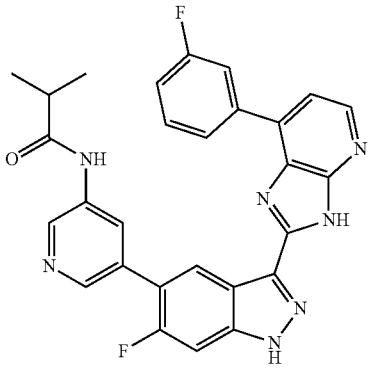
942	
943	
944	
945	

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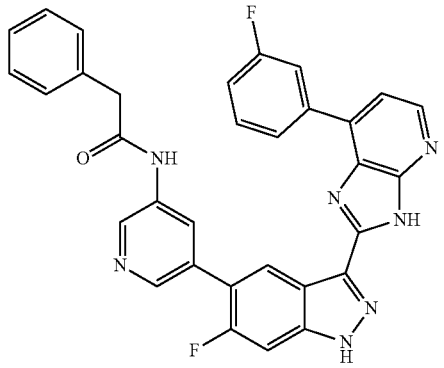

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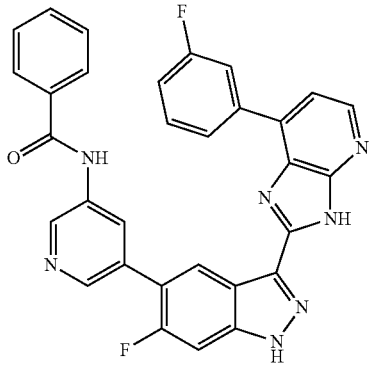

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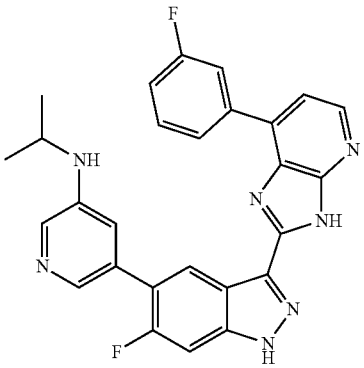

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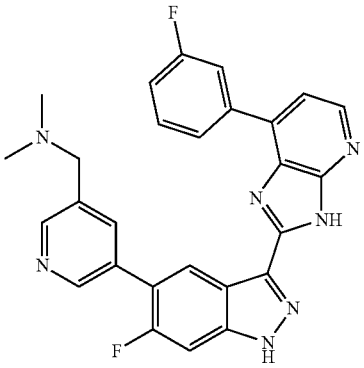

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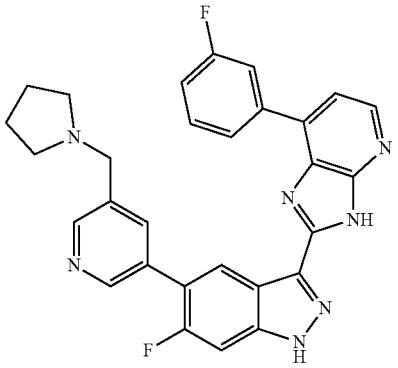

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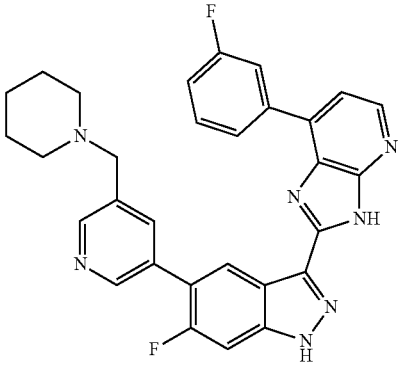

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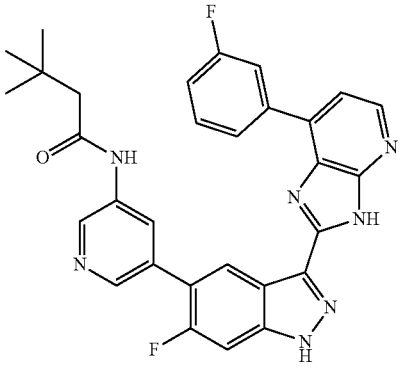

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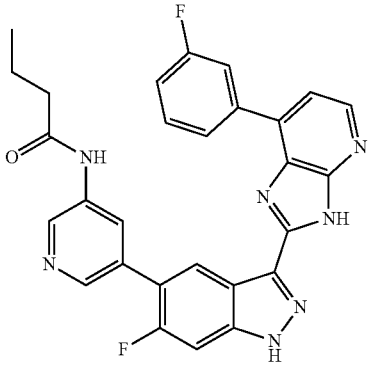

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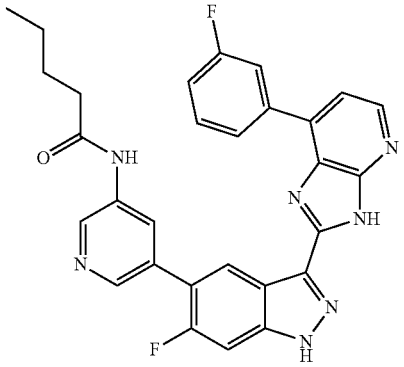
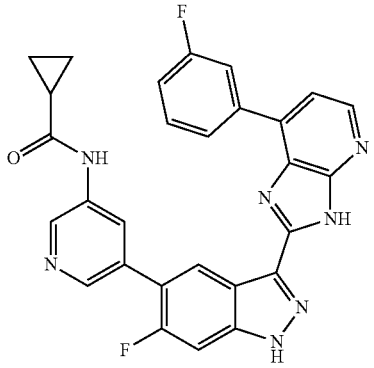
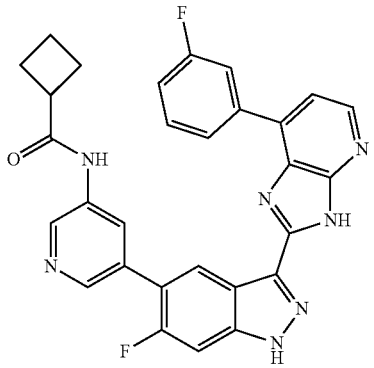
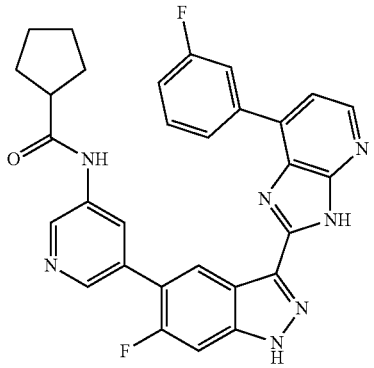
954	
955	
956	
957	

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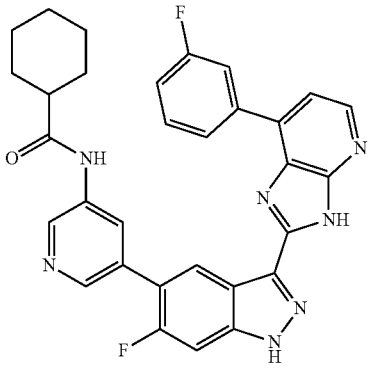
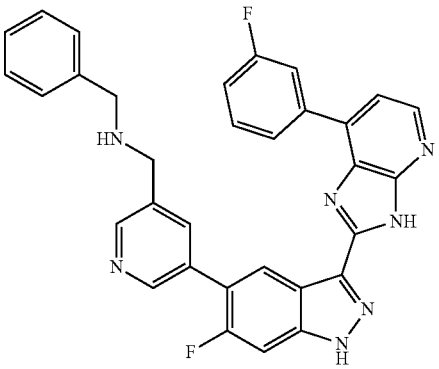
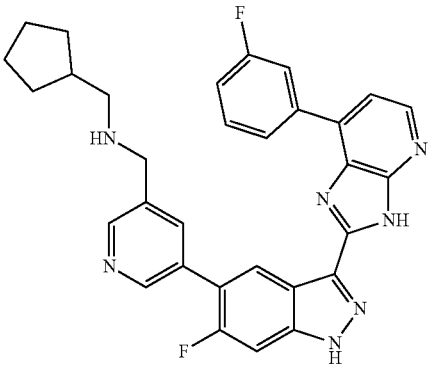
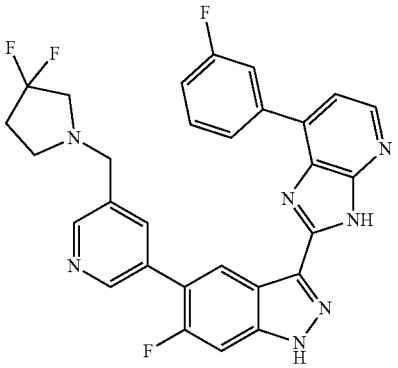
958	
959	
960	
961	

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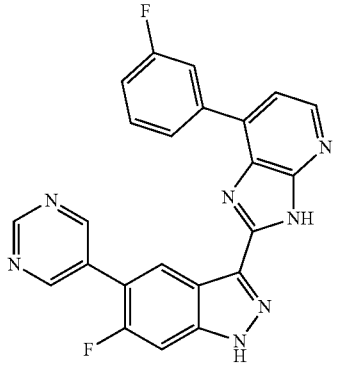

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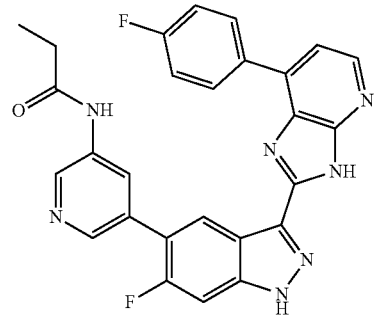

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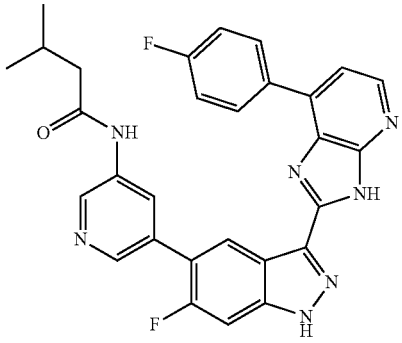

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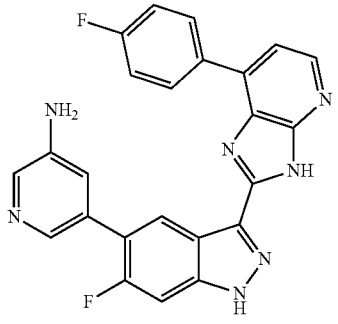

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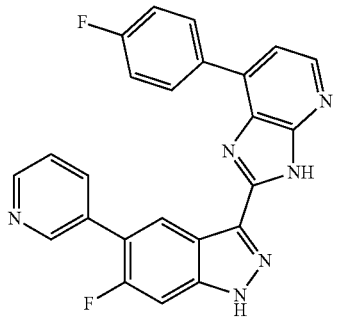

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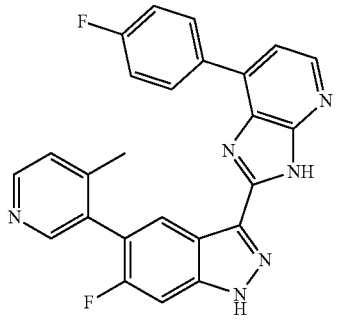

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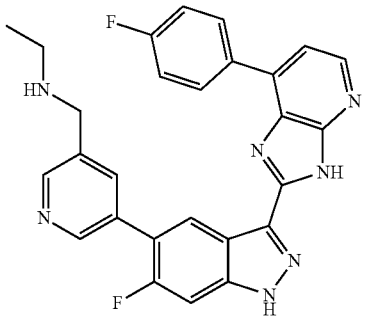

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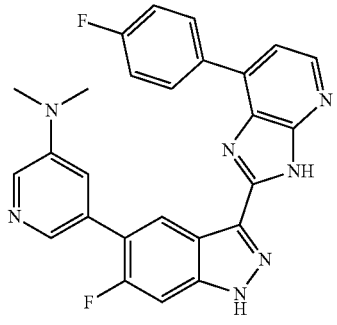

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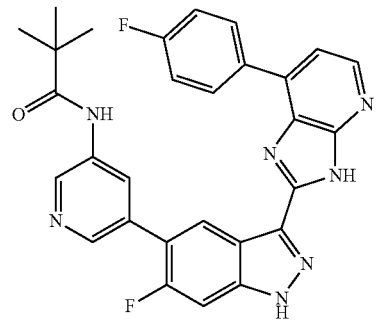

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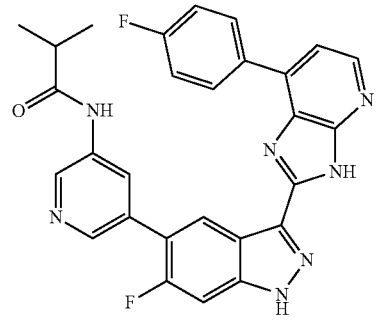

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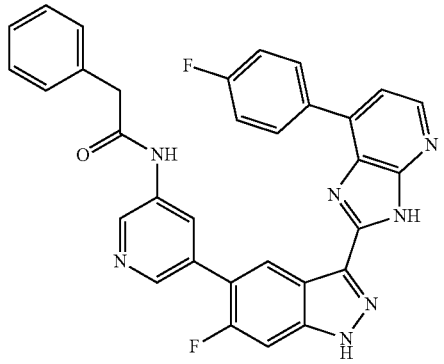

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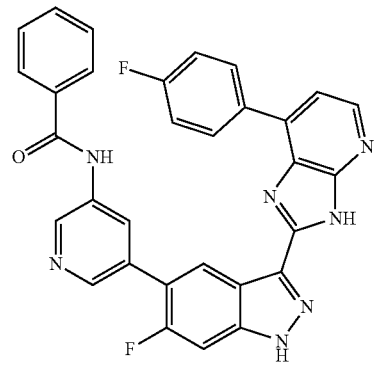

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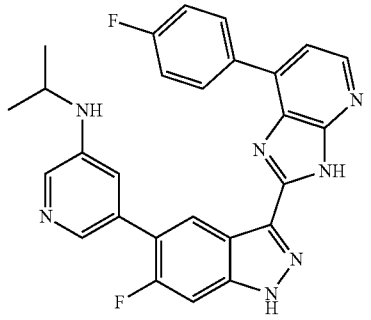

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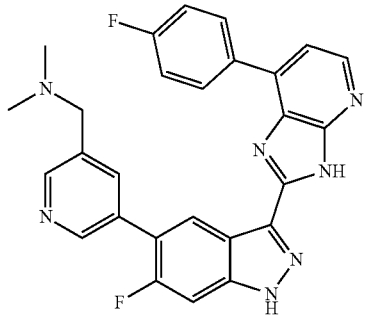

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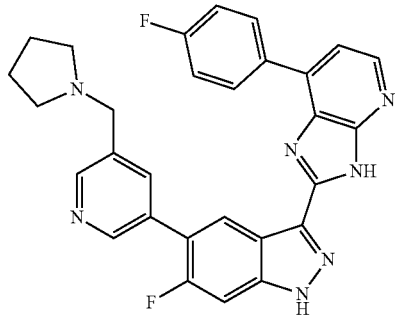

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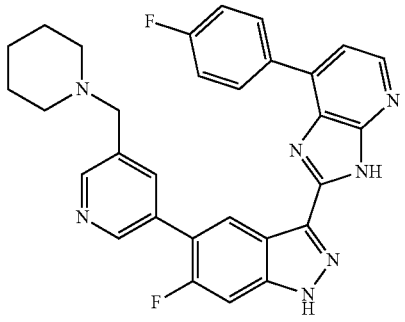

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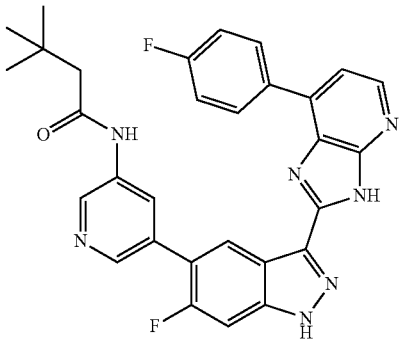

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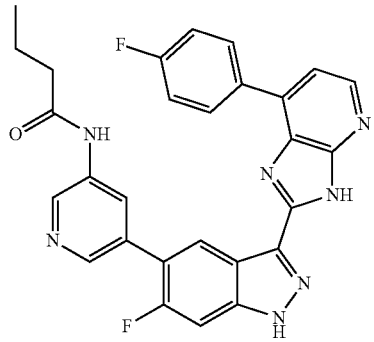

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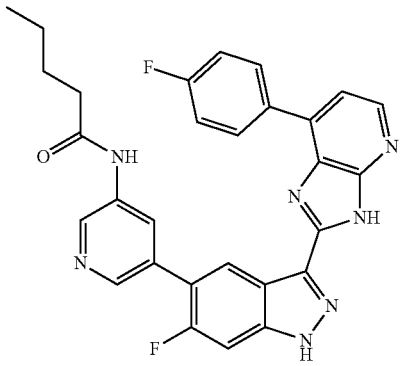

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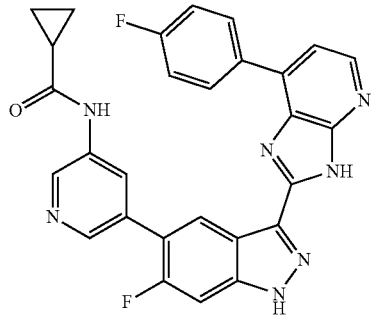

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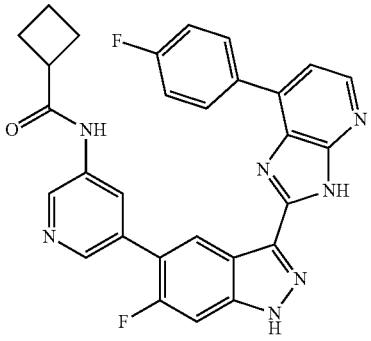

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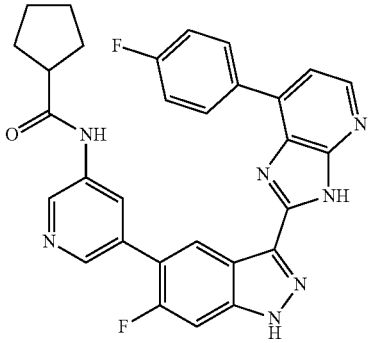

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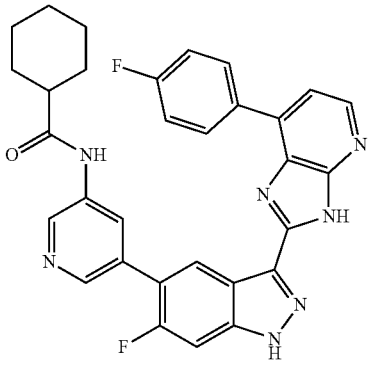

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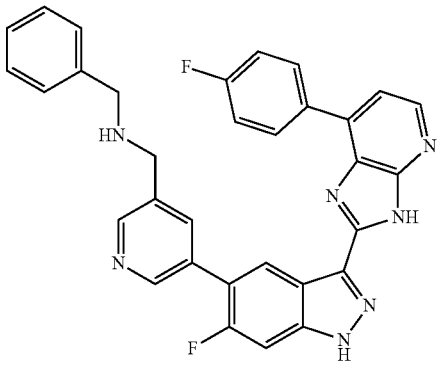

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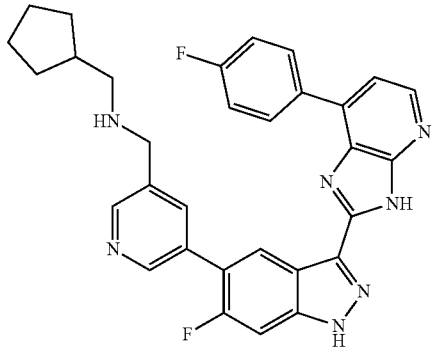

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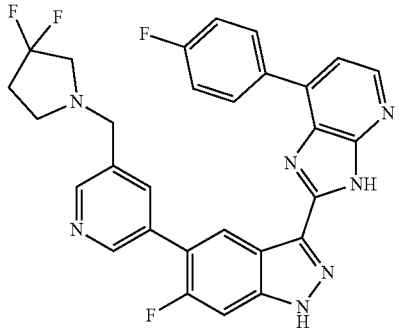

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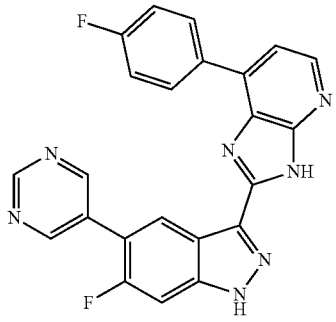

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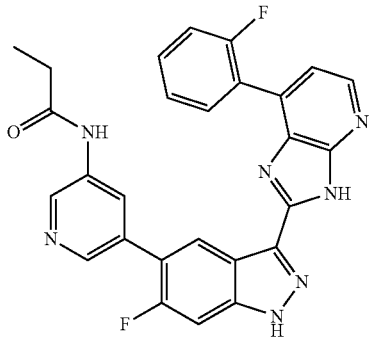

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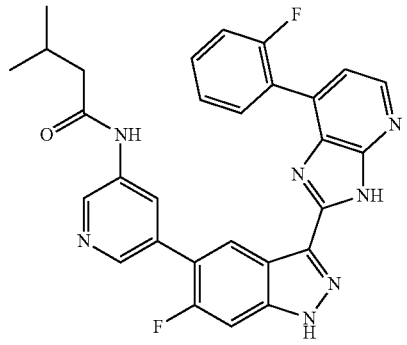

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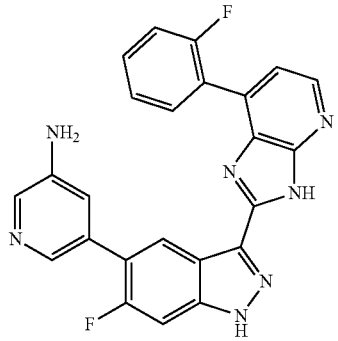

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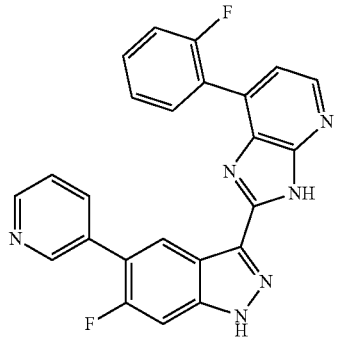

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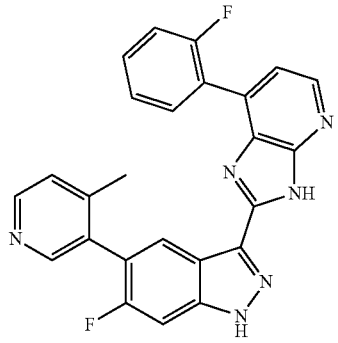

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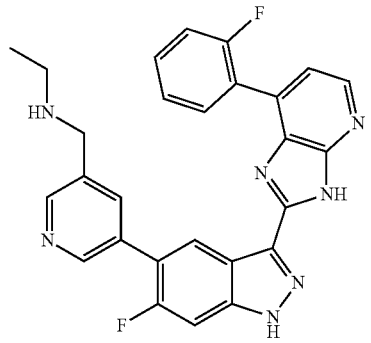

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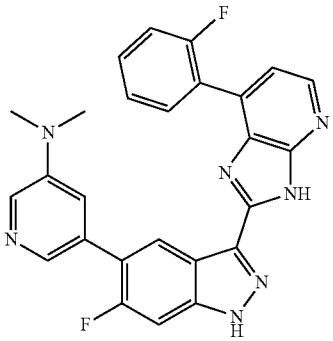

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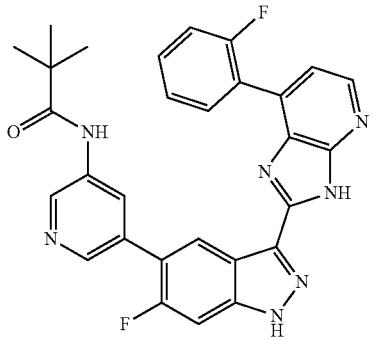

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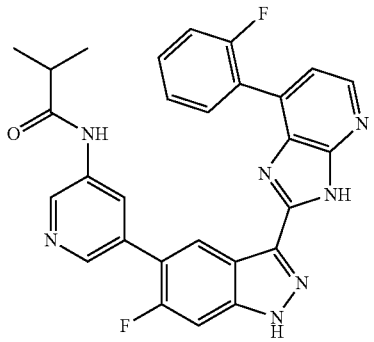

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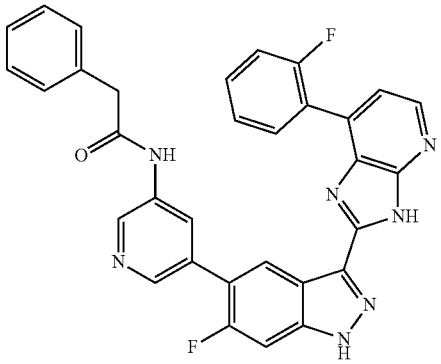

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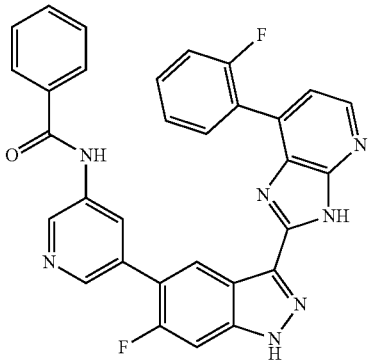

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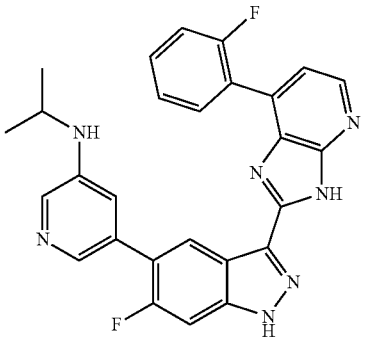

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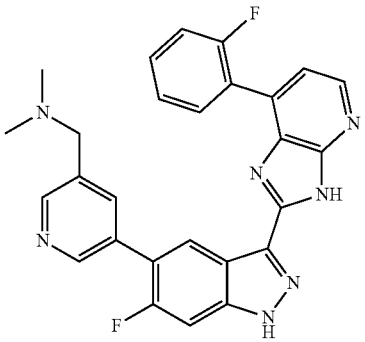

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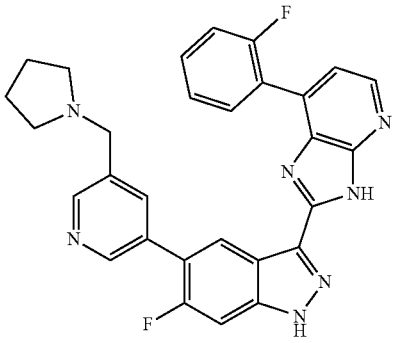
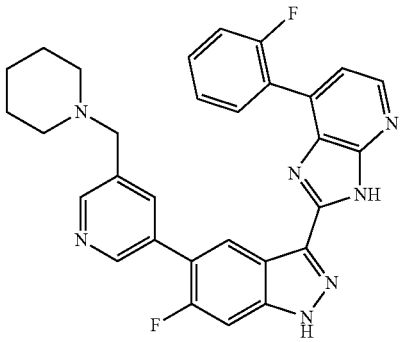
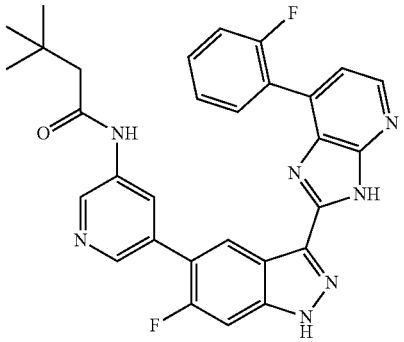
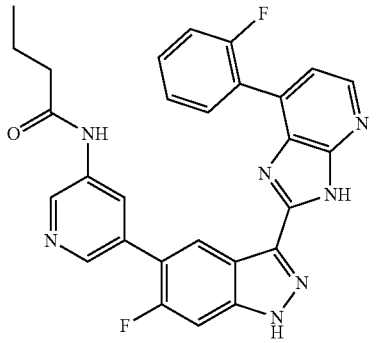
1002	
1003	
1004	
1005	

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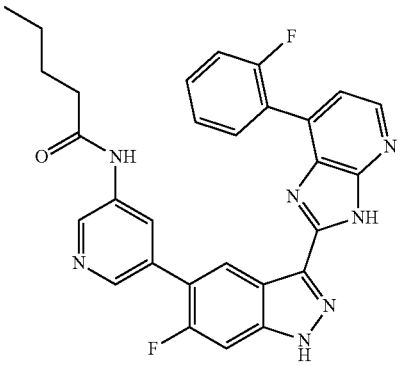
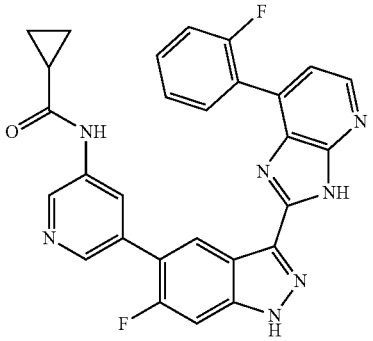
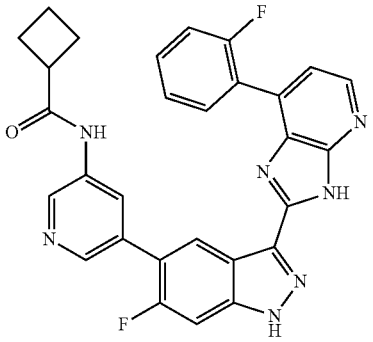
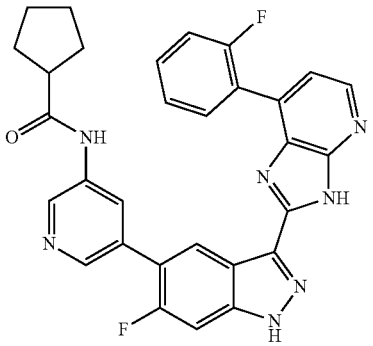
1006	
1007	
1008	
1009	

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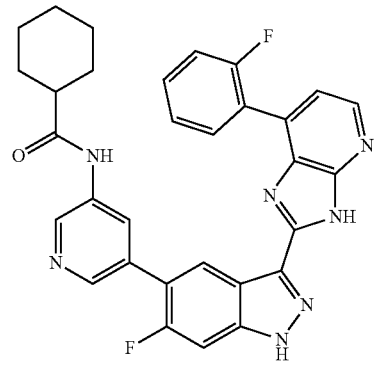
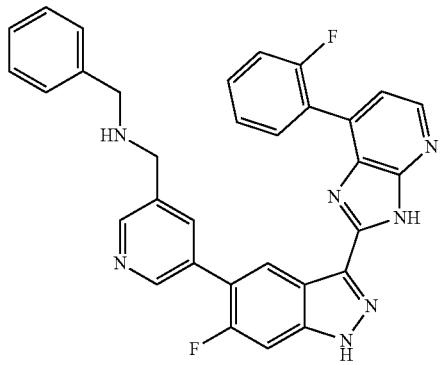
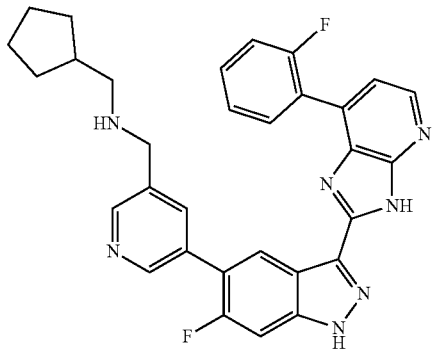
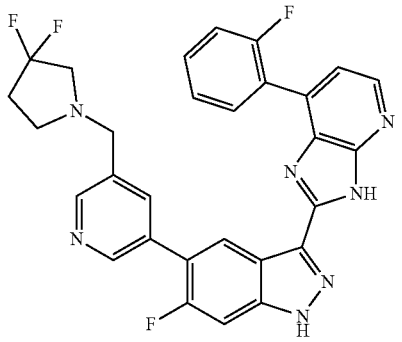
1010	
1011	
1012	
1013	

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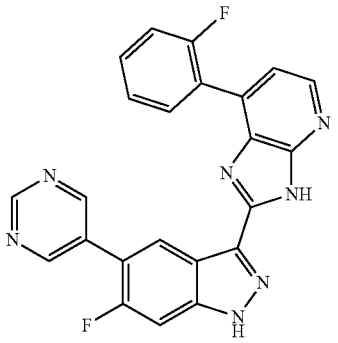
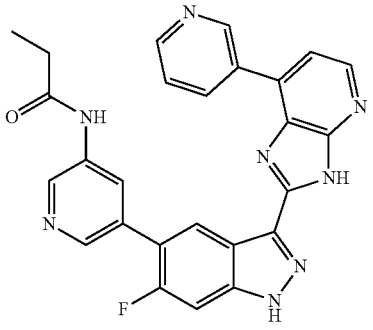
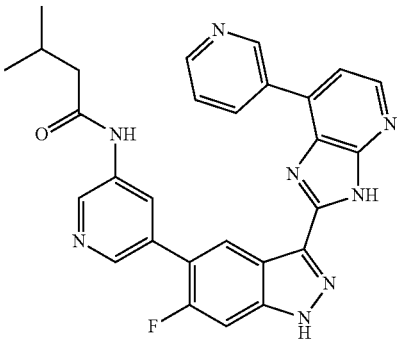
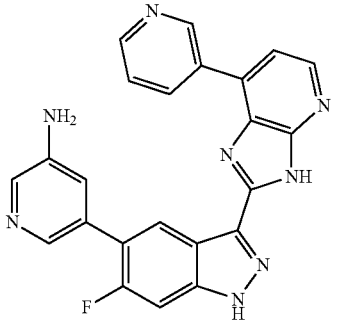
1014	
1015	
1016	
1017	

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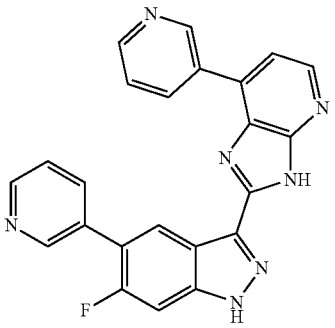
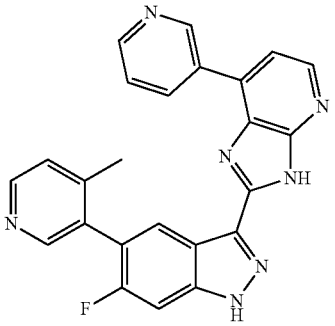
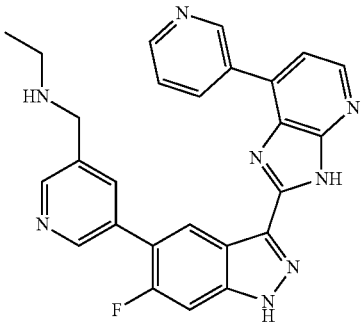
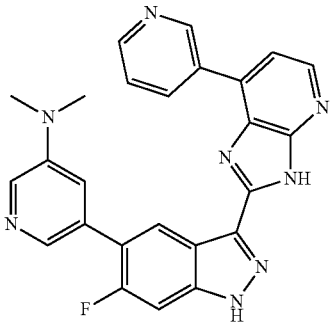
1018	
1019	
1020	
1021	

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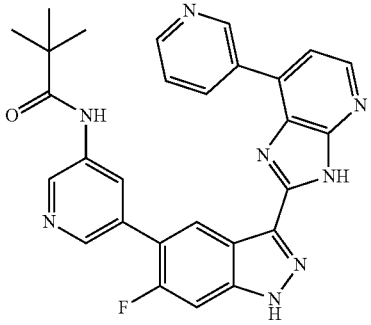
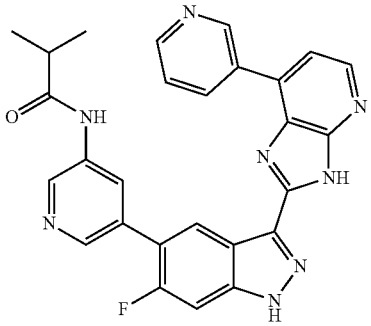
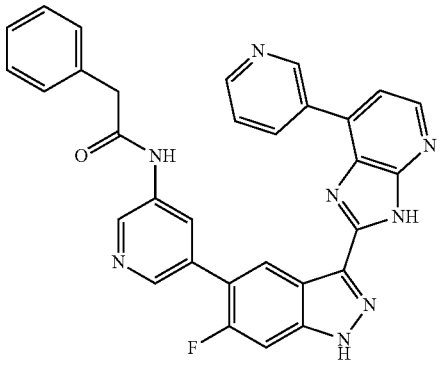
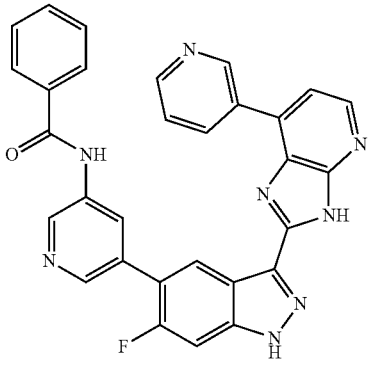
1022	
1023	
1024	
1025	

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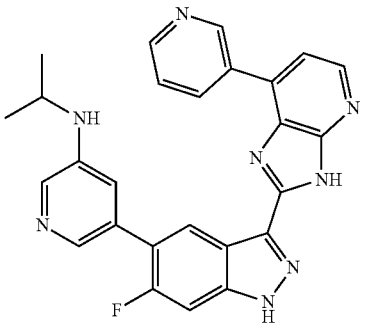
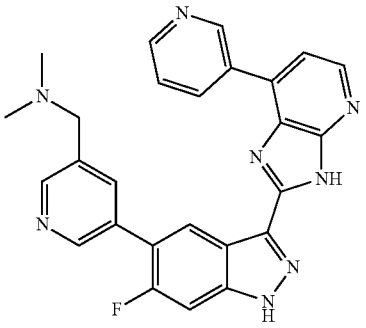
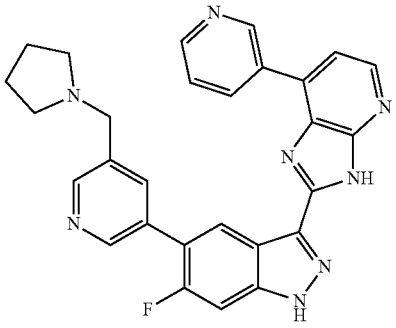
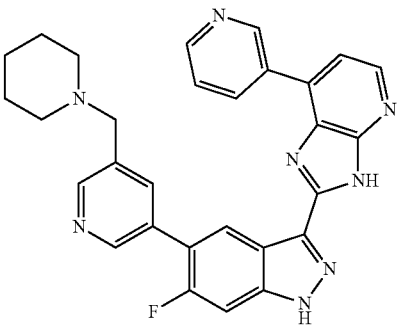
1026	
1027	
1028	
1029	

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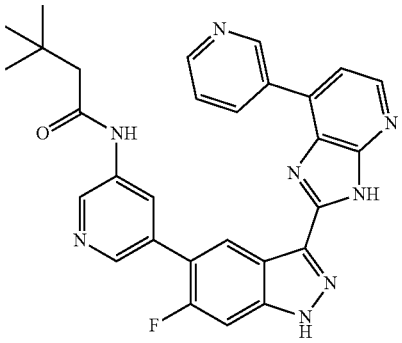
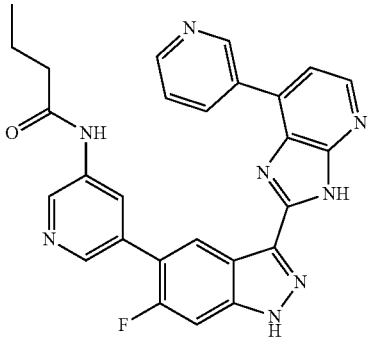
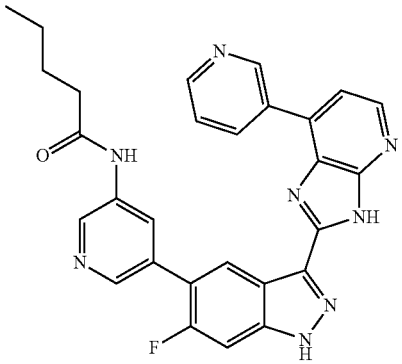
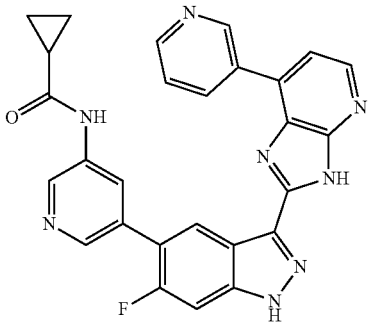
1030	
1031	
1032	
1033	

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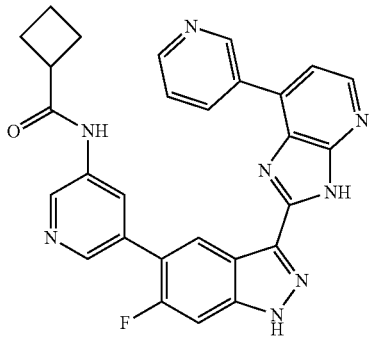
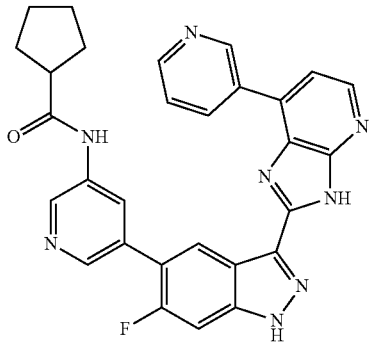
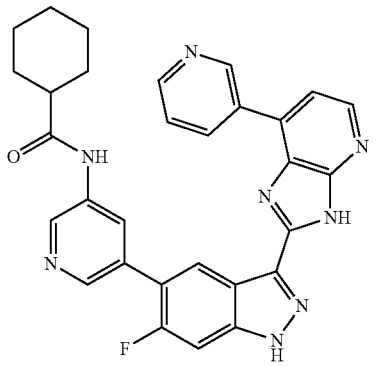
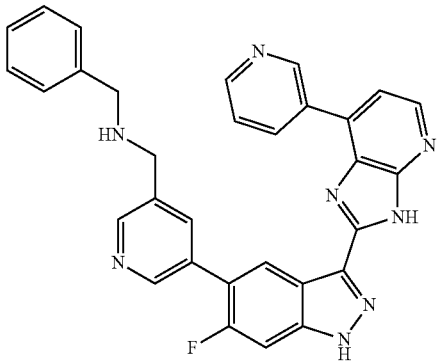
1034	
1035	
1036	
1037	

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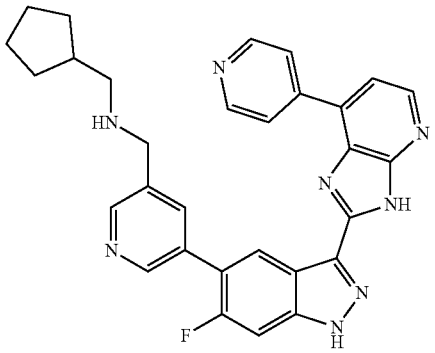
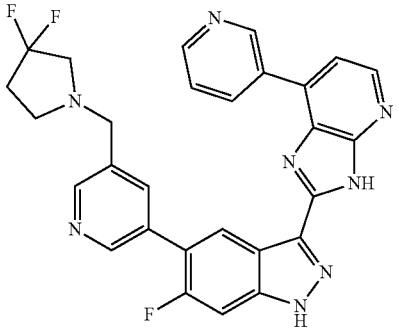
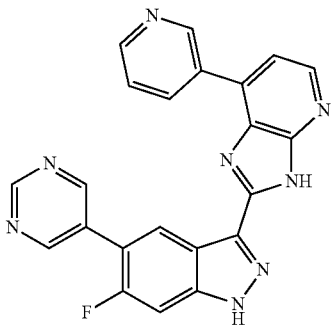
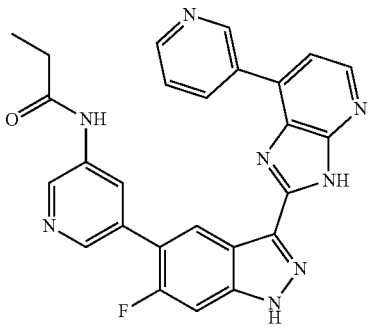
1038	
1039	
1040	
1041	

TABLE 1-continued

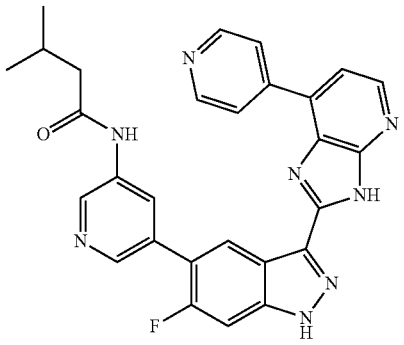
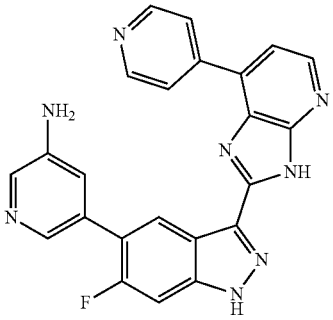
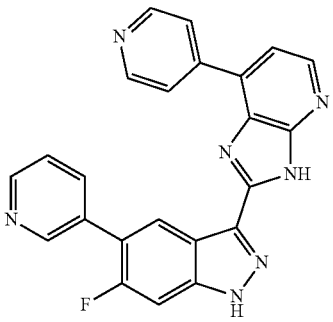
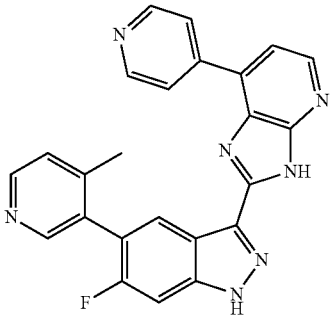
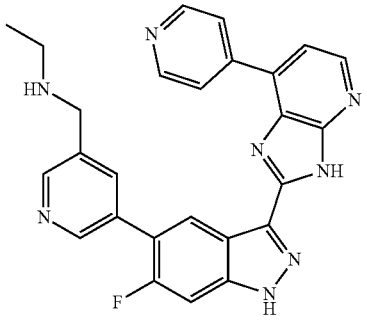
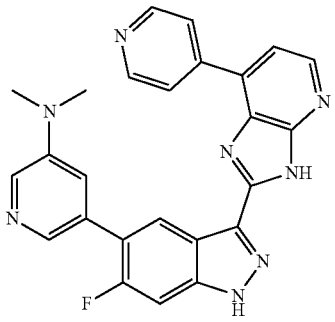
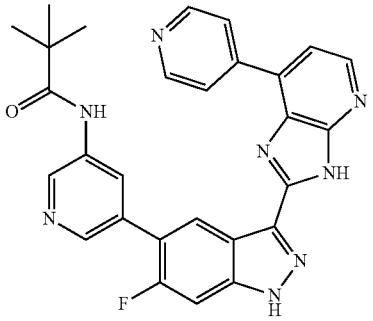
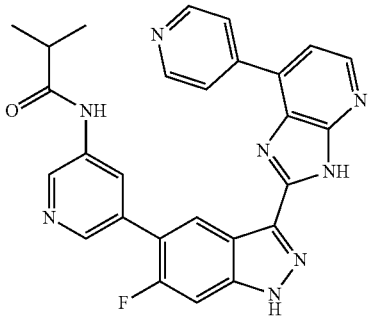
1042	
1043	
1044	
1045	

TABLE 1-continued

1046	
1047	
1048	
1049	

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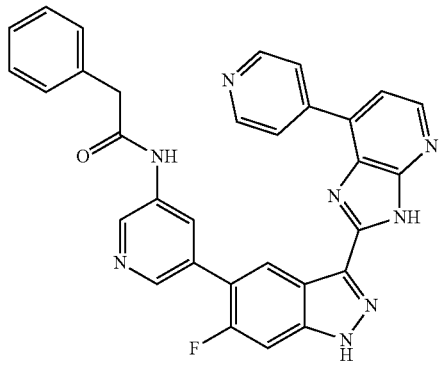
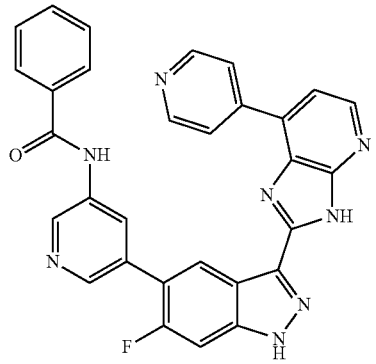
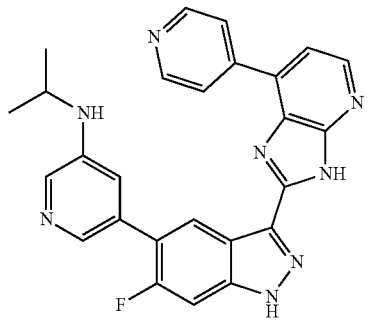
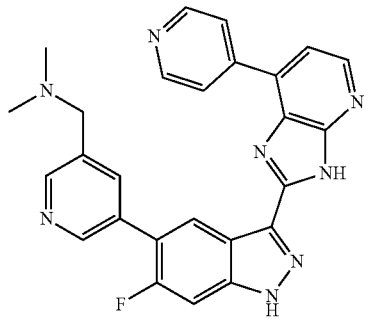
1050	
1051	
1052	
1053	

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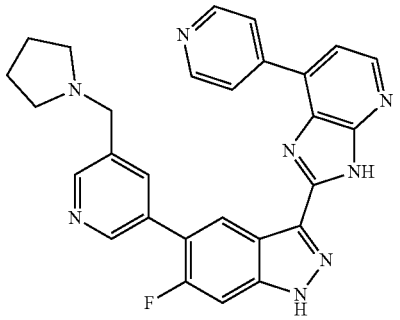
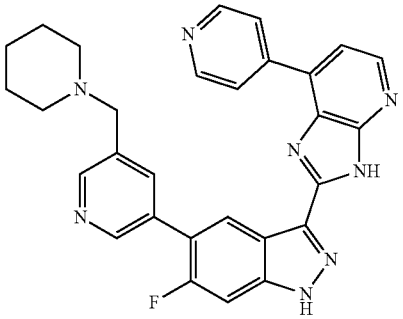
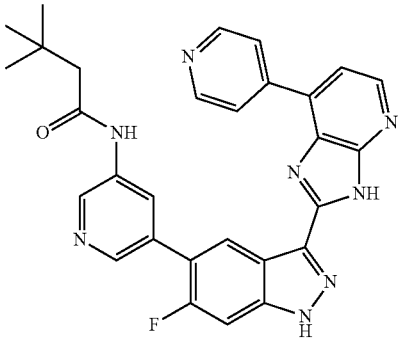
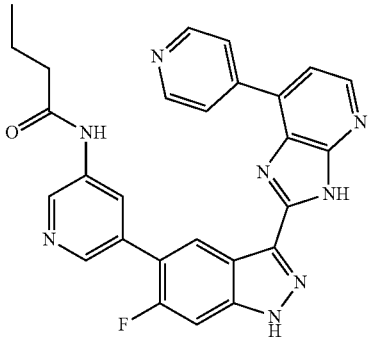
1054	
1055	
1056	
1057	

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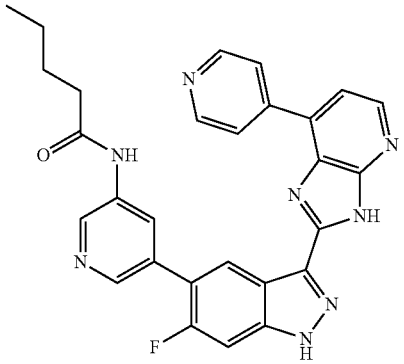
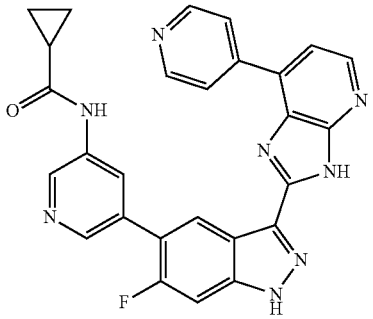
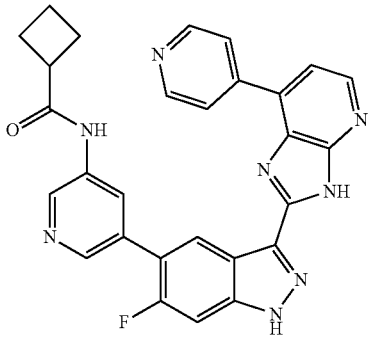
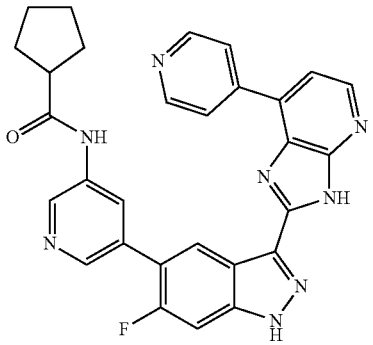
1058	
1059	
1060	
1061	

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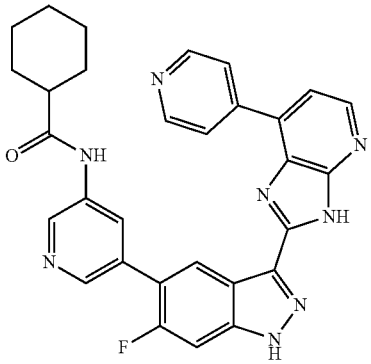
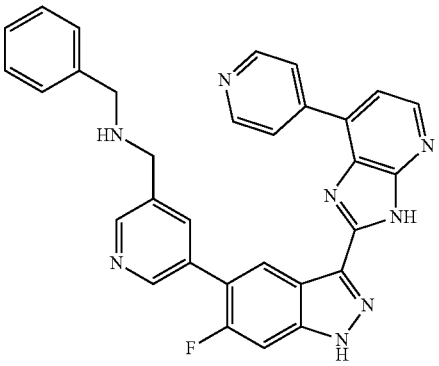
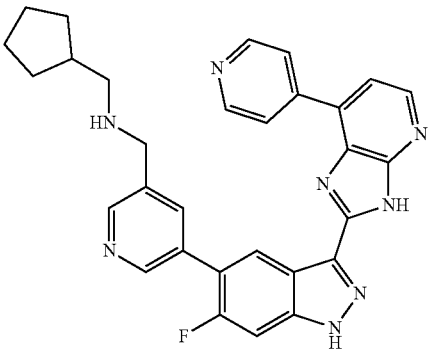
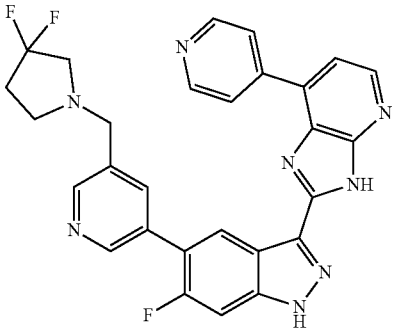
1062	
1063	
1064	
1065	

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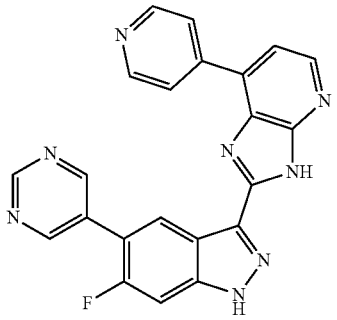
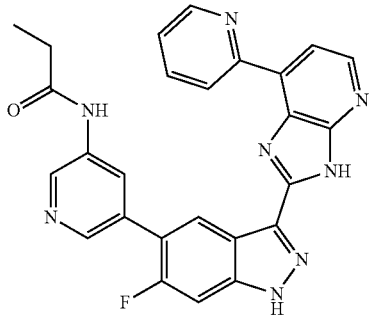
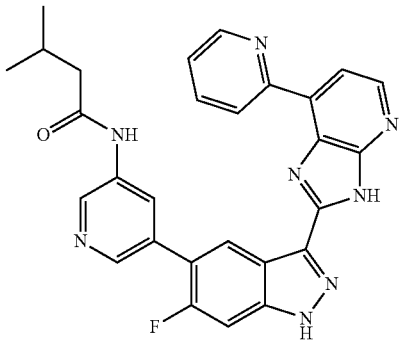
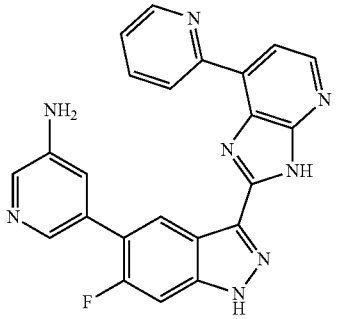
1066	
1067	
1068	
1069	

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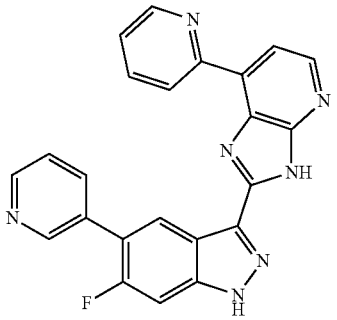
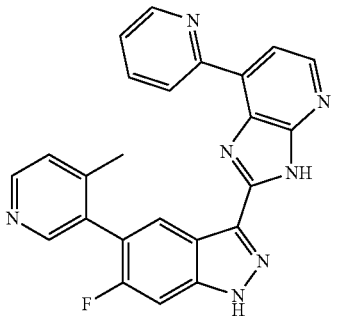
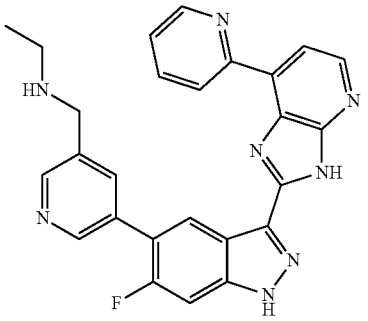
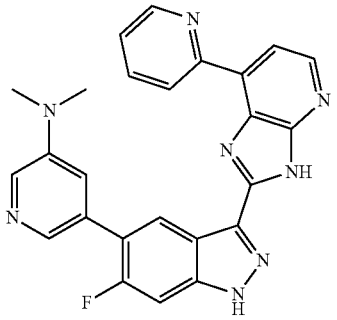
1070	
1071	
1072	
1073	

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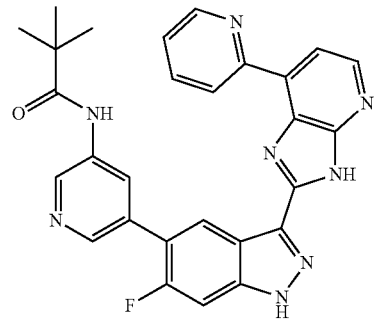

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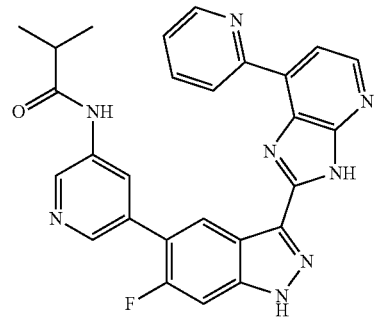

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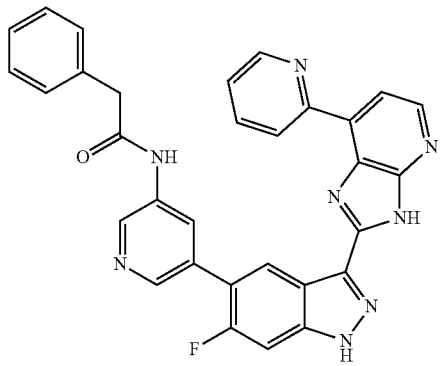

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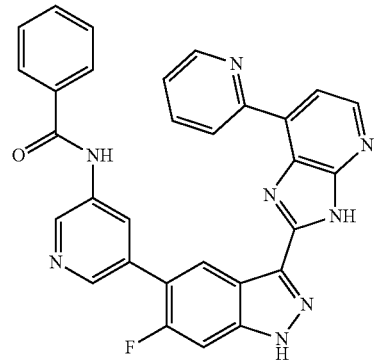

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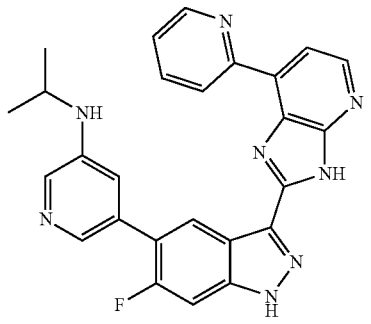

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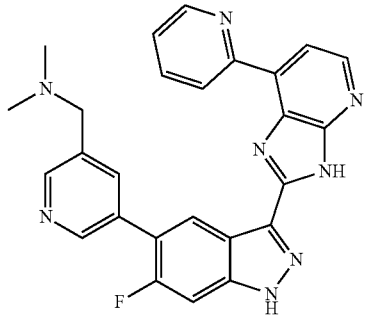

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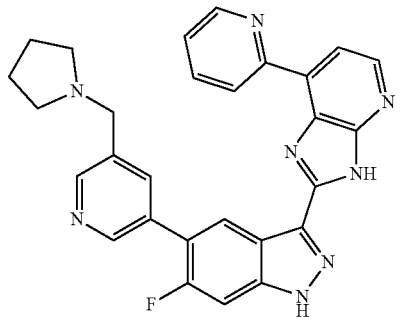

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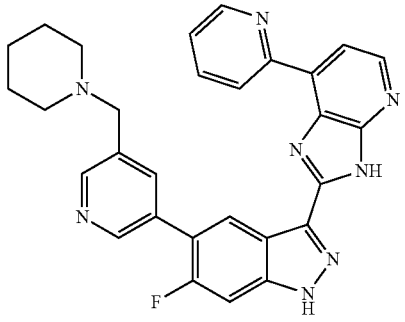

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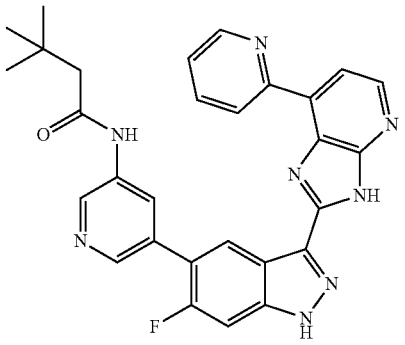
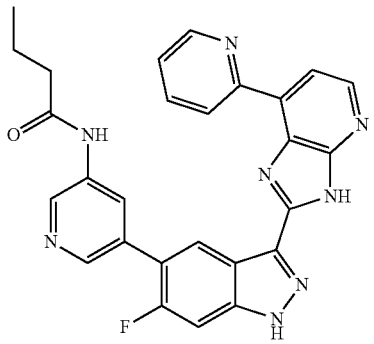
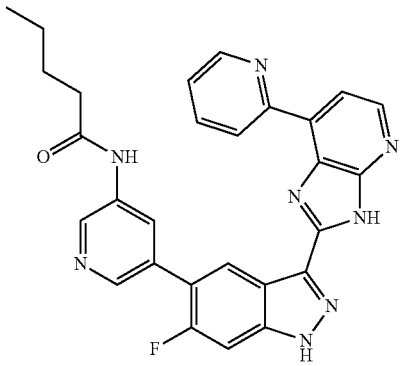
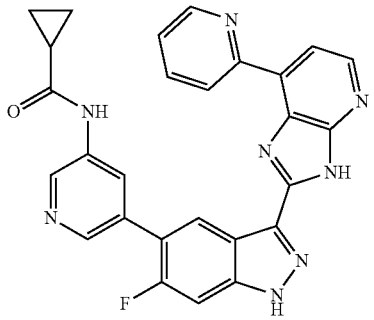
1082	
1083	
1084	
1085	

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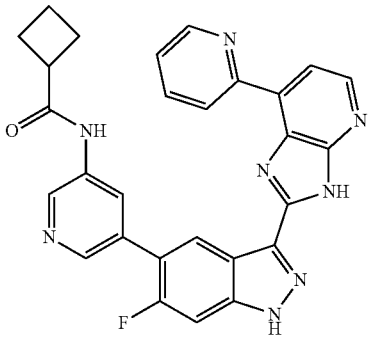
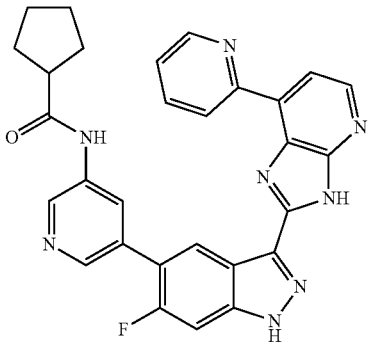
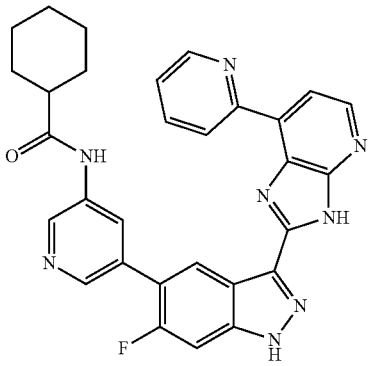
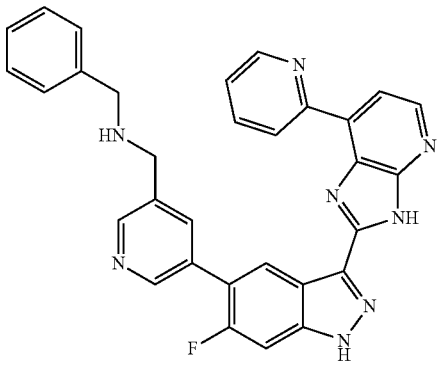
1086	
1087	
1088	
1089	

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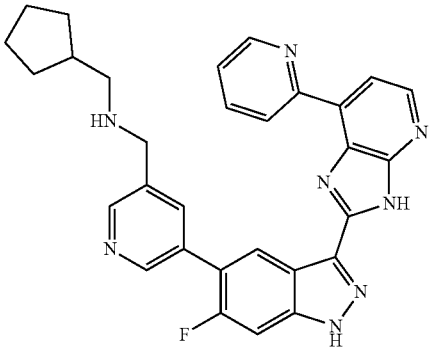
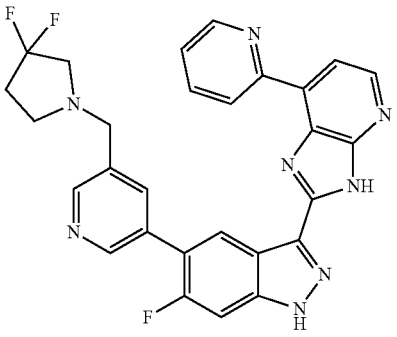
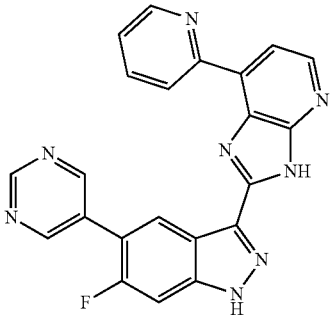
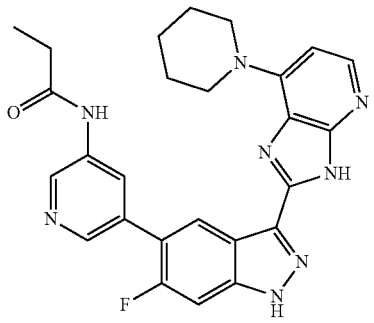
1090	
1091	
1092	
1093	

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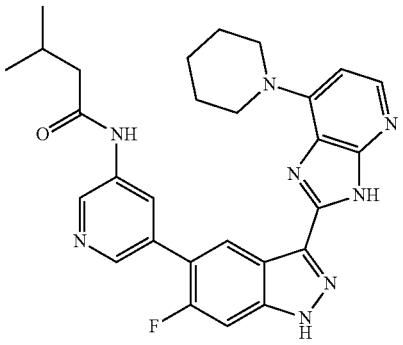
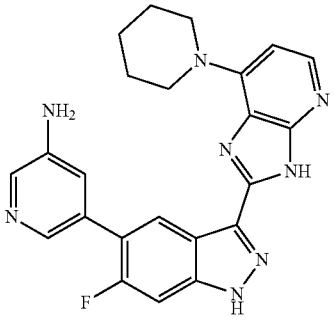
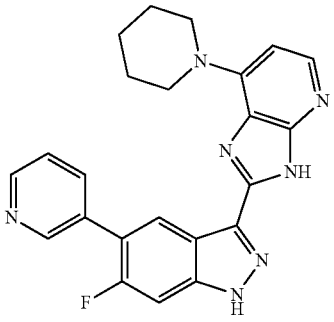
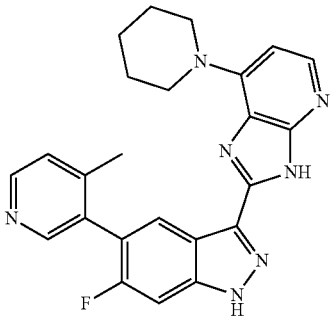
1094	
1095	
1096	
1097	

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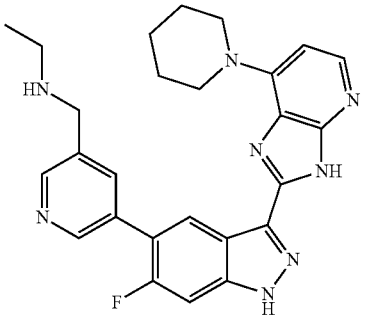
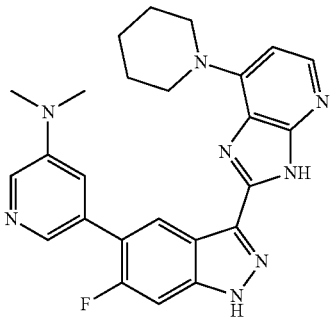
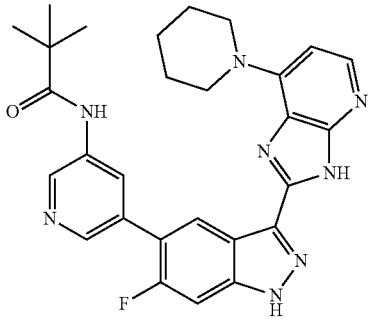
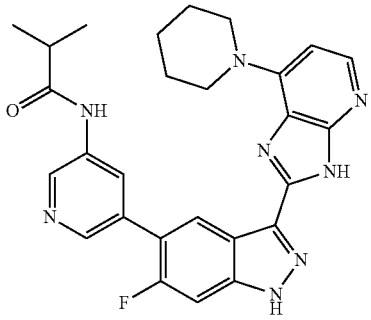
1098	
1099	
1100	
1101	

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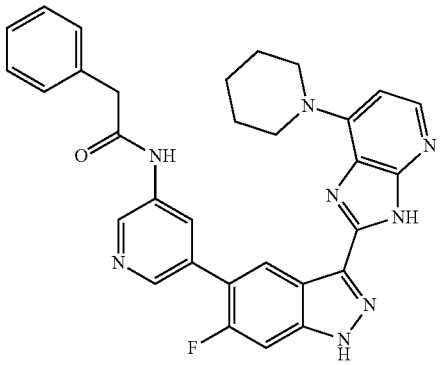
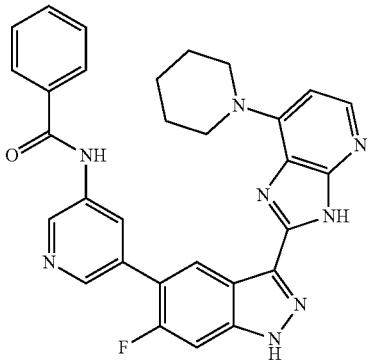
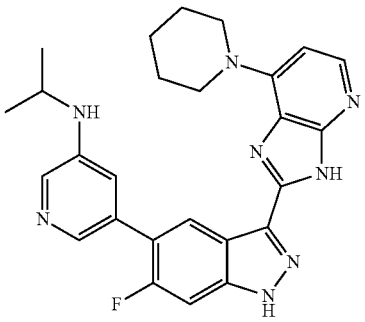
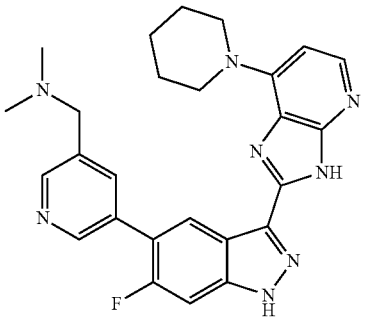
1102	
1103	
1104	
1105	

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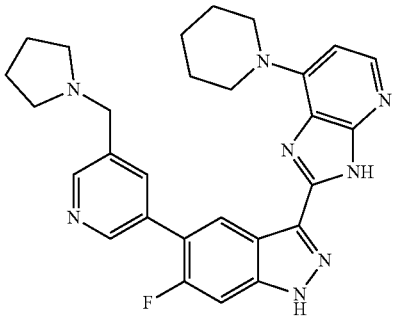
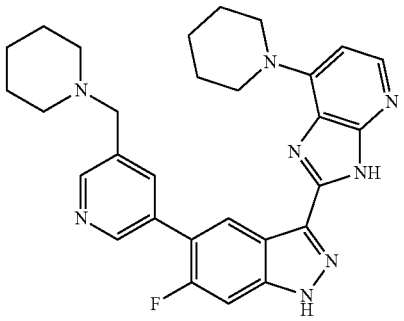
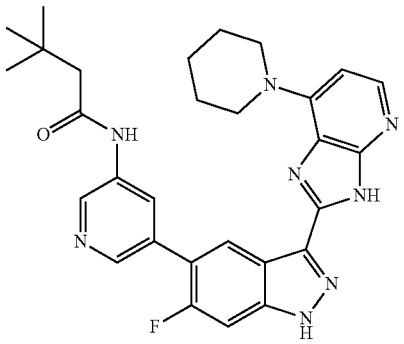
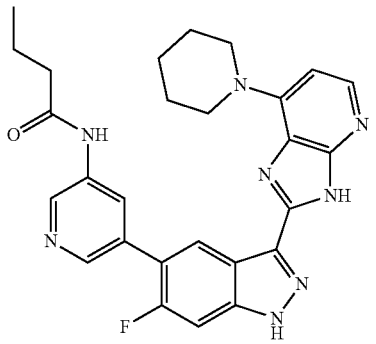
1106	
1107	
1108	
1109	

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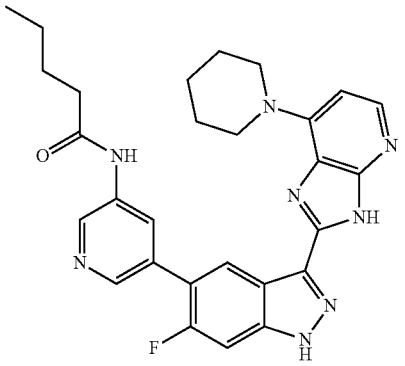
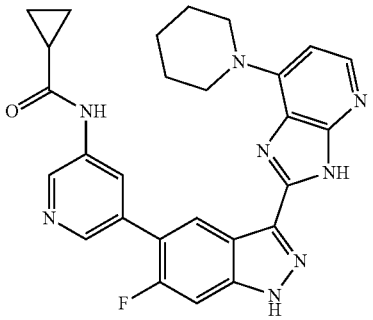
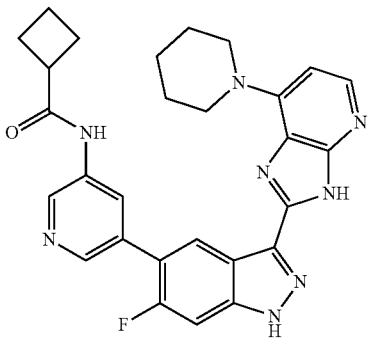
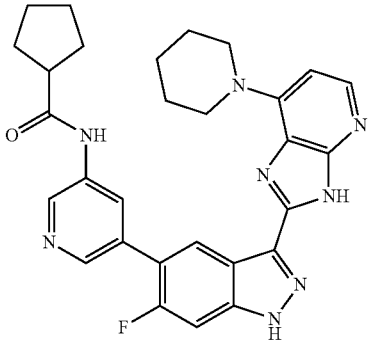
1110	
1111	
1112	
1113	

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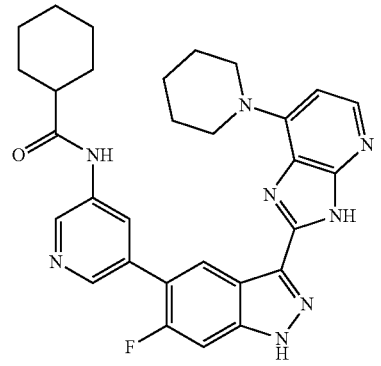
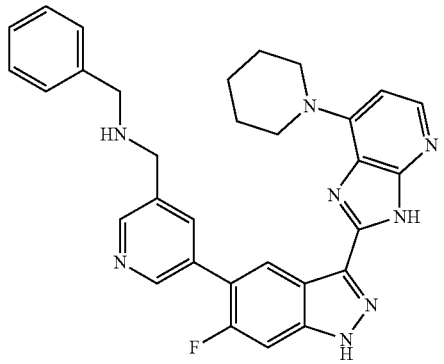
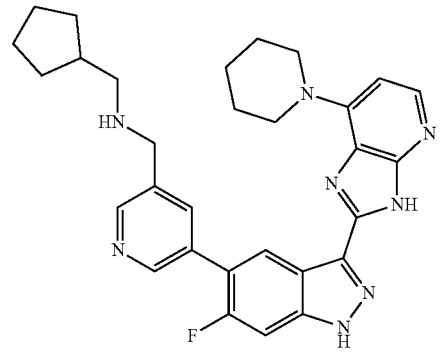
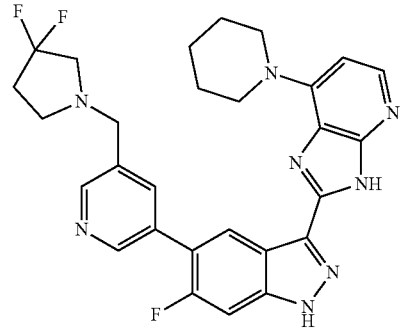
1114	
1115	
1116	
1117	

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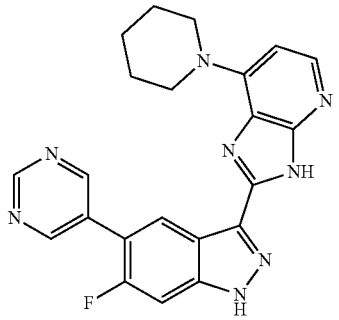
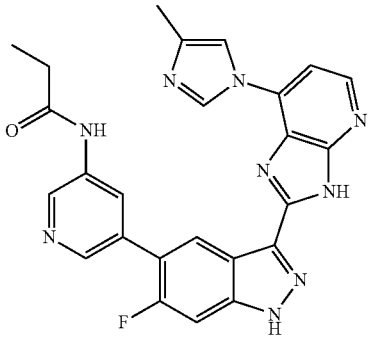
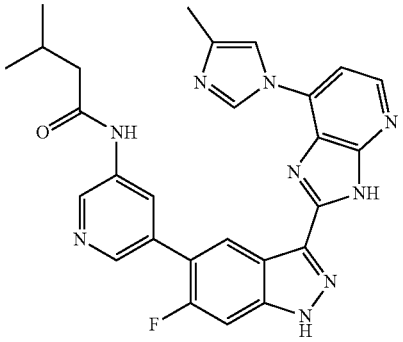
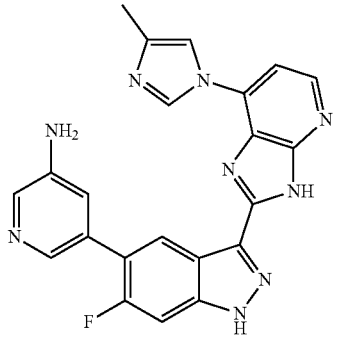
1118	
1119	
1120	
1121	

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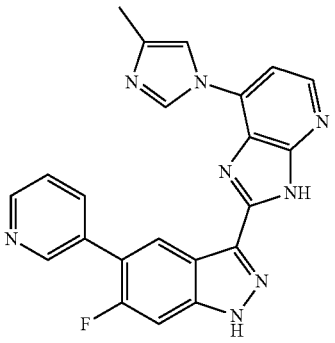
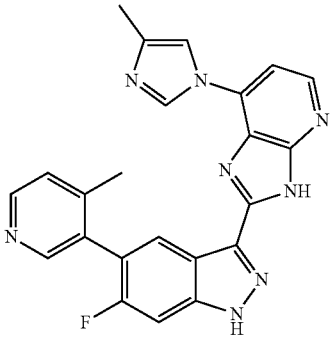
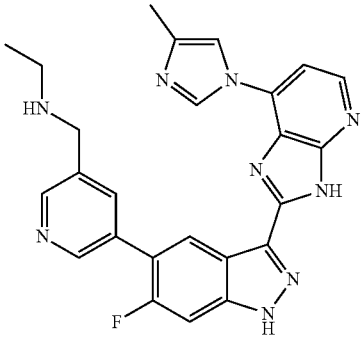
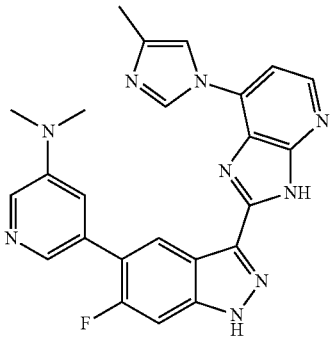
1122	
1123	
1124	
1125	

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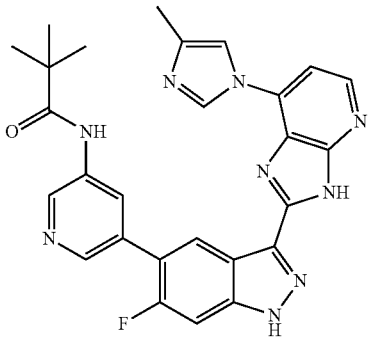
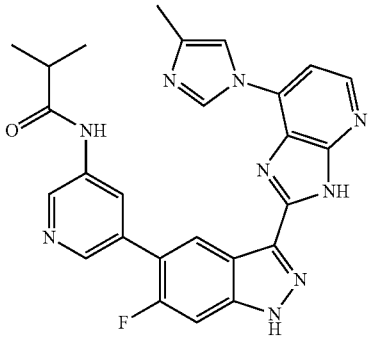
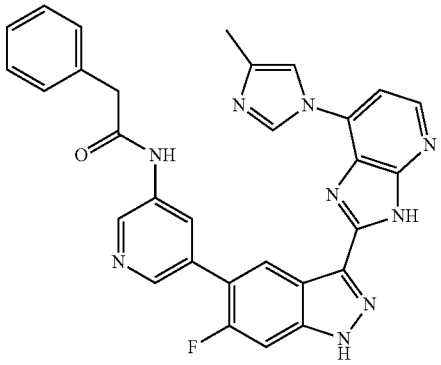
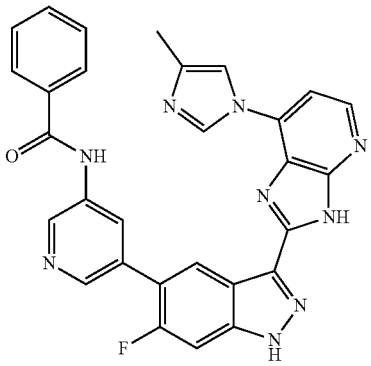
1126	
1127	
1128	
1129	

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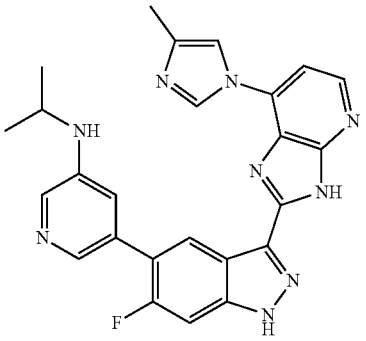
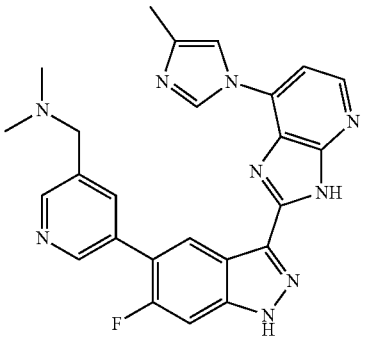
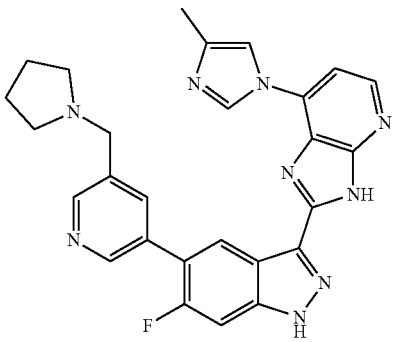
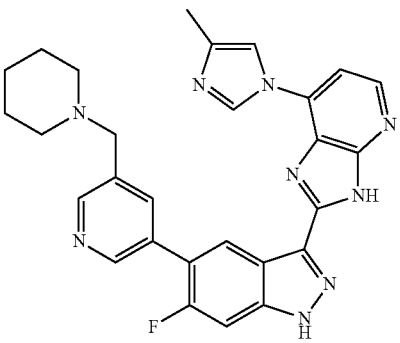
1130	
1131	
1132	
1133	

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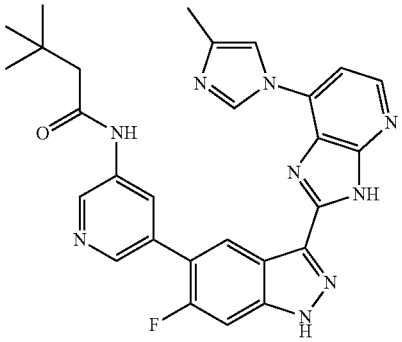
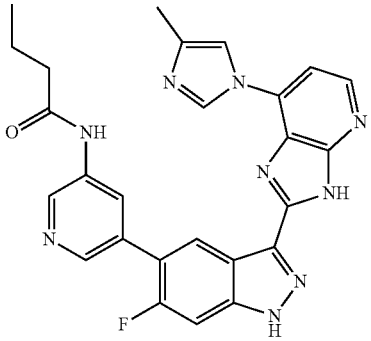
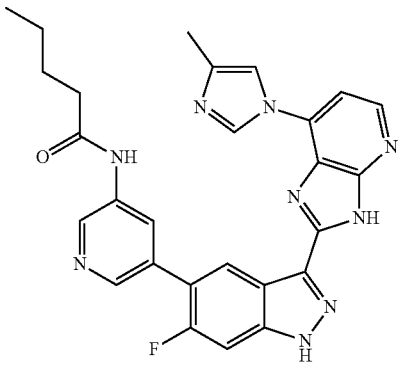
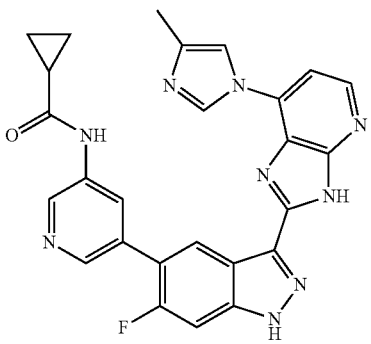
1134	
1135	
1136	
1137	

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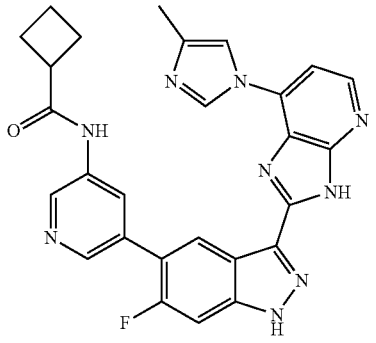
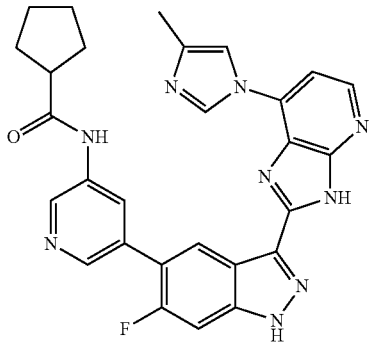
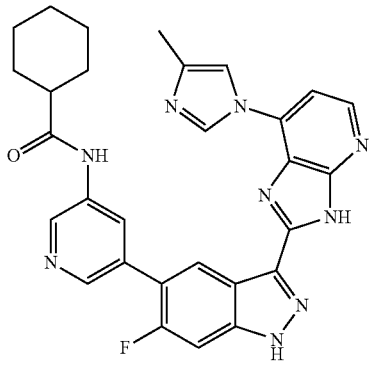
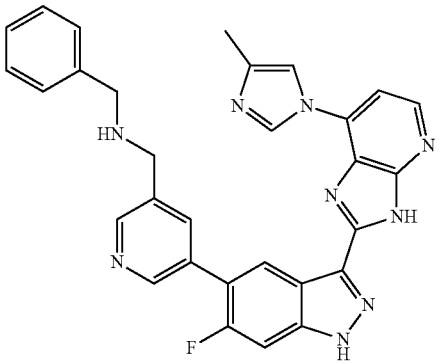
1138	
1139	
1140	
1141	

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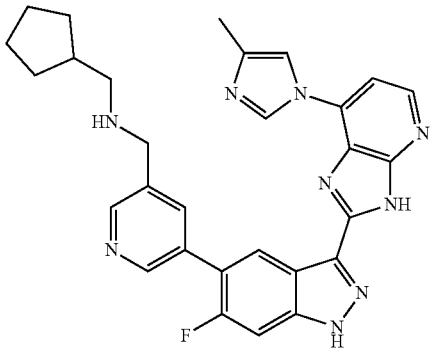
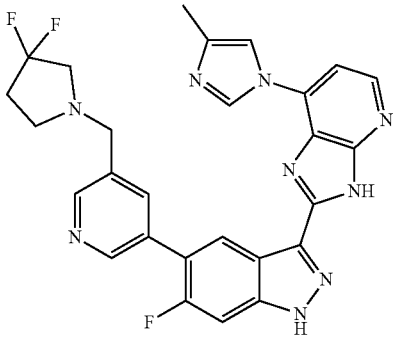
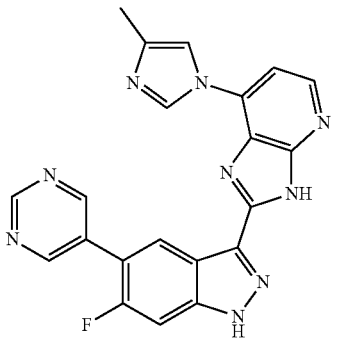
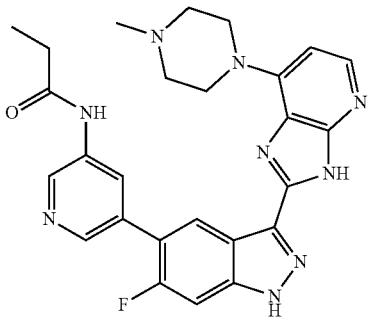
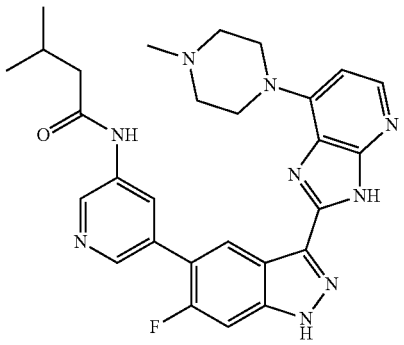
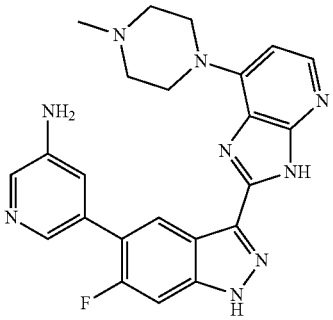
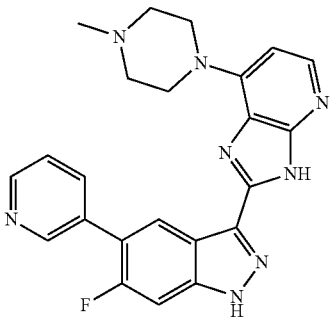
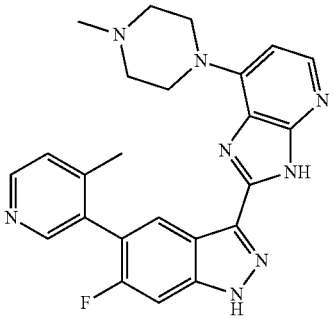
1142	
1143	
1144	
1145	

TABLE 1-continued

1146	
1147	
1148	
1149	

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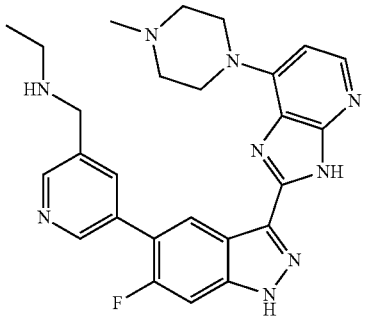
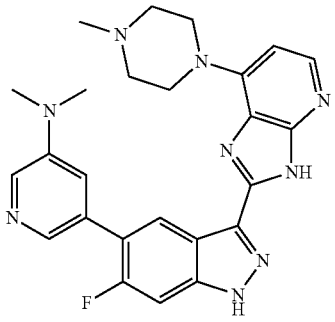
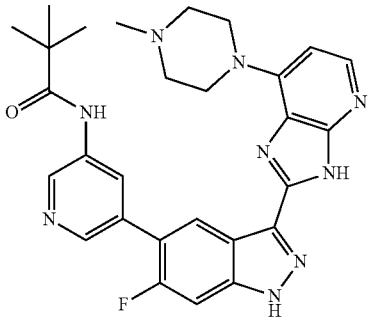
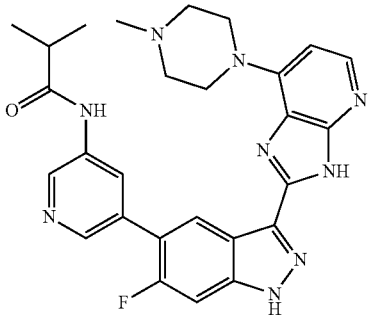
1150	
1151	
1152	
1153	

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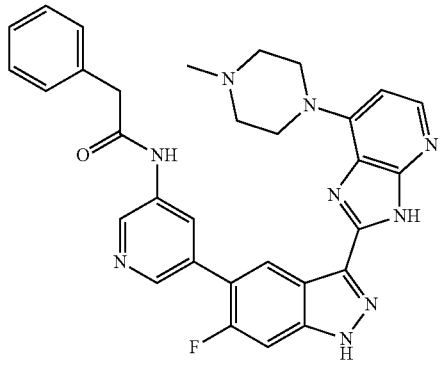
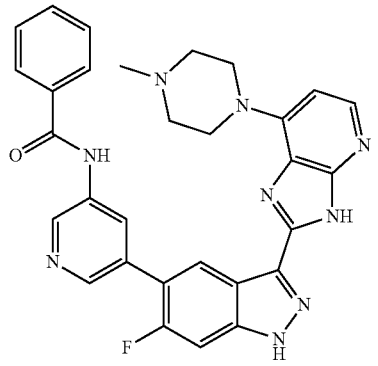
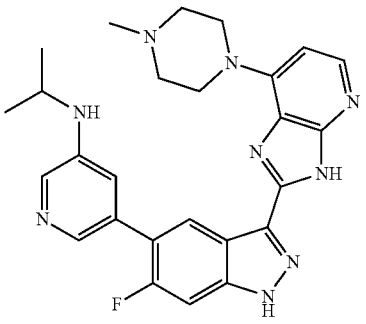
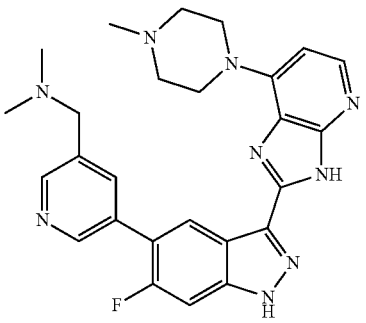
1154	
1155	
1156	
1157	

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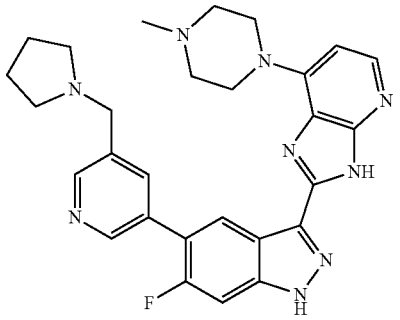
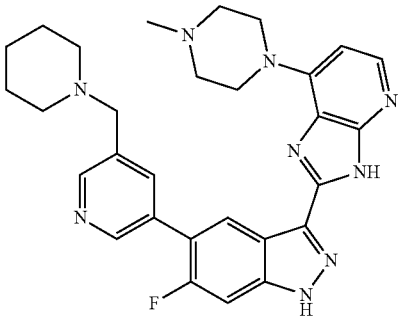
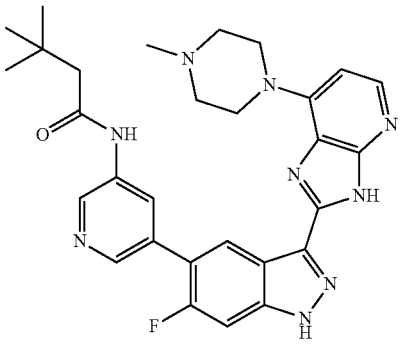
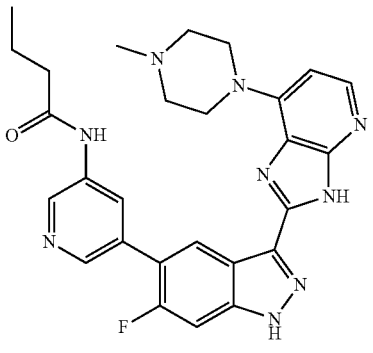
1158	
1159	
1160	
1161	

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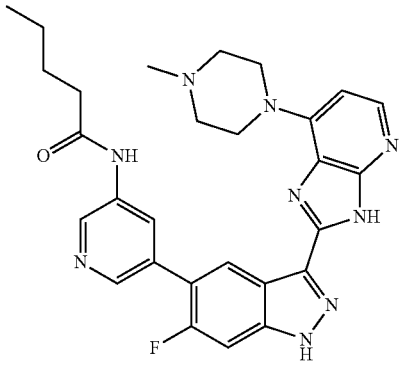
1162



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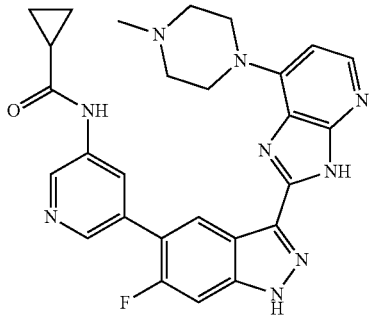

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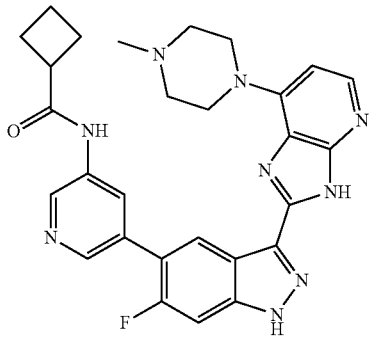

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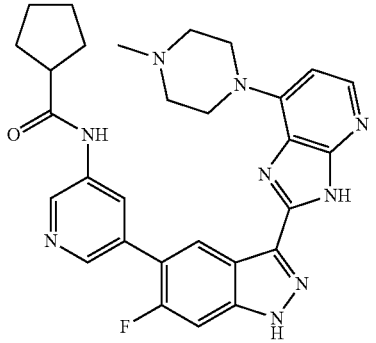

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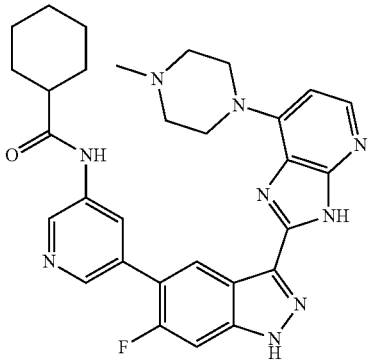
1166



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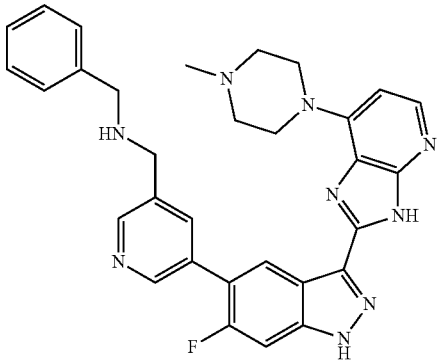
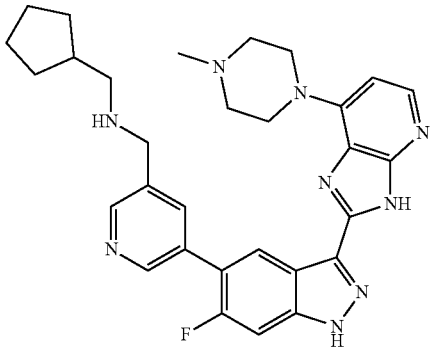


1168



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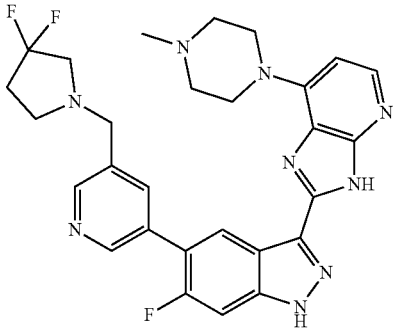

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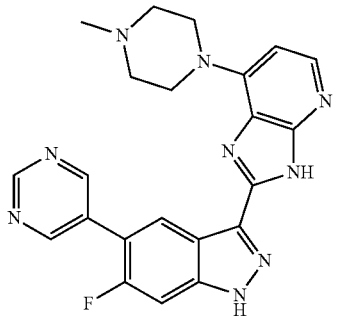
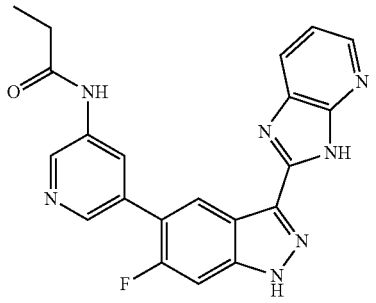
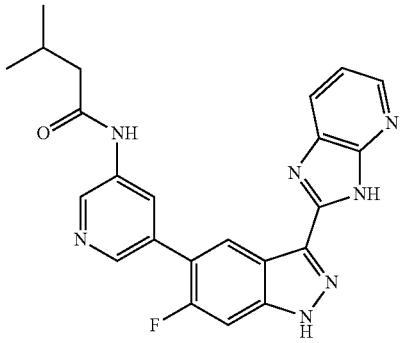
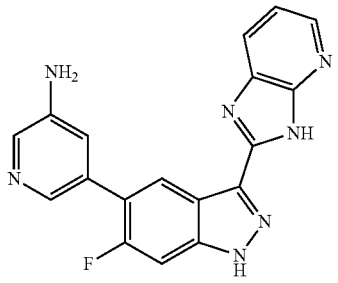
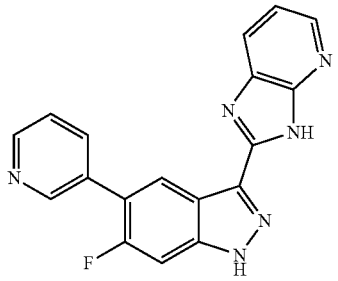
1170	
1171	
1172	
1173	
1174	

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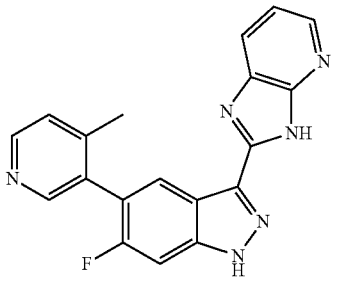
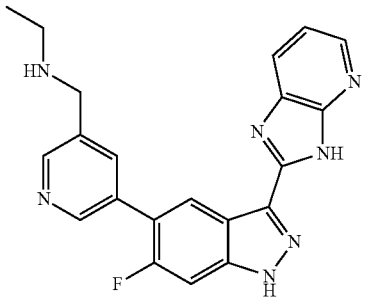
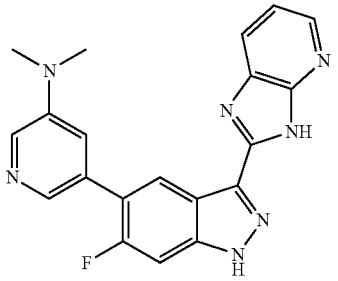
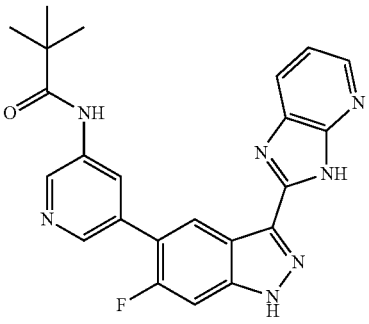
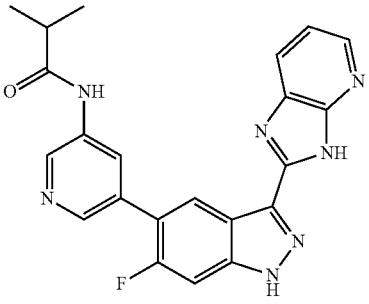
1175	
1176	
1177	
1178	
1179	

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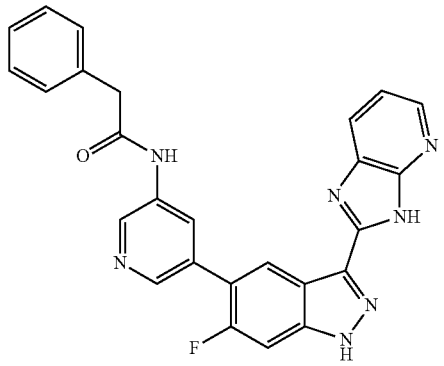
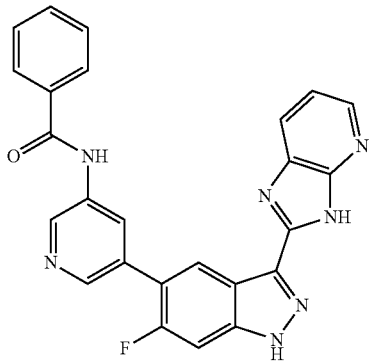
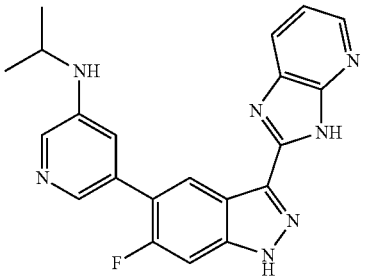
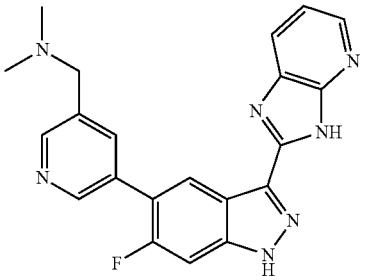
1180	
1181	
1182	
1183	

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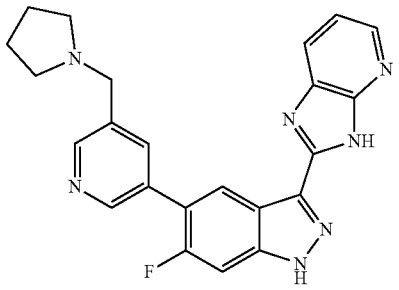
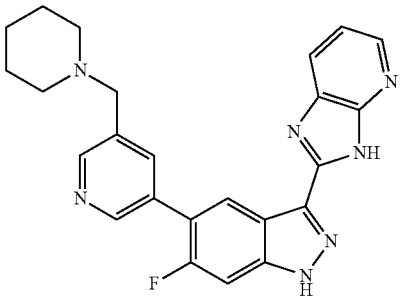
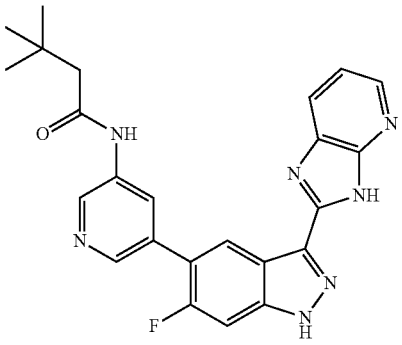
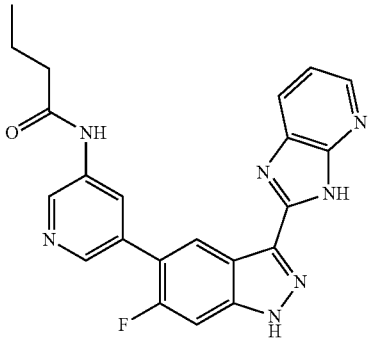
1184	
1185	
1186	
1187	

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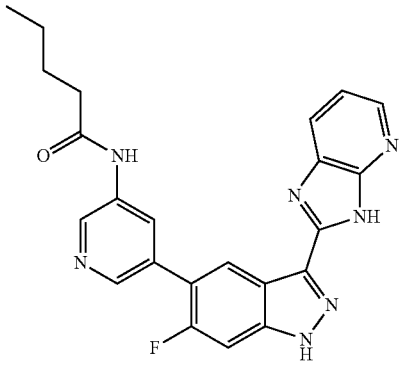
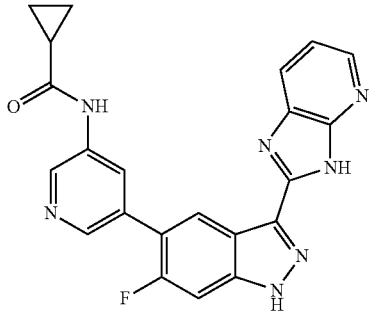
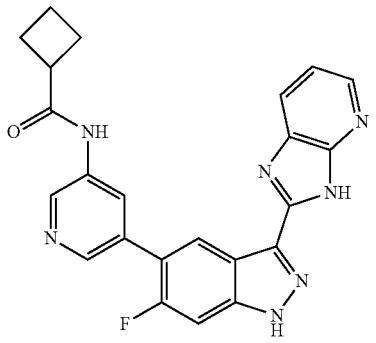
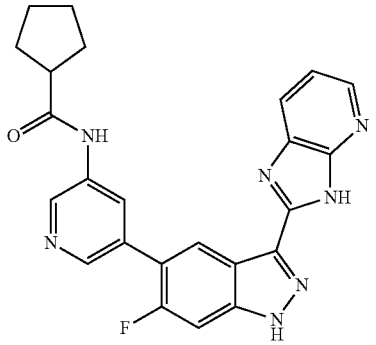
1188	
1189	
1190	
1191	

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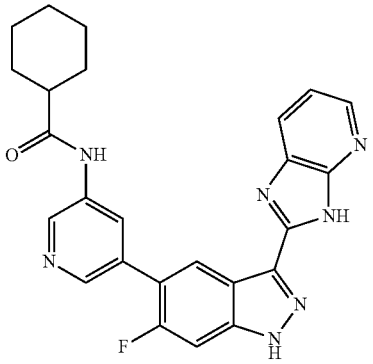
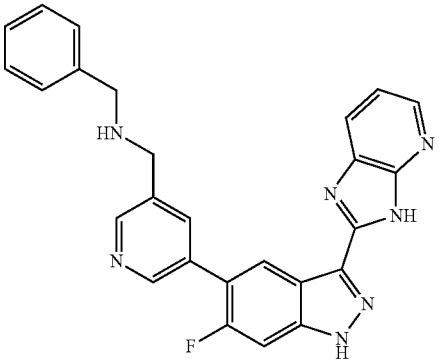
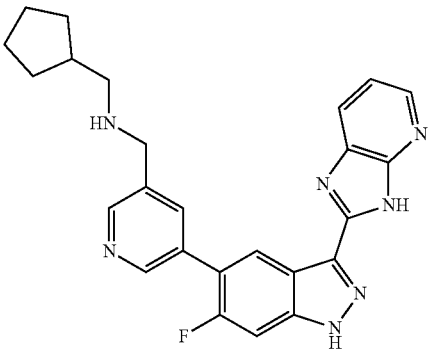
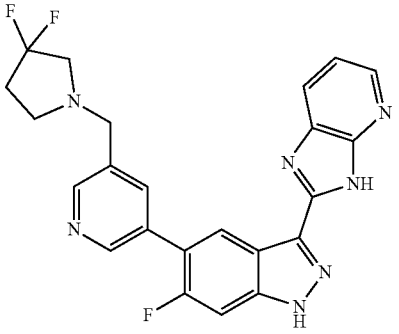
1192	
1193	
1194	
1195	

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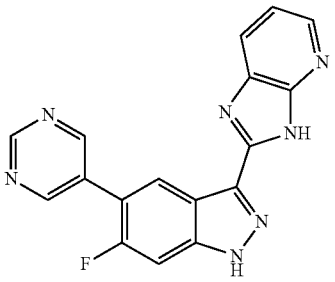
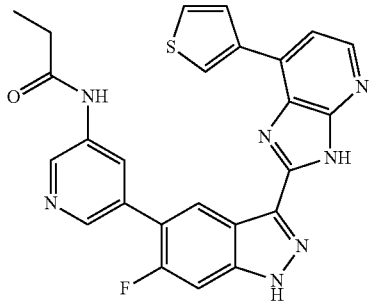
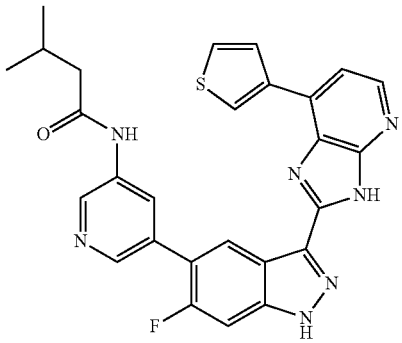
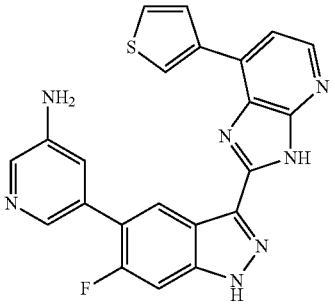
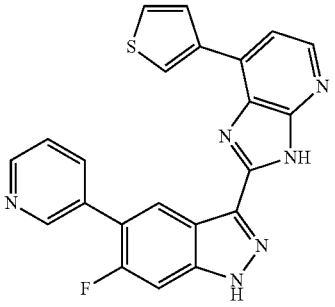
1196	
1197	
1198	
1199	
1200	

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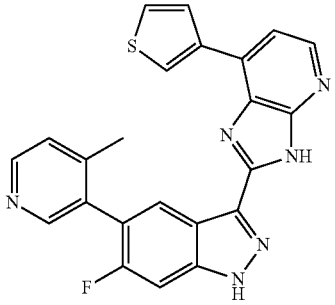
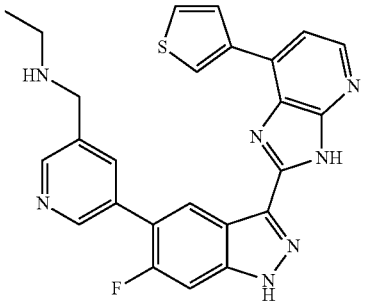
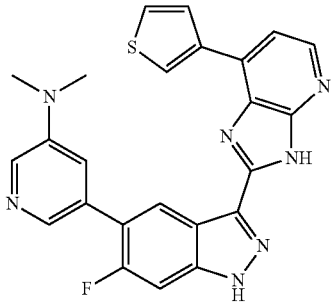
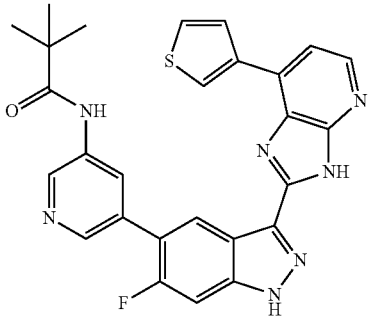
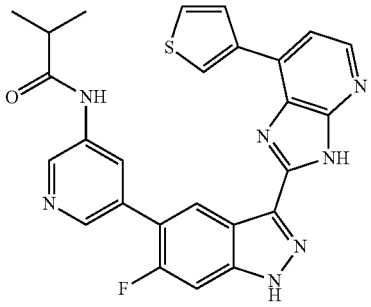
1201	
1202	
1203	
1204	
1205	

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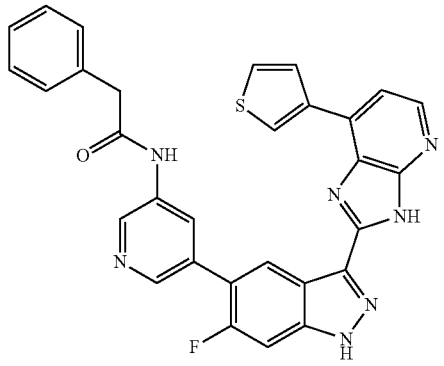

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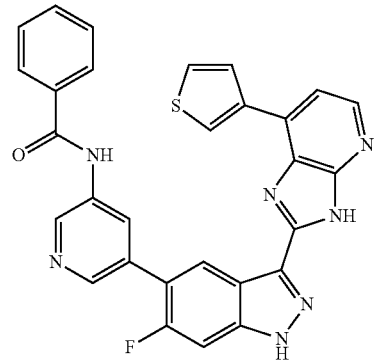

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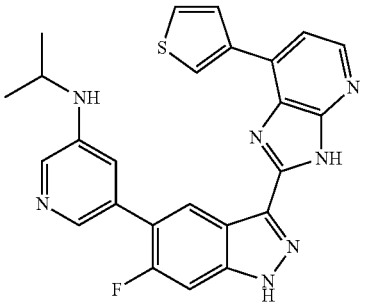

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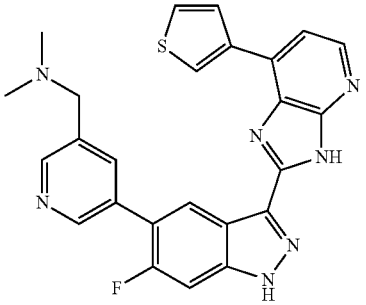

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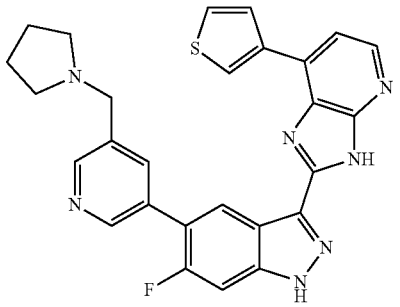

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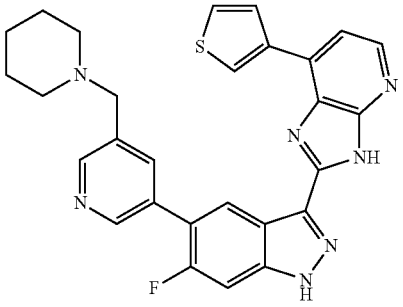

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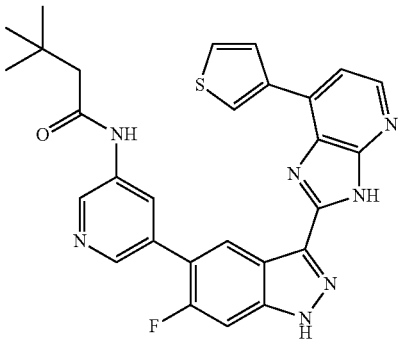

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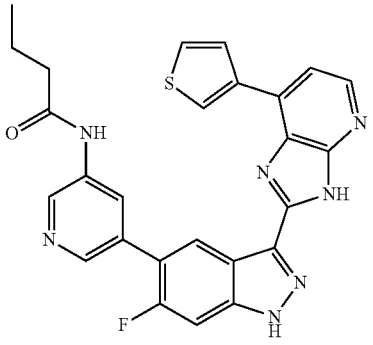

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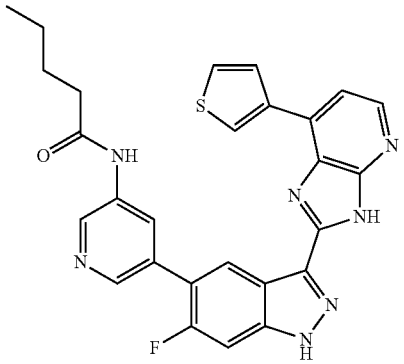
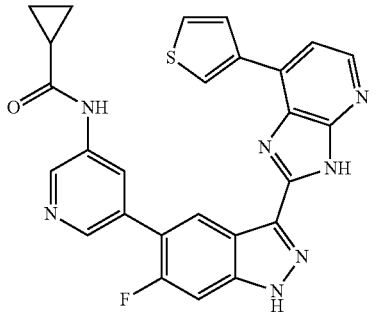
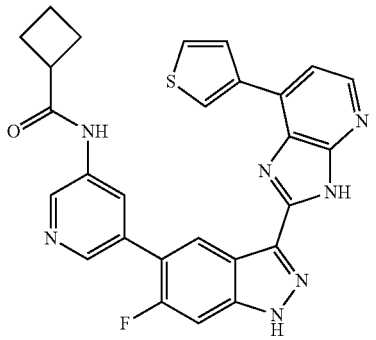
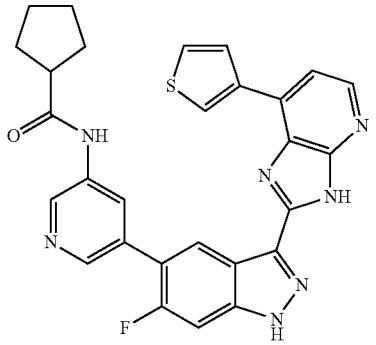
1214	
1215	
1216	
1217	

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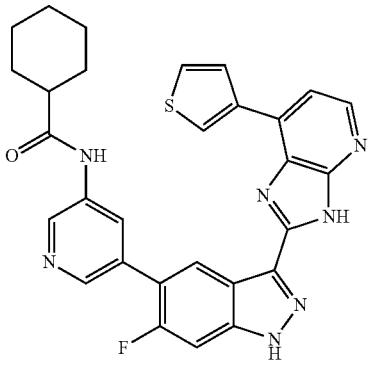
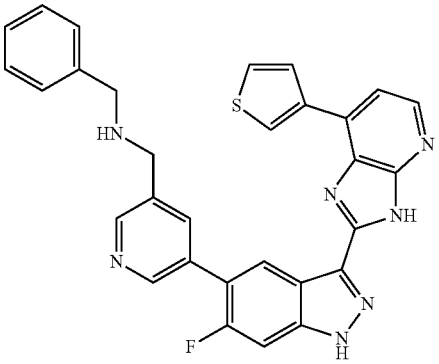
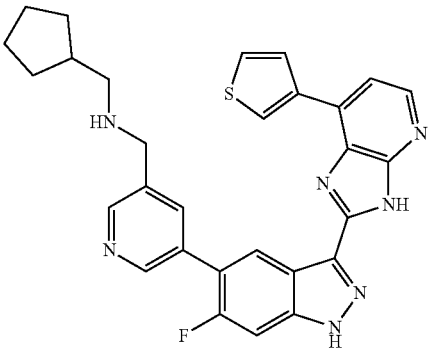
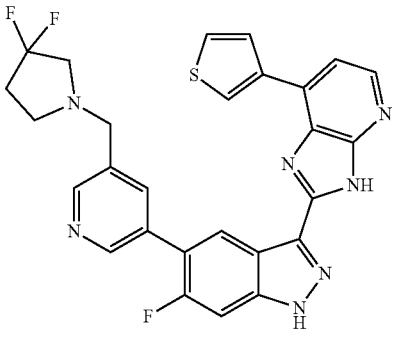
1218	
1219	
1220	
1221	

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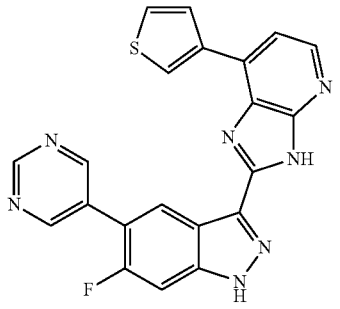
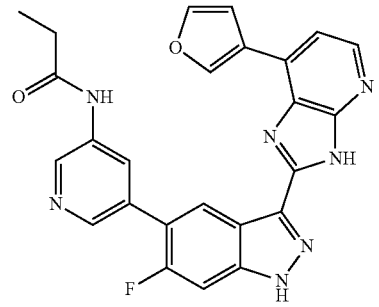
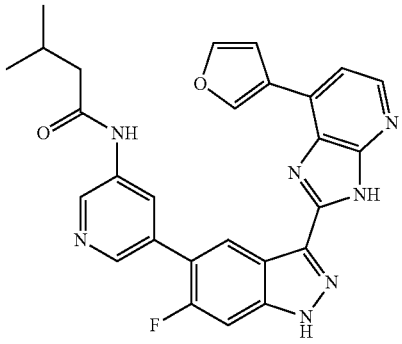
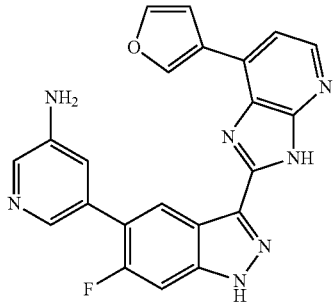
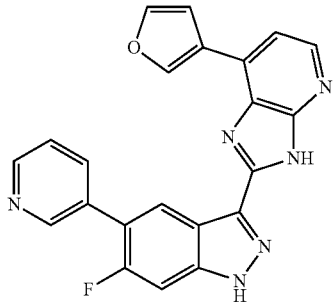
1222	
1223	
1224	
1225	
1226	

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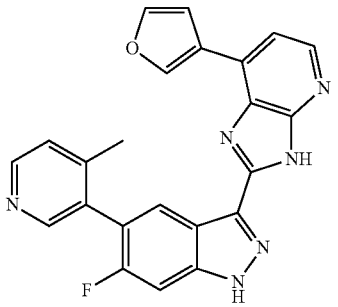
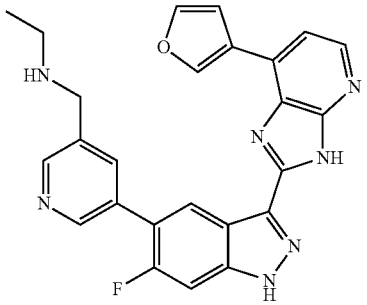
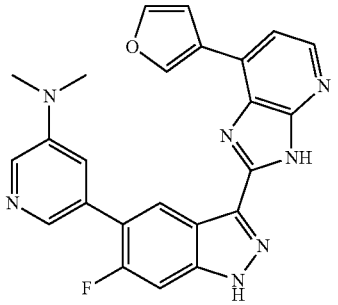
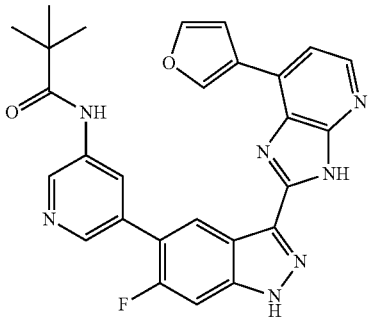
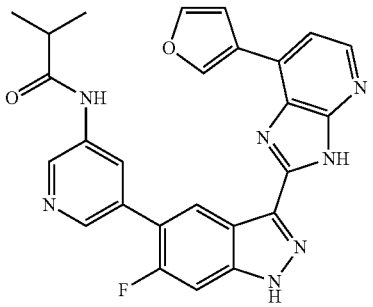
1227	
1228	
1229	
1230	
1231	

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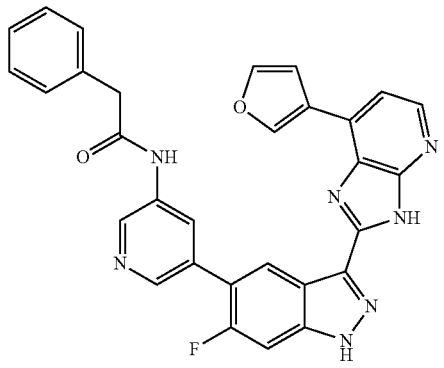
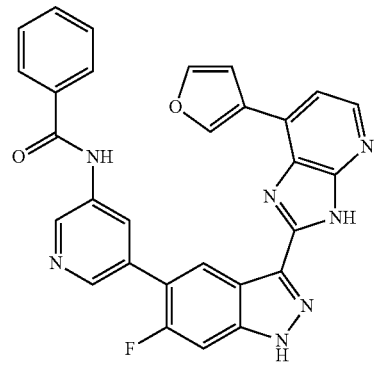
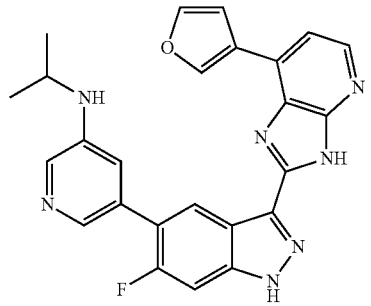
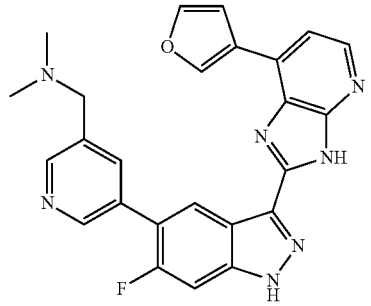
1232	
1233	
1234	
1235	

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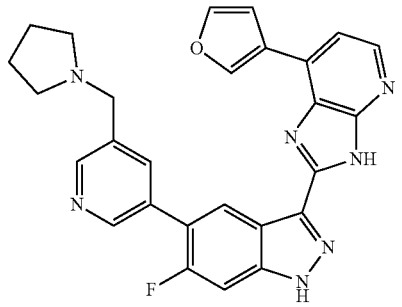
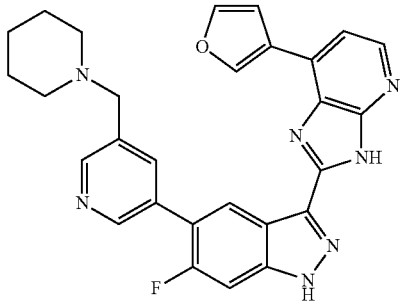
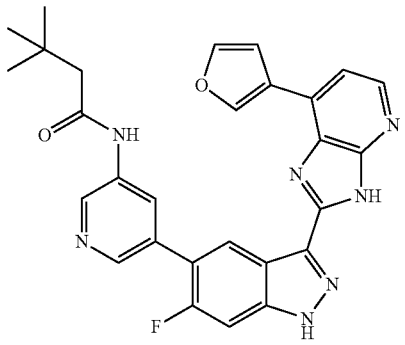
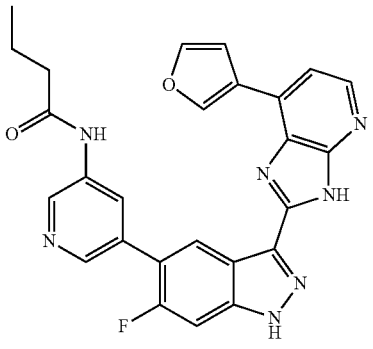
1236	
1237	
1238	
1239	

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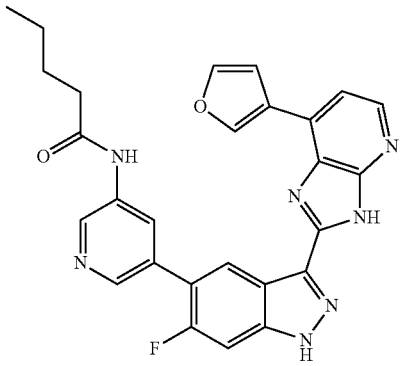
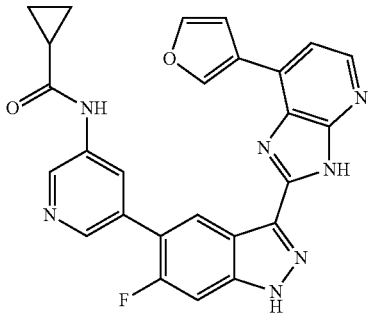
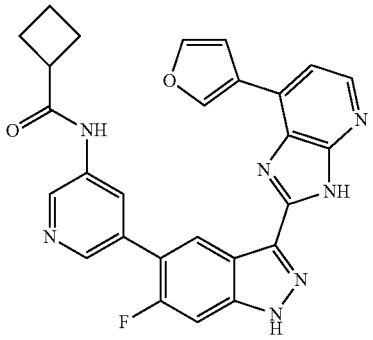
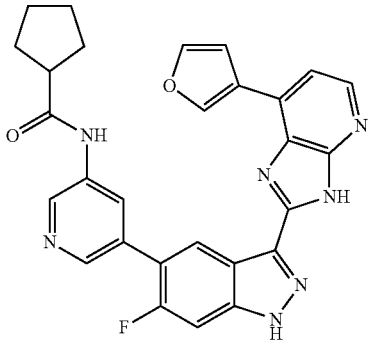
1240	
1241	
1242	
1243	

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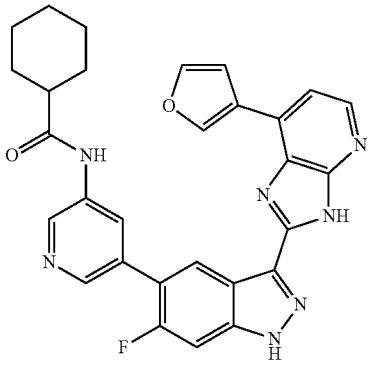
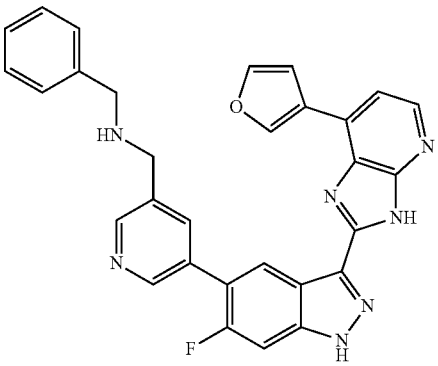
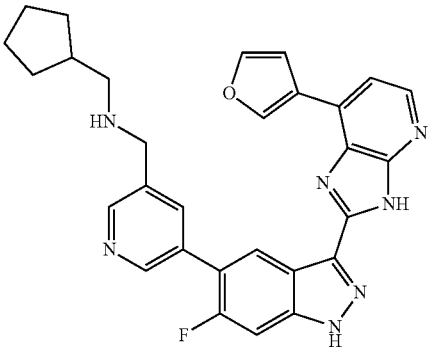
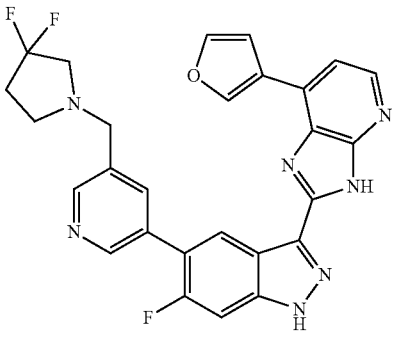
1244	
1245	
1246	
1247	

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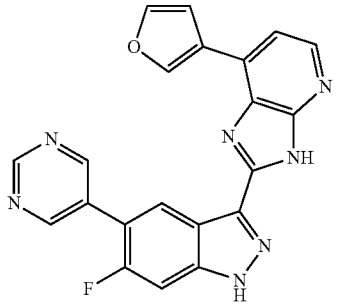
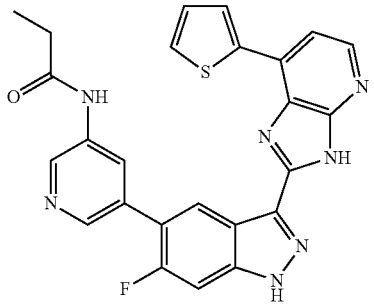
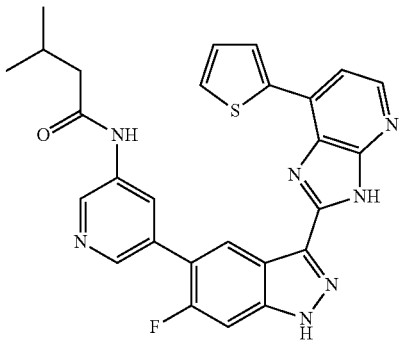
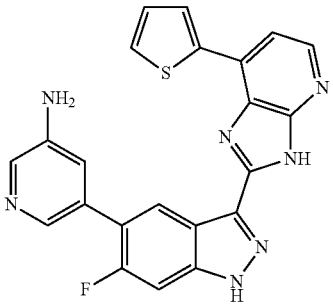
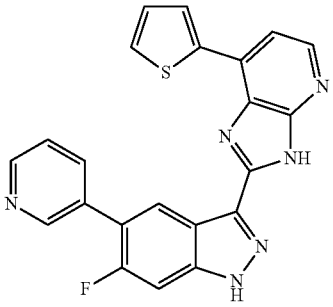
1248	
1249	
1250	
1251	
1252	

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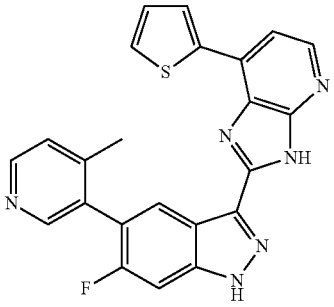
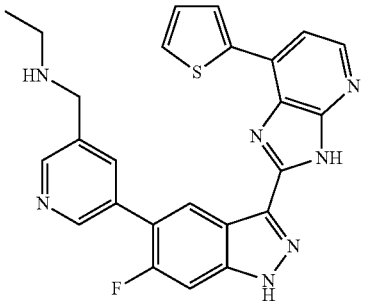
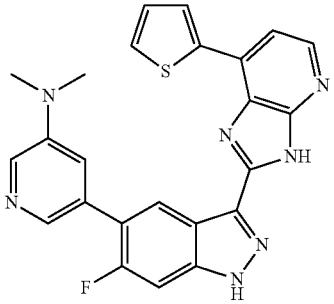
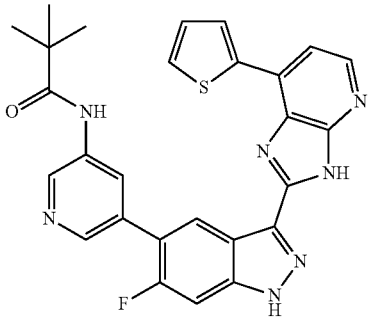
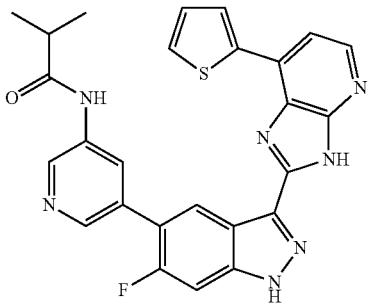
1253	
1254	
1255	
1256	
1257	

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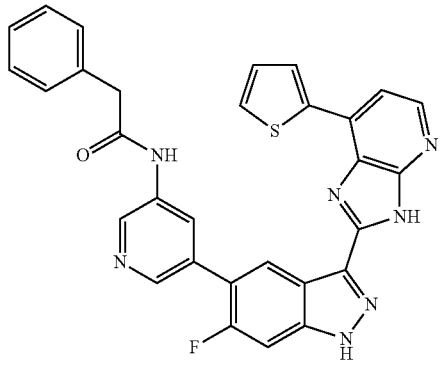
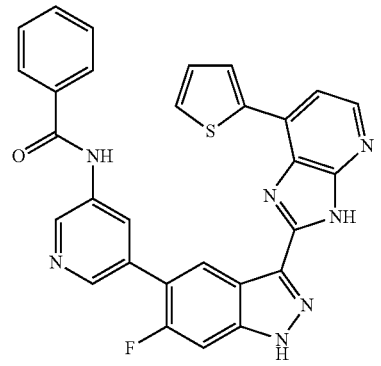
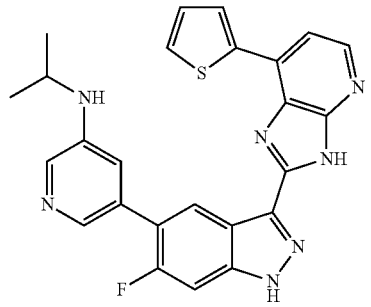
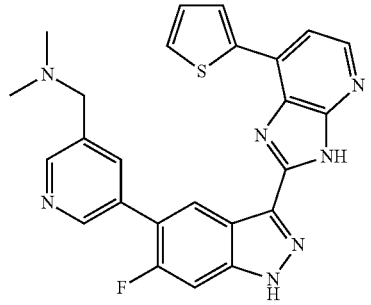
1258	
1259	
1260	
1261	

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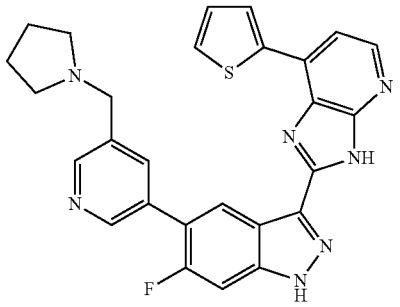
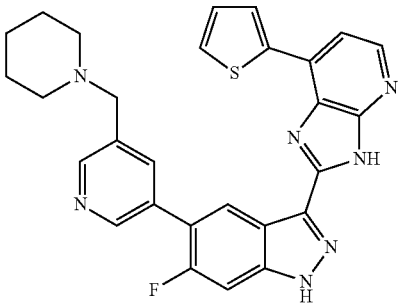
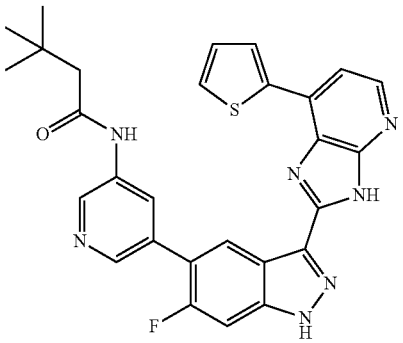
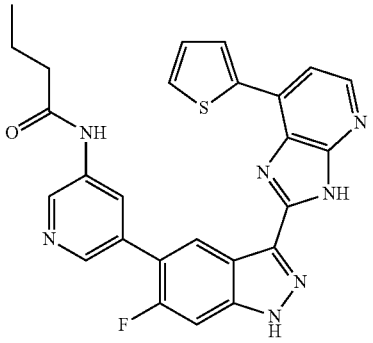
1262	
1263	
1264	
1265	

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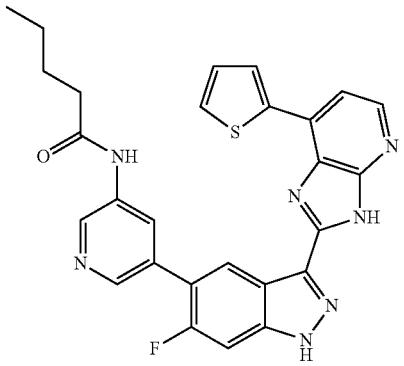
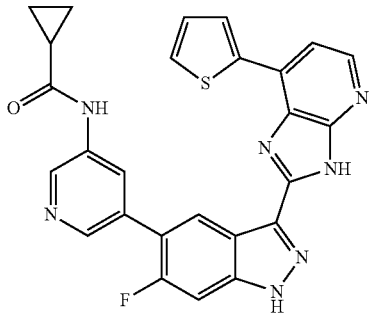
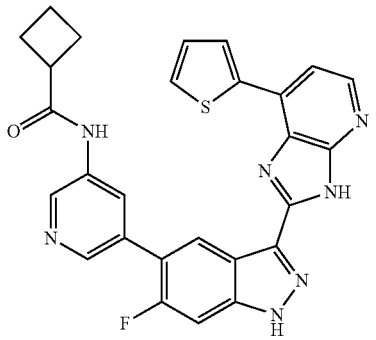
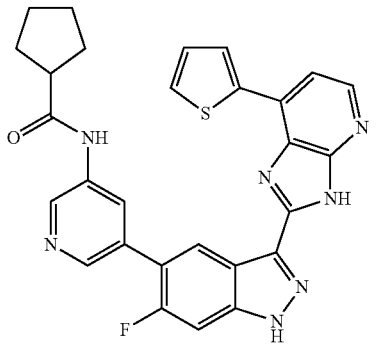
1266	
1267	
1268	
1269	

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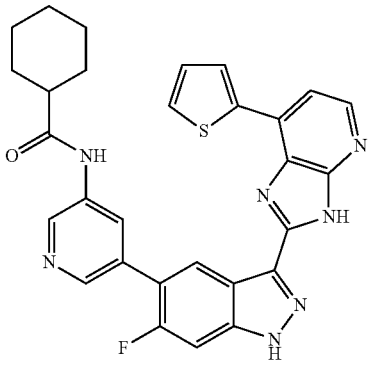
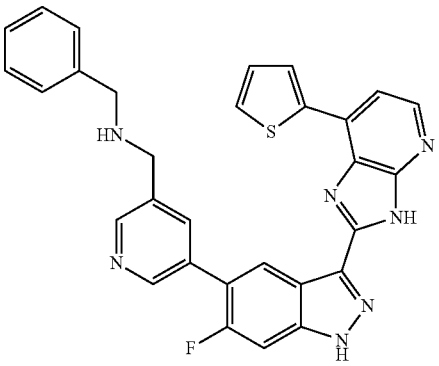
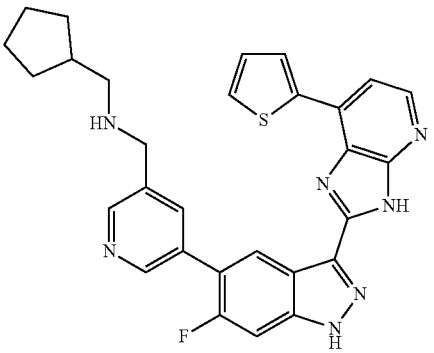
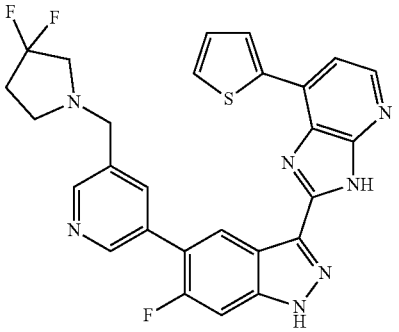
1270	
1271	
1272	
1273	

TABLE 1-continued

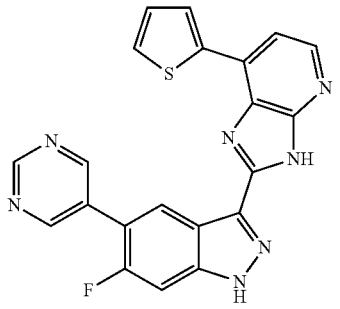
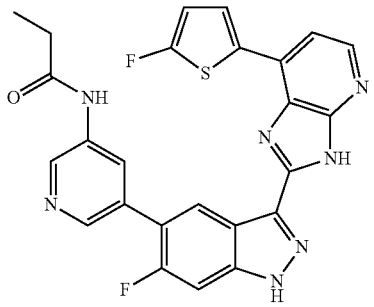
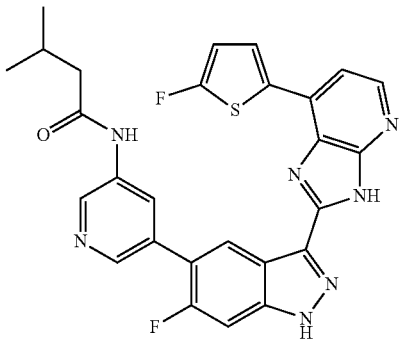
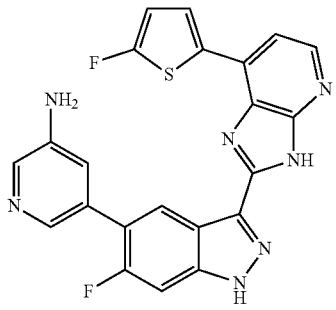
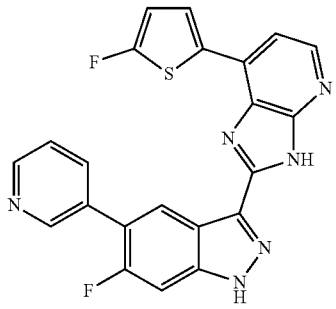
1274	
1275	
1276	
1277	
1278	

TABLE 1-continued

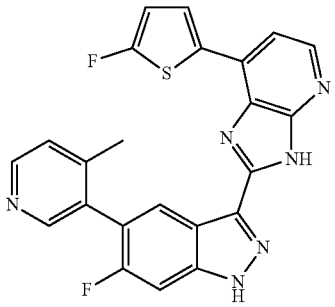
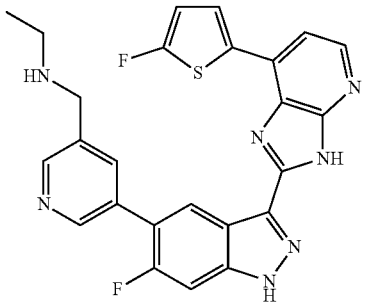
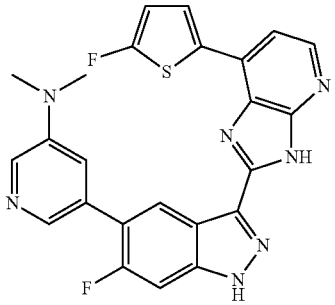
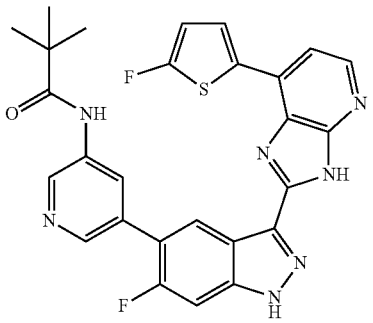
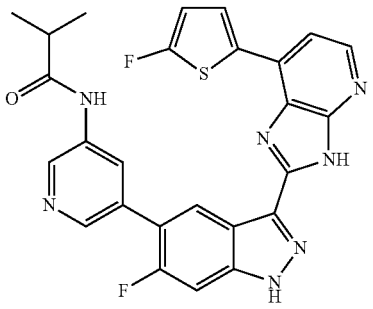
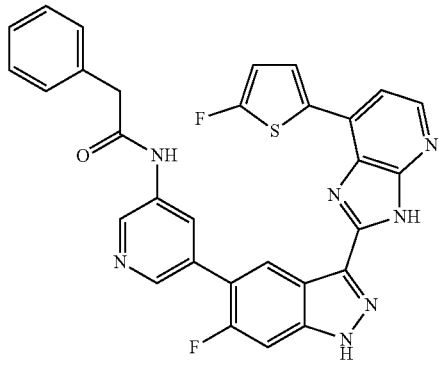
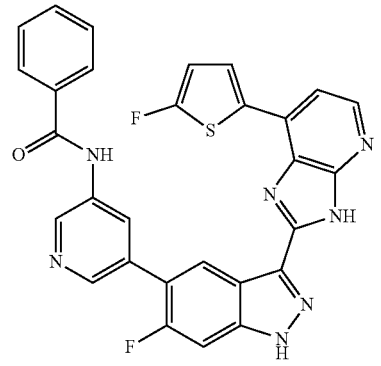
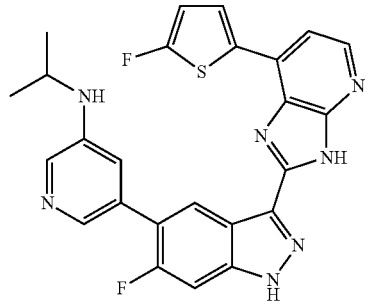
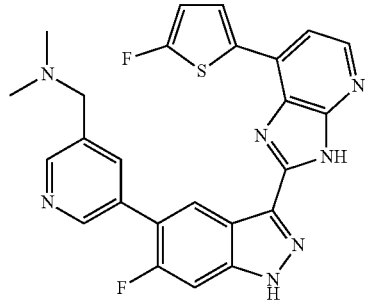
1279	
1280	
1281	
1282	
1283	

TABLE 1-continued

1284	
1285	
1286	
1287	

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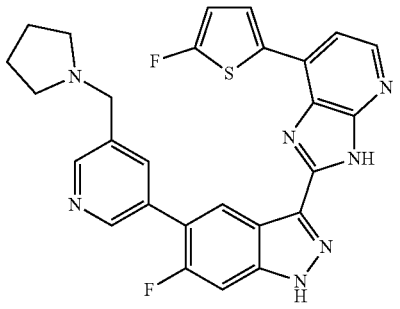
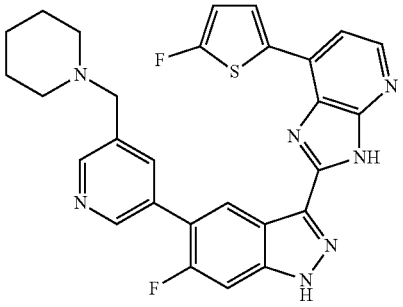
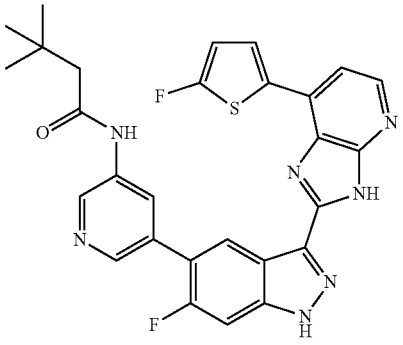
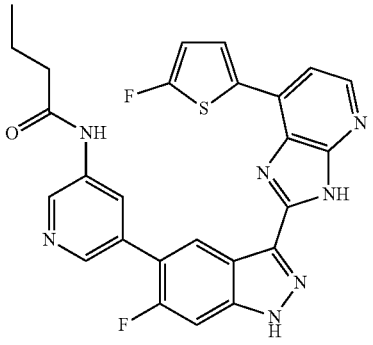
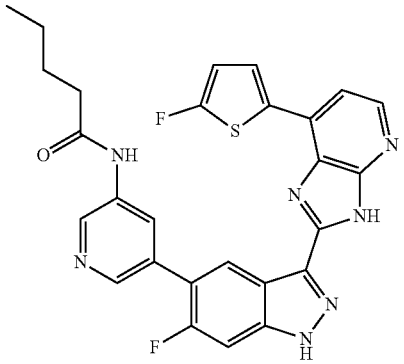
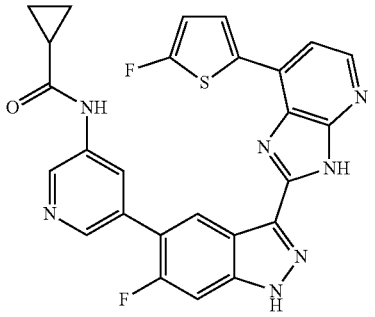
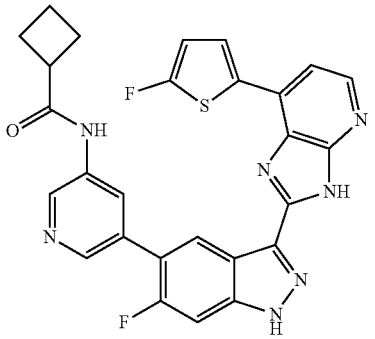
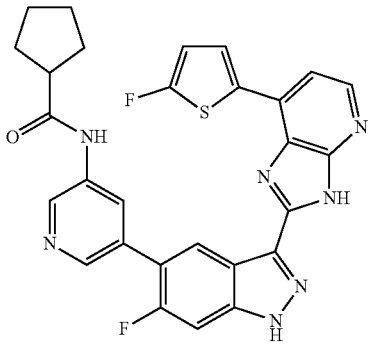
1288	
1289	
1290	
1291	

TABLE 1-continued

1292	
1293	
1294	
1295	

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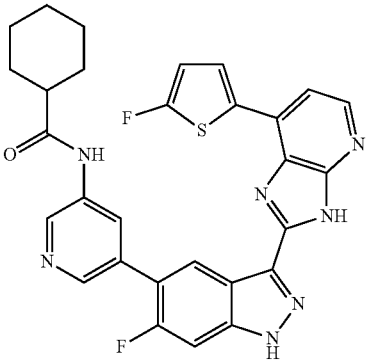
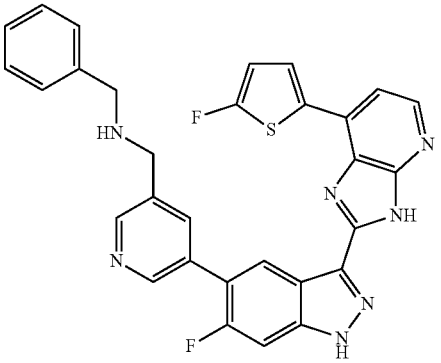
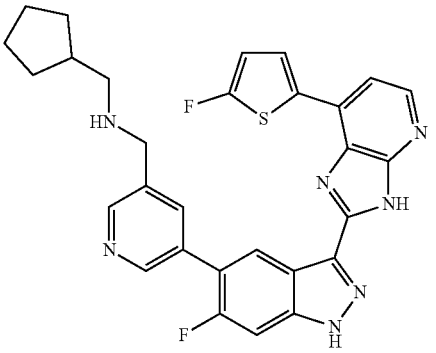
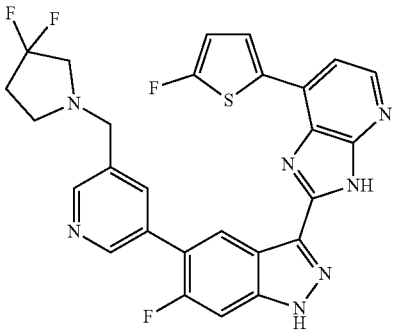
1296	
1297	
1298	
1299	

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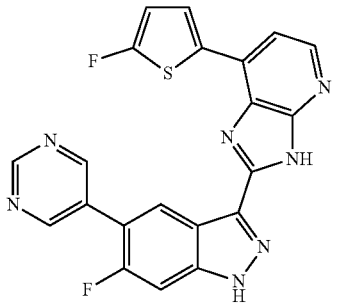
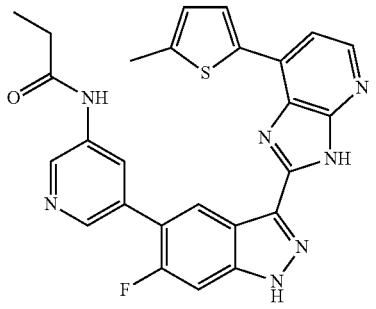
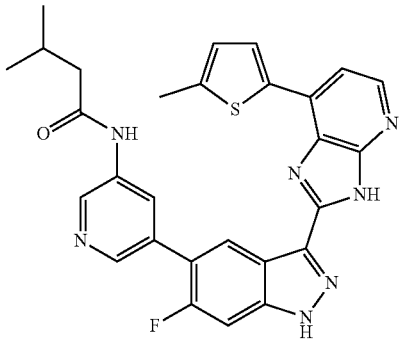
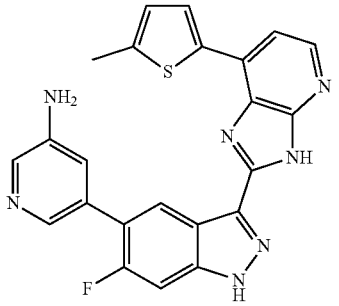
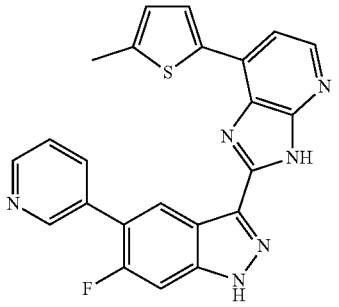
1300	
1301	
1302	
1303	
1304	

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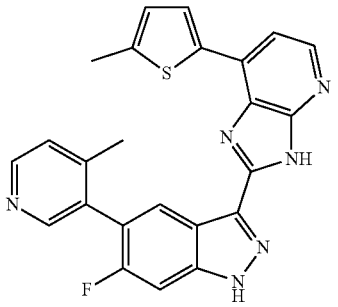
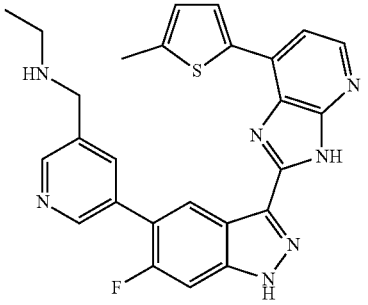
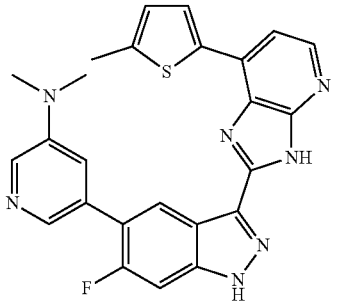
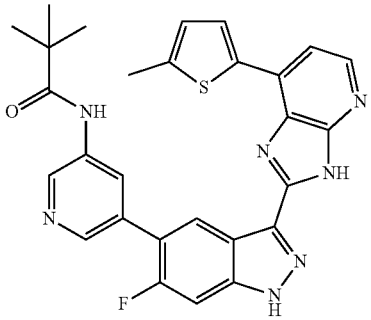
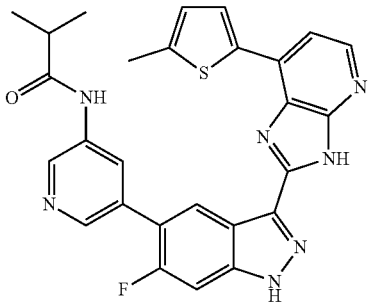
1305	
1306	
1307	
1308	
1309	

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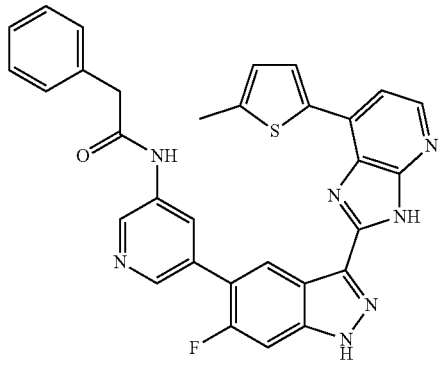

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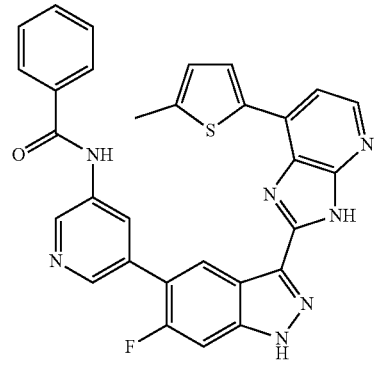

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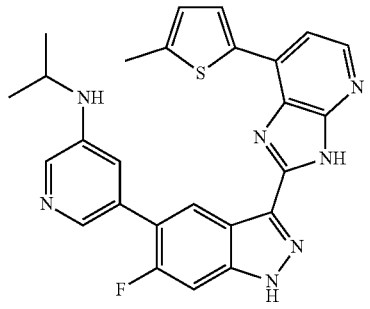

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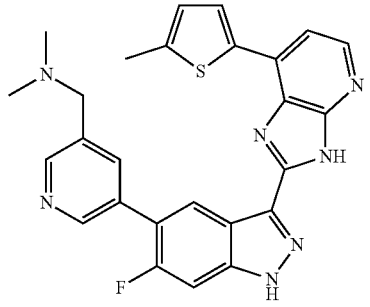

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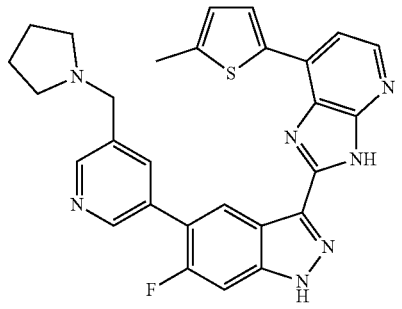

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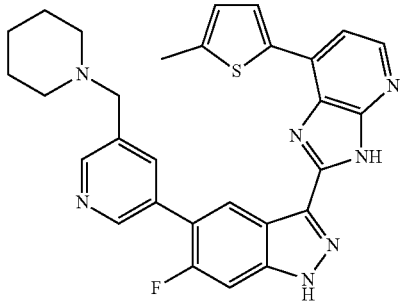

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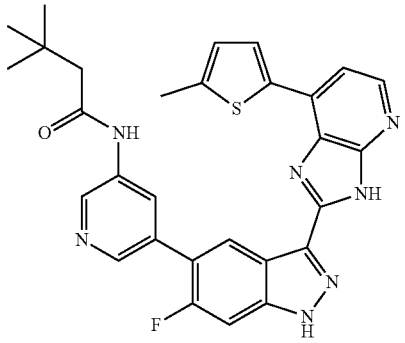

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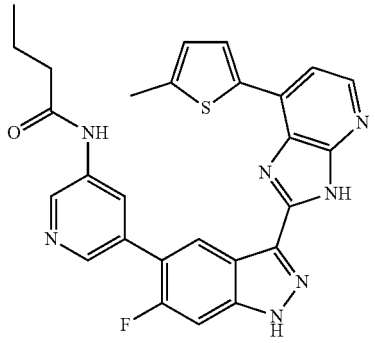

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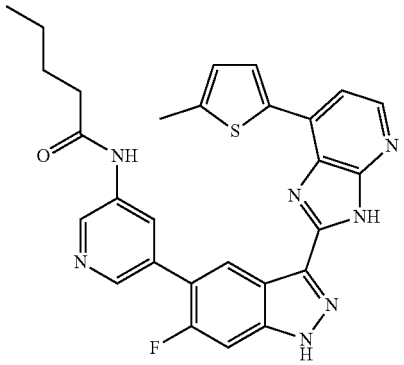
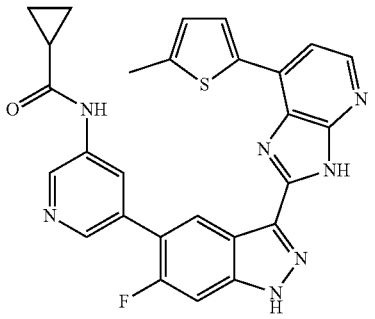
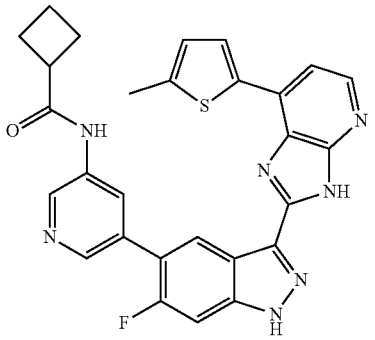
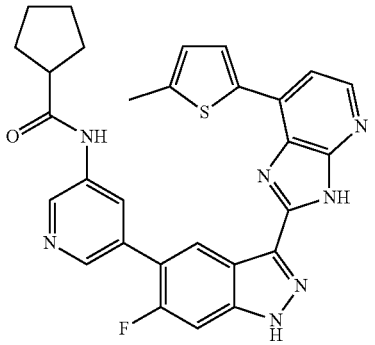
1318	
1319	
1320	
1321	

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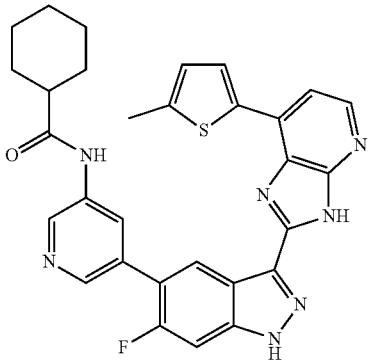
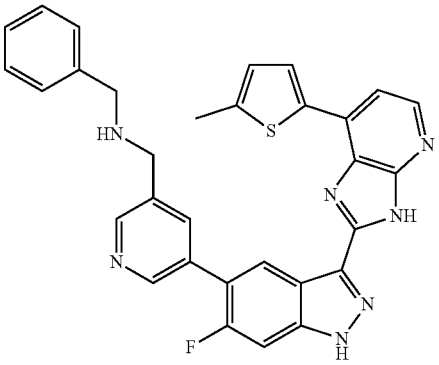
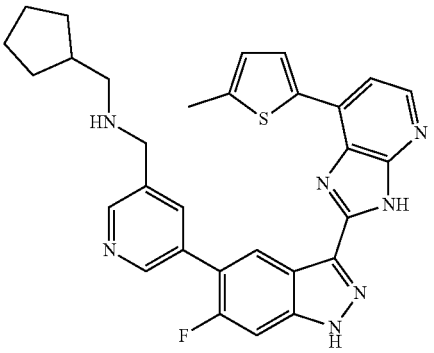
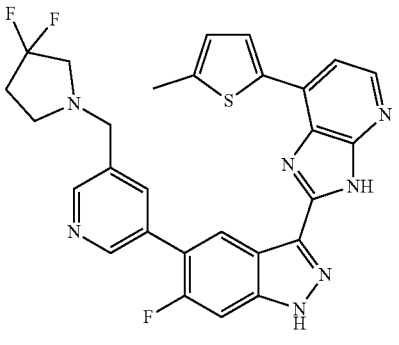
1322	
1323	
1324	
1325	

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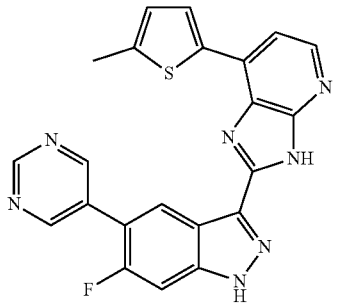
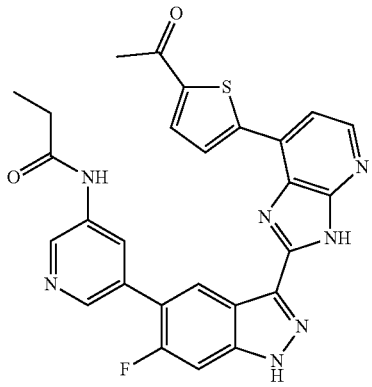
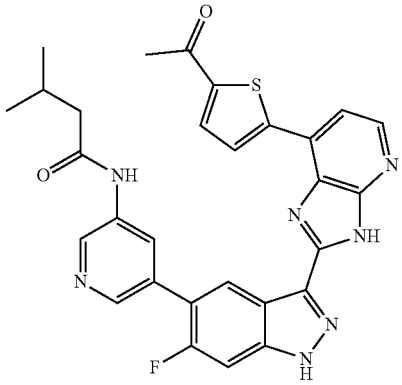
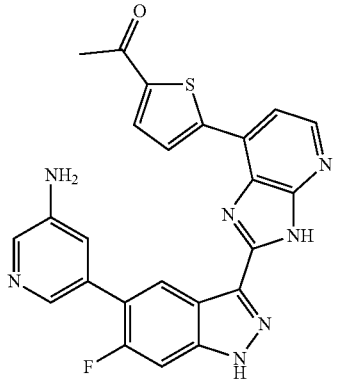
1326	
1327	
1328	
1329	

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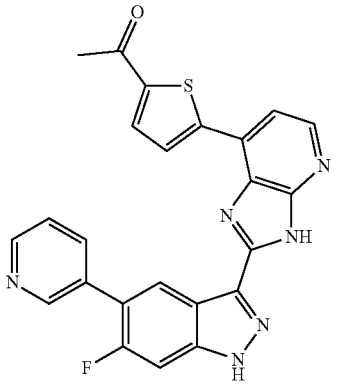
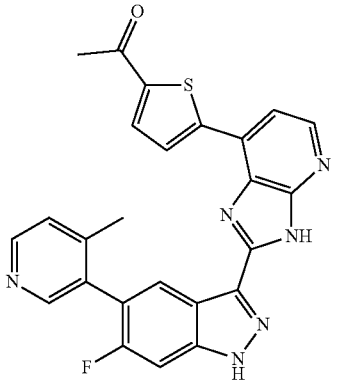
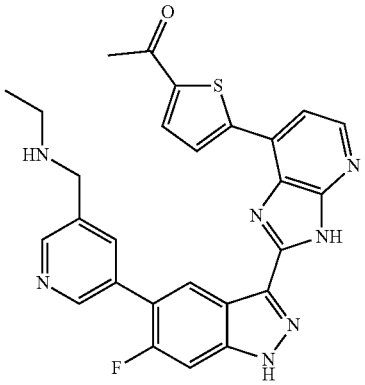
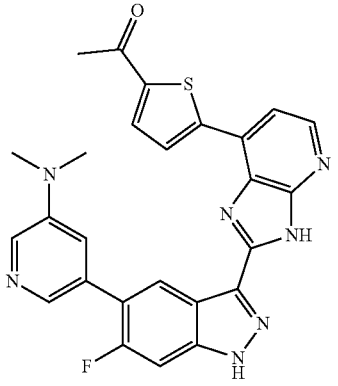
1330	
1331	
1332	
1333	

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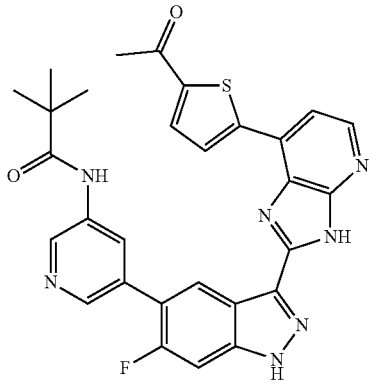
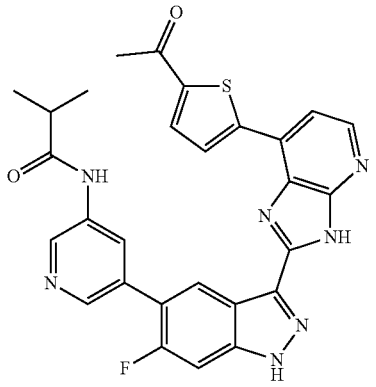
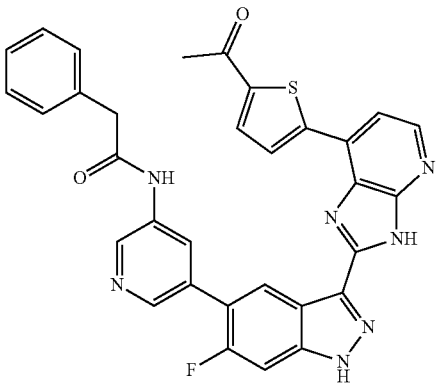
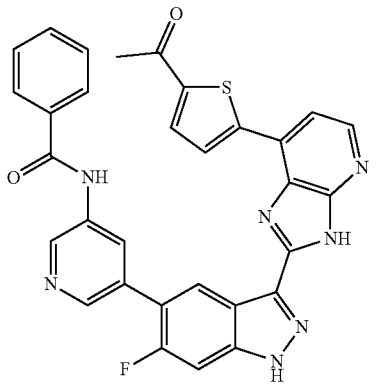
1334	
1335	
1336	
1337	

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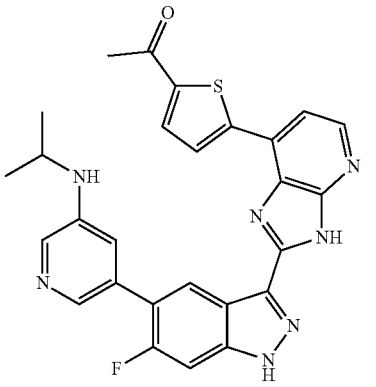
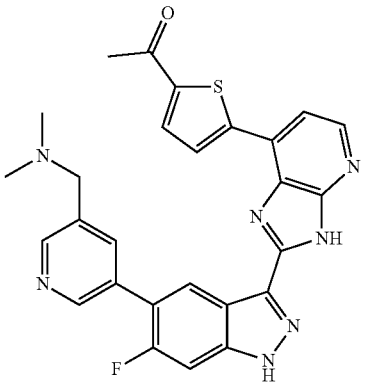
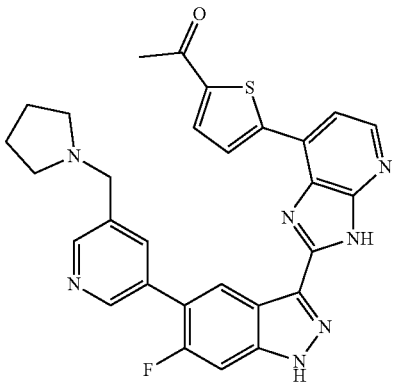
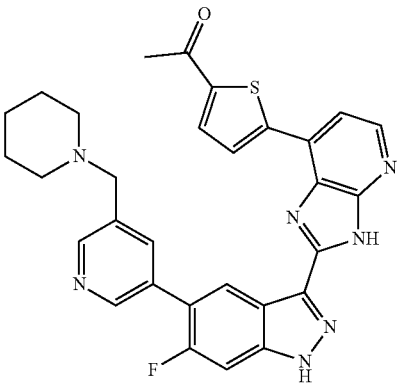
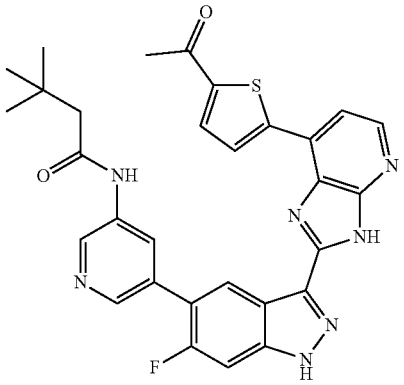
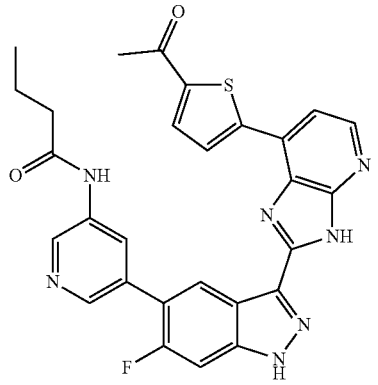
1338	
1339	
1340	
1341	

TABLE 1-continued

1342



1343



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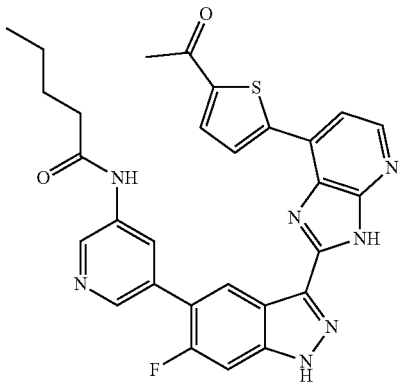

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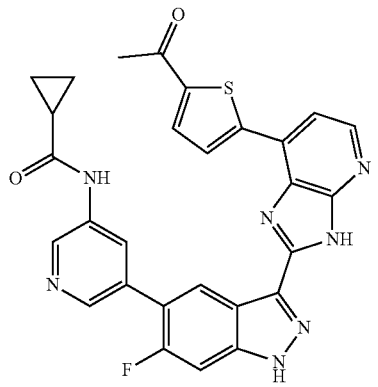

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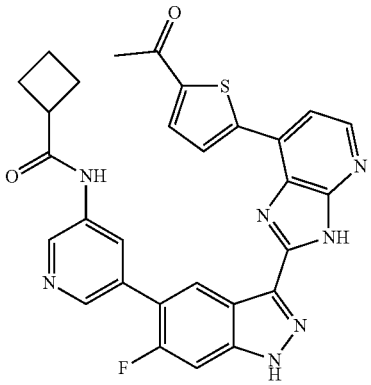

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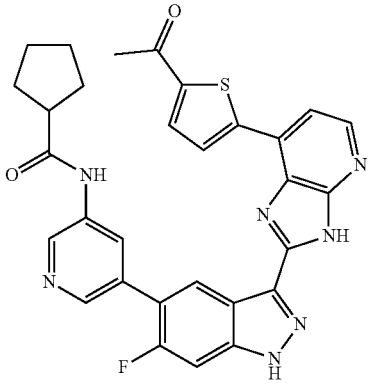

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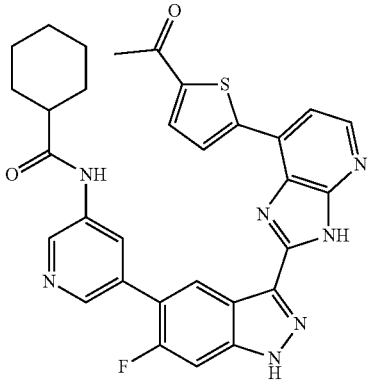

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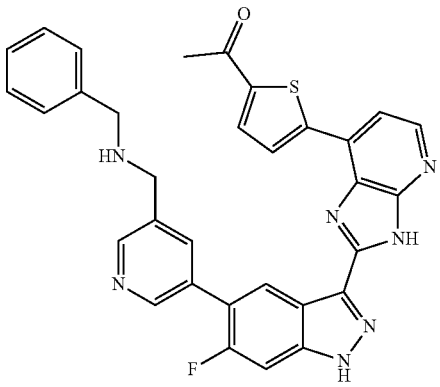

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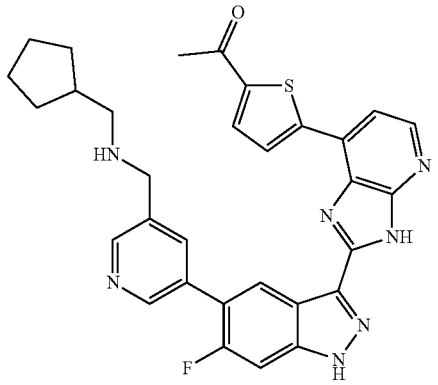

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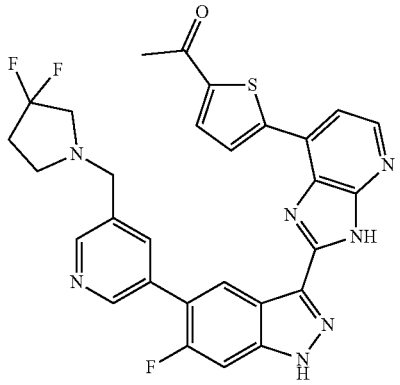

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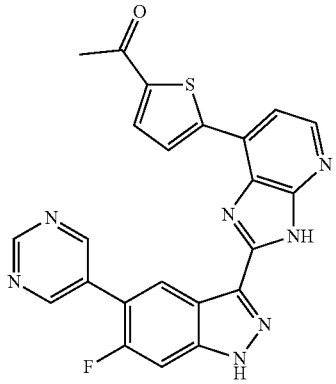

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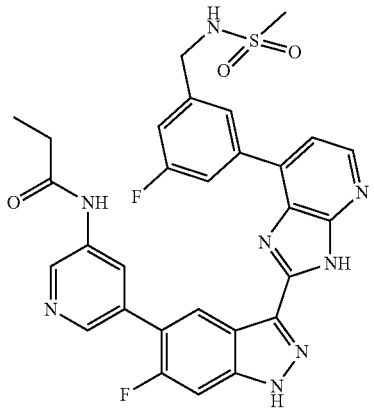

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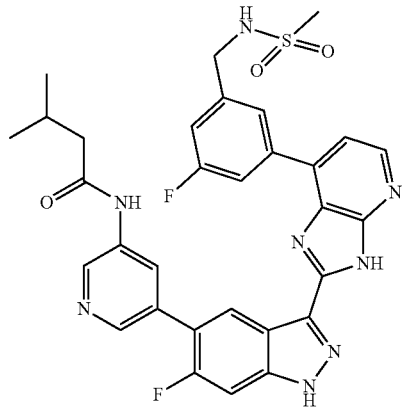

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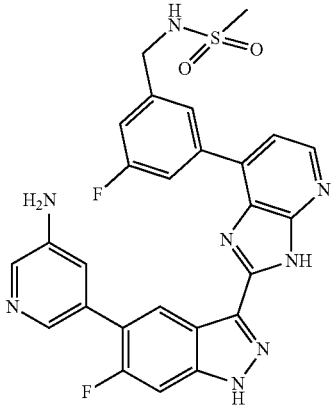

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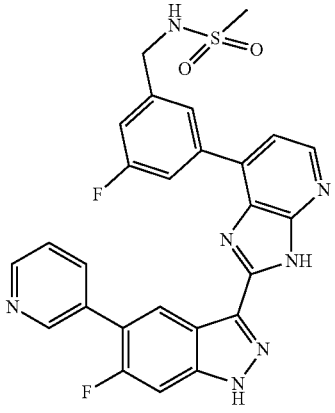

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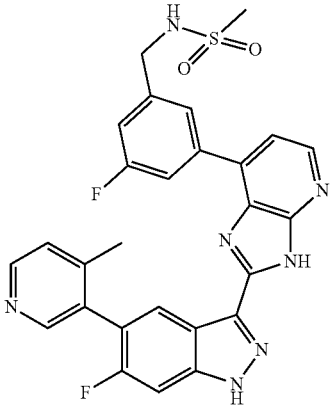
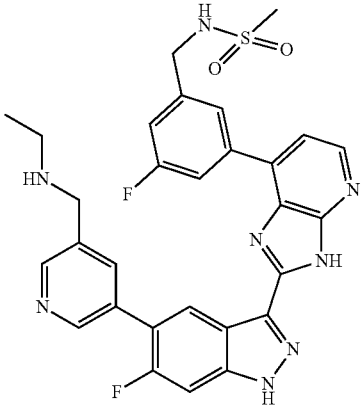
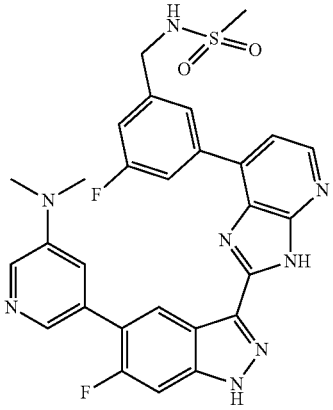
1357	
1358	
1359	

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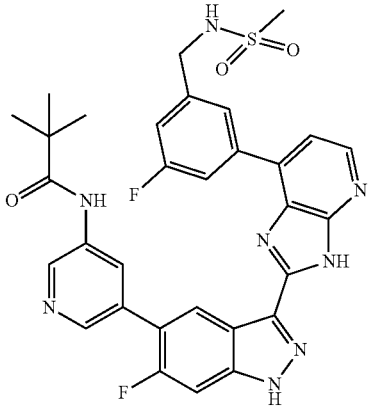
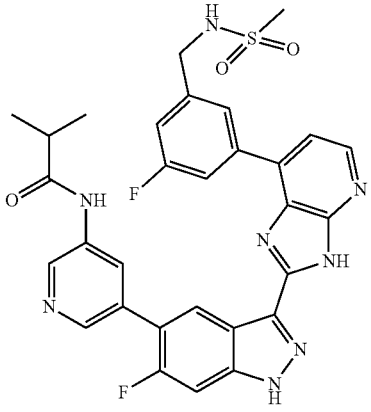
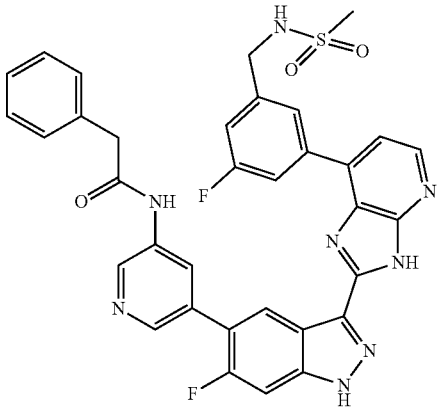
1360	
1361	
1362	

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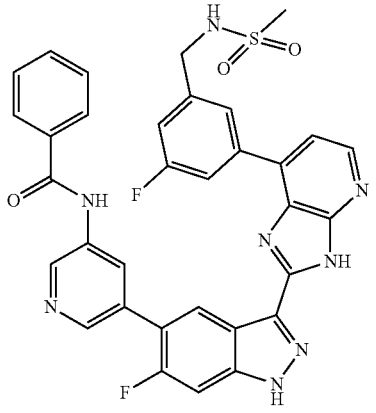
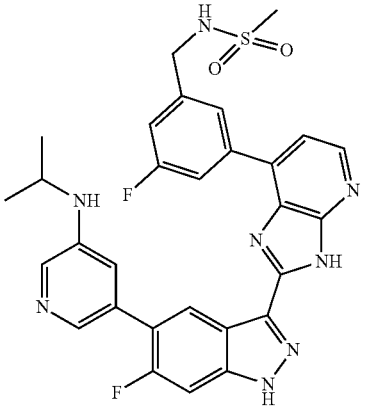
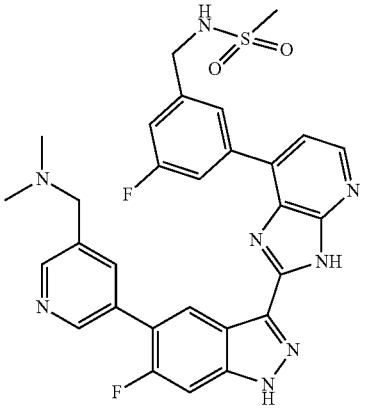
1363	
1364	
1365	

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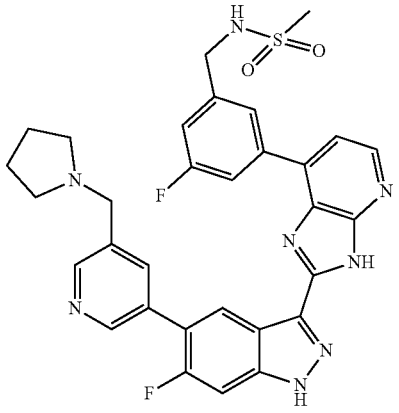
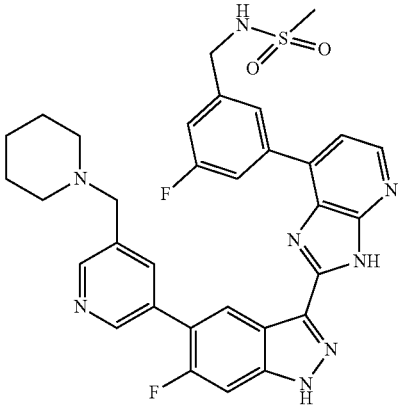
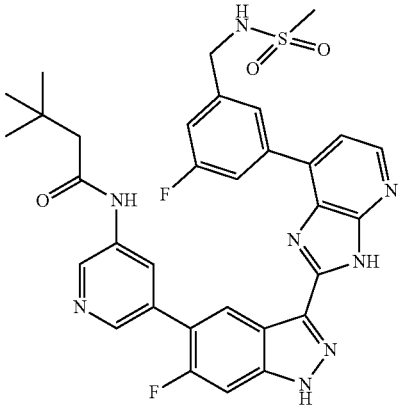
1366	
1367	
1368	

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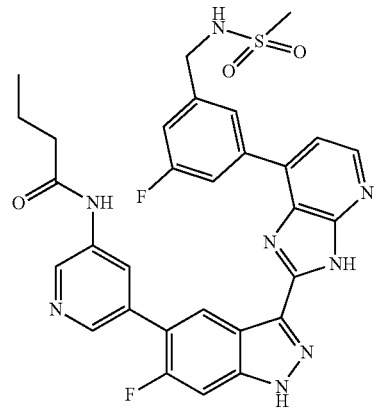
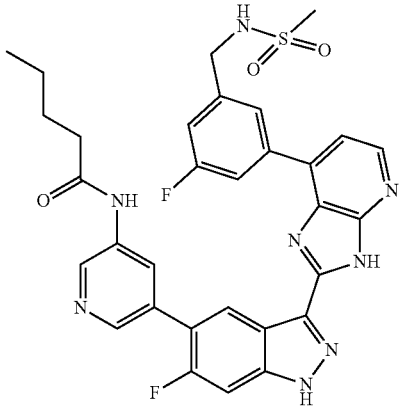
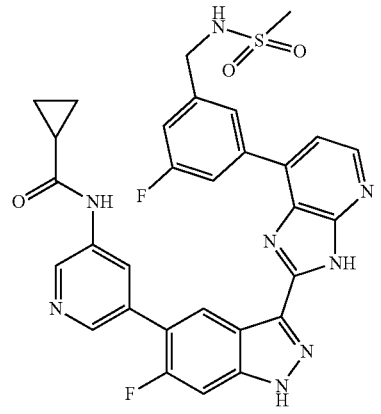
1369	
1370	
1371	

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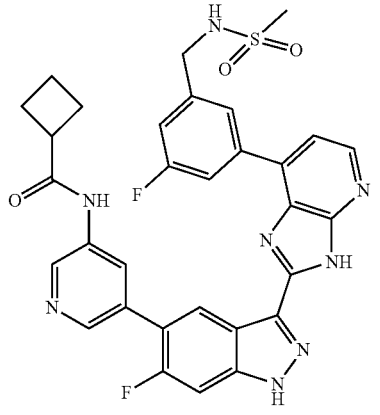
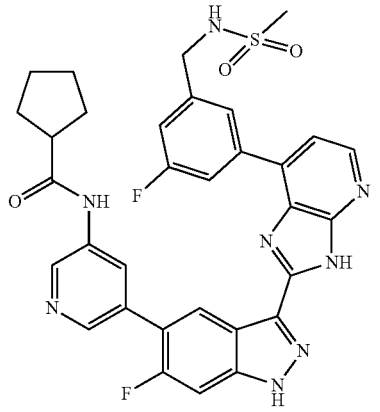
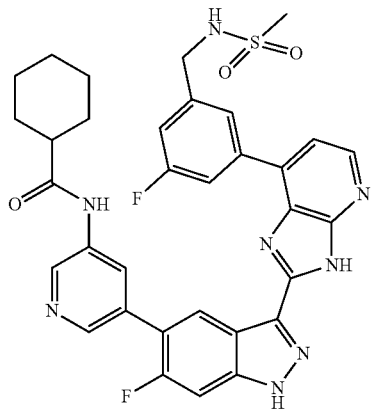
1372	
1373	
1374	

TABLE 1-continued

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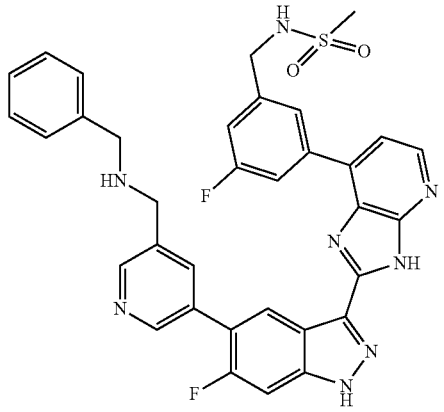

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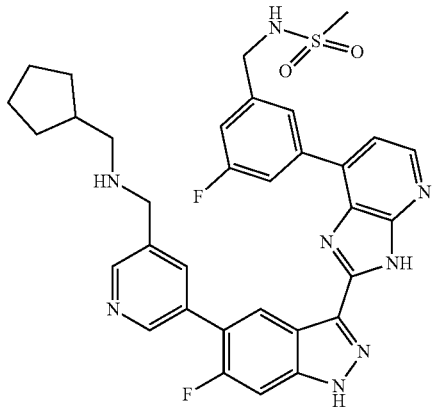

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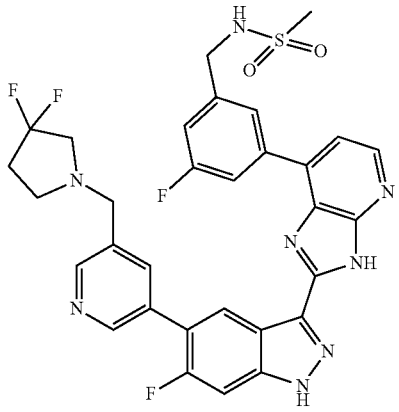

TABLE 1-continued

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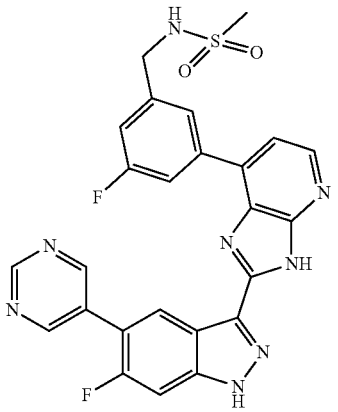

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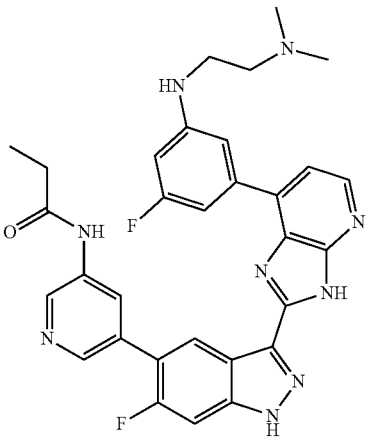

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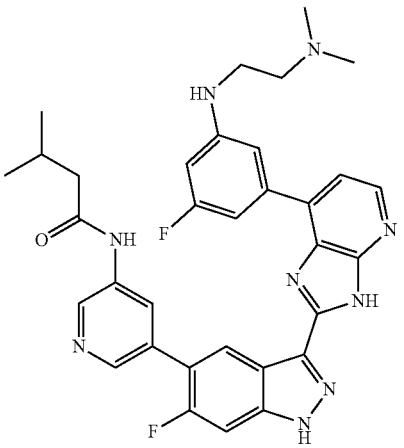

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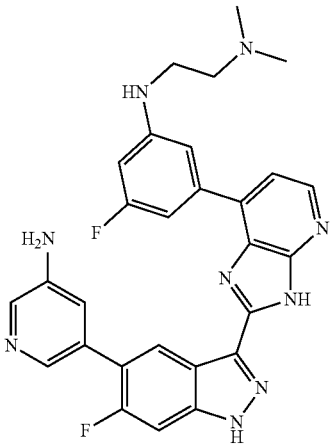
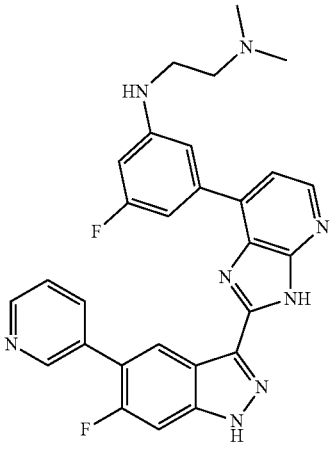
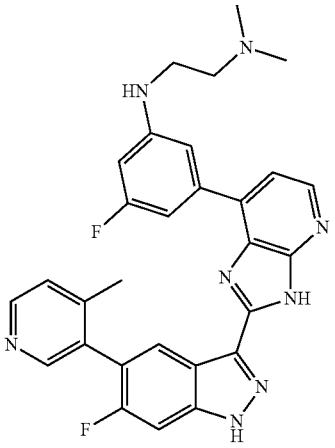
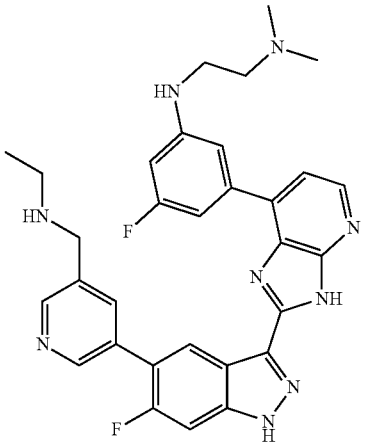
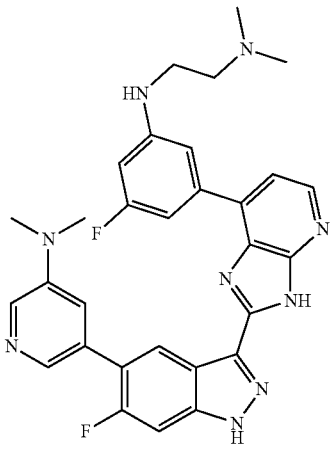
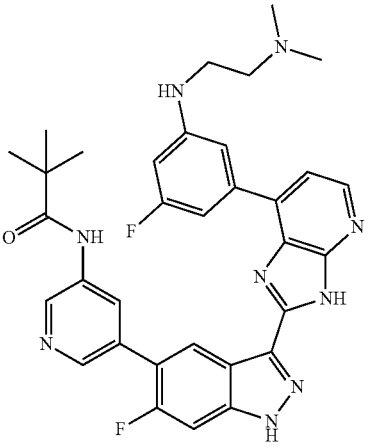
1381	
1382	
1383	

TABLE 1-continued

1384	
1385	
1386	

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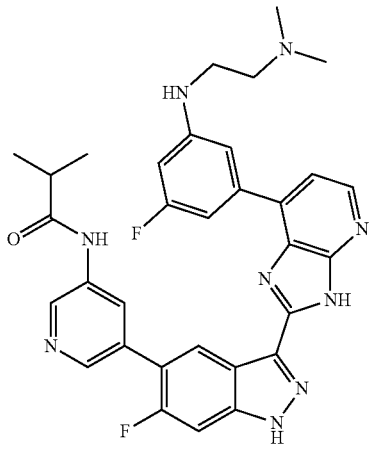
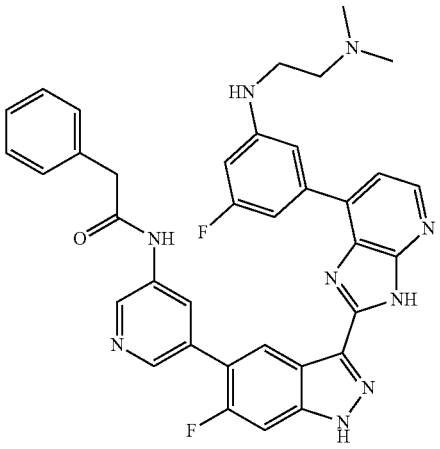
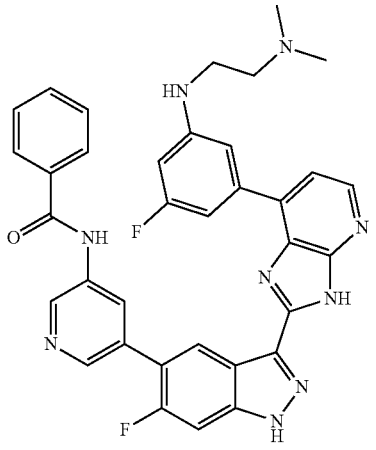
1387	
1388	
1389	

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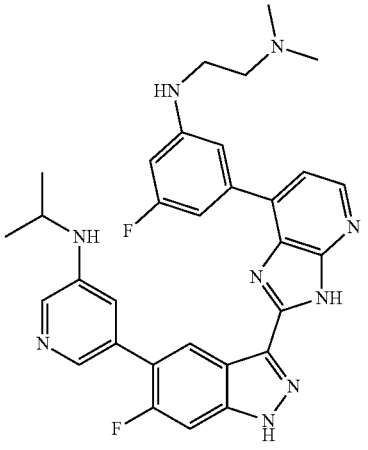
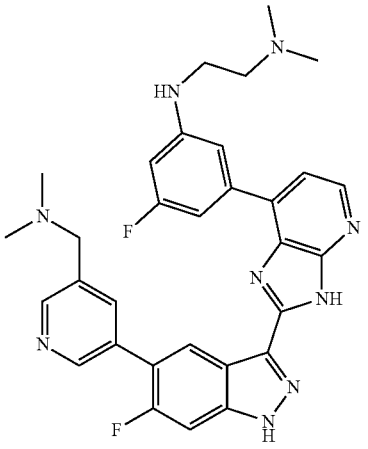
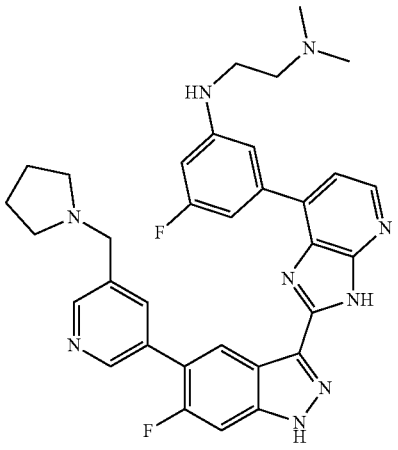
1390	
1391	
1392	

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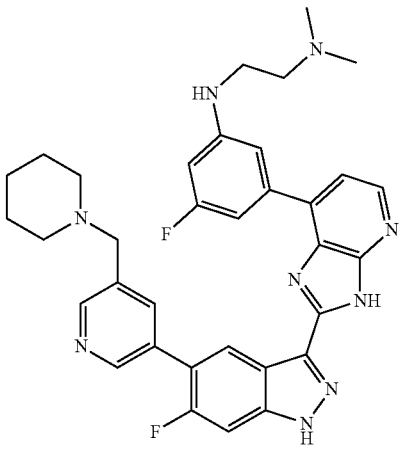
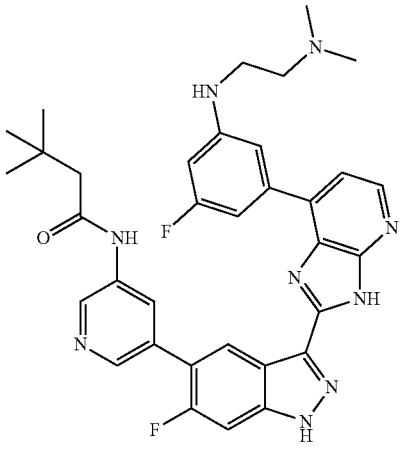
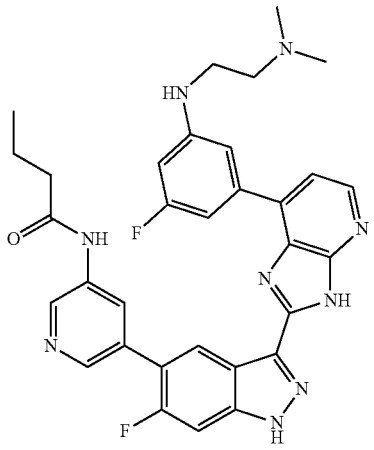
1393	
1394	
1395	

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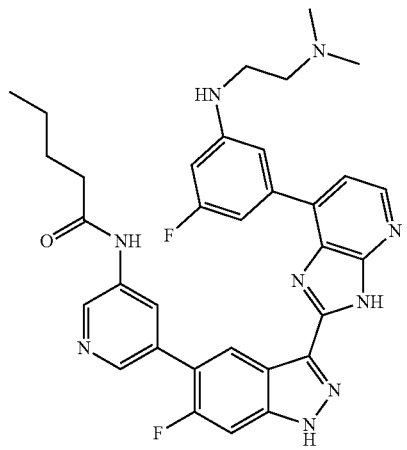
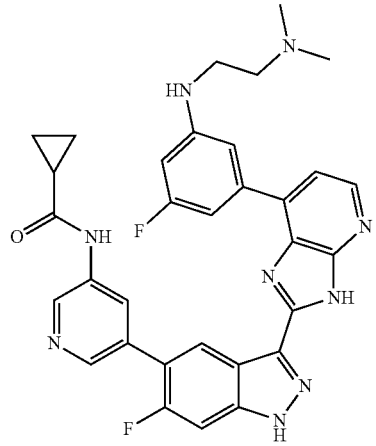
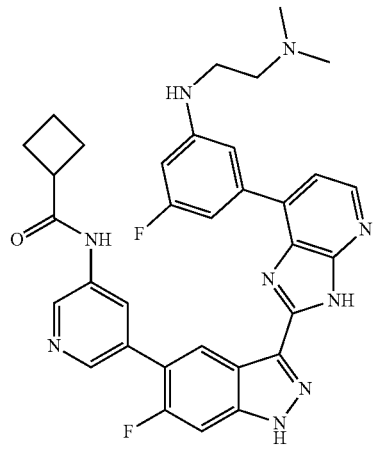
1396	
1397	
1398	

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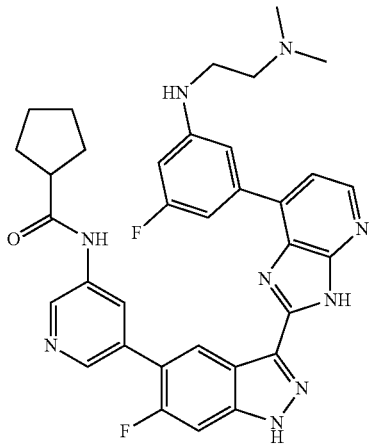
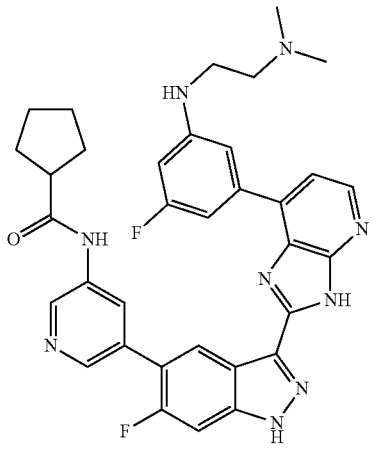
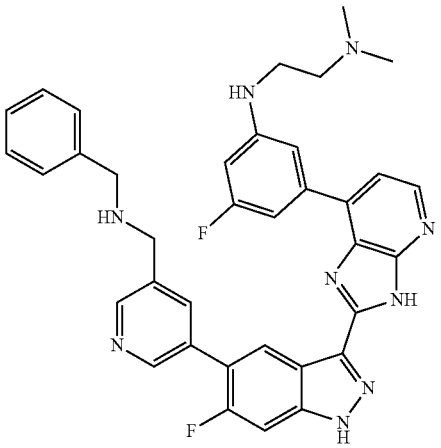
1399	
1400	
1401	

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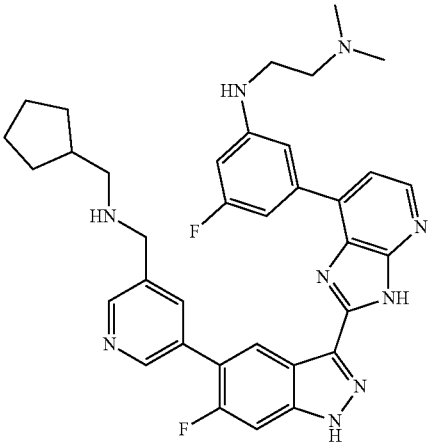
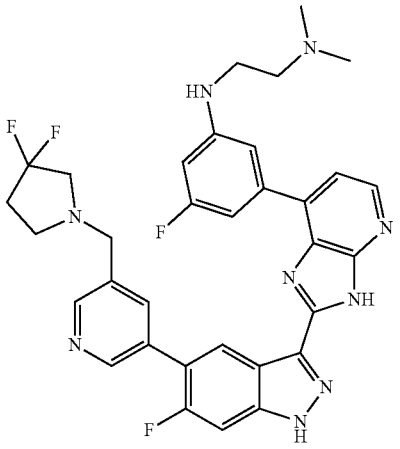
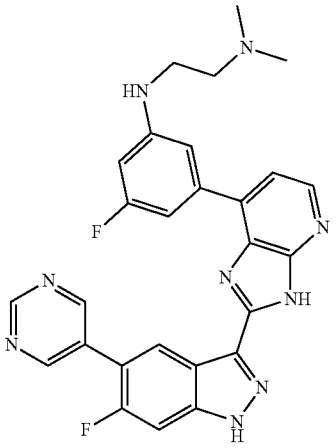
1402	
1403	
1404	

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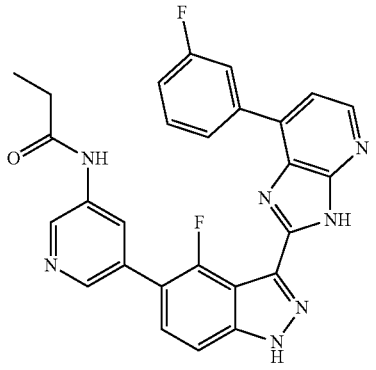
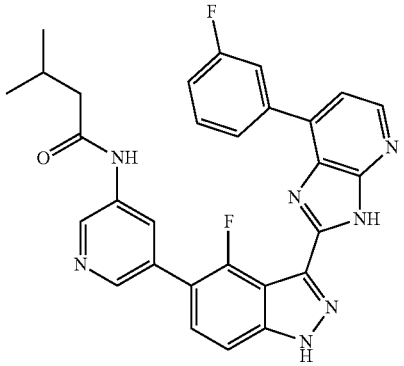
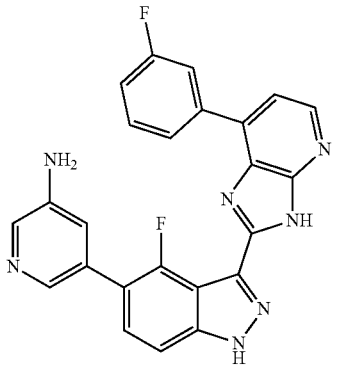
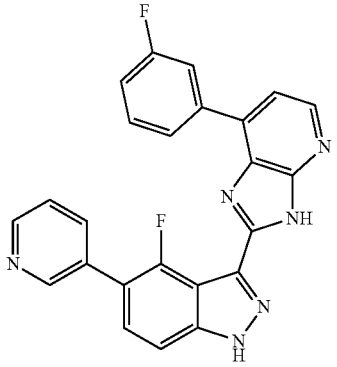
1405	
1406	
1407	
1408	

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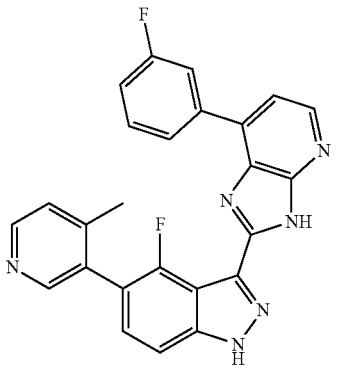
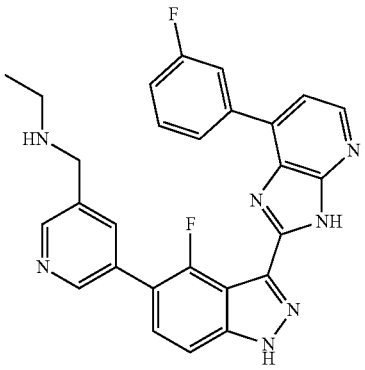
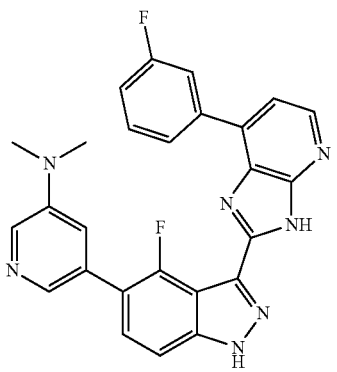
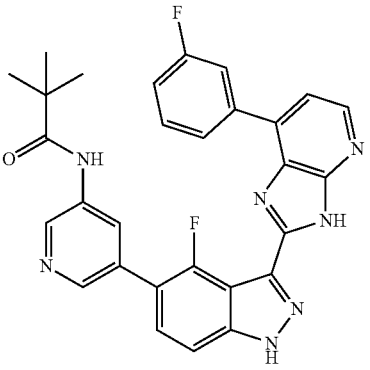
1409	
1410	
1411	
1412	

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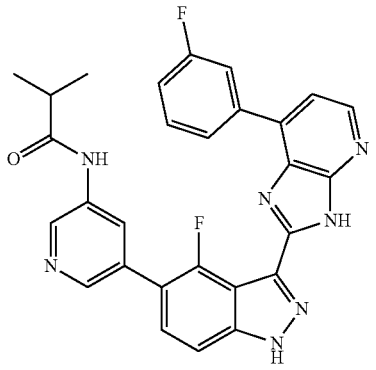
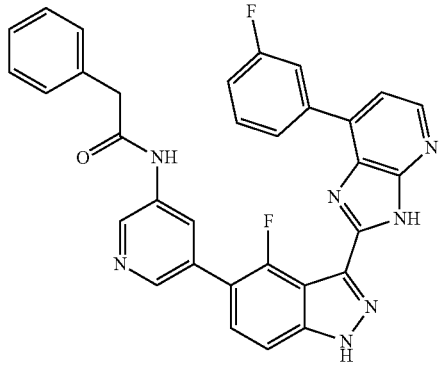
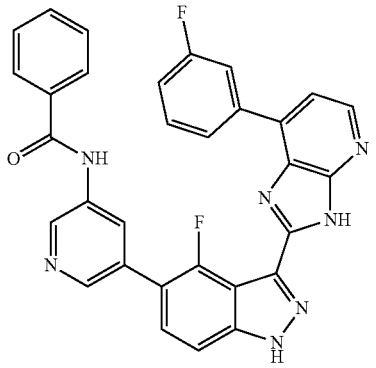
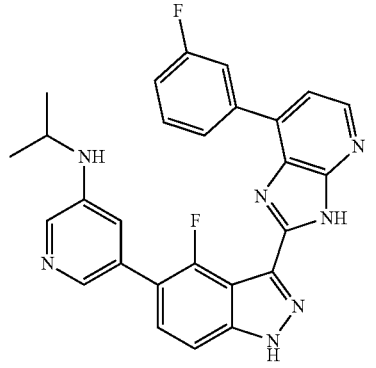
1413	
1414	
1415	
1416	

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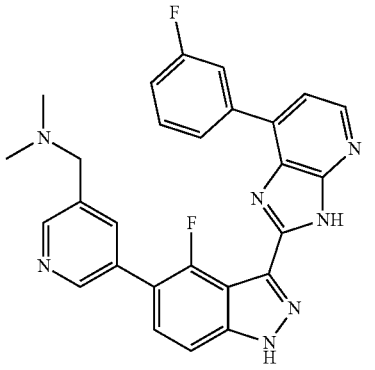
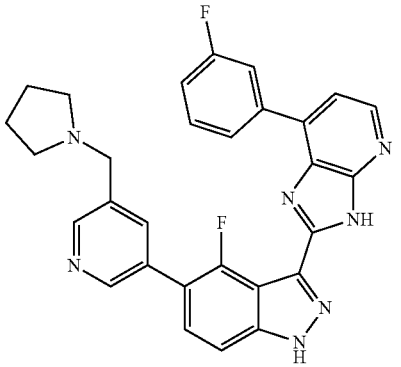
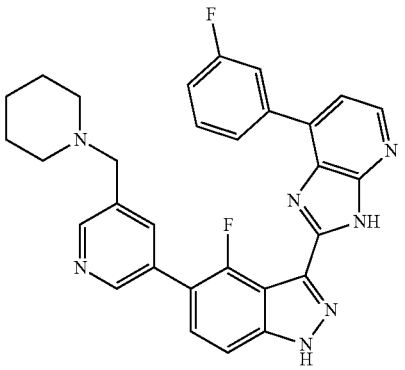
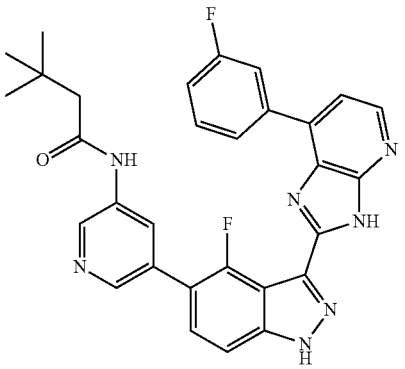
1417	
1418	
1419	
1420	

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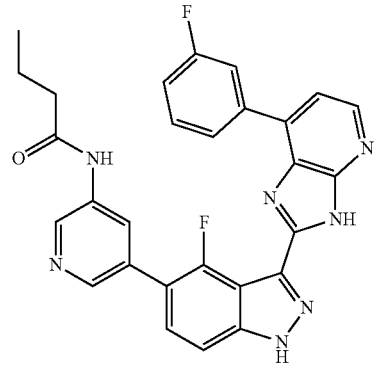
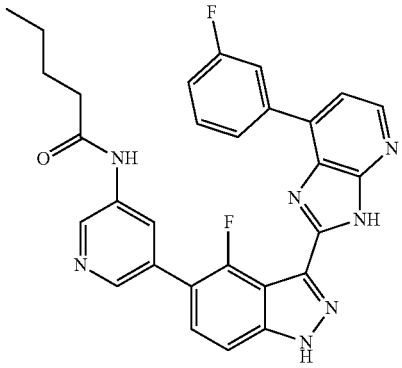
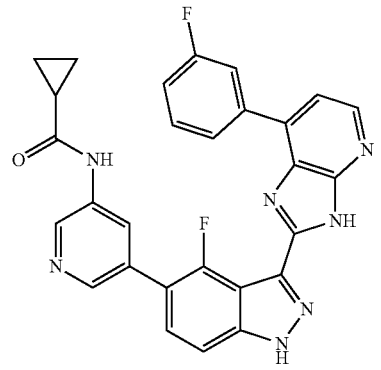
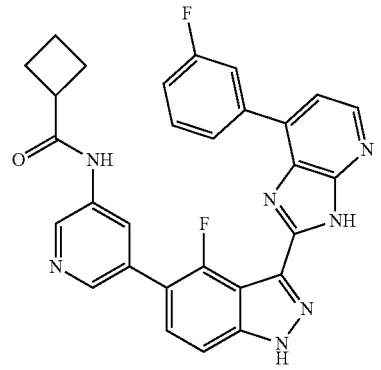
1421	
1422	
1423	
1424	

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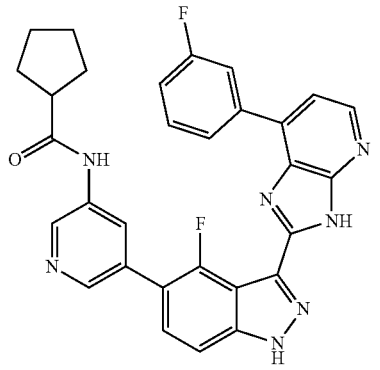
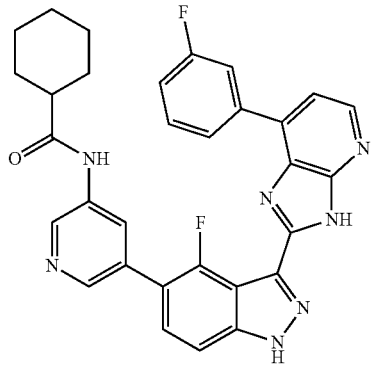
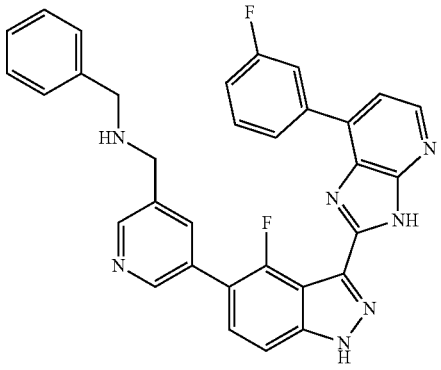
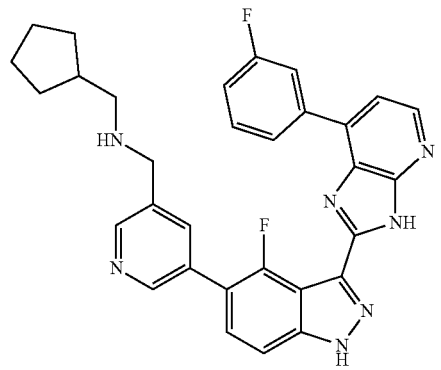
1425	
1426	
1427	
1428	

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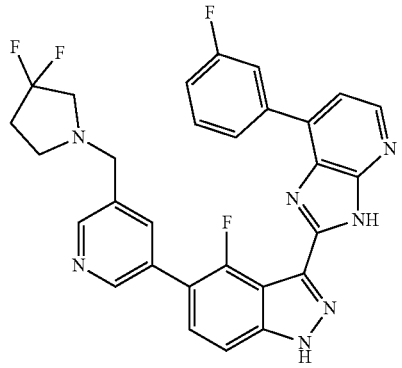
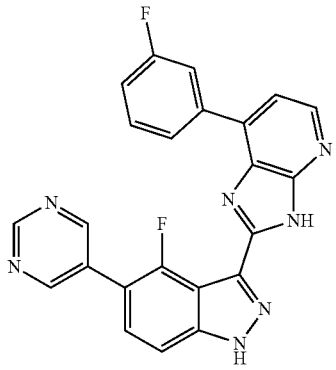
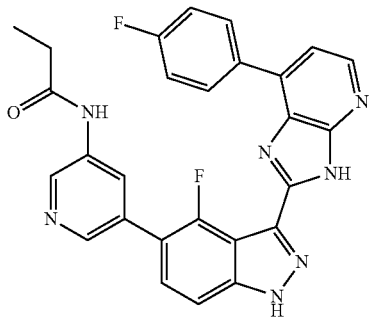
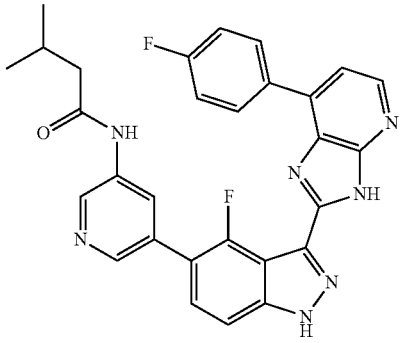
1429	
1430	
1431	
1432	

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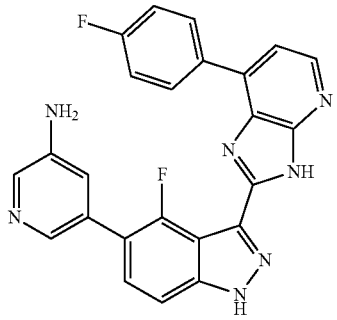
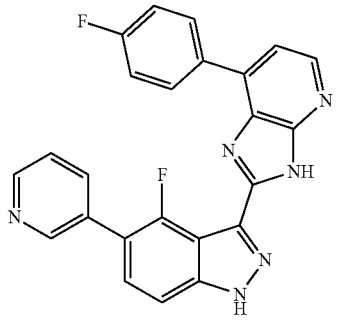
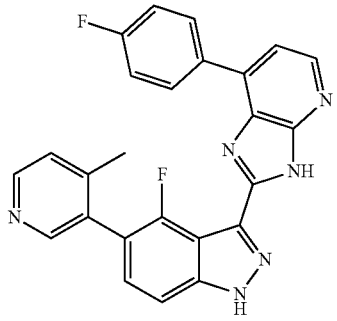
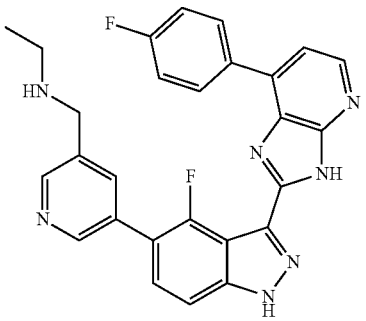
1433	
1434	
1435	
1436	

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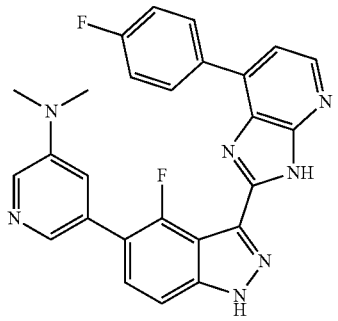
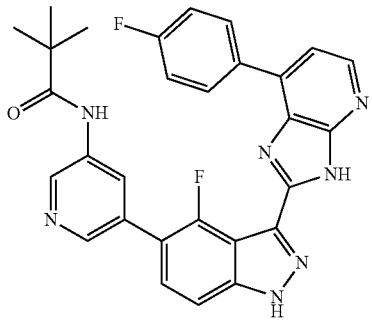
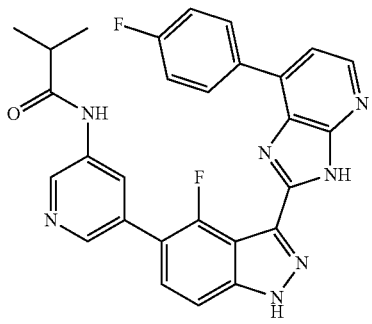
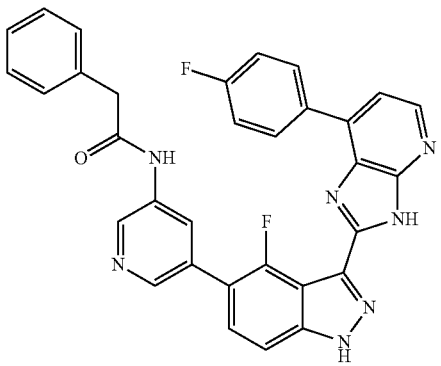
1437	
1438	
1439	
1440	

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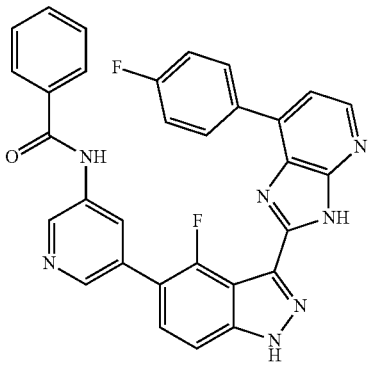
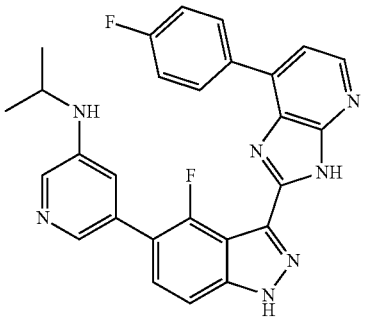
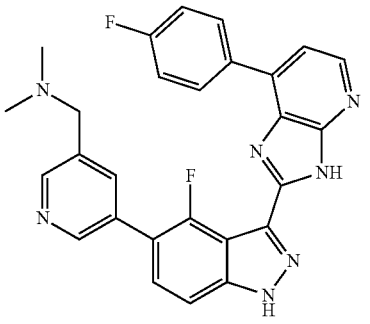
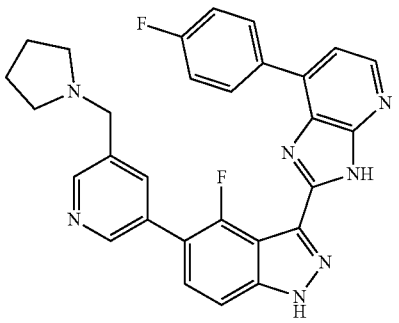
1441	
1442	
1443	
1444	

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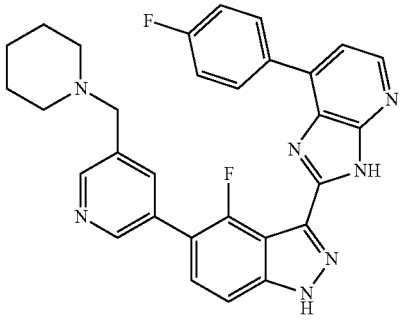
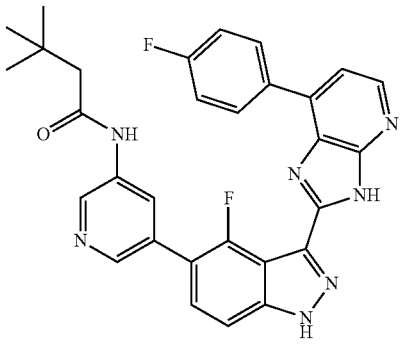
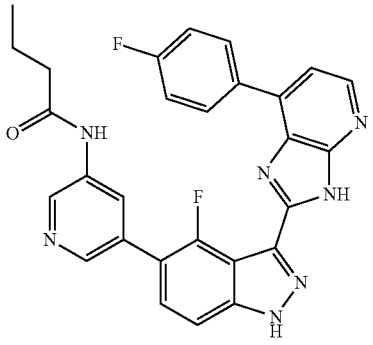
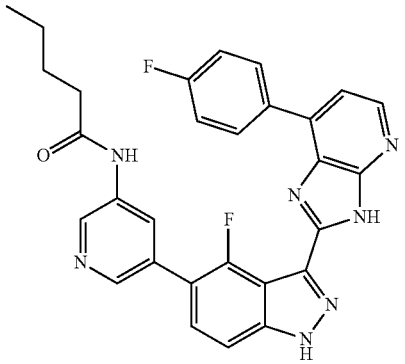
1445	
1446	
1447	
1448	

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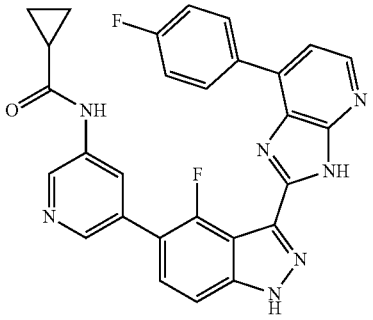
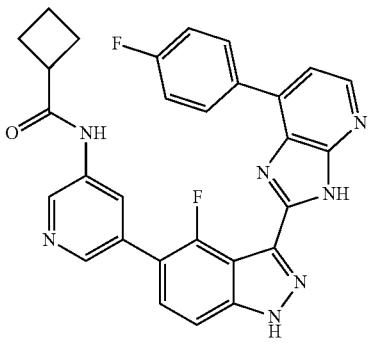
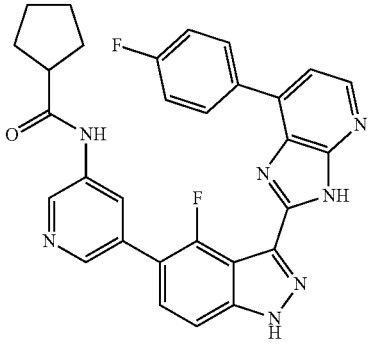
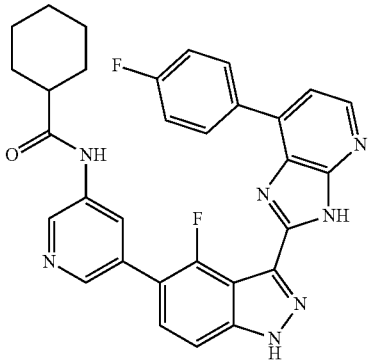
1449	
1450	
1451	
1452	

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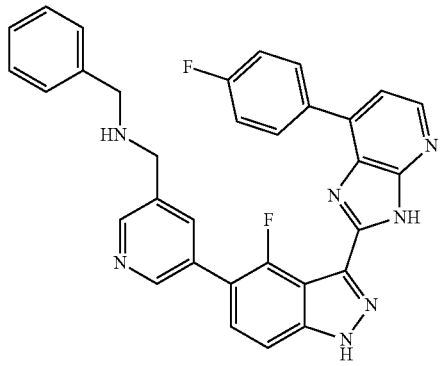
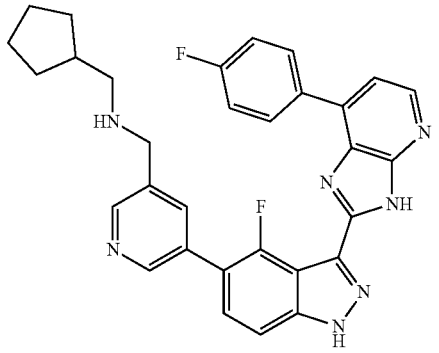
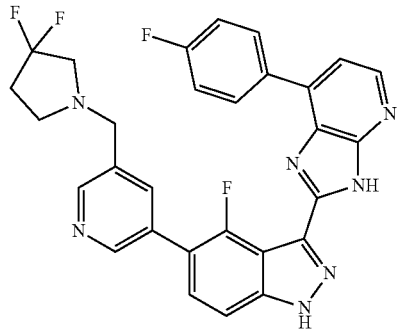
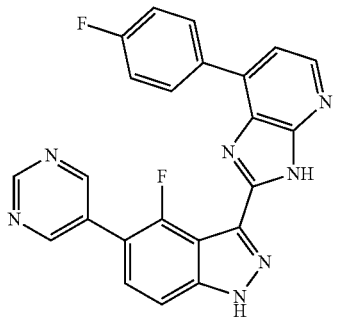
1453	
1454	
1455	
1456	

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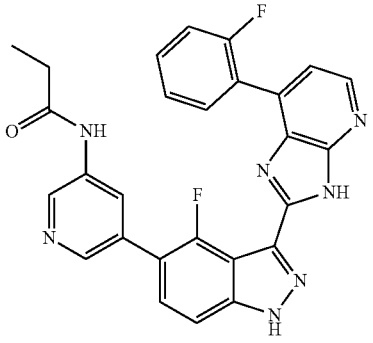
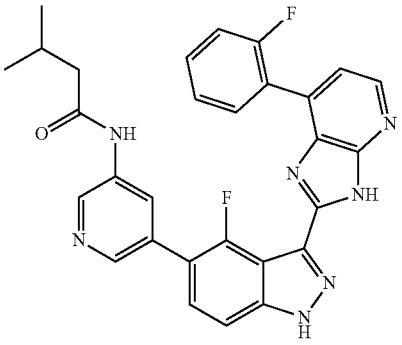
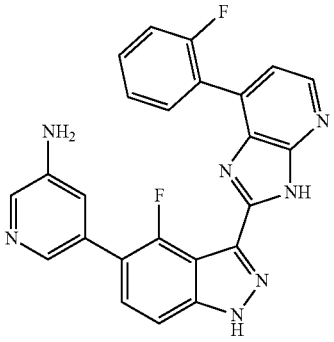
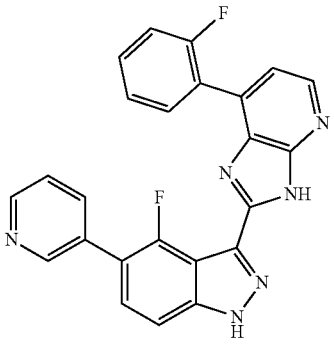
1457	
1458	
1459	
1460	

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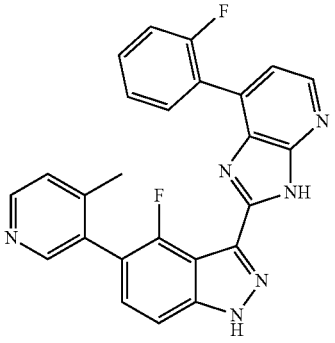
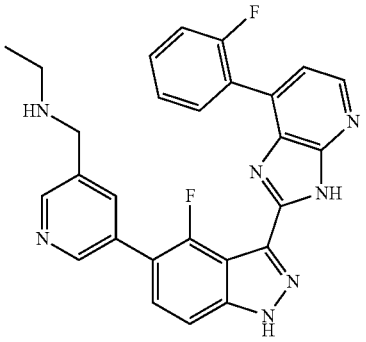
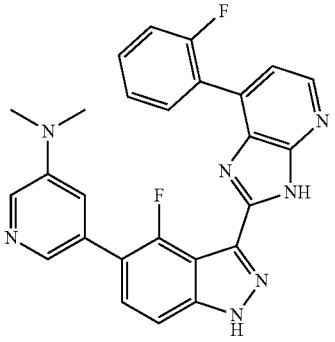
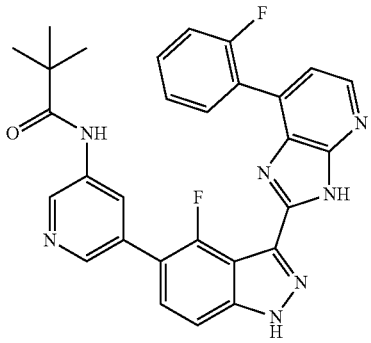
1461	
1462	
1463	
1464	

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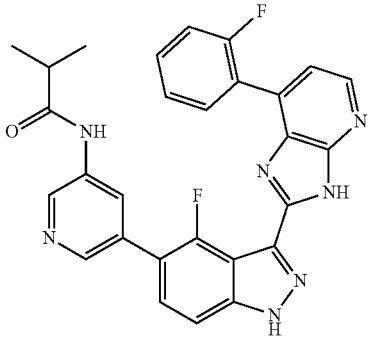
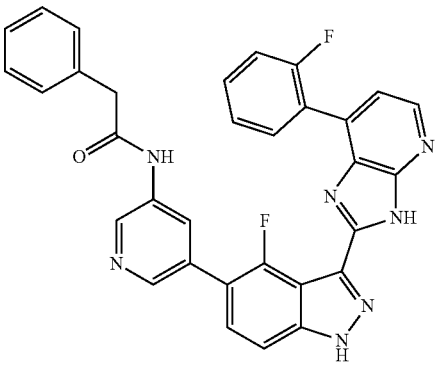
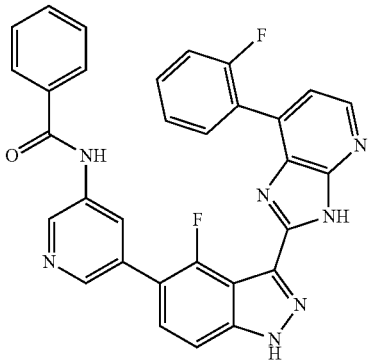
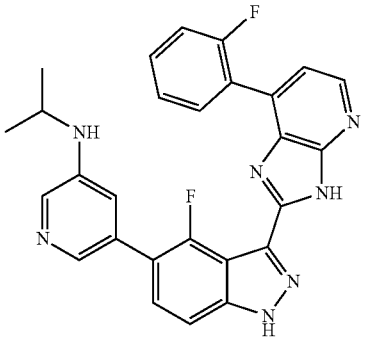
1465	
1466	
1467	
1468	

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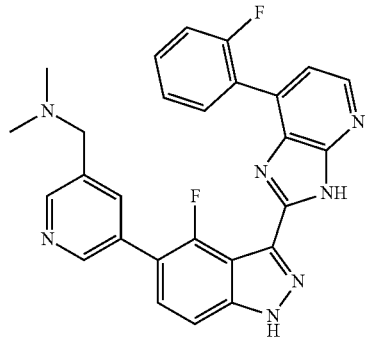
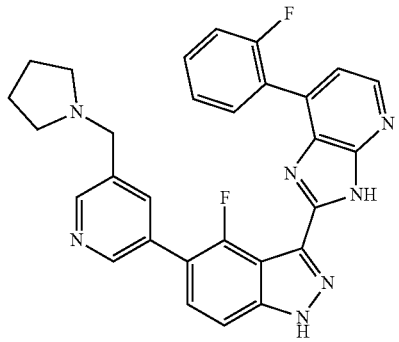
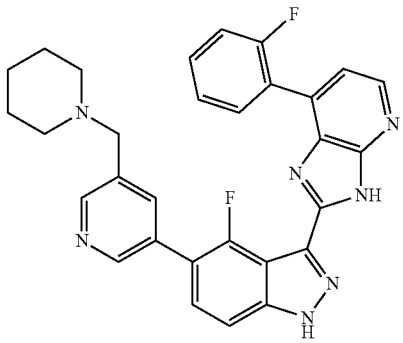
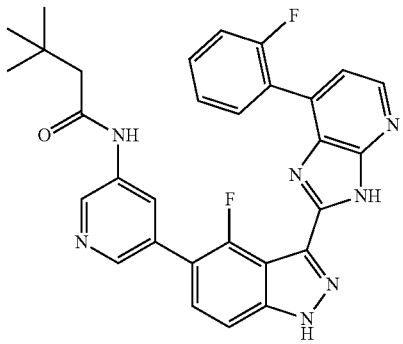
1469	
1470	
1471	
1472	

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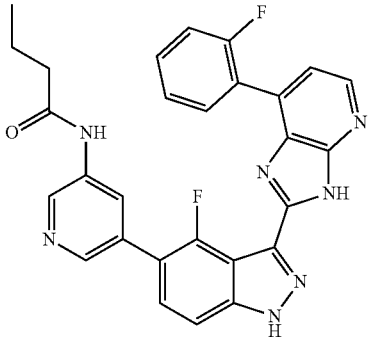
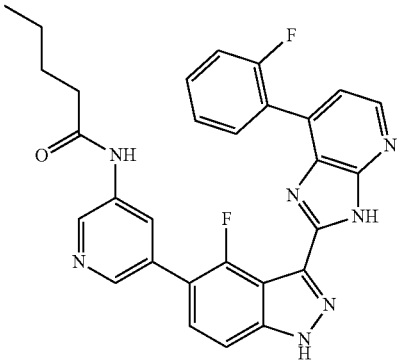
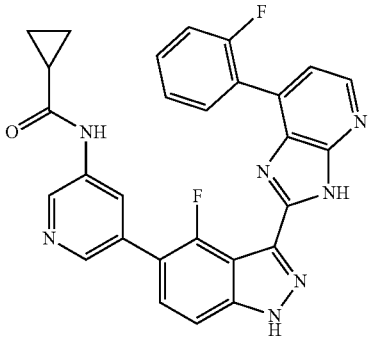
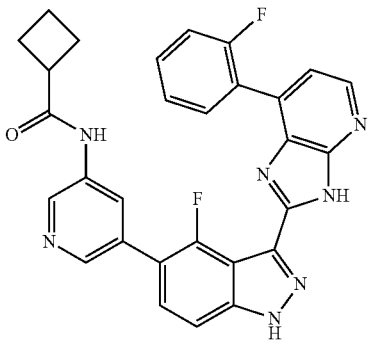
1473	
1474	
1475	
1476	

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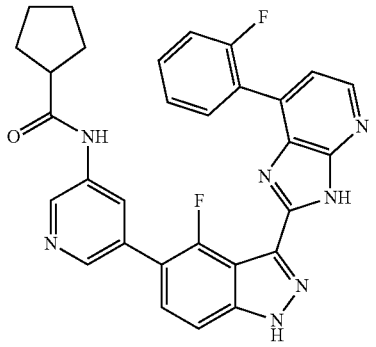
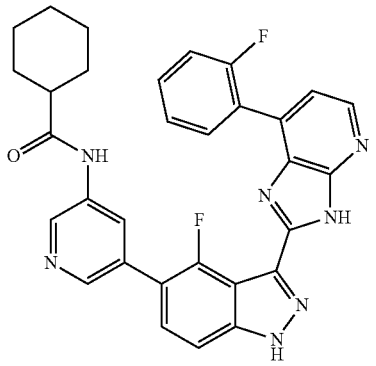
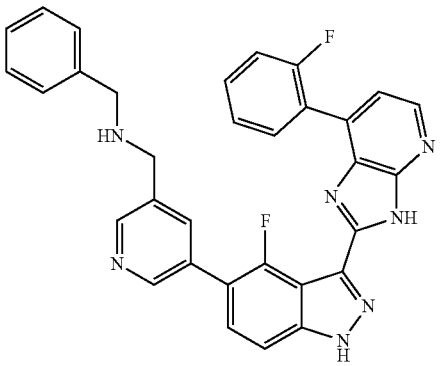
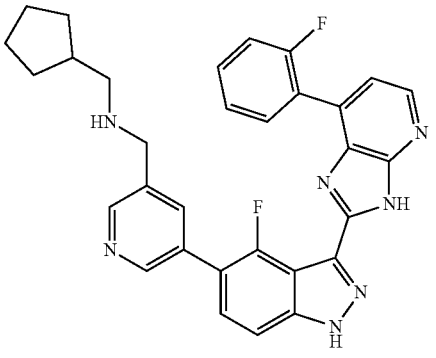
1477	
1478	
1479	
1480	

TABLE 1-continued

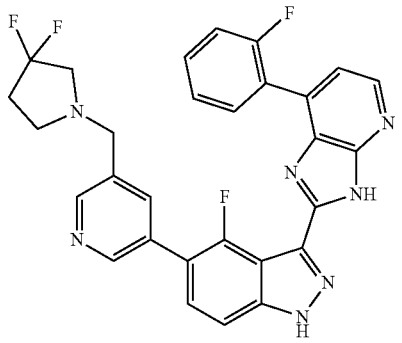
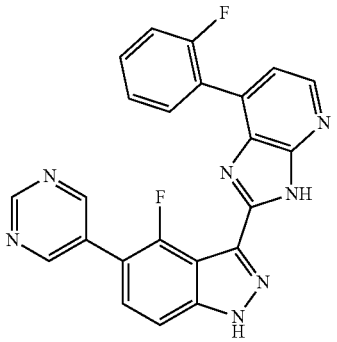
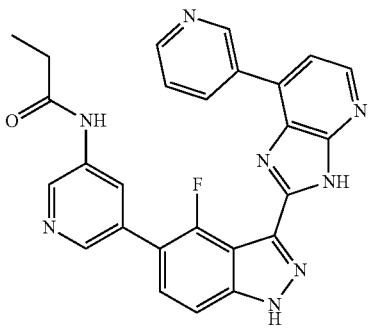
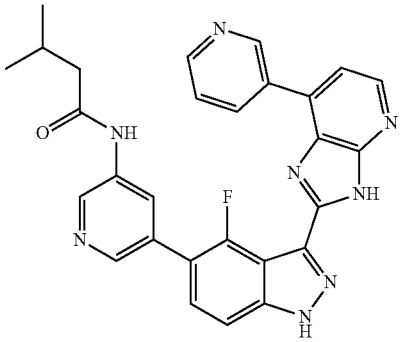
1481	
1482	
1483	
1484	

TABLE 1-continued

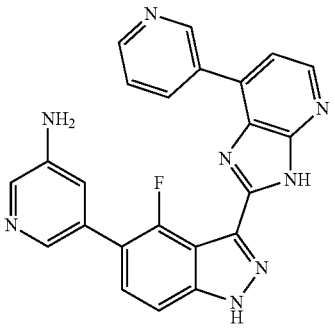
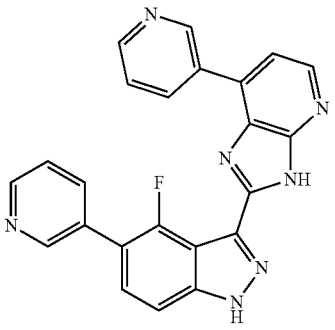
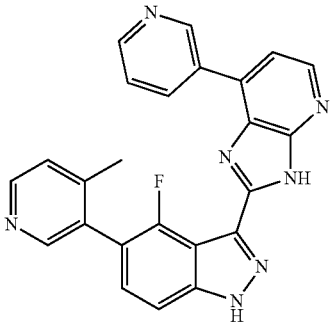
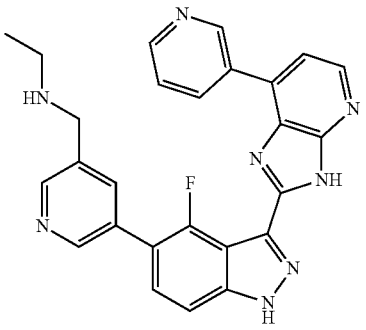
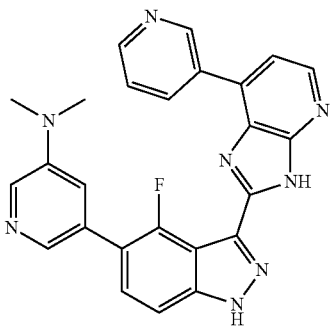
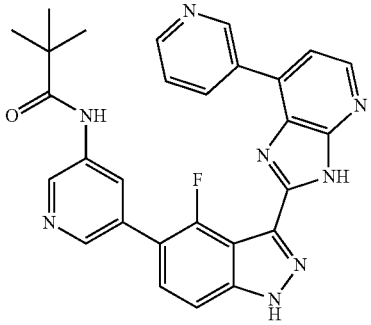
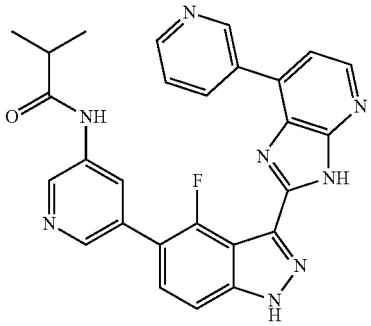
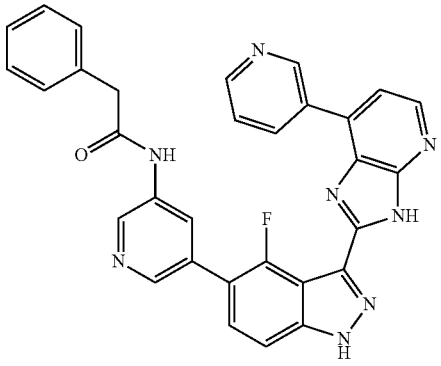
1485	
1486	
1487	
1488	

TABLE 1-continued

1489	
1490	
1491	
1492	

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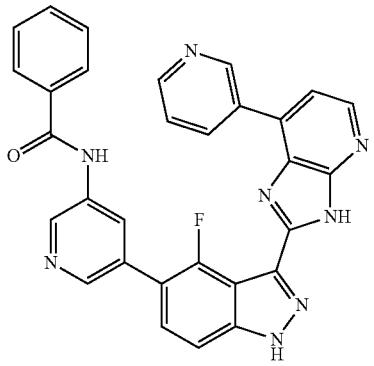
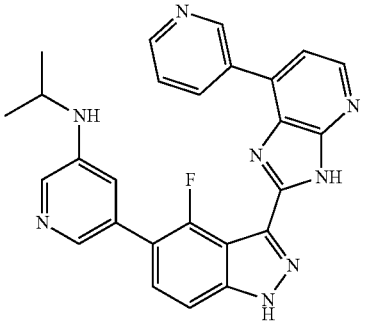
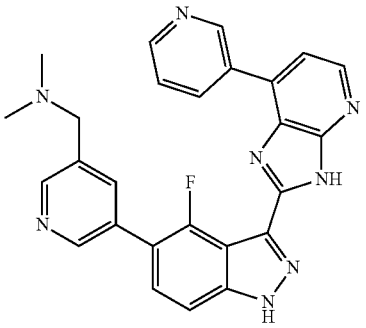
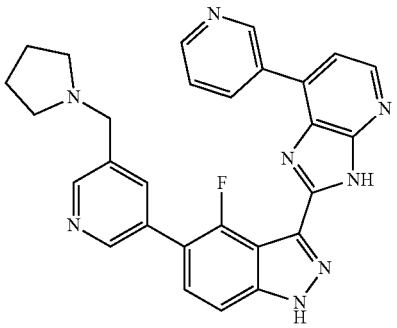
1493	
1494	
1495	
1496	

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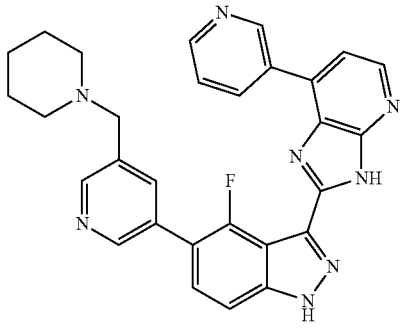
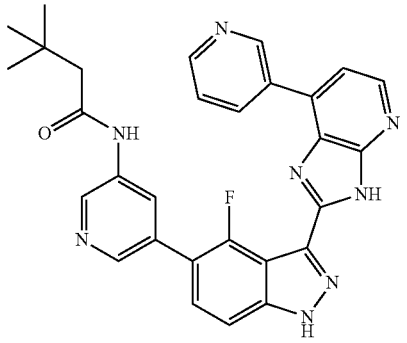
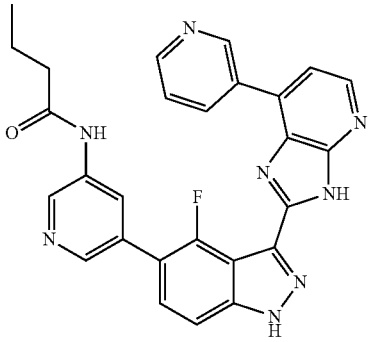
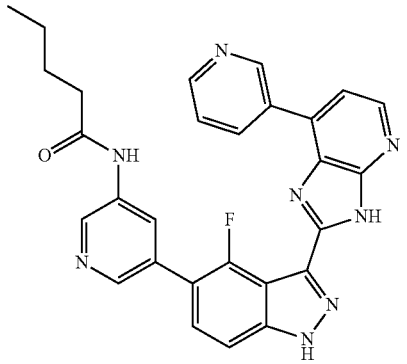
1497	
1498	
1499	
1500	

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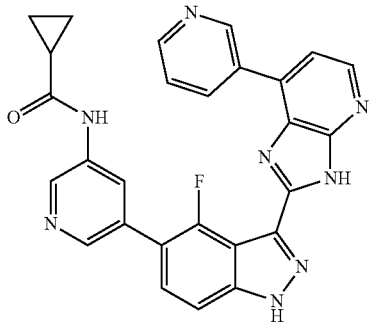

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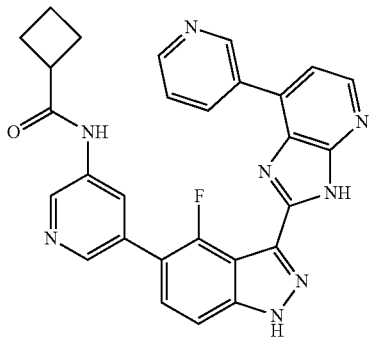

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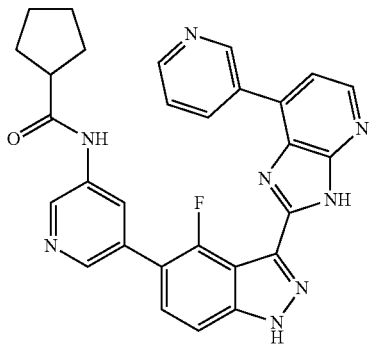

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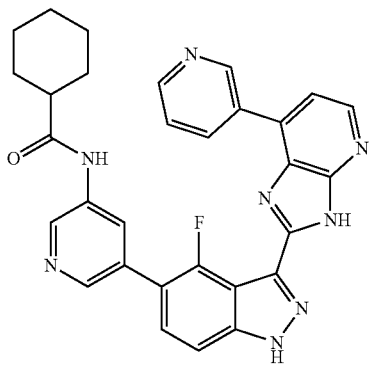

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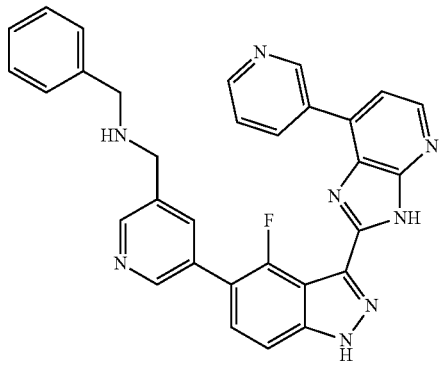

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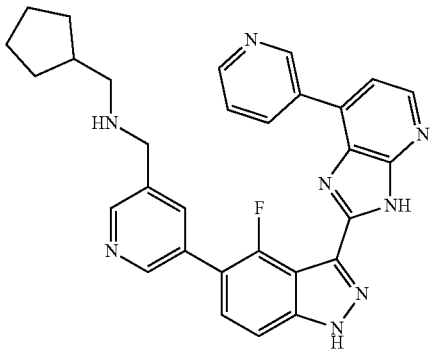

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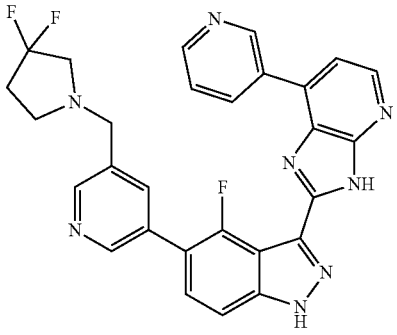

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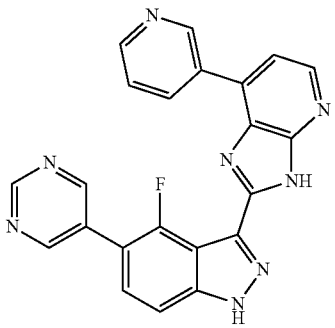

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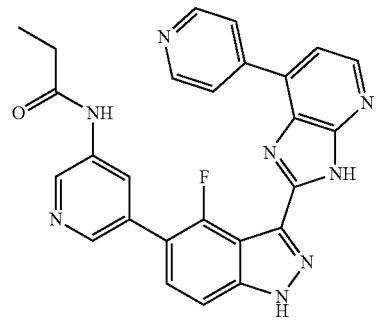
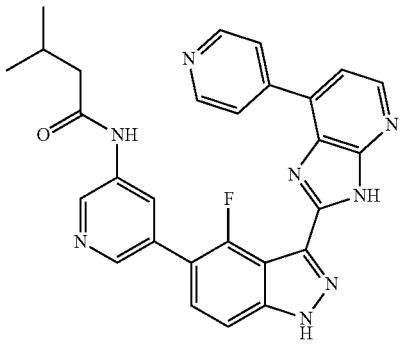
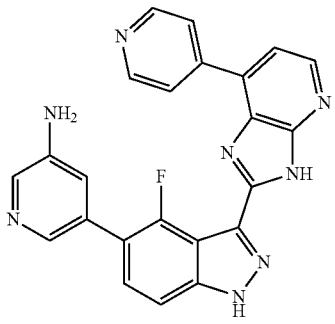
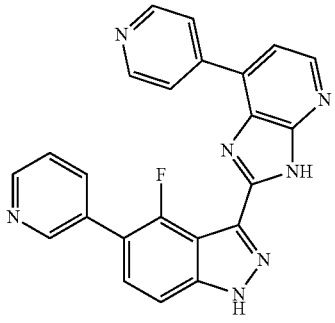
1509	
1510	
1511	
1512	

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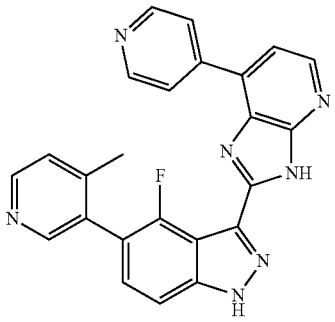
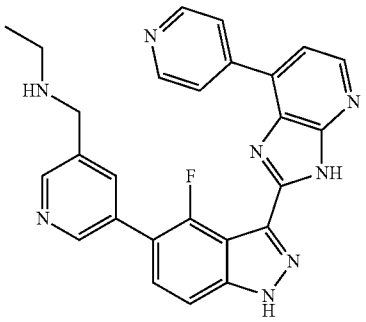
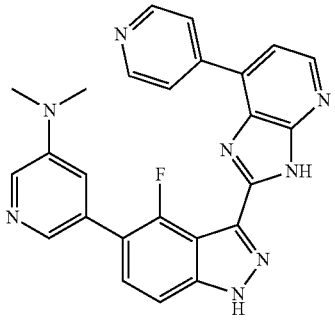
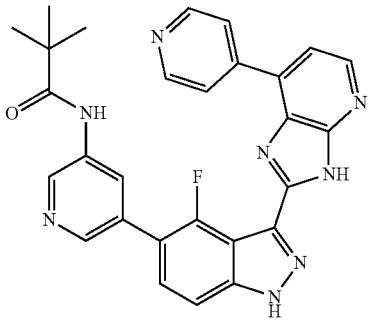
1513	
1514	
1515	
1516	

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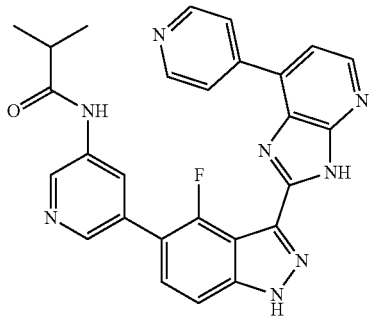
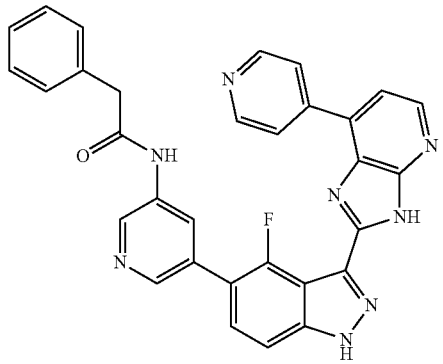
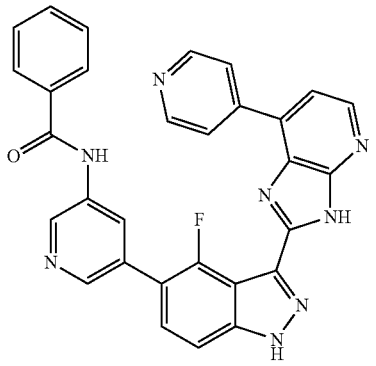
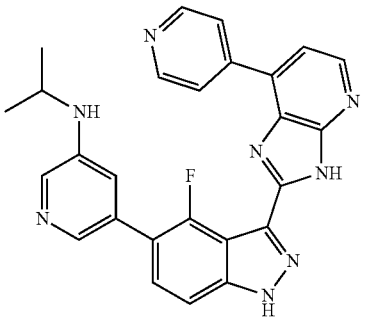
1517	
1518	
1519	
1520	

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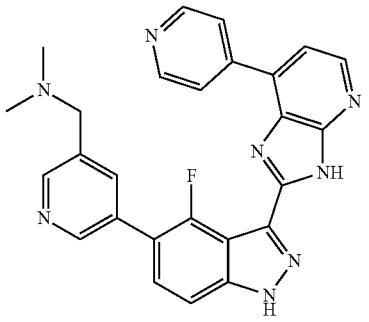
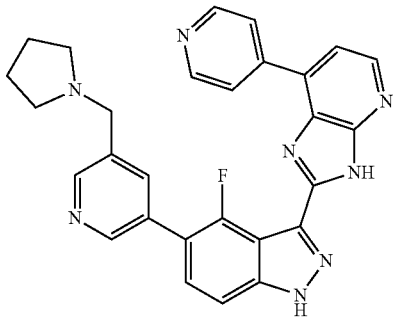
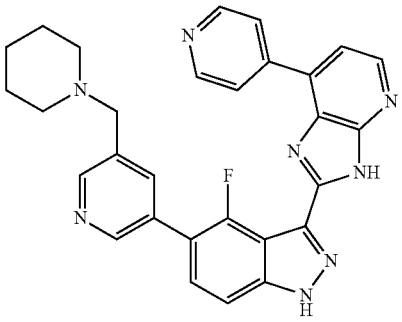
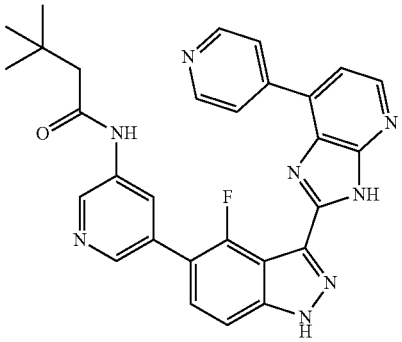
1521	
1522	
1523	
1524	

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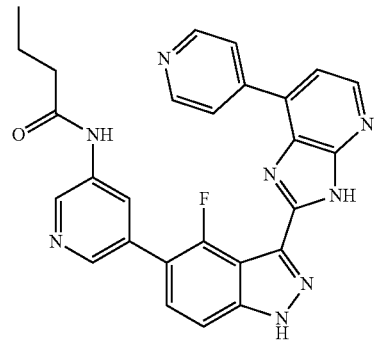
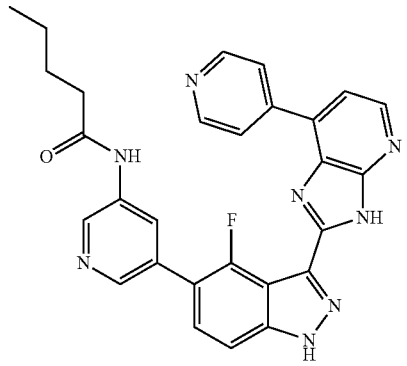
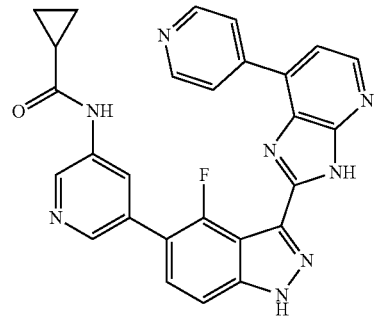
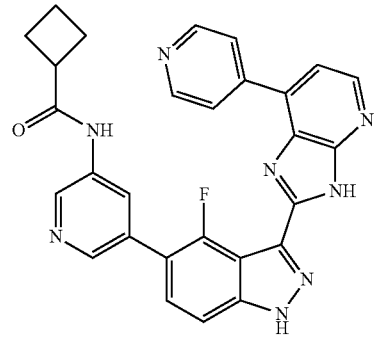
1525	
1526	
1527	
1528	

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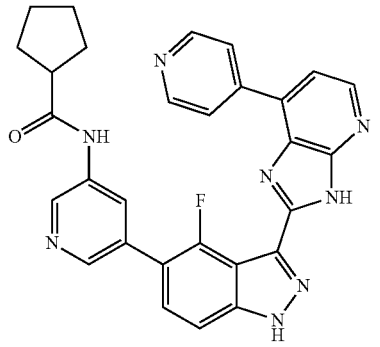
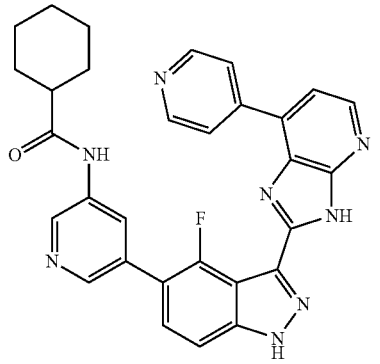
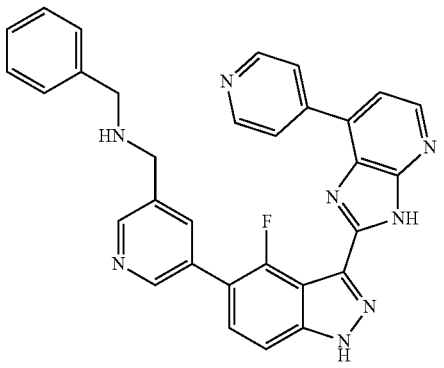
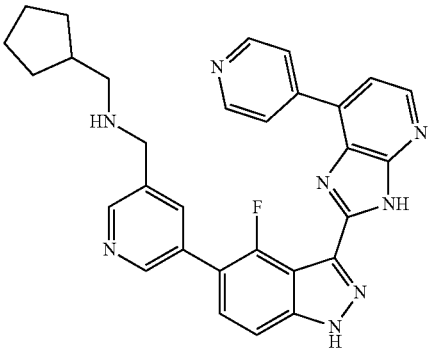
1529	
1530	
1531	
1532	

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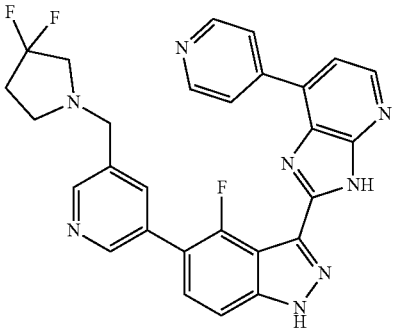
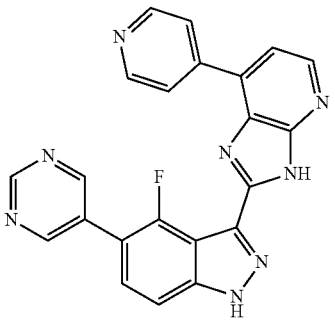
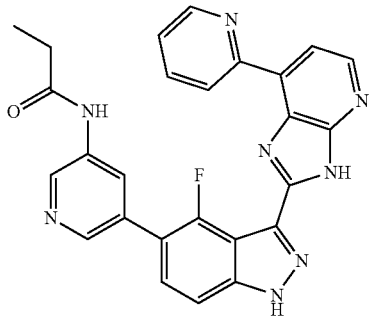
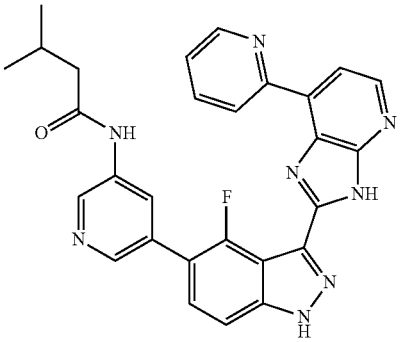
1533	
1534	
1535	
1536	

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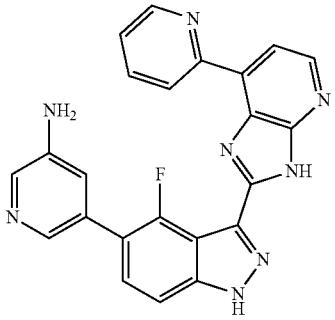
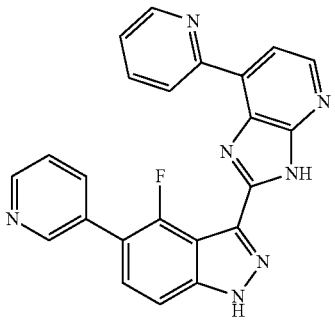
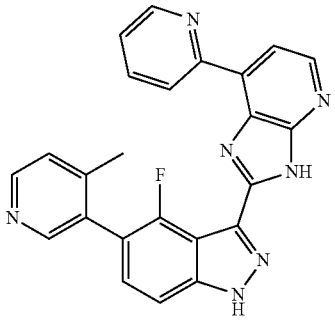
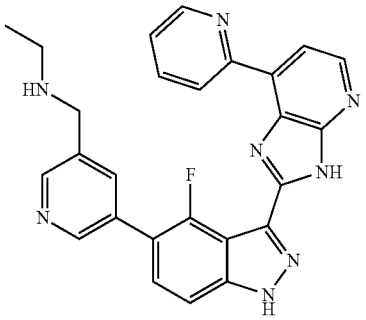
1537	
1538	
1539	
1540	

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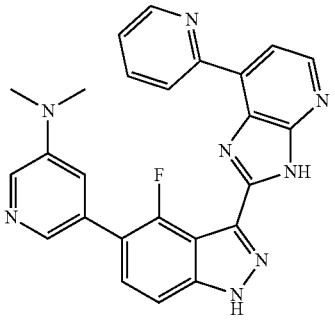
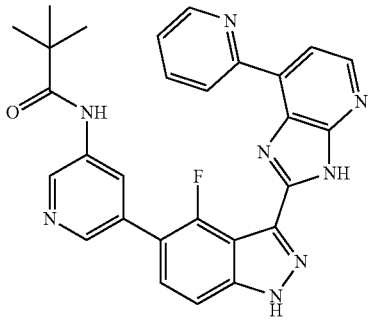
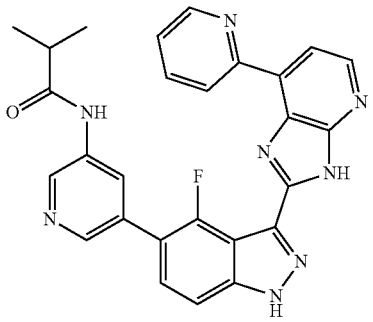
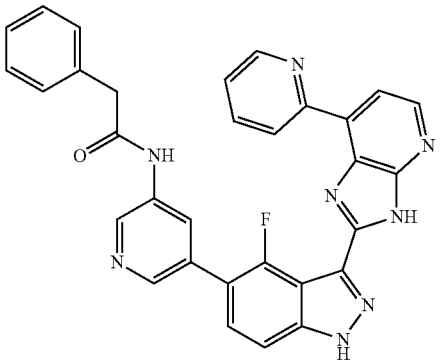
1541	
1542	
1543	
1544	

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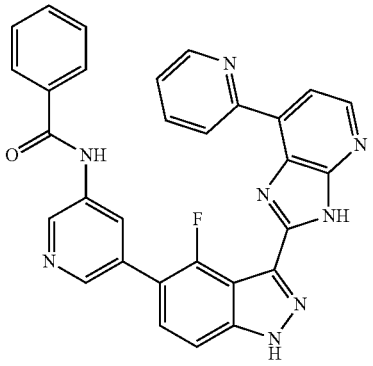
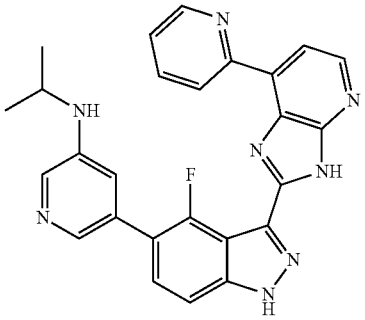
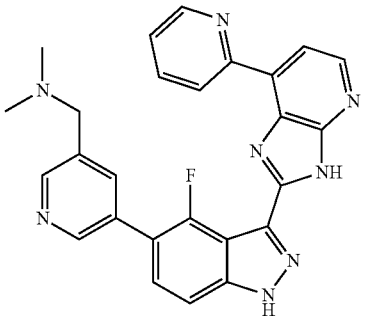
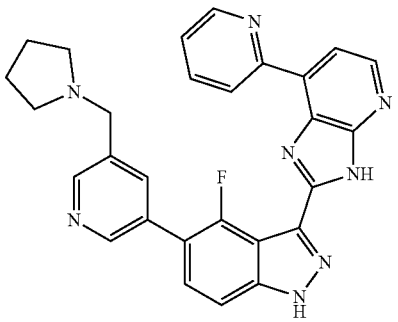
1545	
1546	
1547	
1548	

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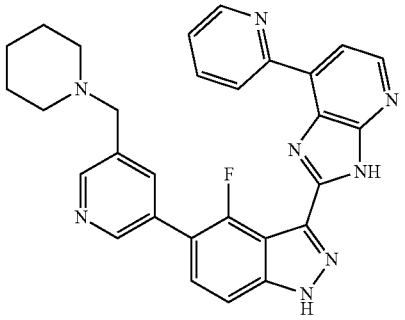
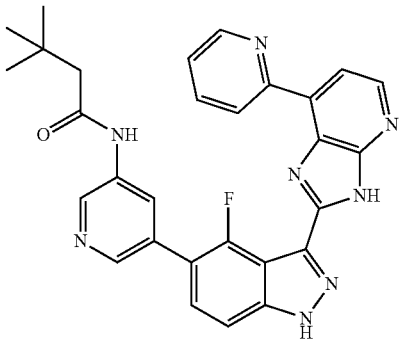
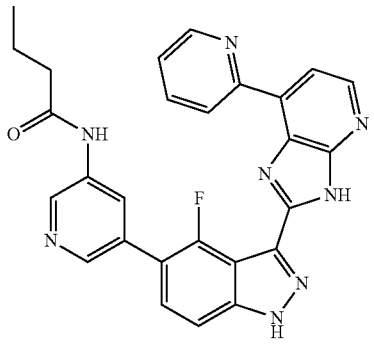
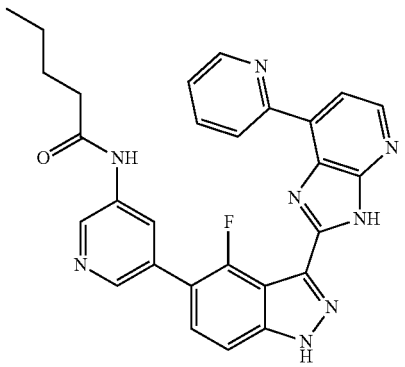
1549	
1550	
1551	
1552	

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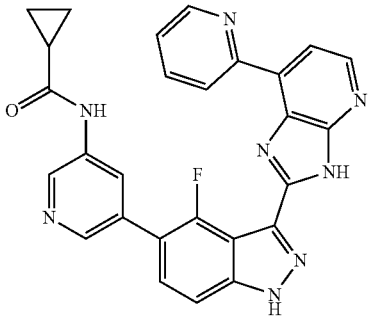
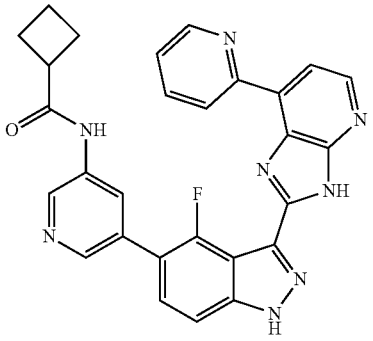
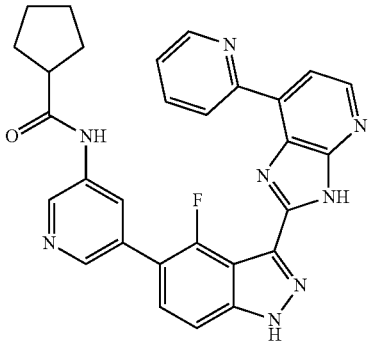
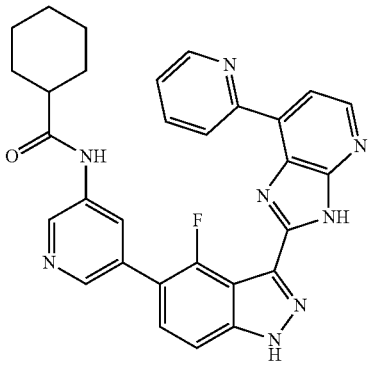
1553	
1554	
1555	
1556	

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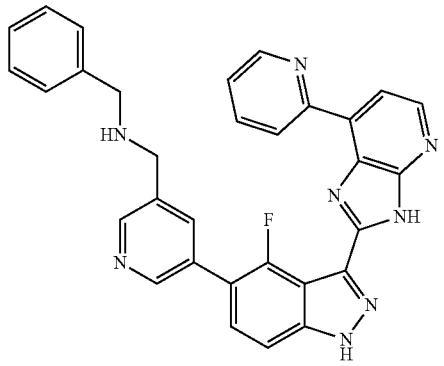
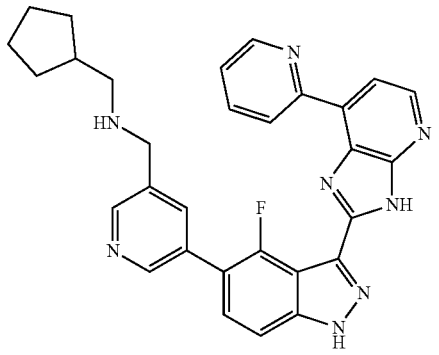
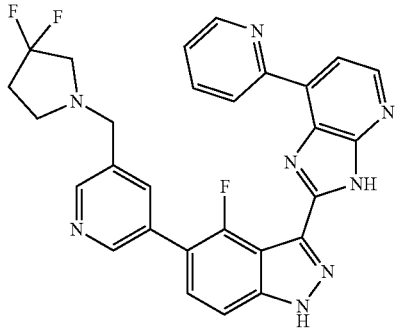
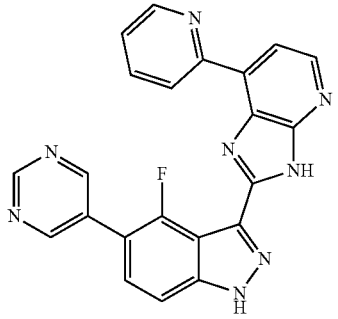
1557	
1558	
1559	
1560	

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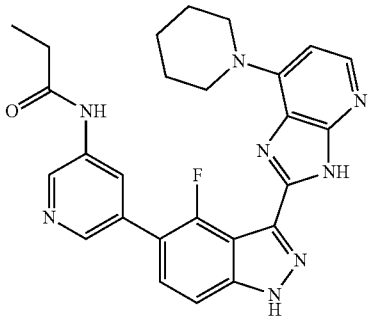
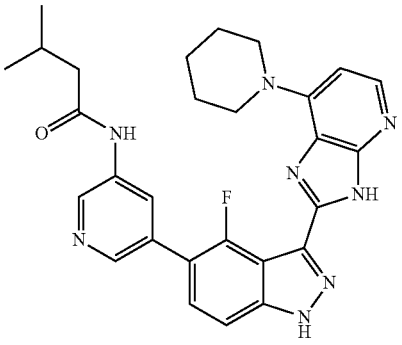
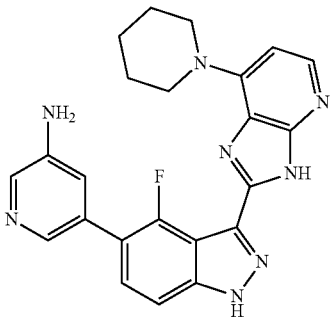
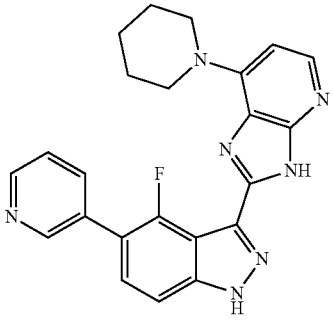
1561	
1562	
1563	
1564	

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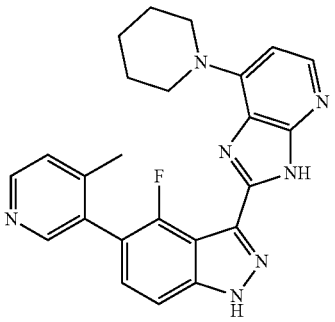
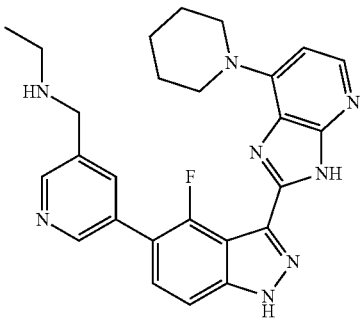
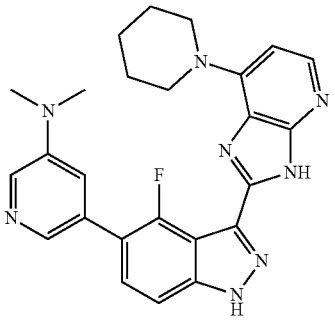
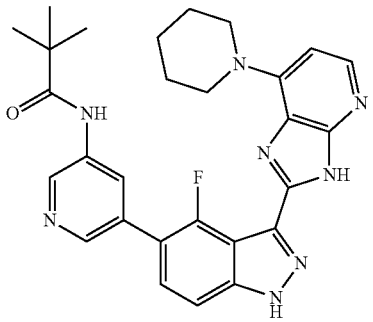
1565	
1566	
1567	
1568	

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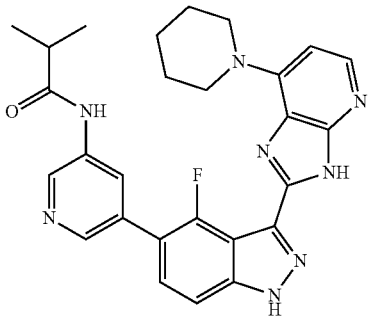
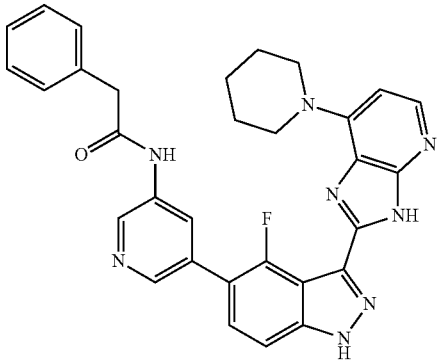
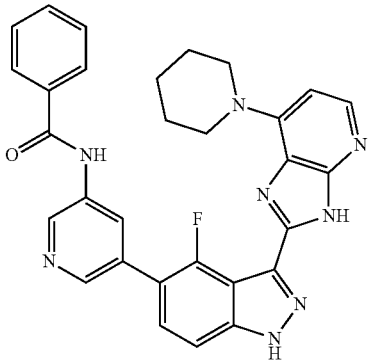
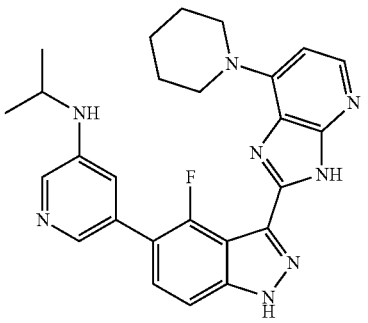
1569	
1570	
1571	
1572	

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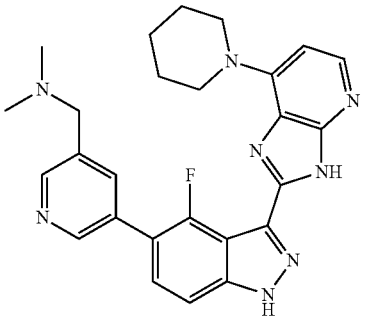
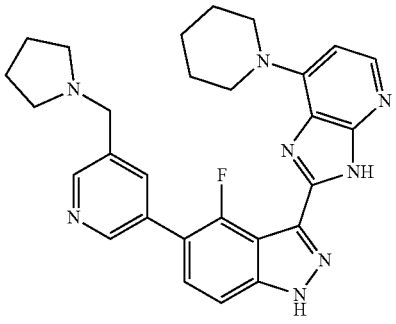
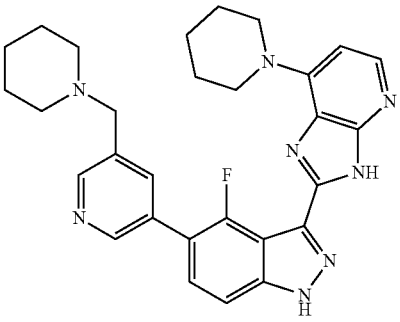
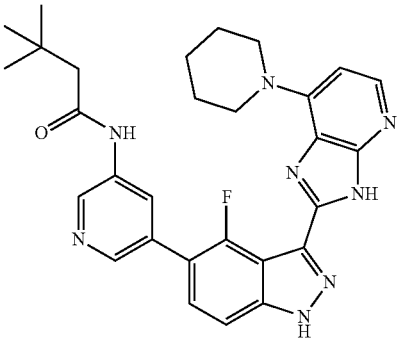
1573	
1574	
1575	
1576	

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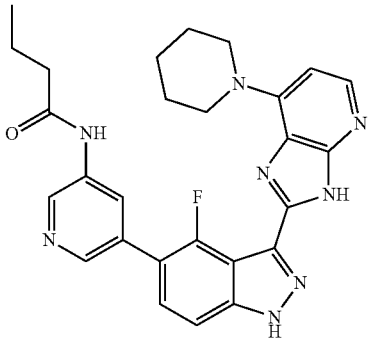
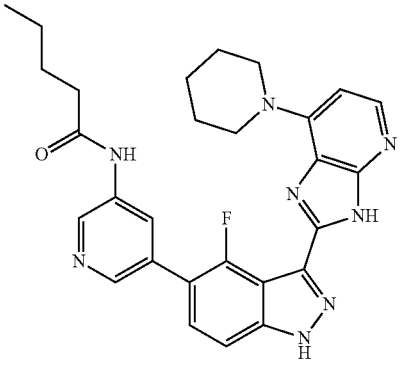
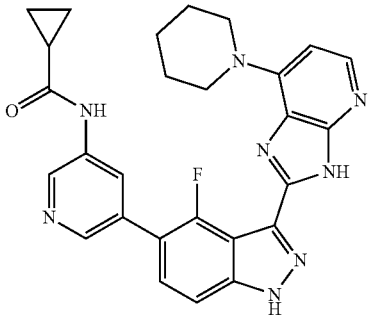
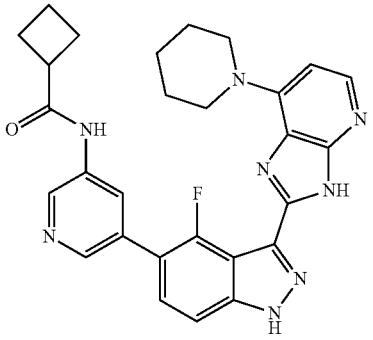
1577	
1578	
1579	
1580	

TABLE 1-continued

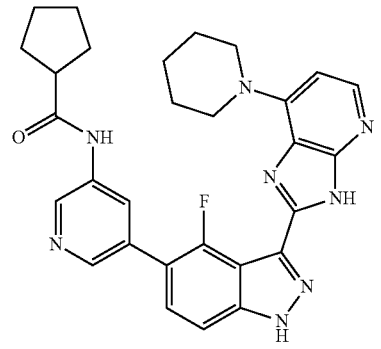
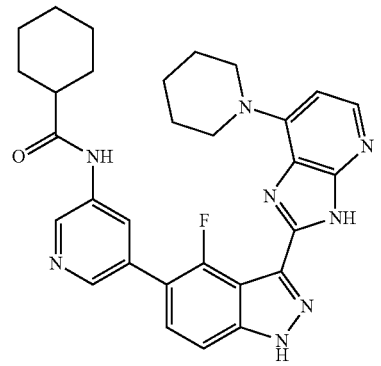
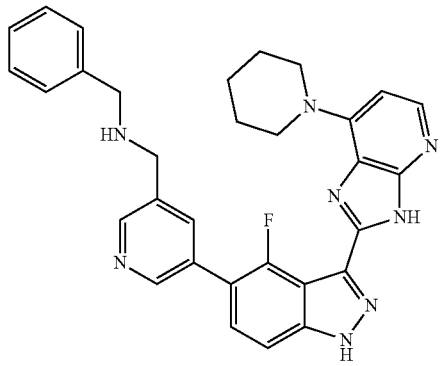
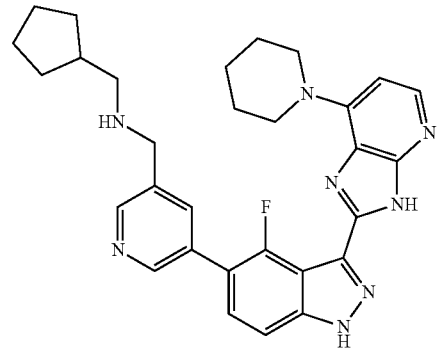
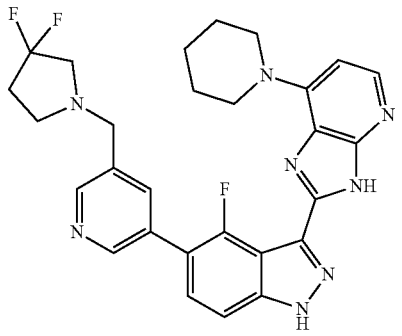
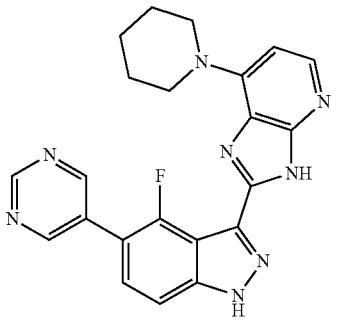
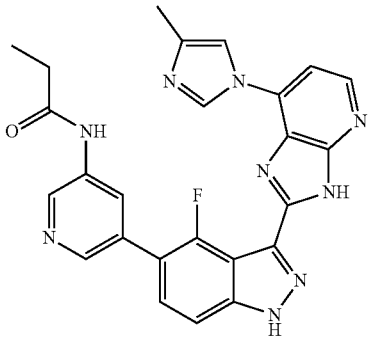
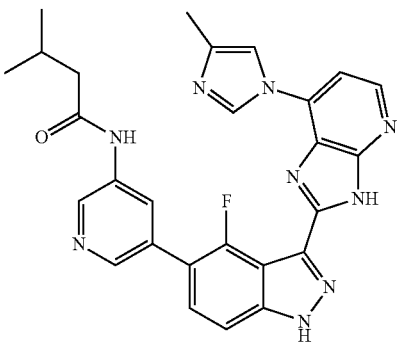
1581	
1582	
1583	
1584	

TABLE 1-continued

1585	
1586	
1587	
1588	

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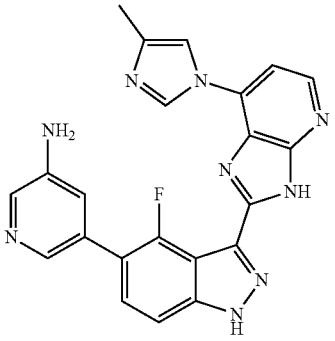
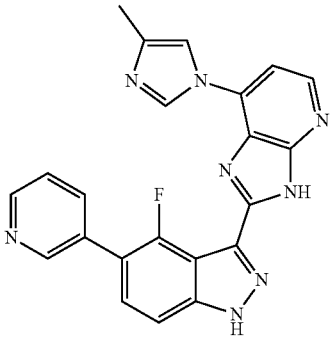
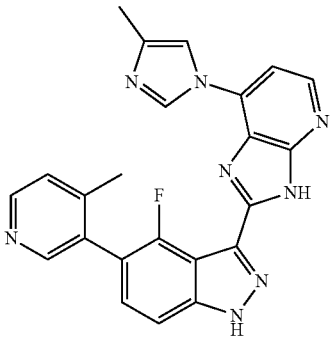
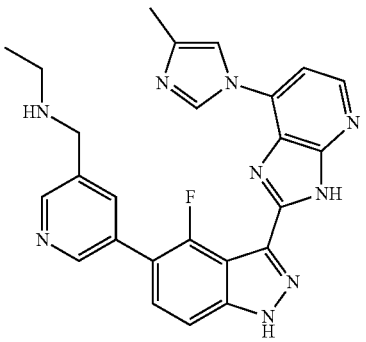
1589	
1590	
1591	
1592	

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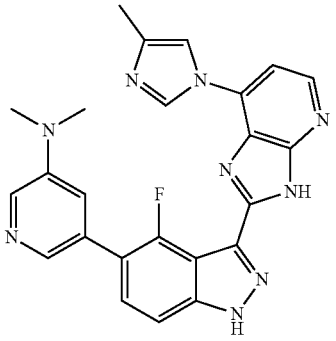
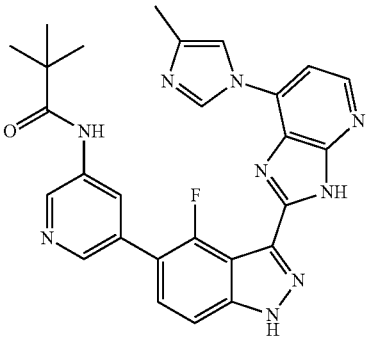
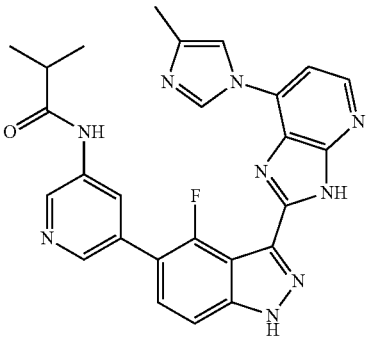
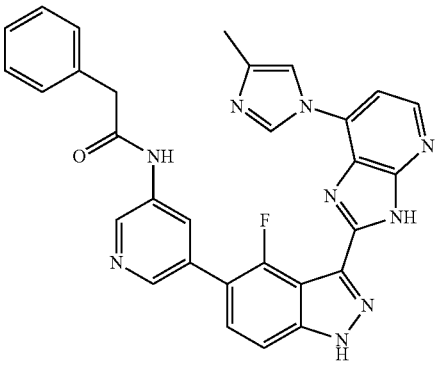
1593	
1594	
1595	
1596	

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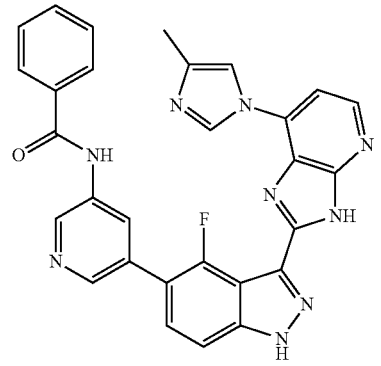
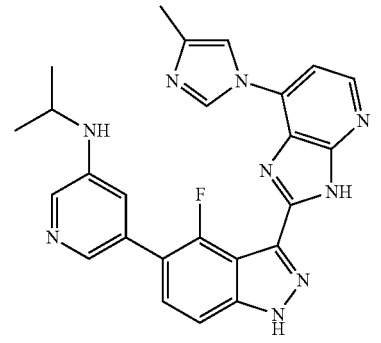
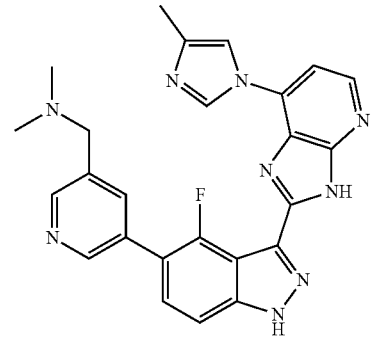
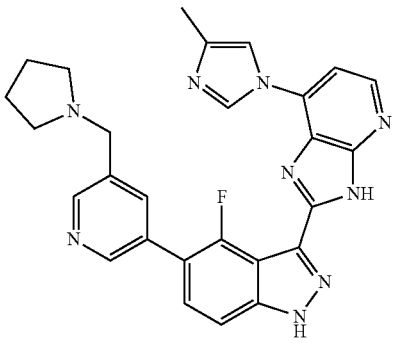
1597	
1598	
1599	
1600	

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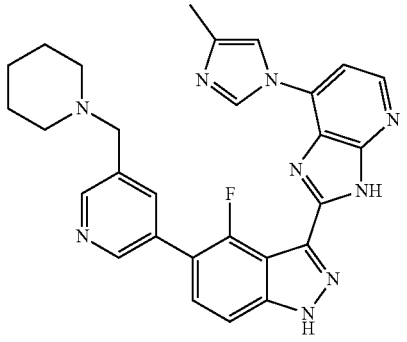
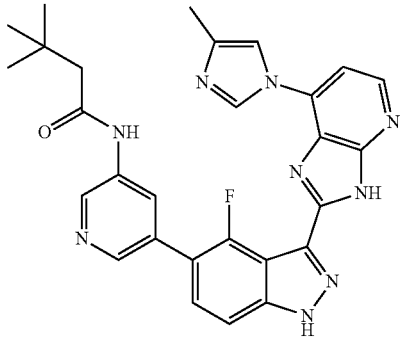
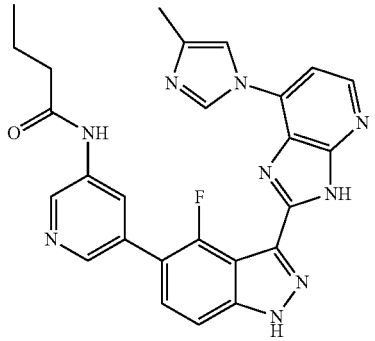
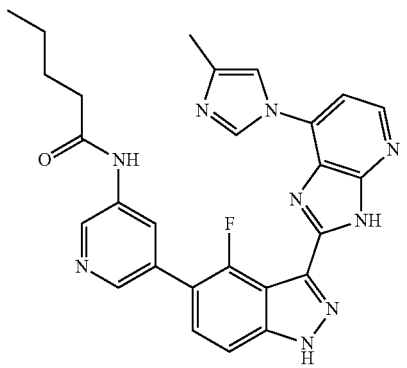
1601	
1602	
1603	
1604	

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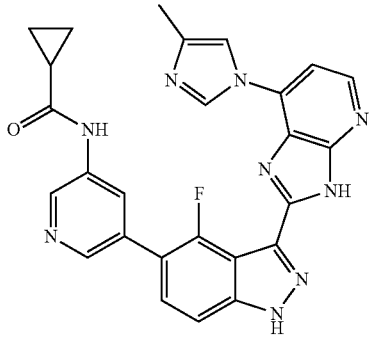
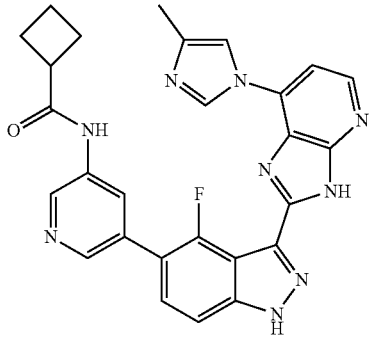
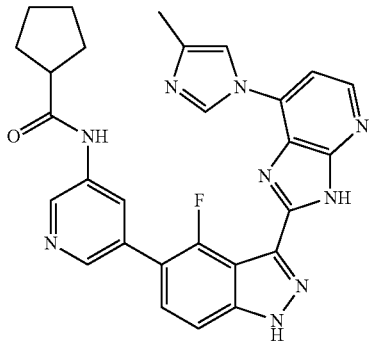
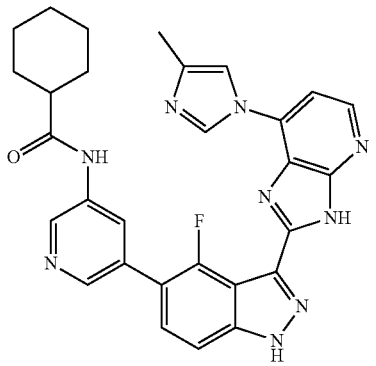
1605	
1606	
1607	
1608	

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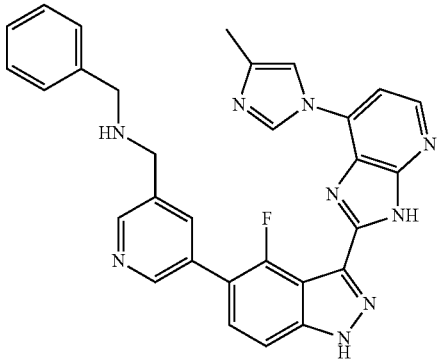
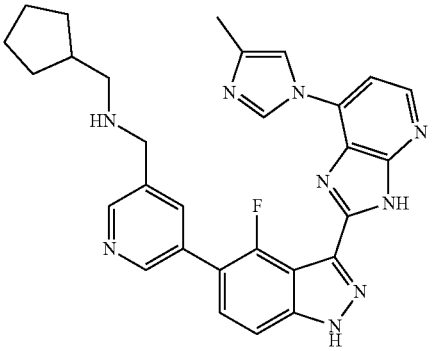
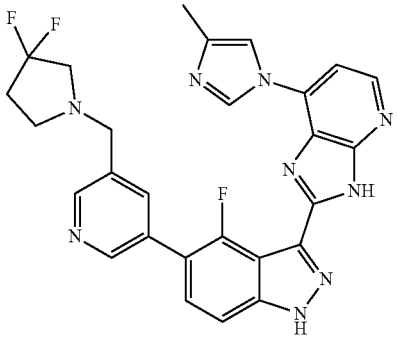
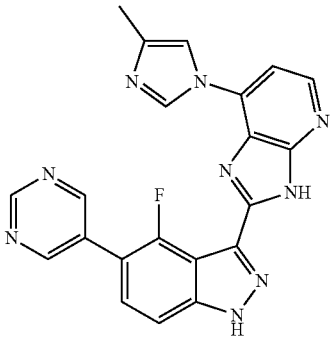
1609	
1610	
1611	
1612	

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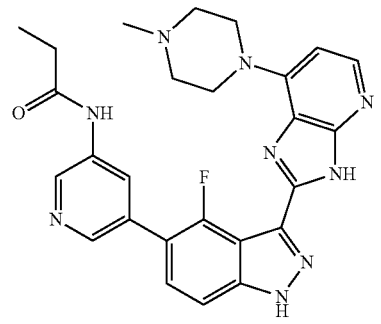
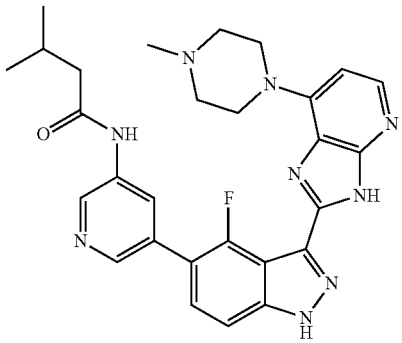
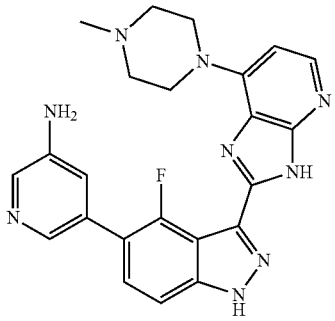
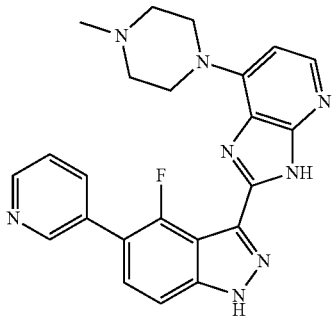
1613	
1614	
1615	
1616	

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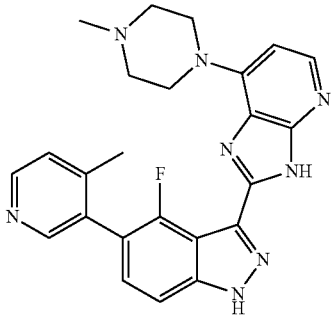
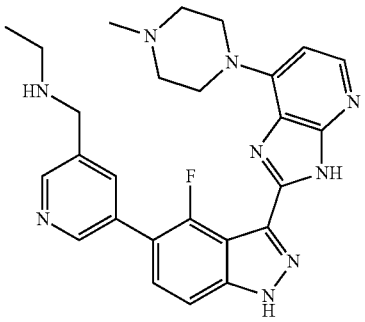
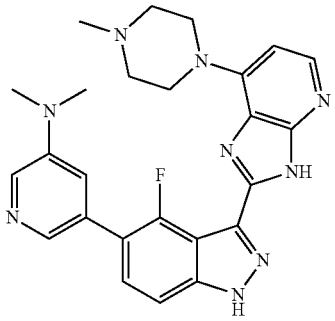
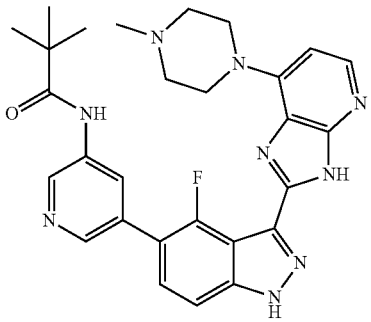
1617	
1618	
1619	
1620	

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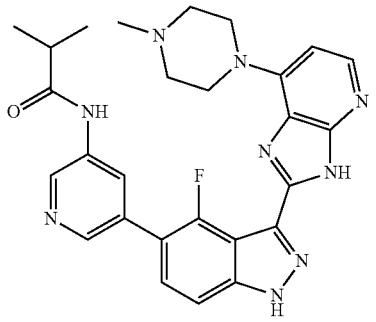

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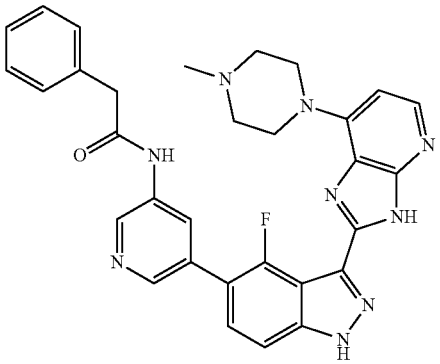

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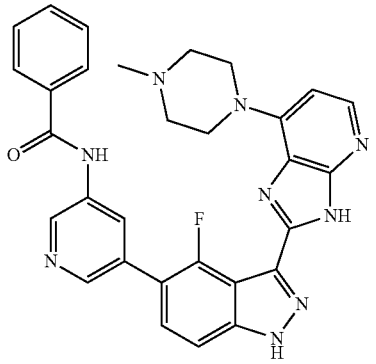

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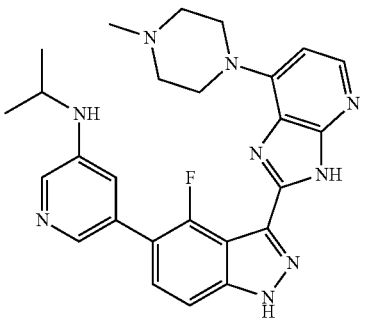

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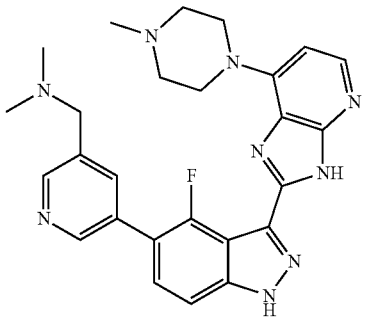

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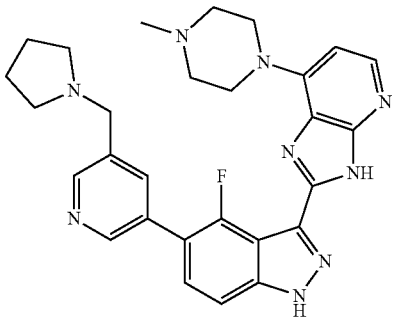

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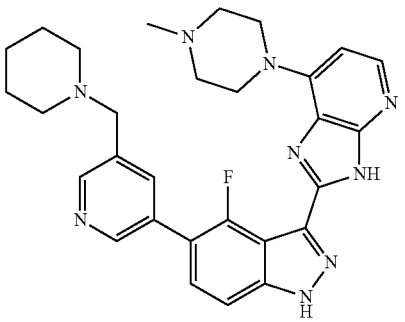

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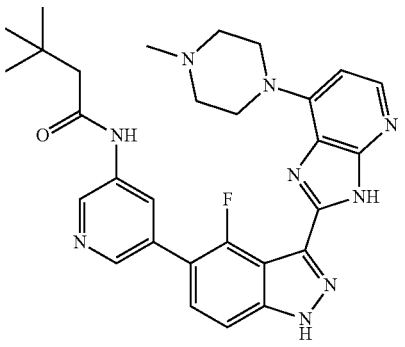

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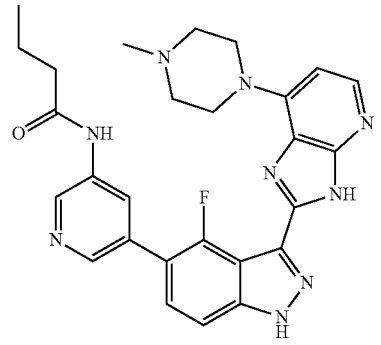
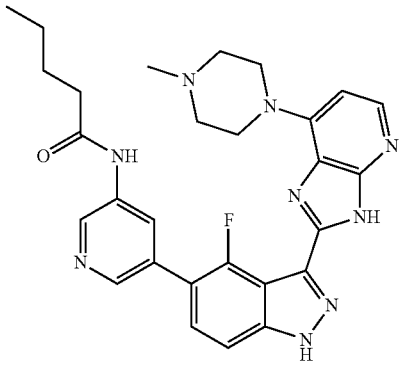
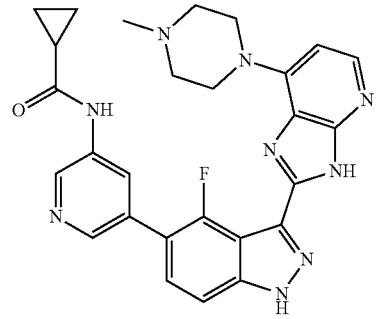
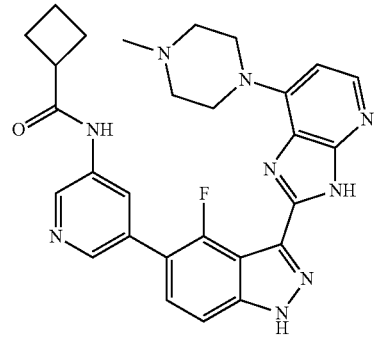
1629	
1630	
1631	
1632	

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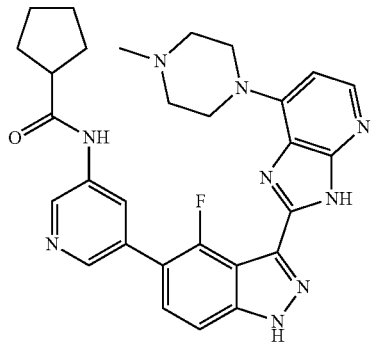
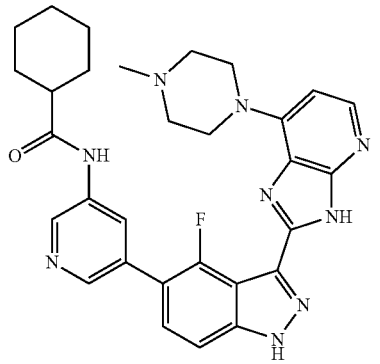
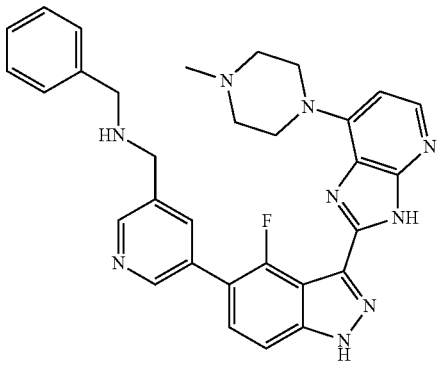
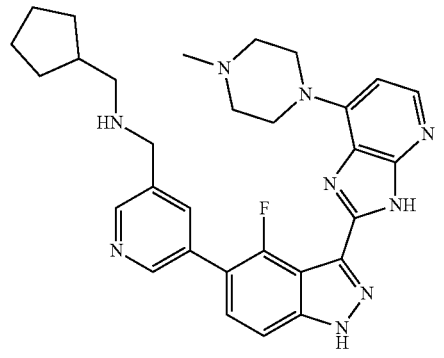
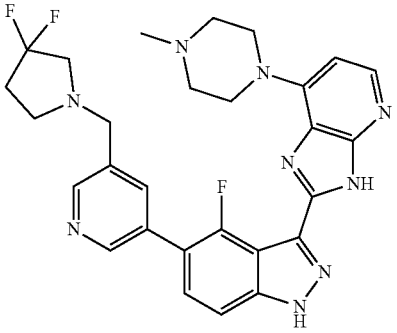
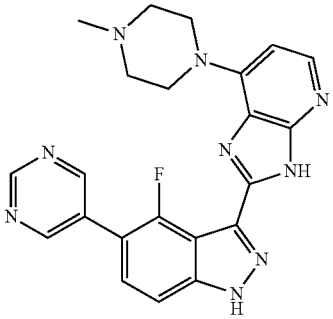
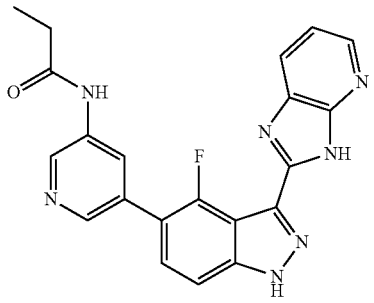
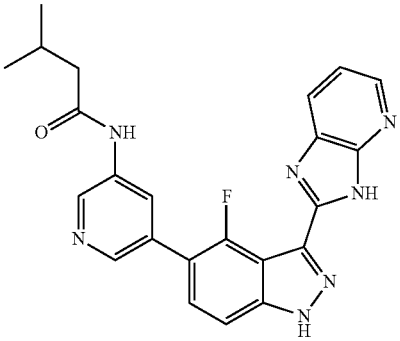
1633	
1634	
1635	
1636	

TABLE 1-continued

1637	
1638	
1639	
1640	

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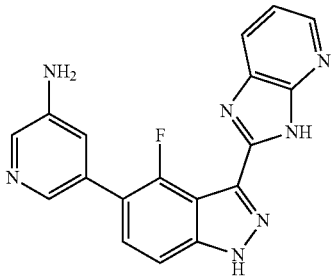
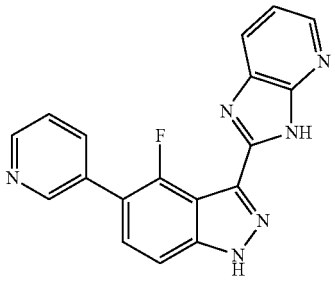
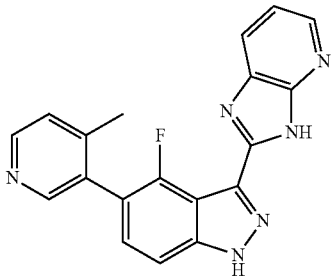
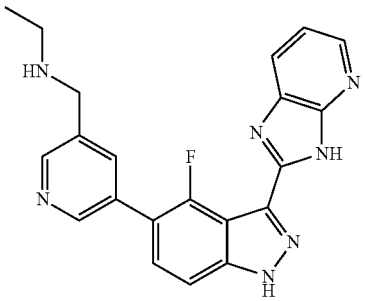
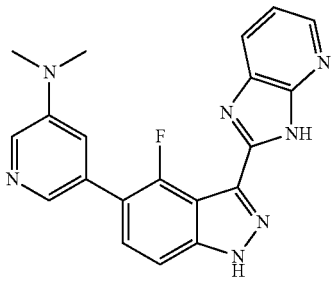
1641	
1642	
1643	
1644	
1645	

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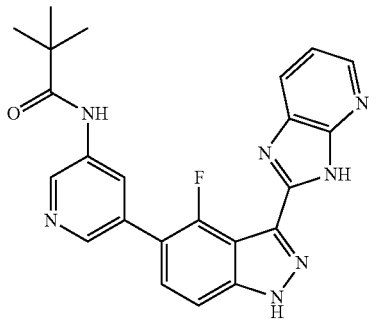
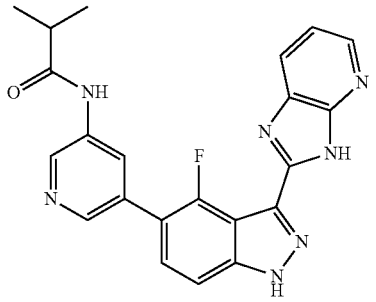
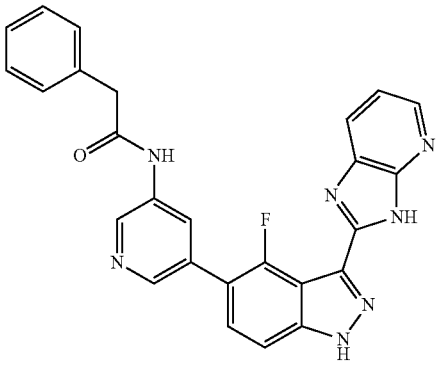
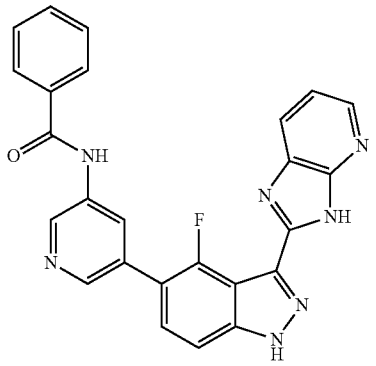
1646	
1647	
1648	
1649	

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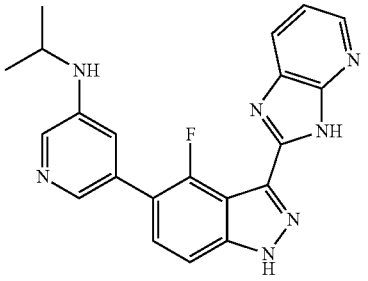
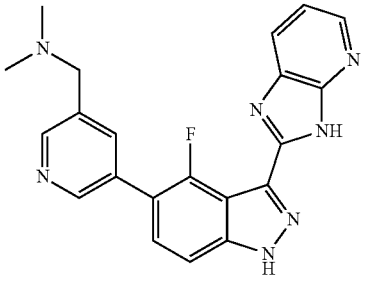
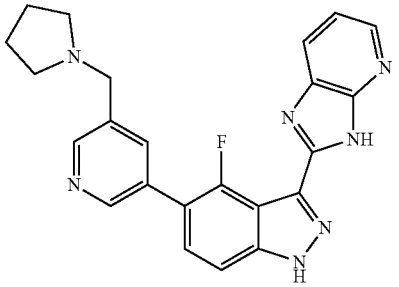
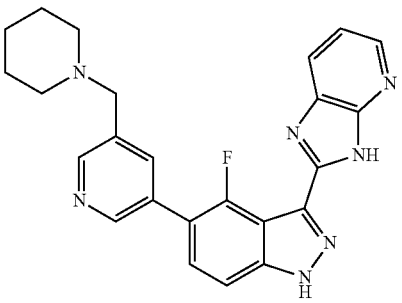
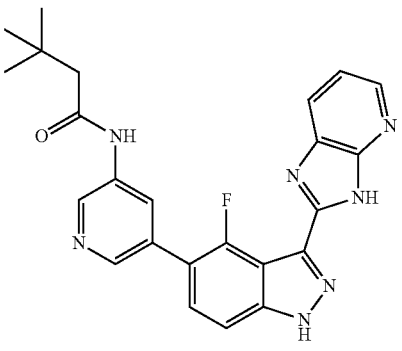
1650	
1651	
1652	
1653	
1654	

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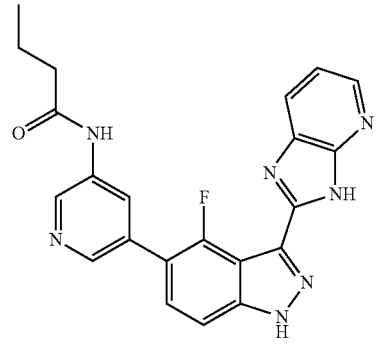
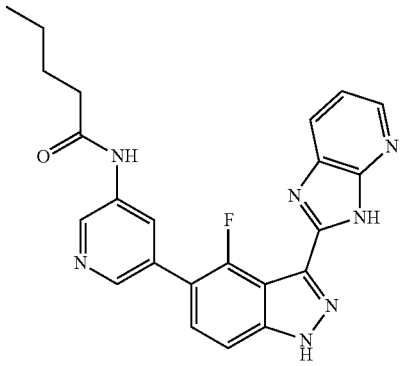
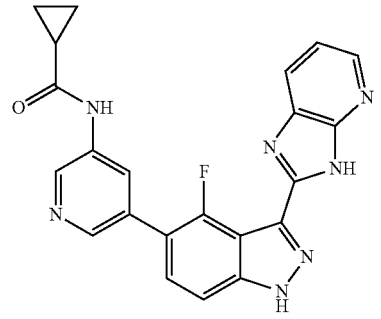
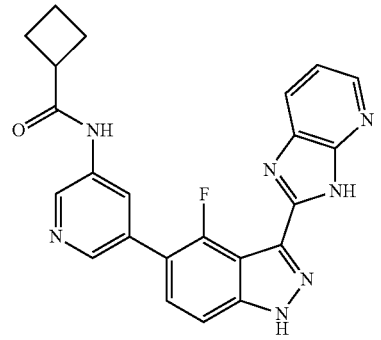
1655	
1656	
1657	
1658	

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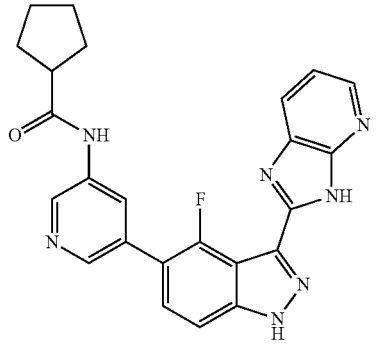
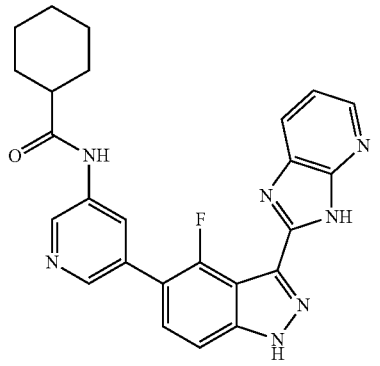
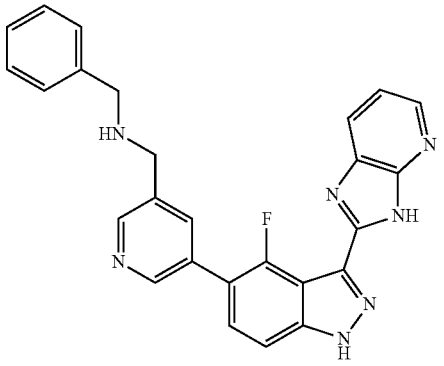
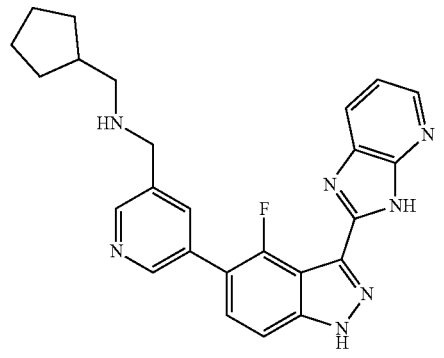
1659	
1660	
1661	
1662	

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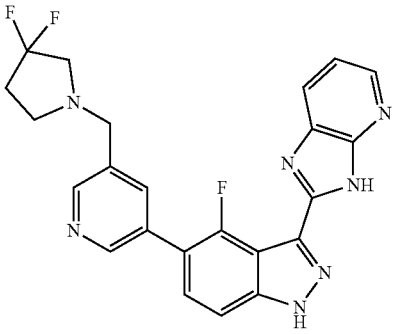
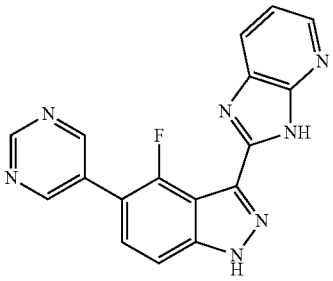
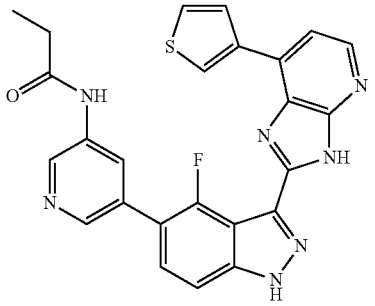
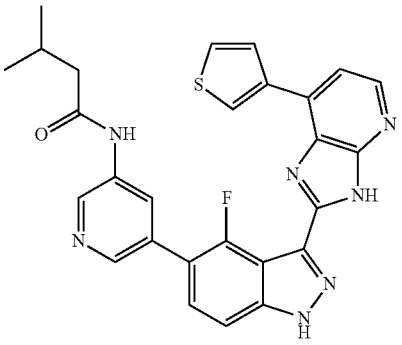
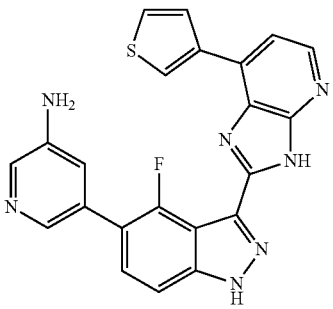
1663	
1664	
1665	
1666	
1667	

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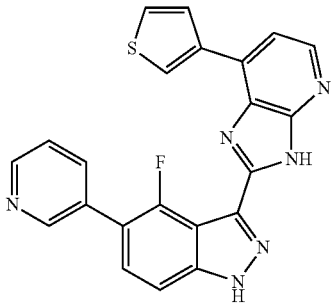
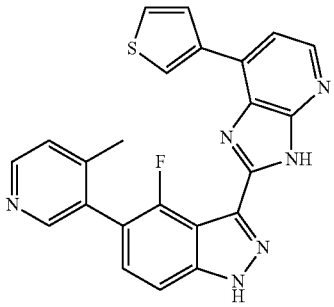
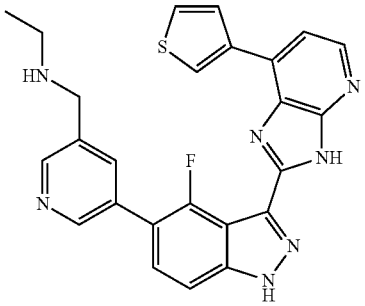
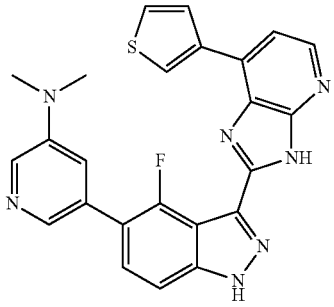
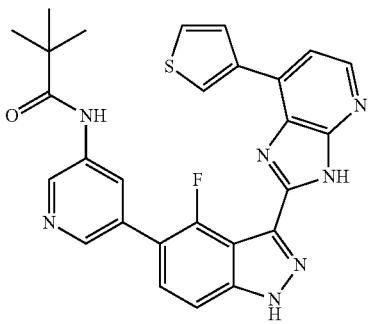
1668	
1669	
1670	
1671	
1672	

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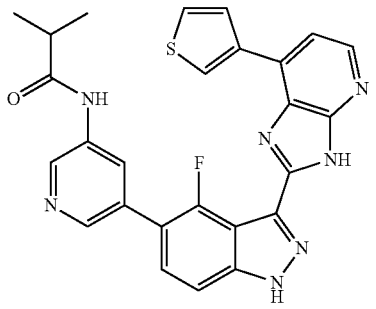
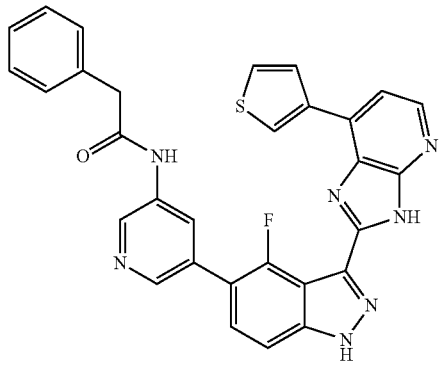
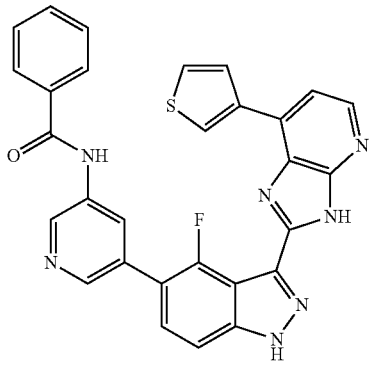
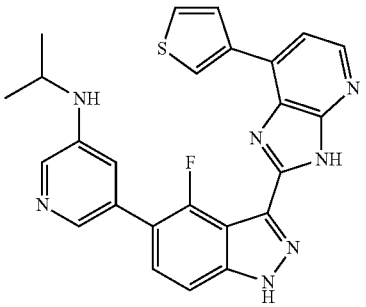
1673	
1674	
1675	
1676	

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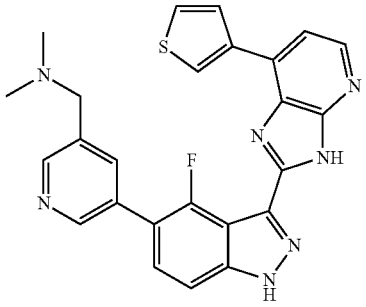
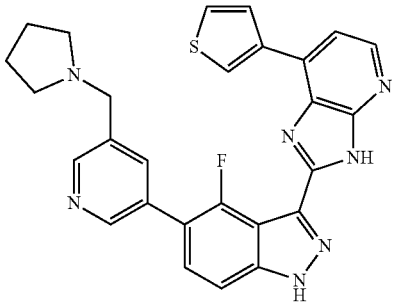
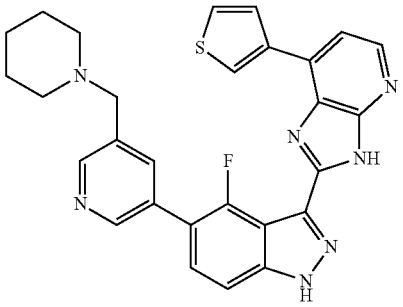
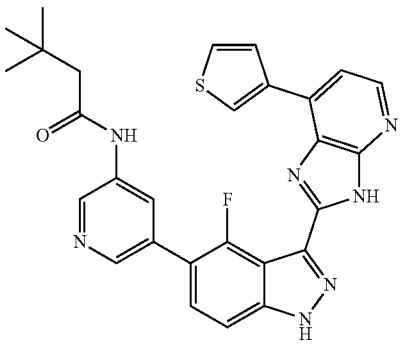
1677	
1678	
1679	
1680	

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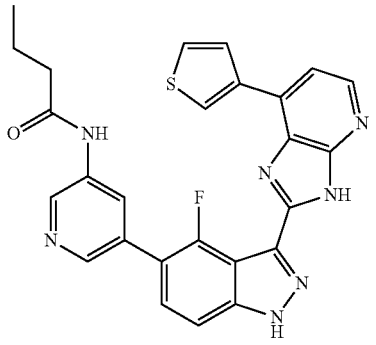
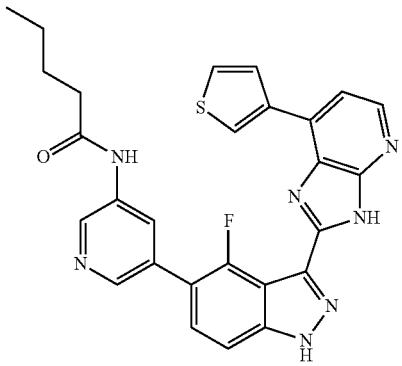
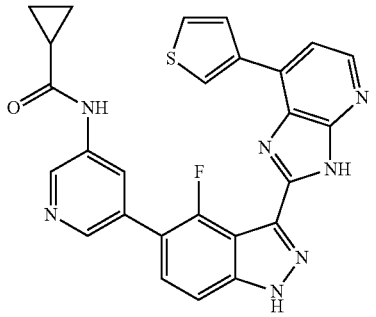
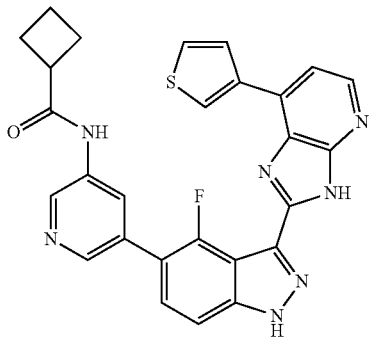
1681	
1682	
1683	
1684	

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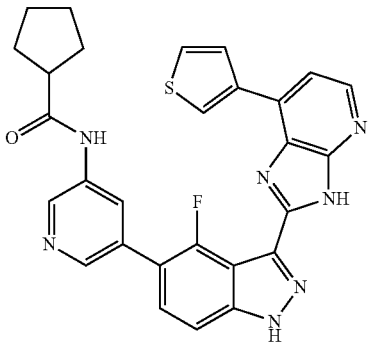
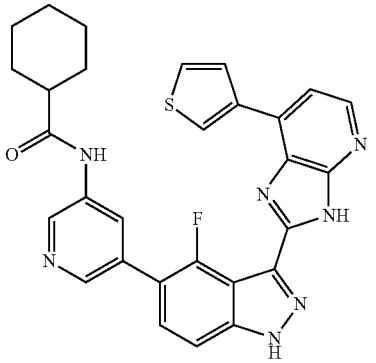
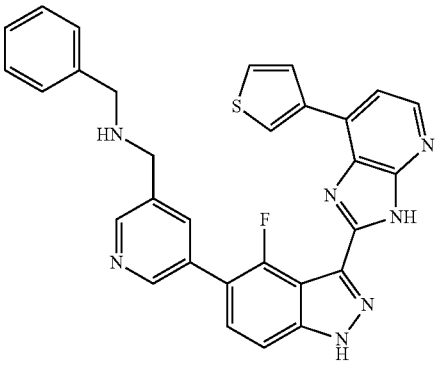
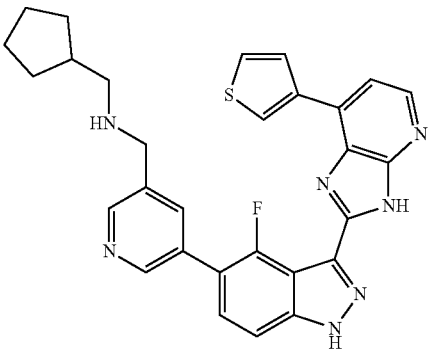
1685	
1686	
1687	
1688	

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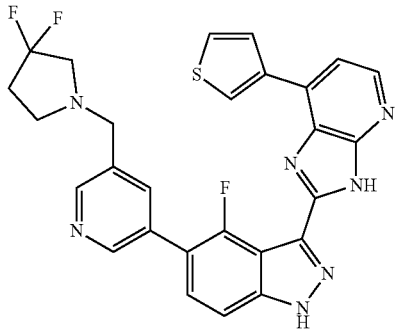
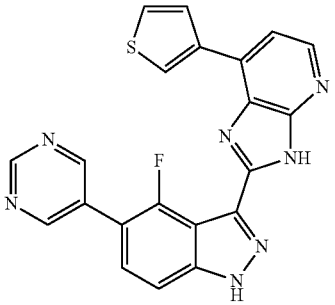
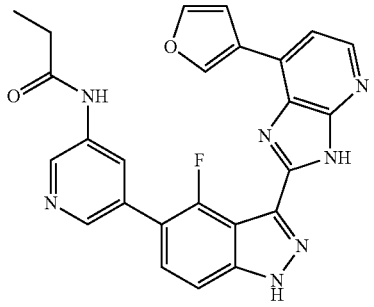
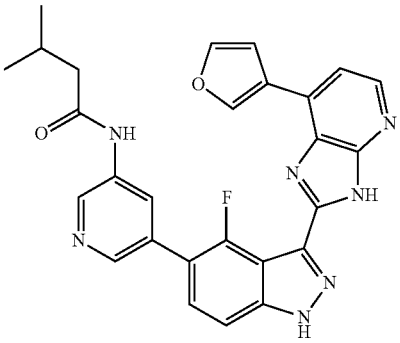
1689	
1690	
1691	
1692	

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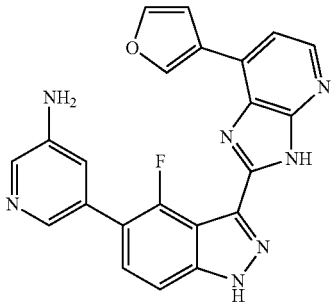
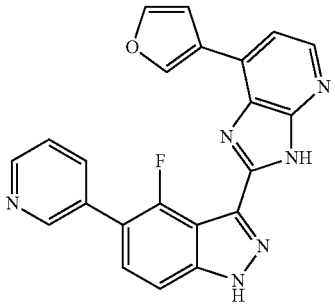
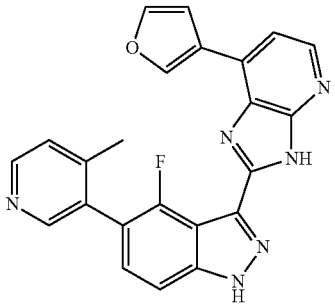
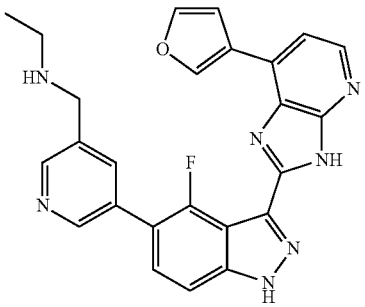
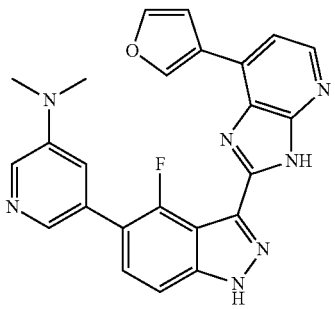
1693	
1694	
1695	
1696	
1697	

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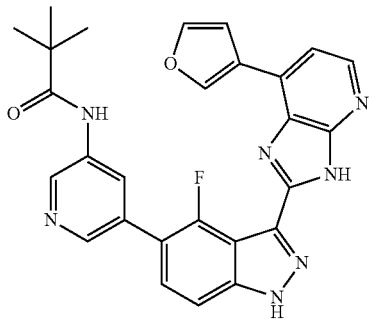
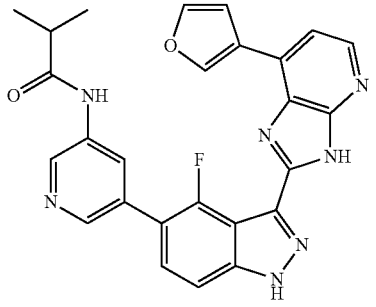
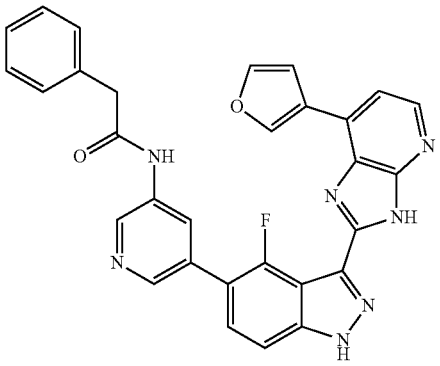
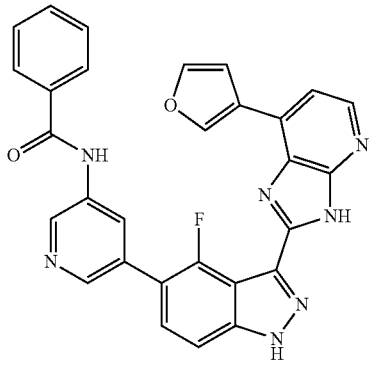
1698	
1699	
1700	
1701	

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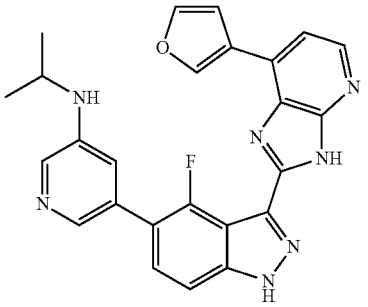
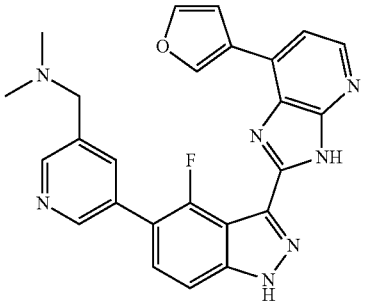
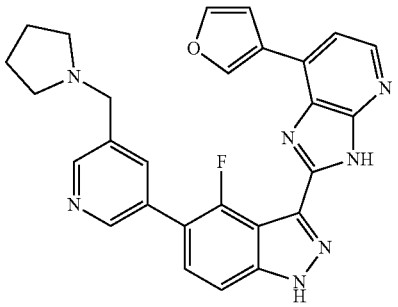
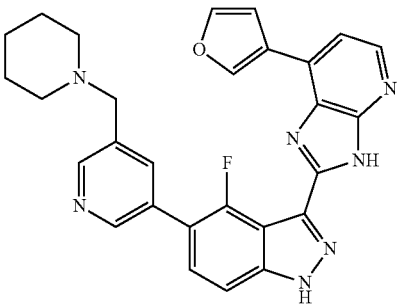
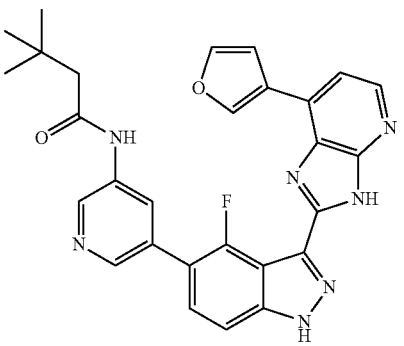
1702	
1703	
1704	
1705	
1706	

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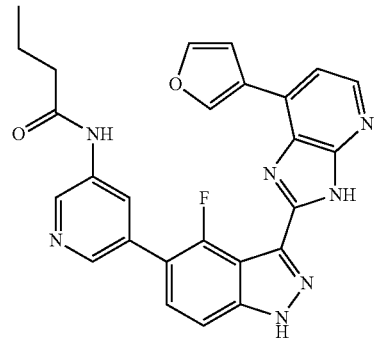
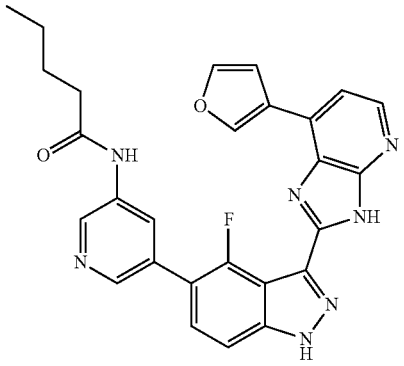
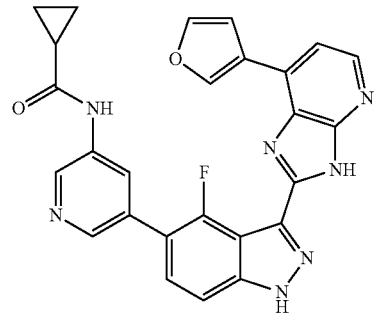
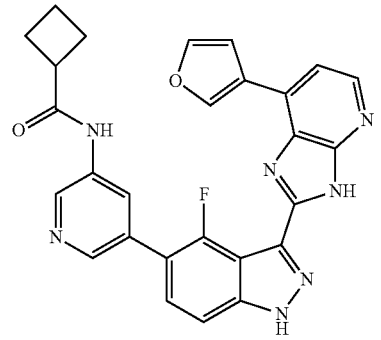
1707	
1708	
1709	
1710	

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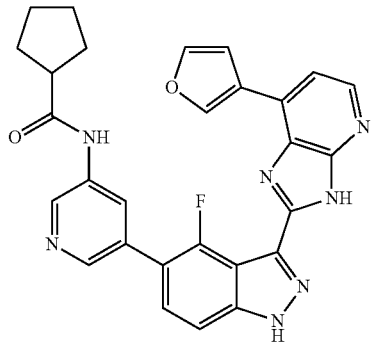
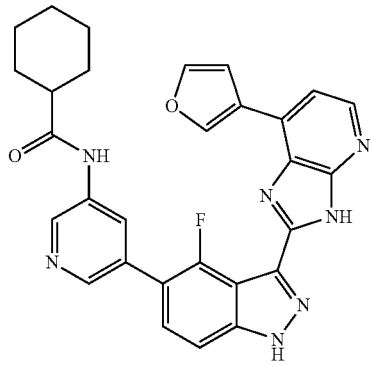
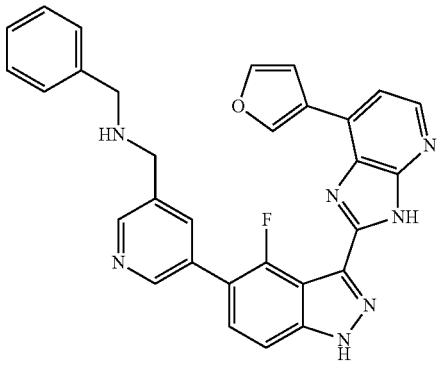
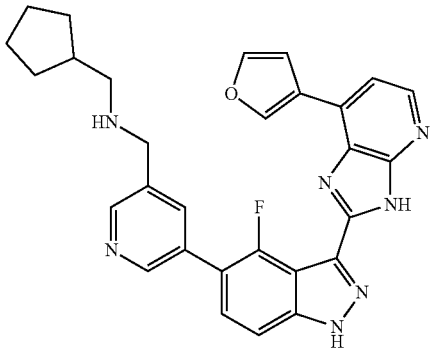
1711	
1712	
1713	
1714	

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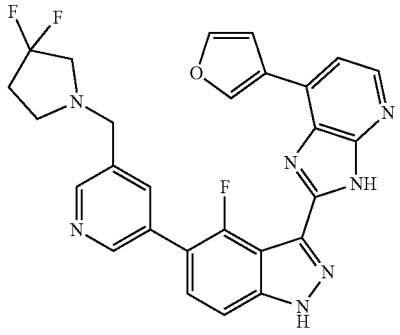
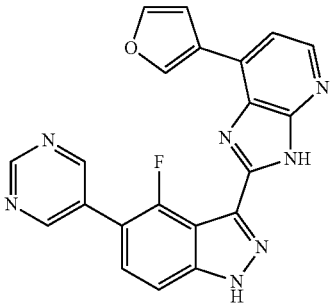
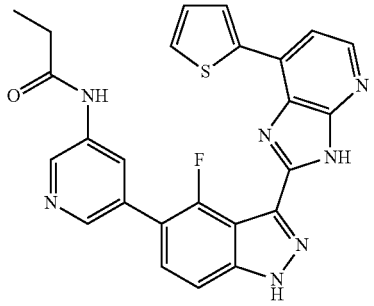
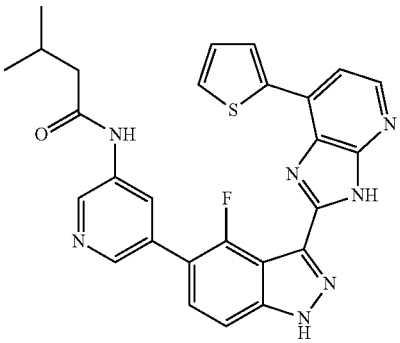
1715	
1716	
1717	
1718	

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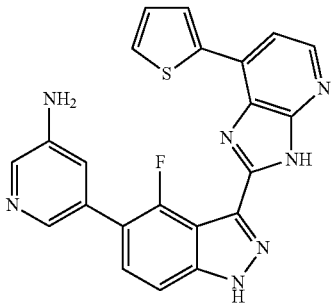
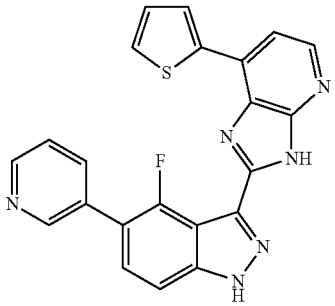
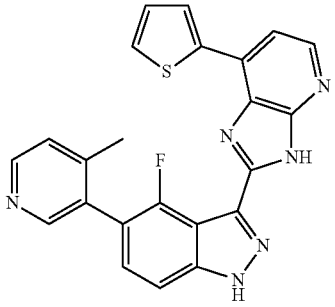
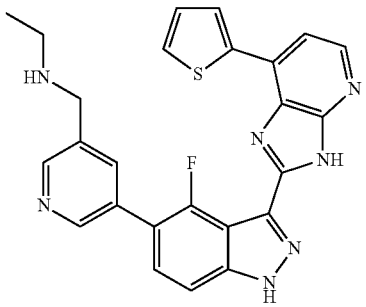
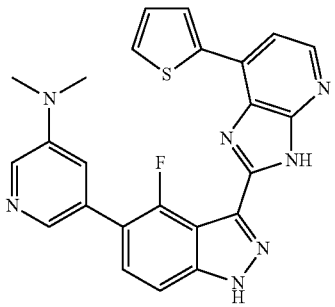
1719	
1720	
1721	
1722	
1723	

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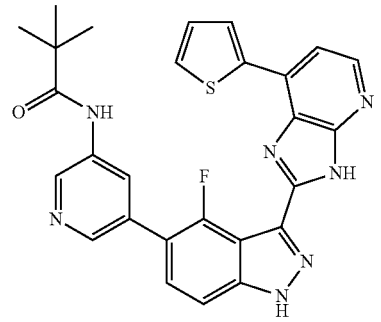

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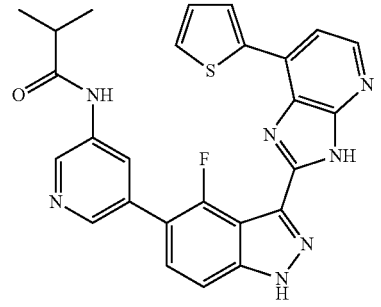

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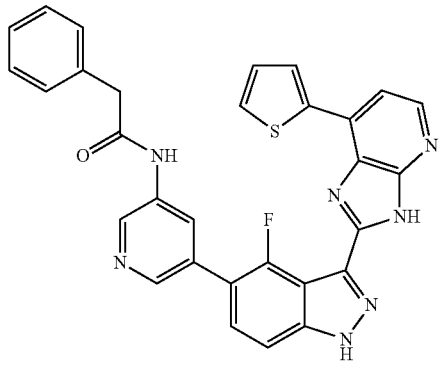

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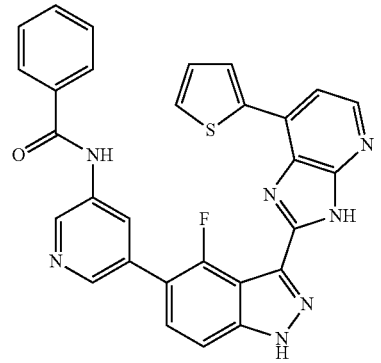

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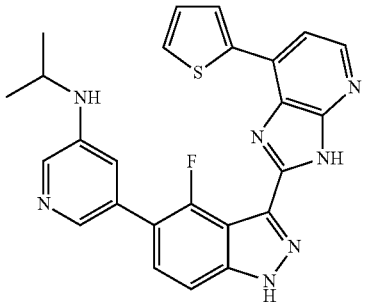

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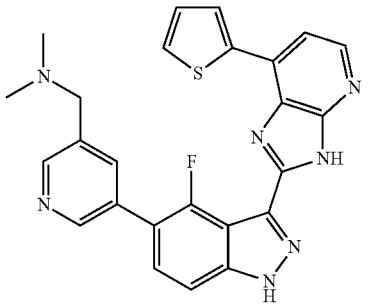

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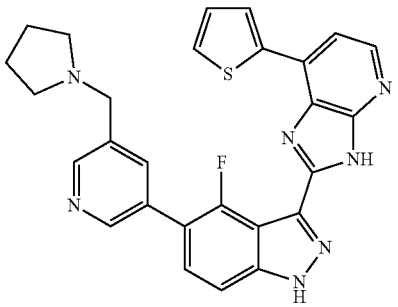

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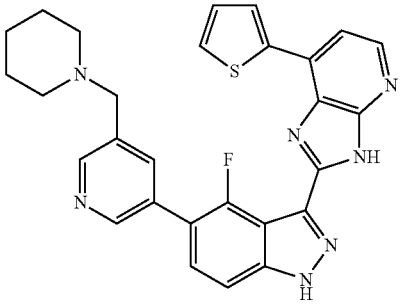

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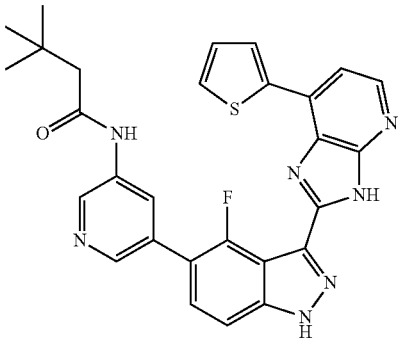

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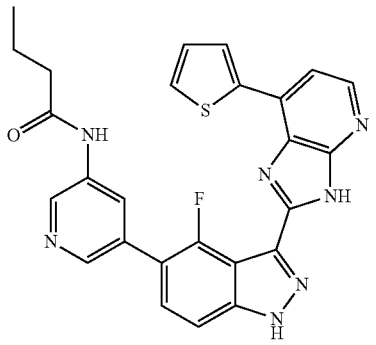
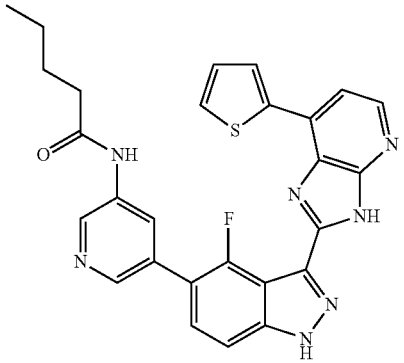
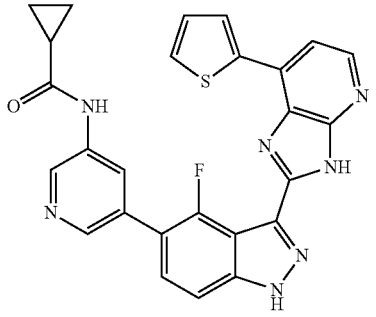
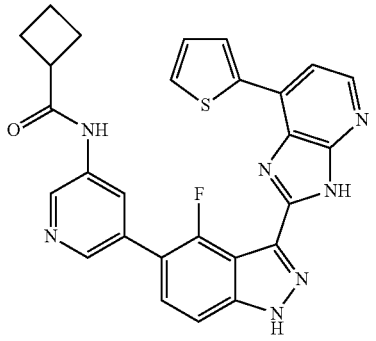
1733	
1734	
1735	
1736	

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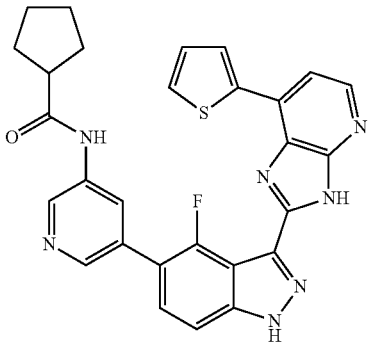
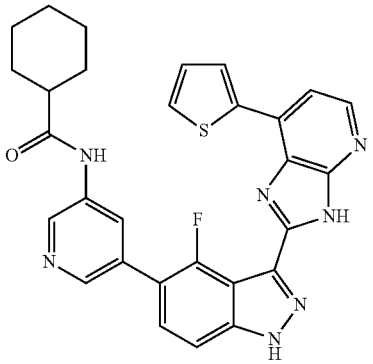
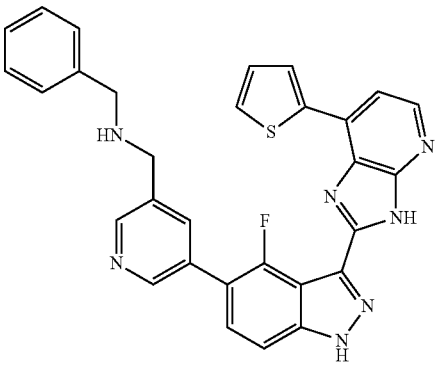
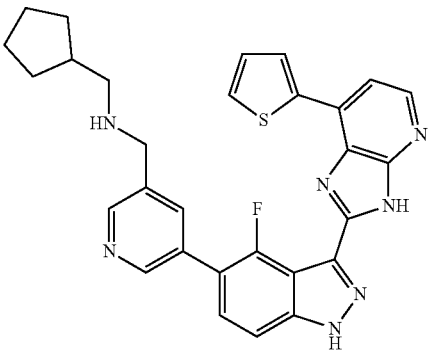
1737	
1738	
1739	
1740	

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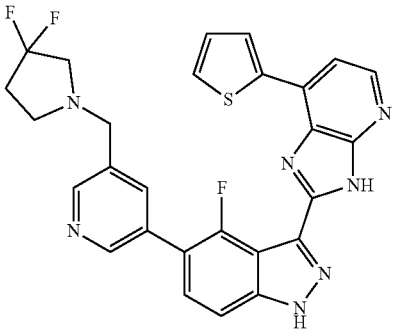
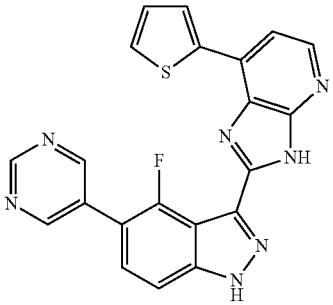
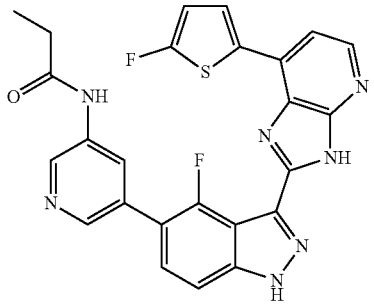
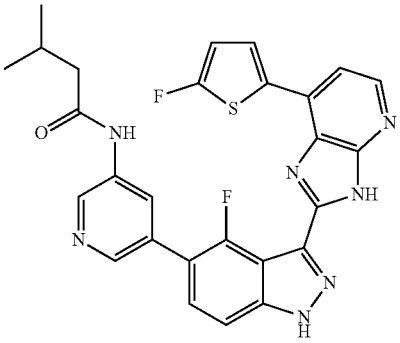
1741	
1742	
1743	
1744	

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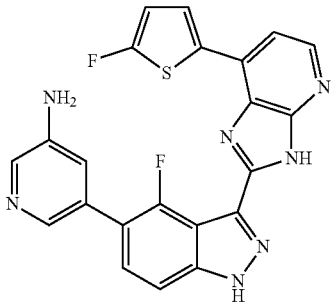
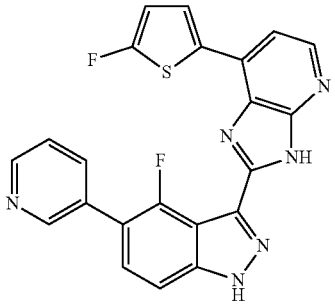
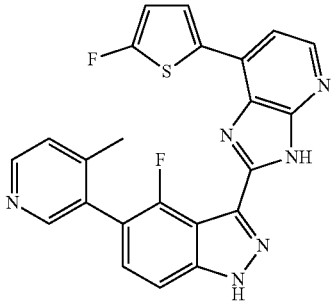
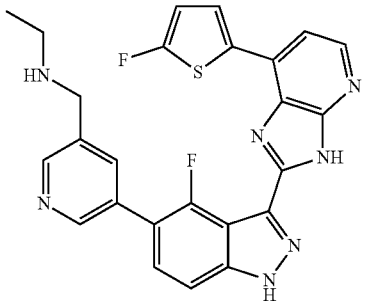
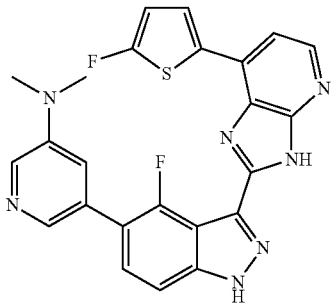
1745	
1746	
1747	
1748	
1749	

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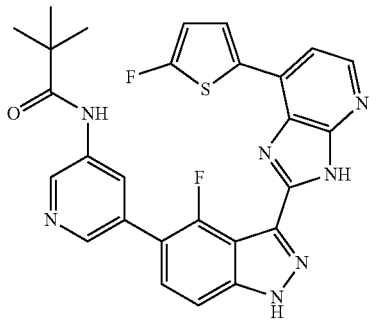
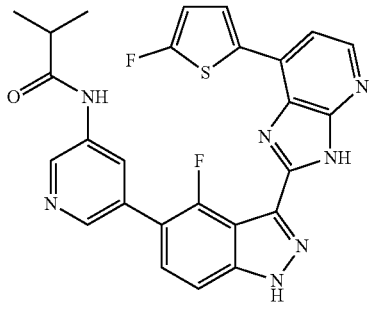
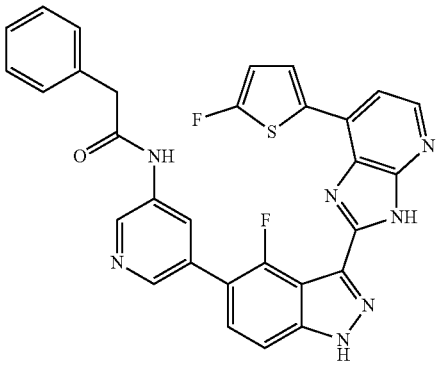
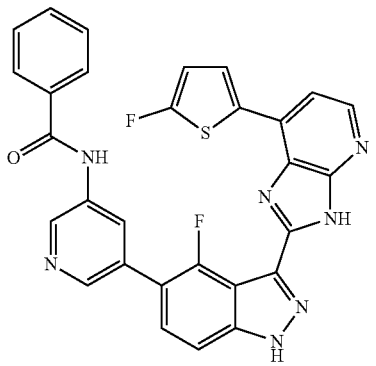
1750	
1751	
1752	
1753	

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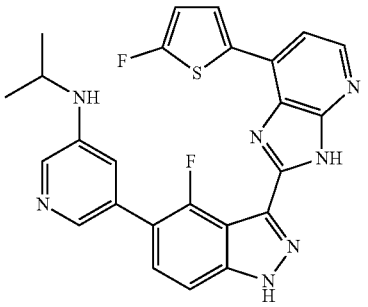
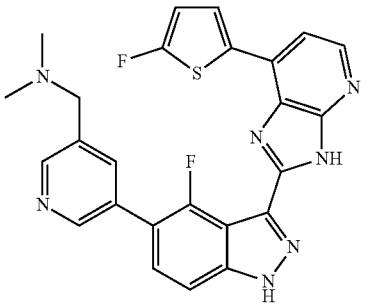
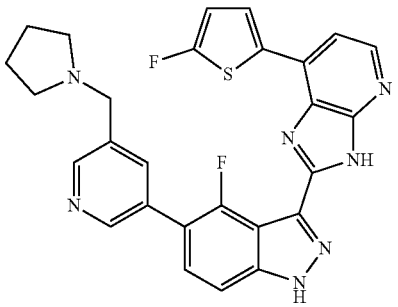
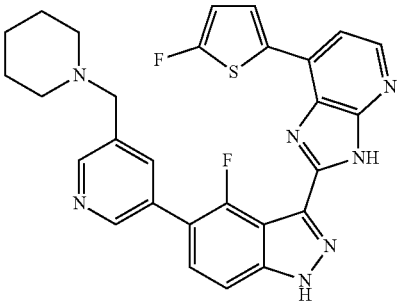
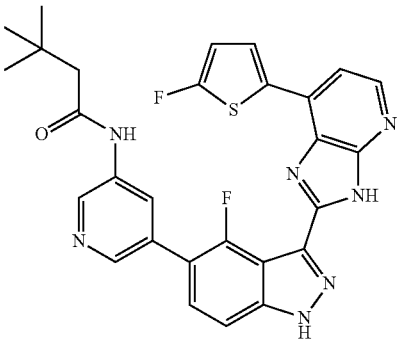
1754	
1755	
1756	
1757	
1758	

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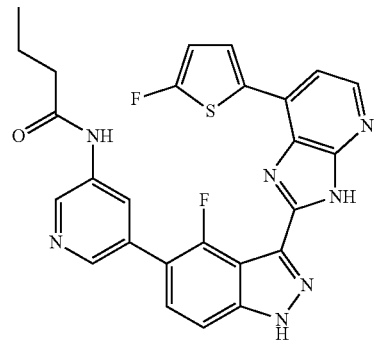
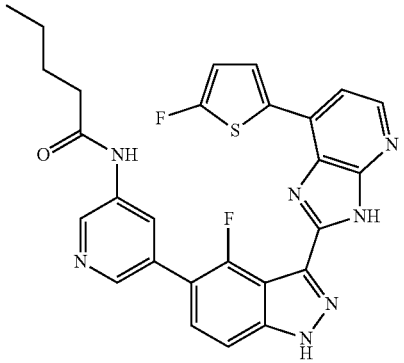
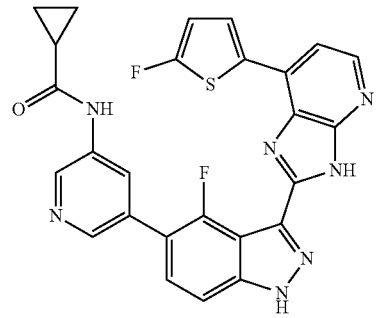
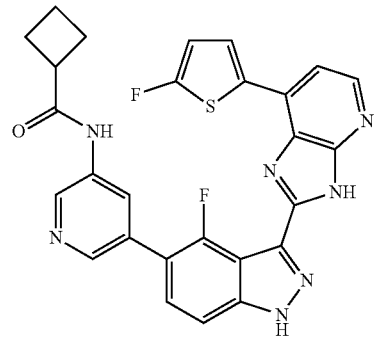
1759	
1760	
1761	
1762	

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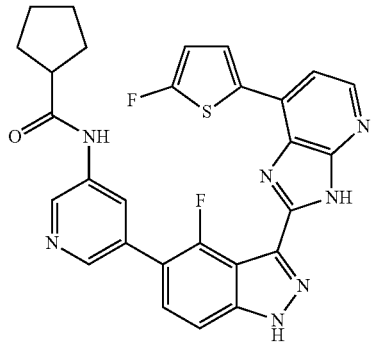
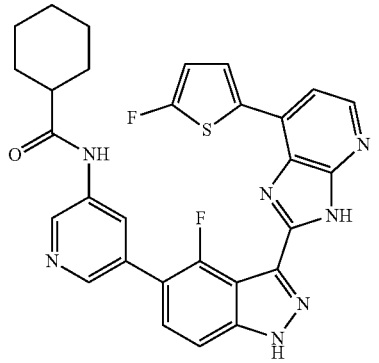
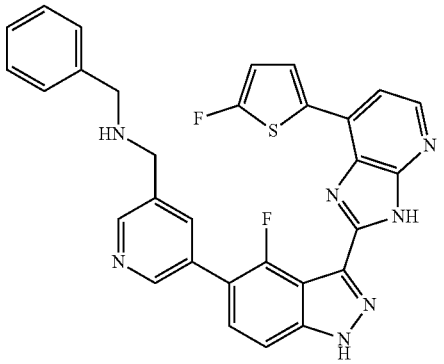
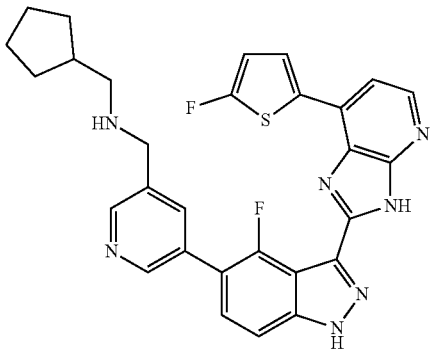
1763	
1764	
1765	
1766	

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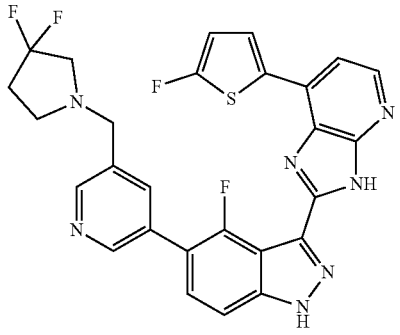
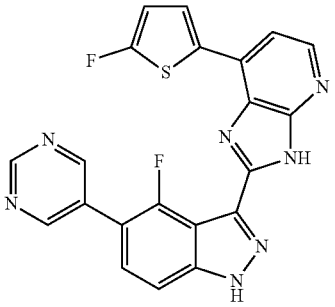
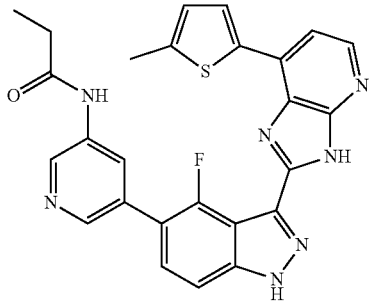
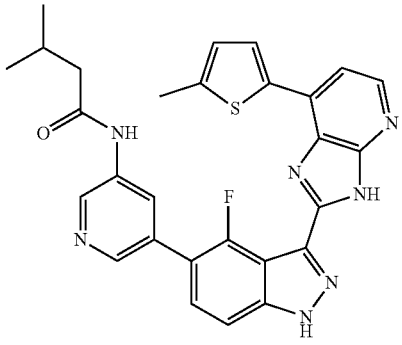
1767	
1768	
1769	
1770	

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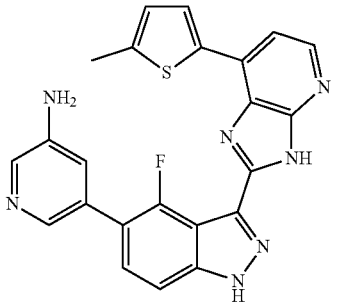
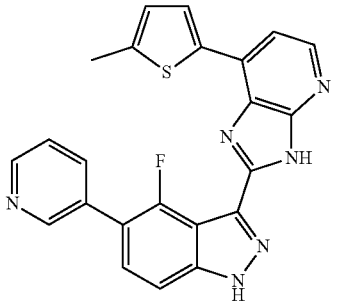
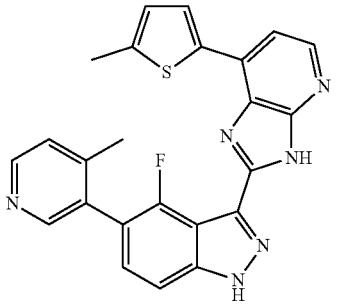
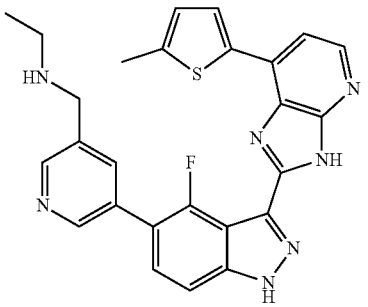
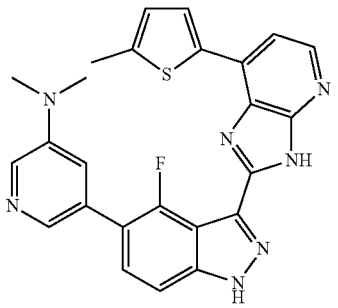
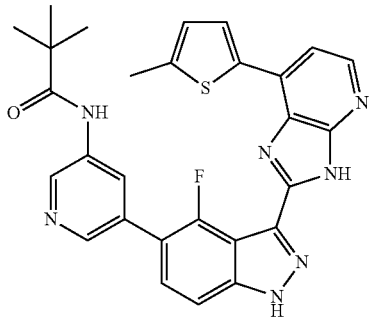
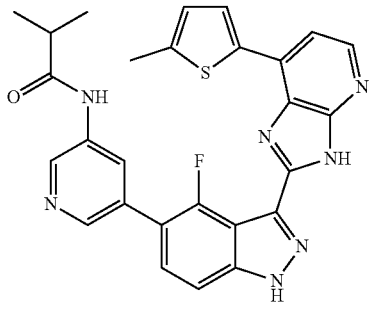
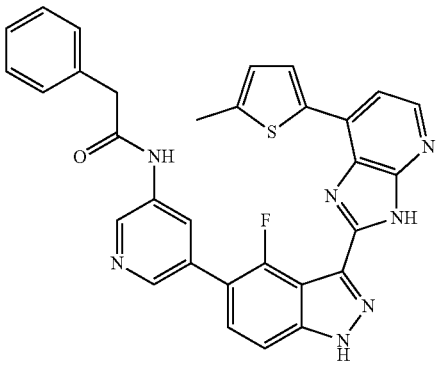
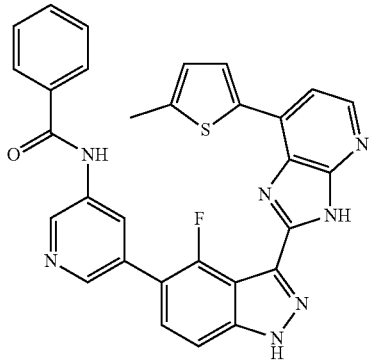
1771	
1772	
1773	
1774	
1775	

TABLE 1-continued

1776	
1777	
1778	
1779	

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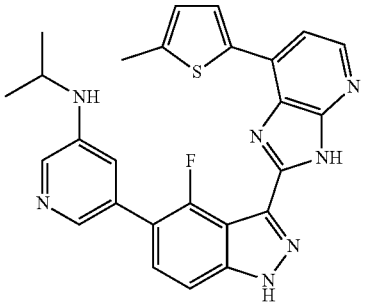
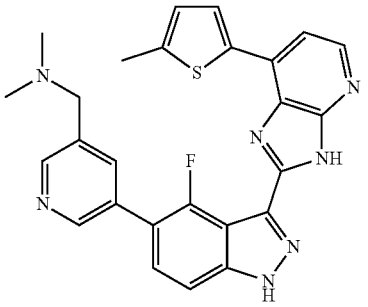
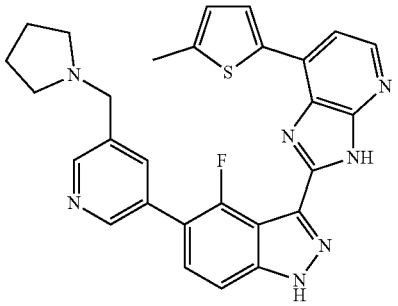
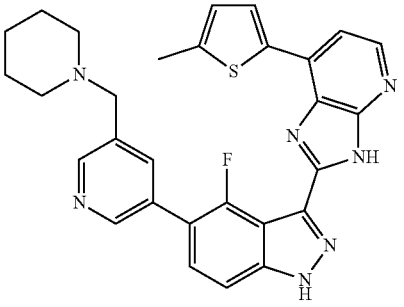
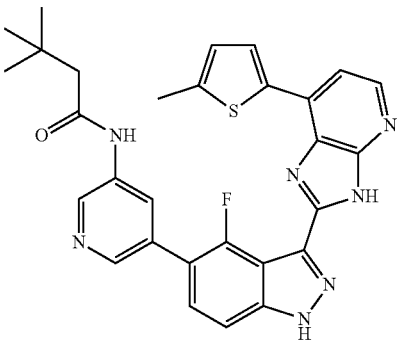
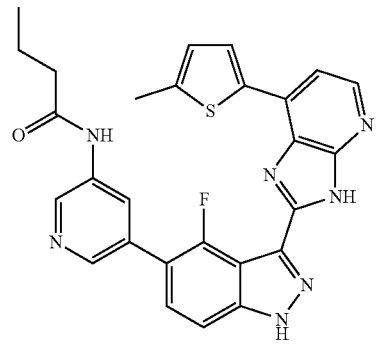
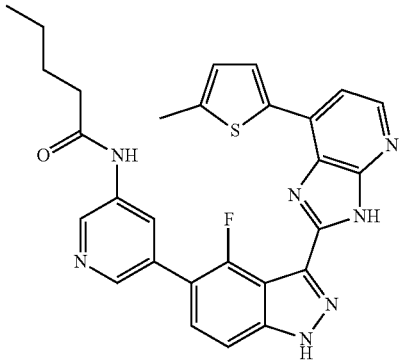
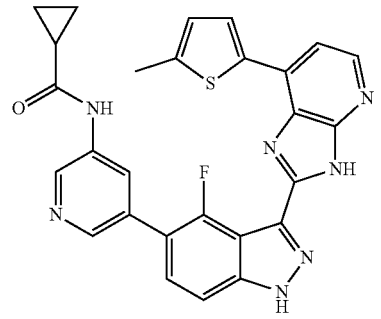
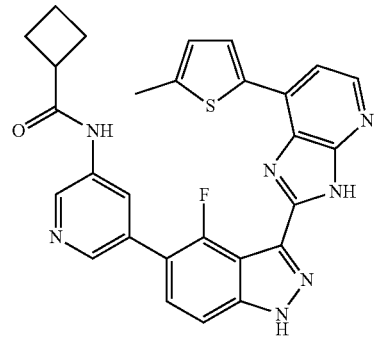
1780	
1781	
1782	
1783	
1784	

TABLE 1-continued

1785	
1786	
1787	
1788	

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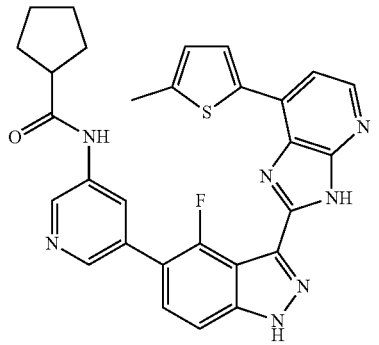
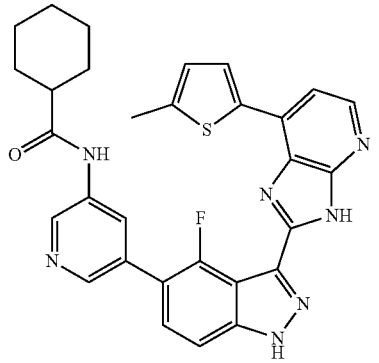
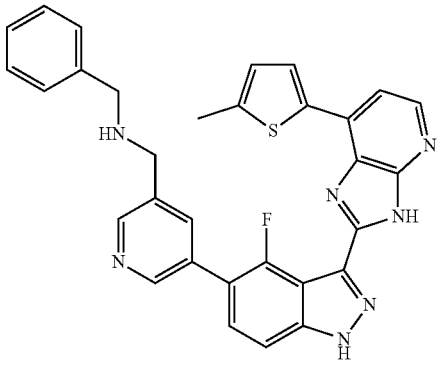
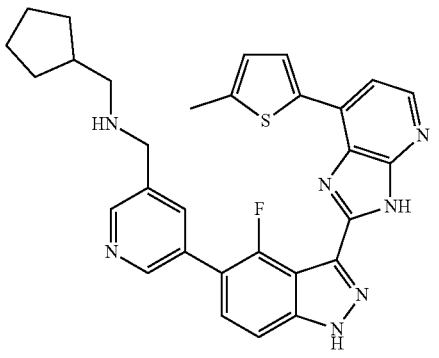
1789	
1790	
1791	
1792	

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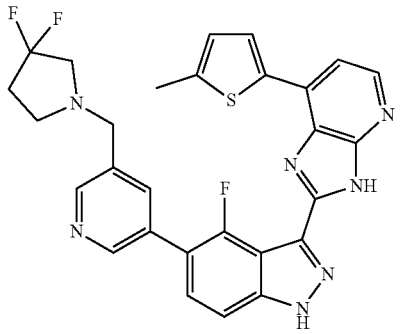
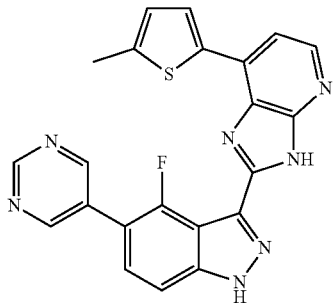
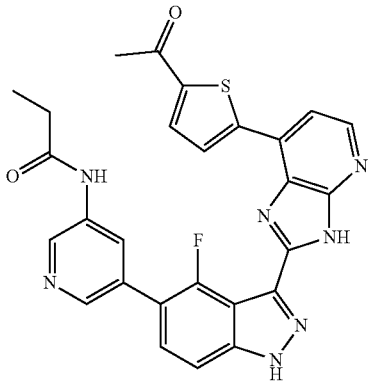
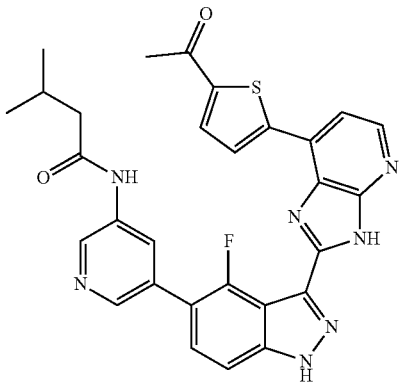
1793	
1794	
1795	
1796	

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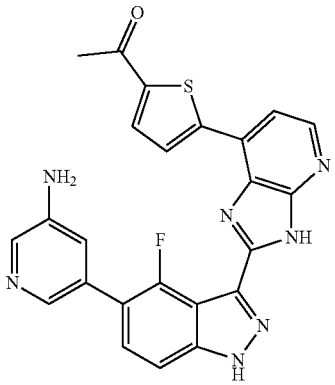
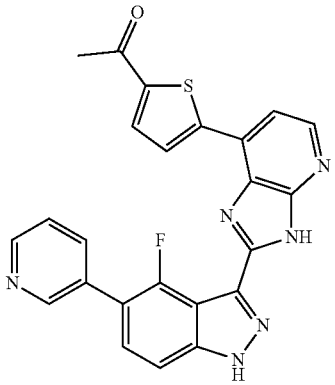
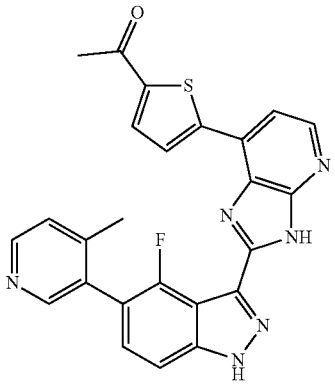
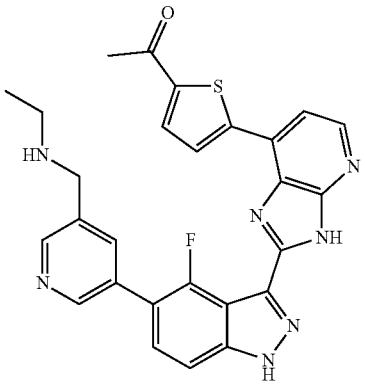
1797	
1798	
1799	
1800	

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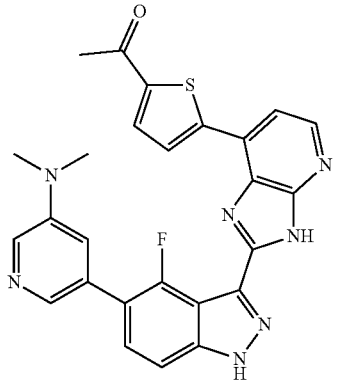
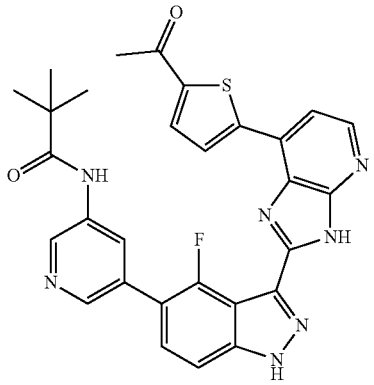
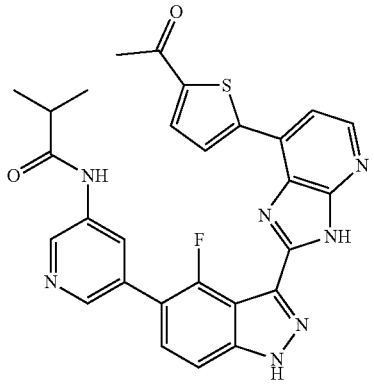
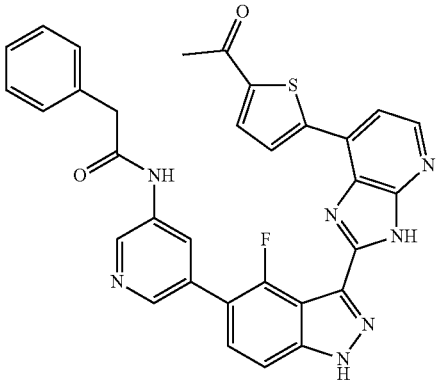
1801	
1802	
1803	
1804	

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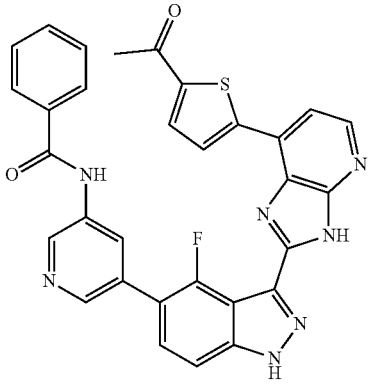
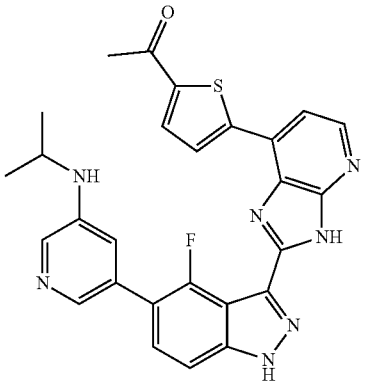
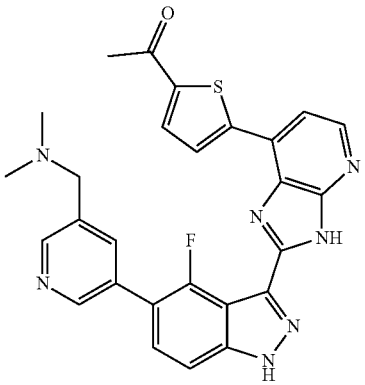
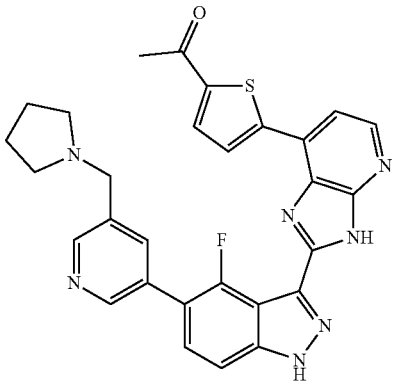
1805	
1806	
1807	
1808	

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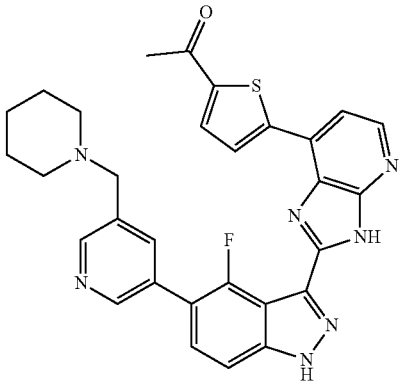
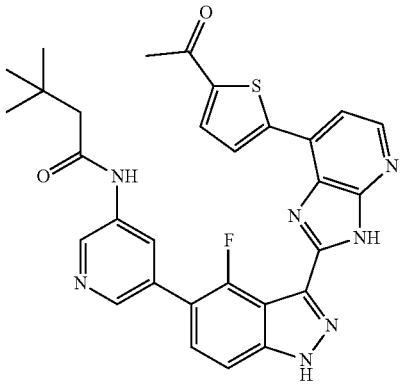
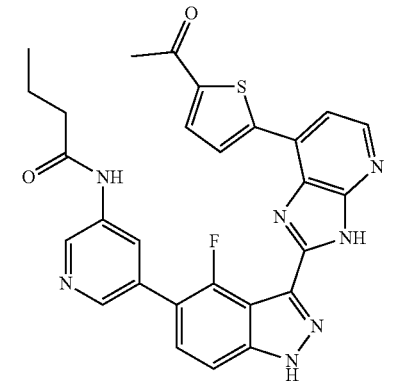
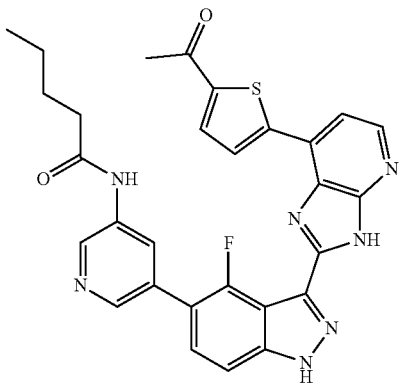
1809	
1810	
1811	
1812	

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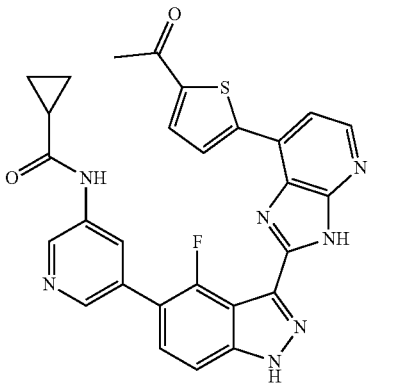
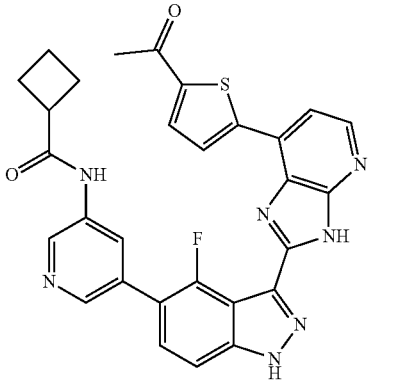
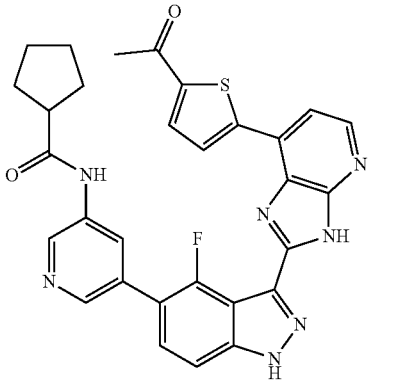
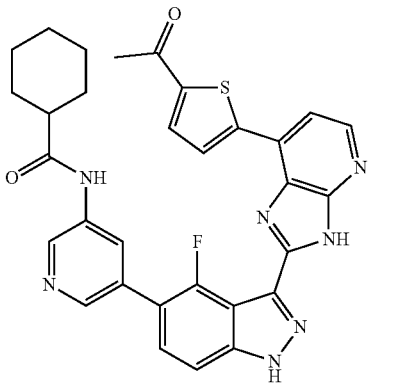
1813	
1814	
1815	
1816	

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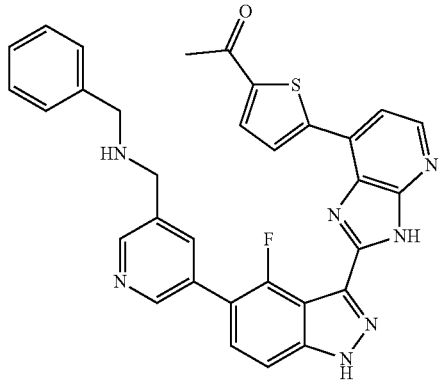
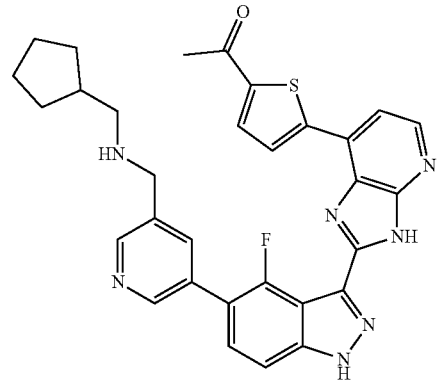
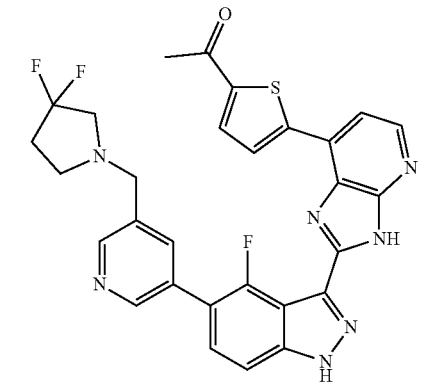
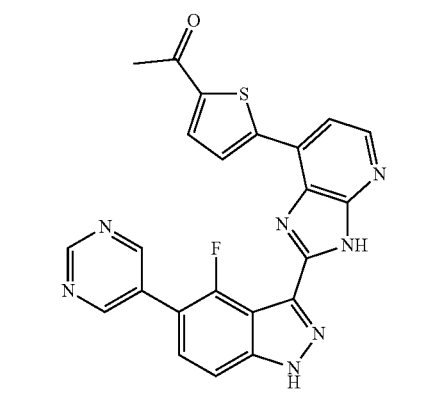
1817	
1818	
1819	
1820	

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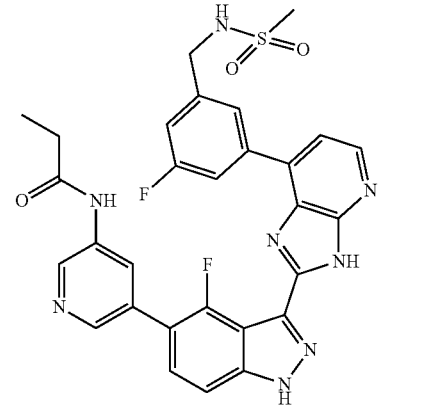
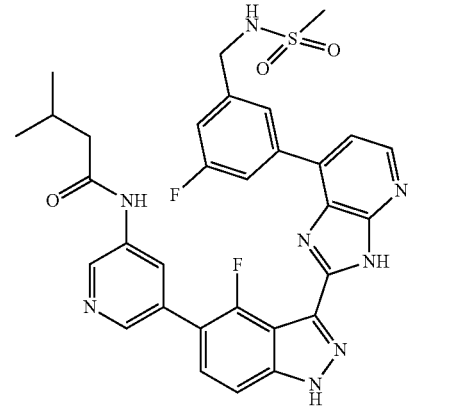
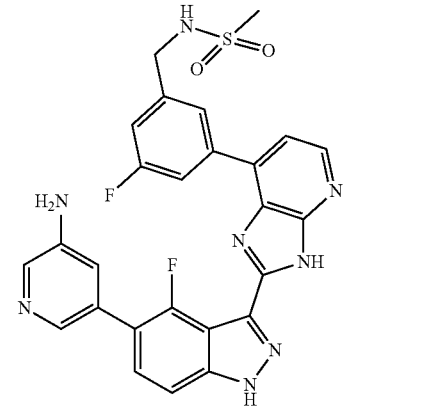
1821	
1822	
1823	

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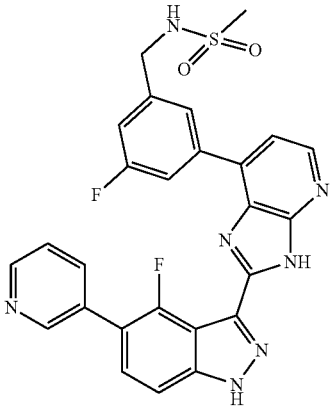
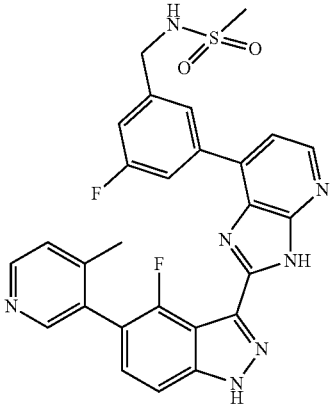
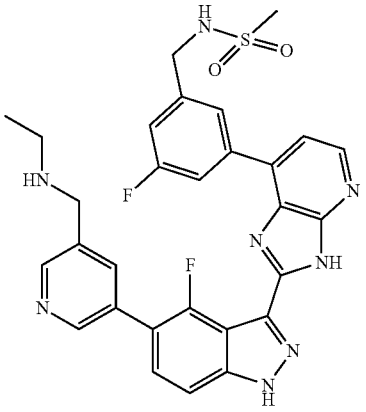
1824	
1825	
1826	

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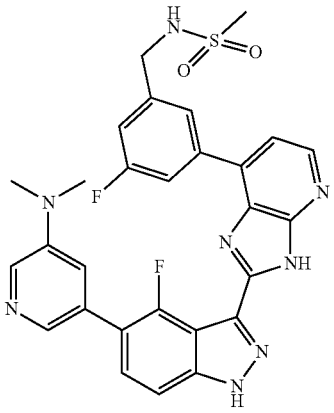
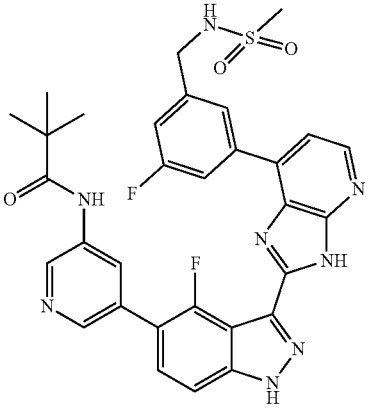
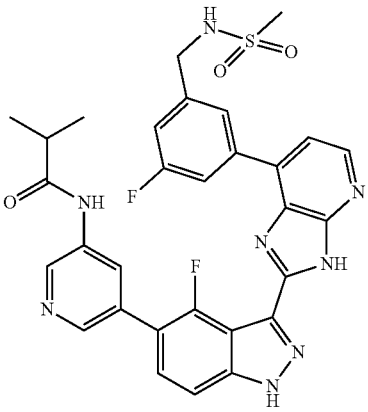
1827	
1828	
1829	

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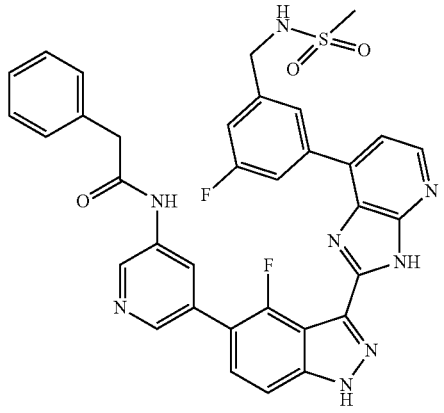
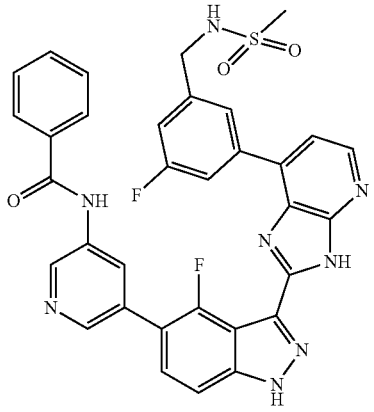


1831



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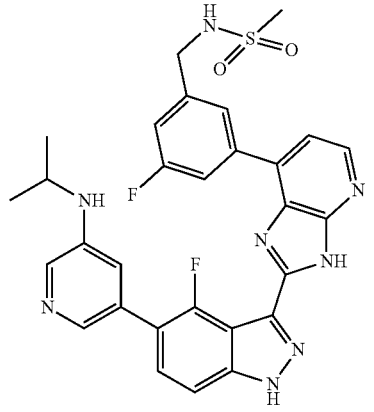

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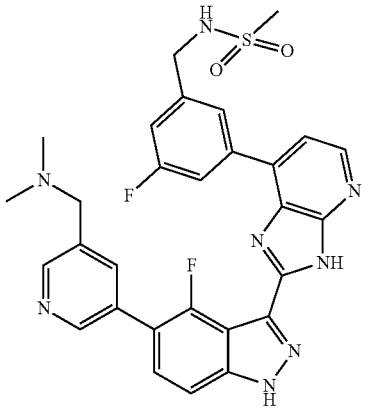
1833



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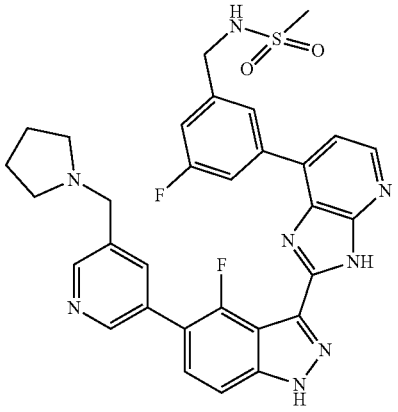
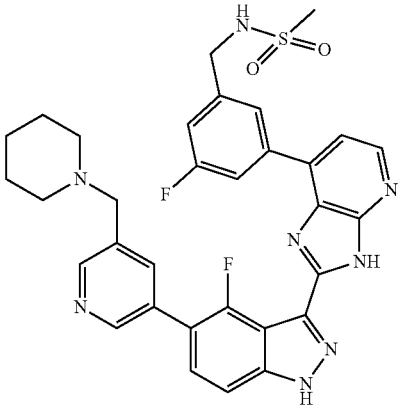


1835



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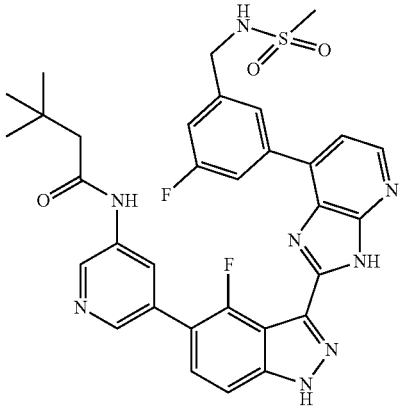
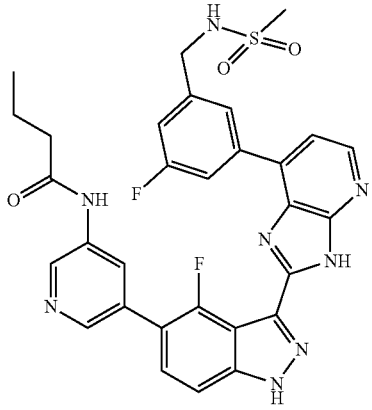
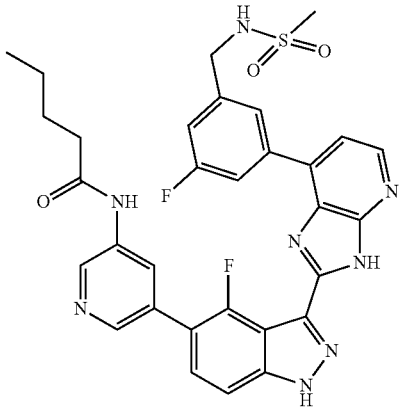
1836	
1837	
1838	

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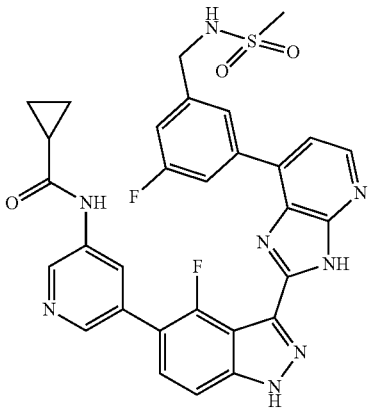
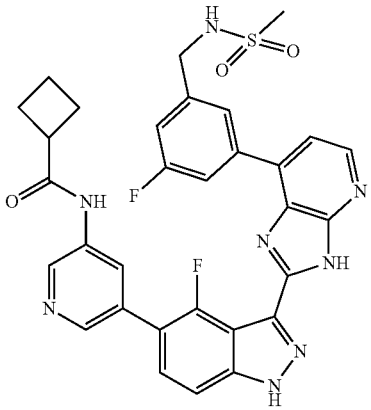
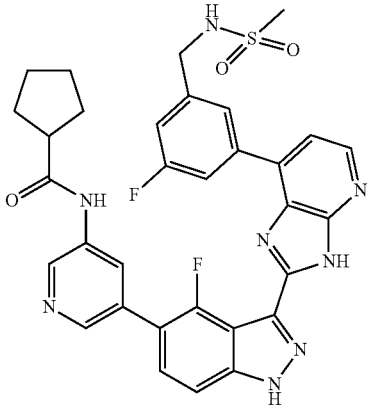
1839	
1840	
1841	

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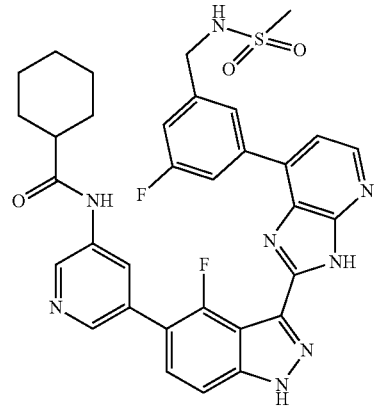
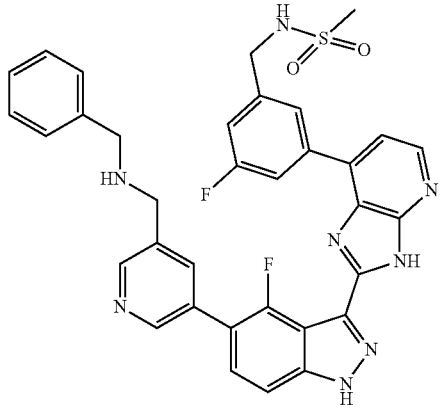
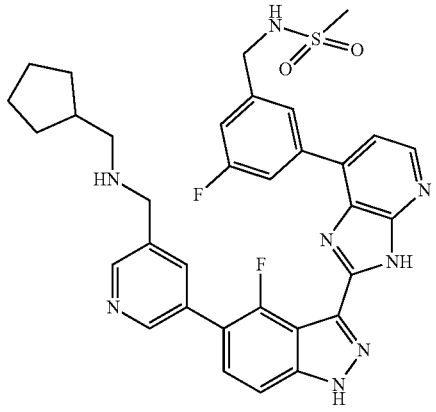
1842	
1843	
1844	

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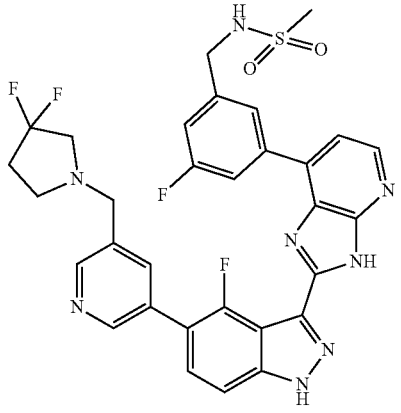
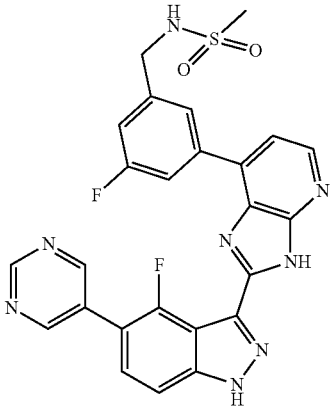
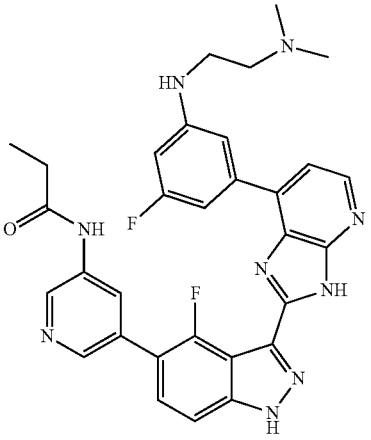
1845	
1846	
1847	

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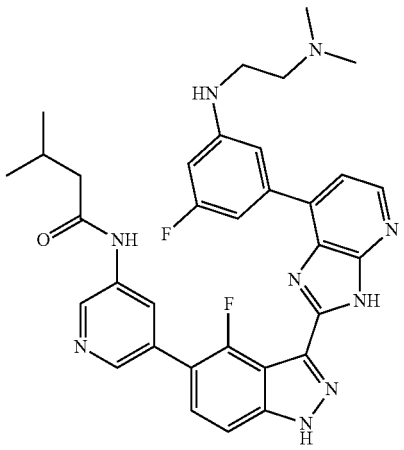
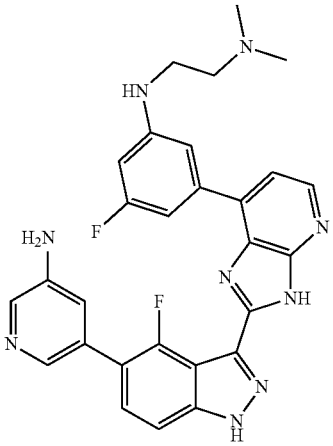
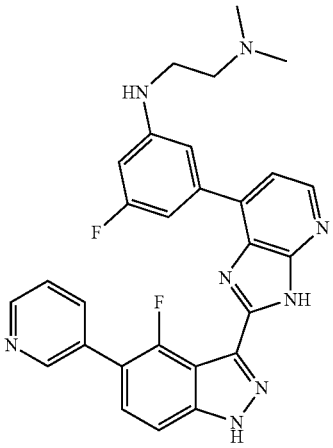
1848	
1849	
1850	

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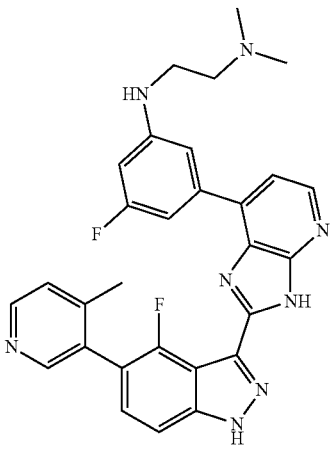
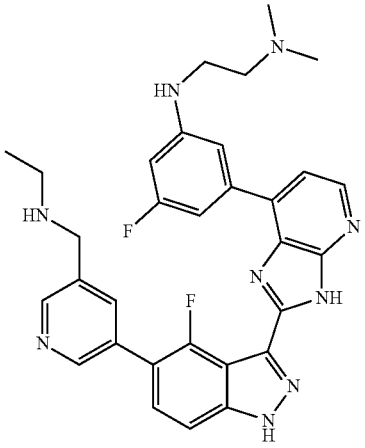
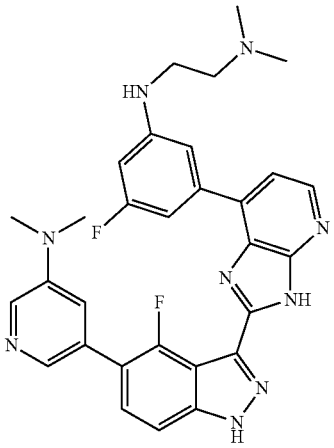
1851	
1852	
1853	

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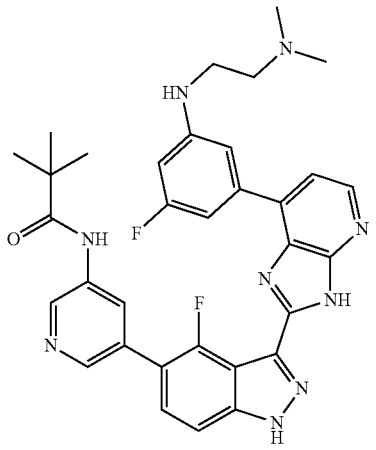
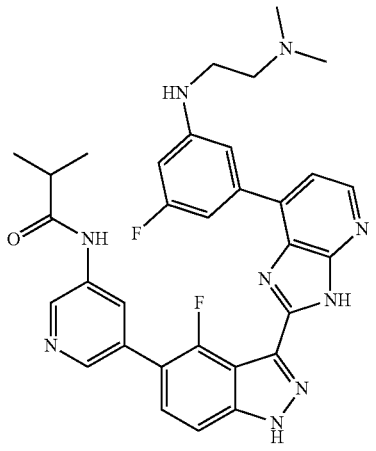
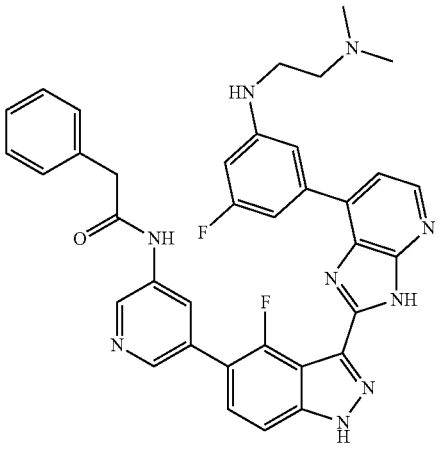
1854	
1855	
1856	

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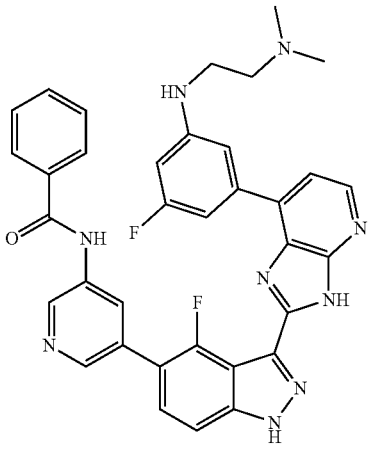
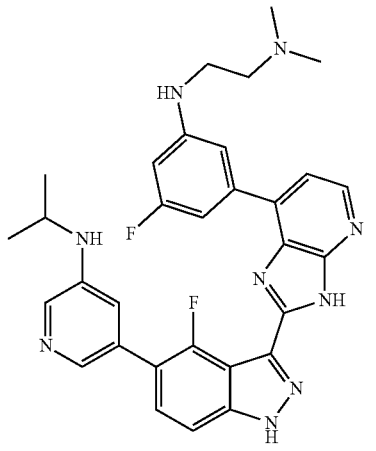
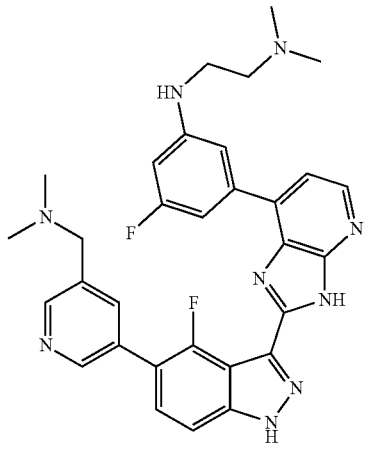
1857	
1858	
1859	

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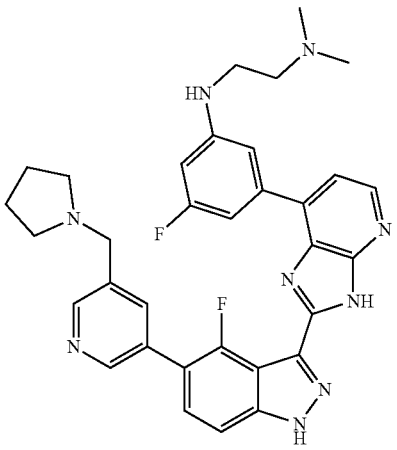
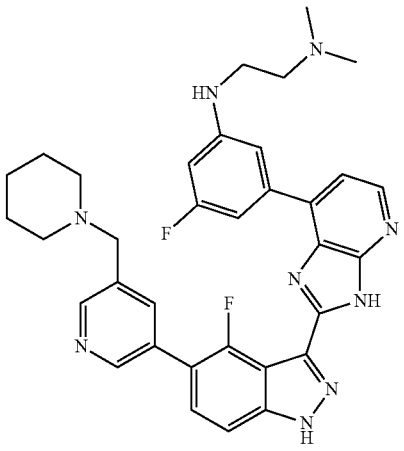
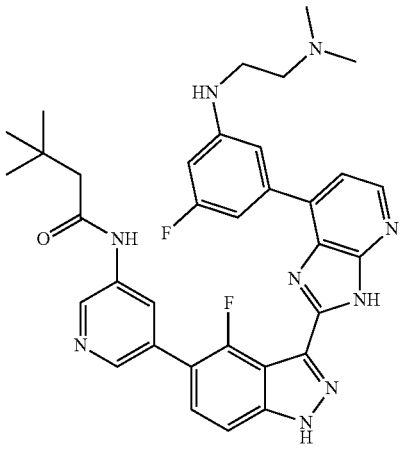
1860	
1861	
1862	

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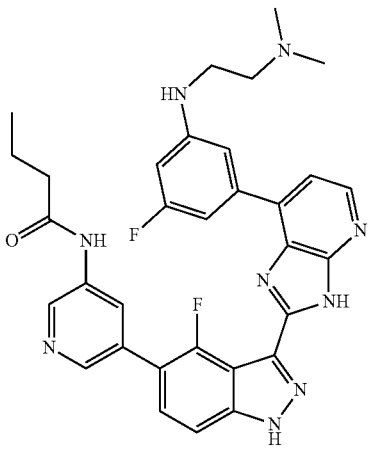
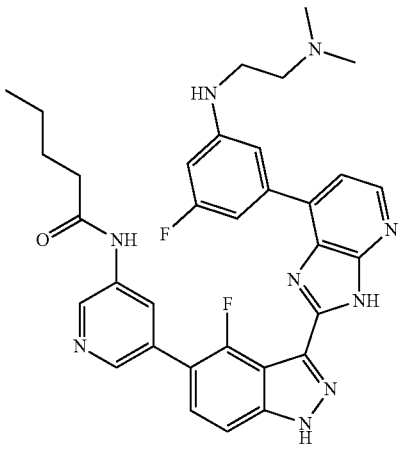
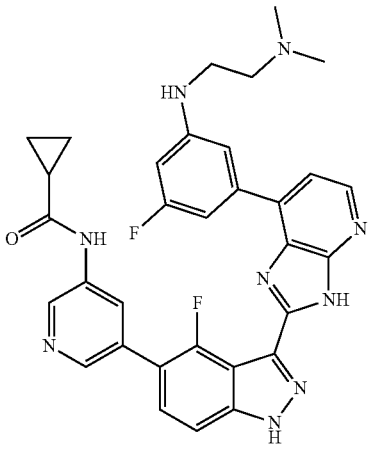
1863	
1864	
1865	

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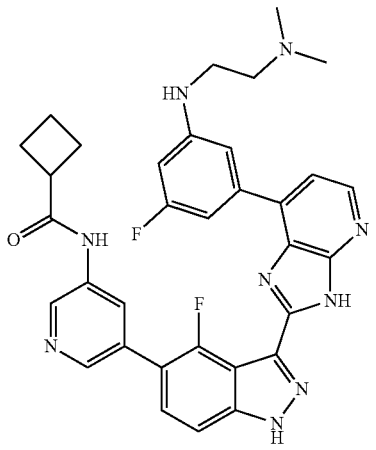
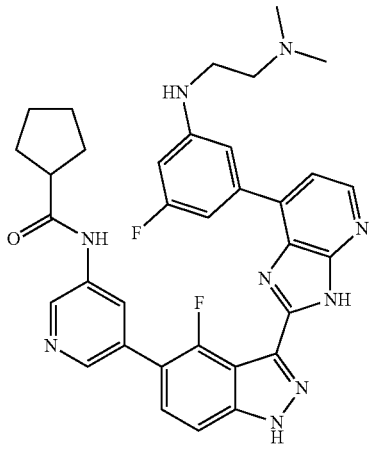
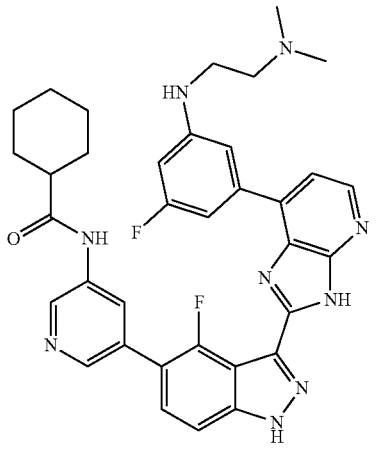
1866	
1867	
1868	

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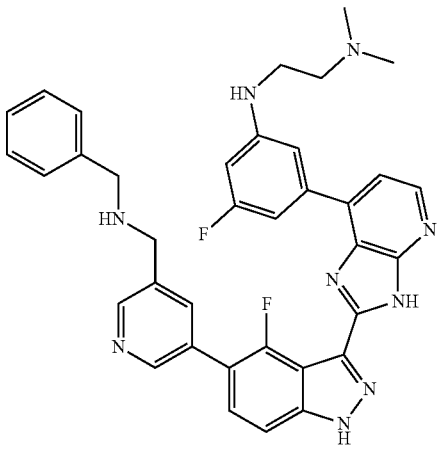
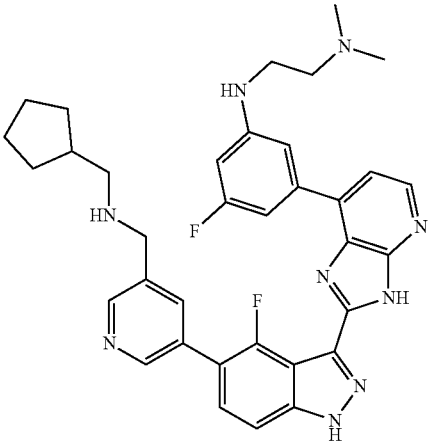
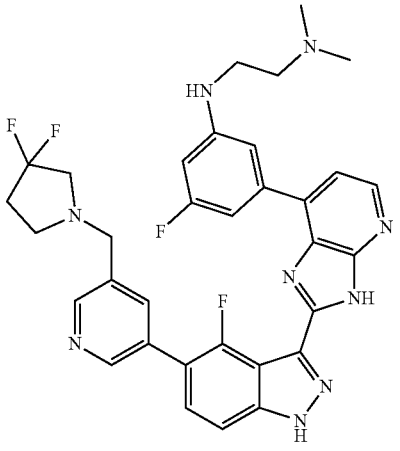
1869	
1870	
1871	

TABLE 1-continued

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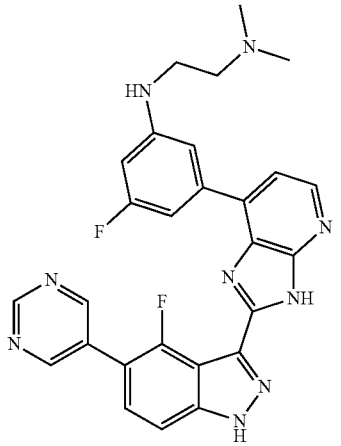

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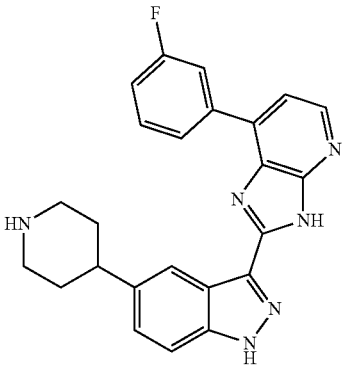

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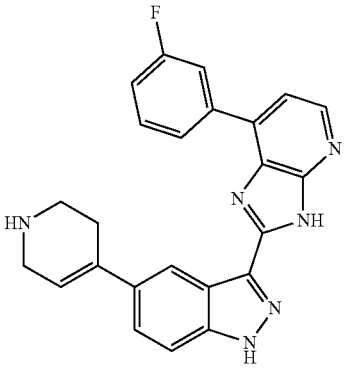

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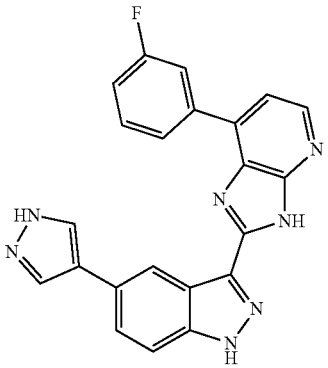

TABLE 1-continued

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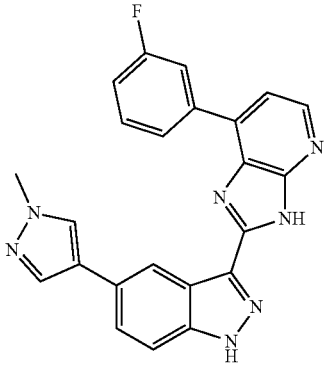

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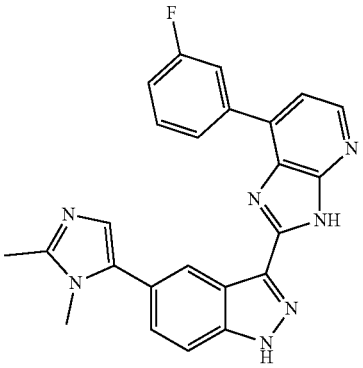

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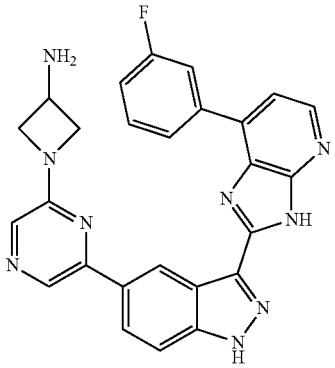

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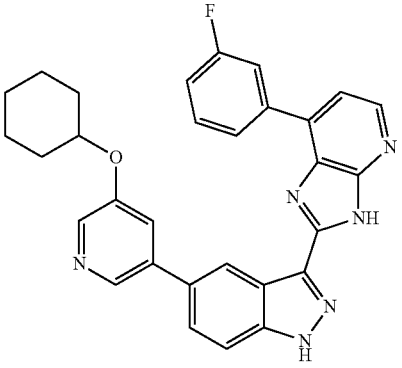

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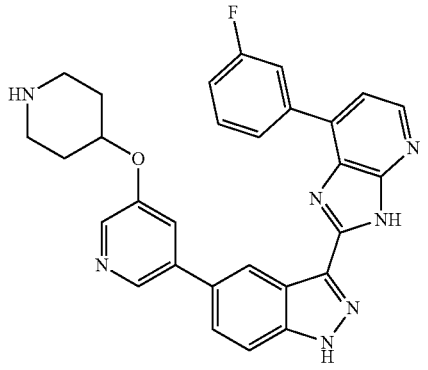
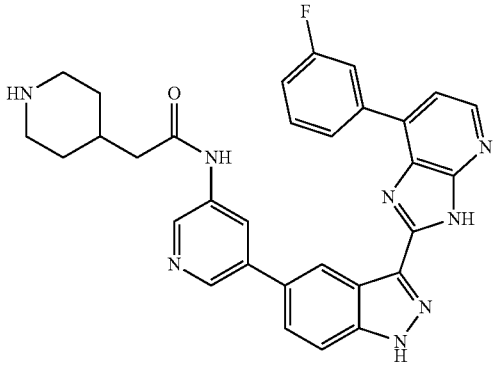
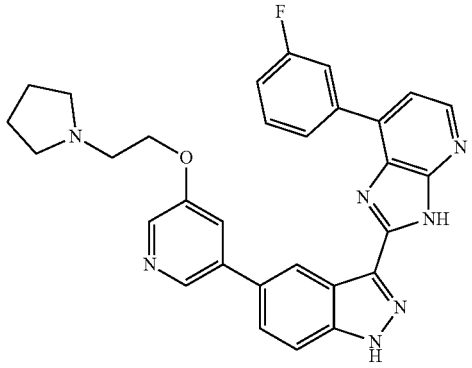
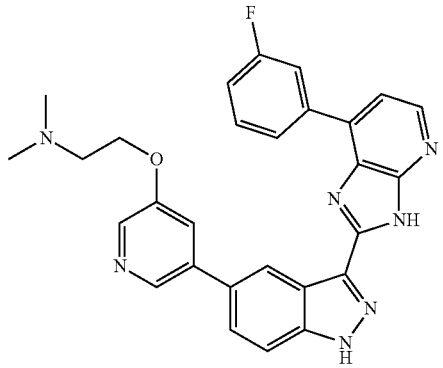
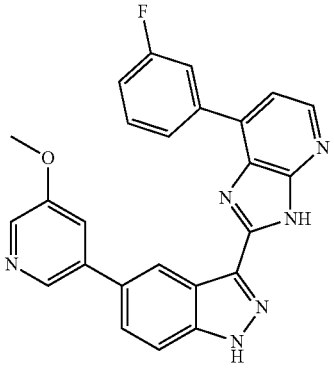
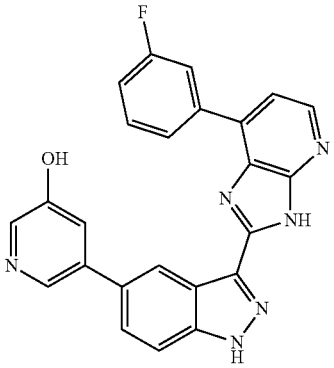
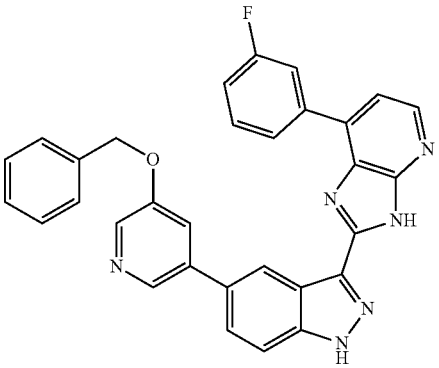
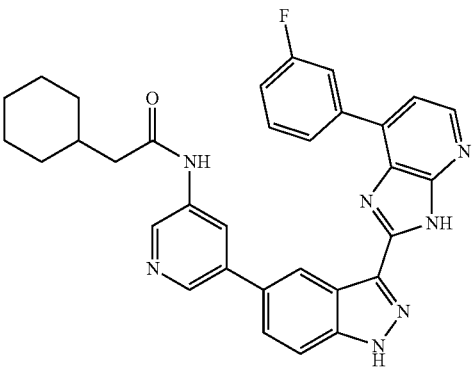
1880	
1881	
1882	
1883	

TABLE 1-continued

1884	
1885	
1886	
1887	

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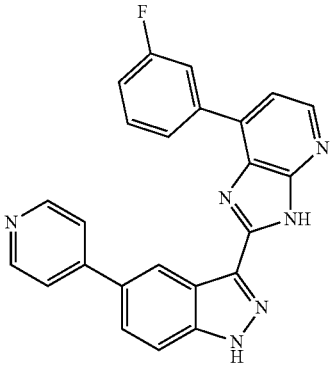

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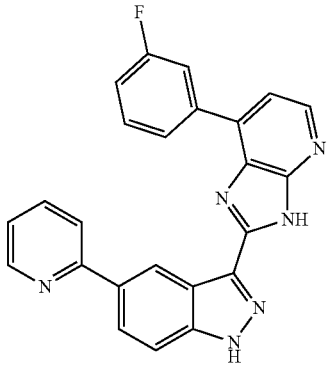

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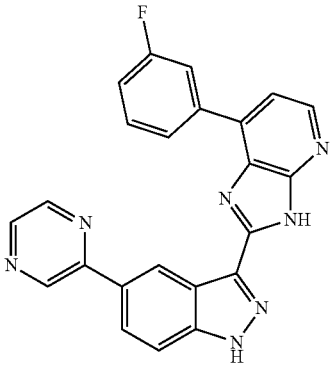

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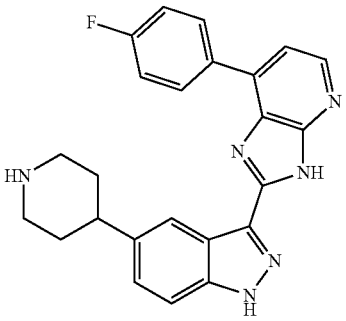

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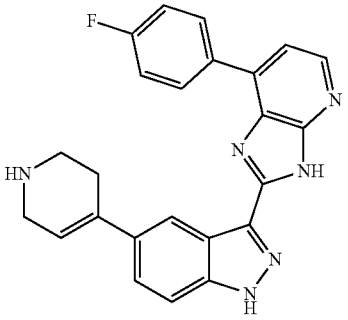

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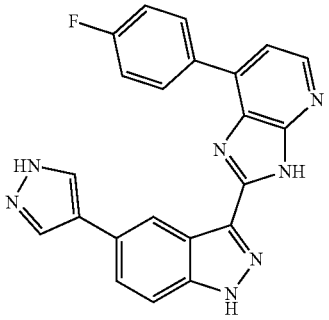

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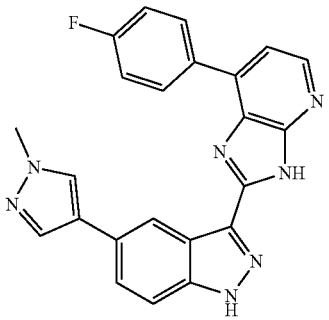

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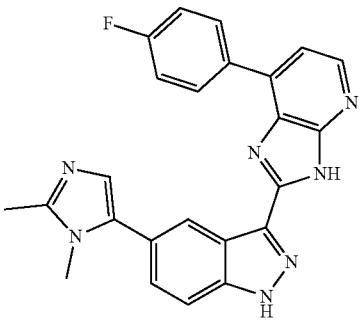

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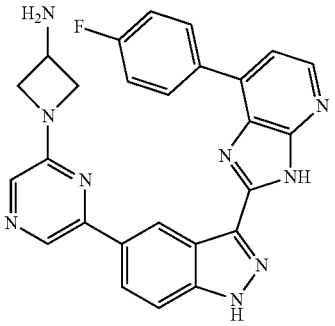
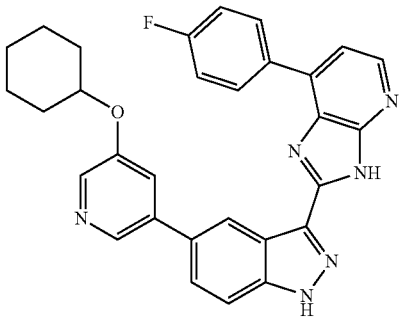
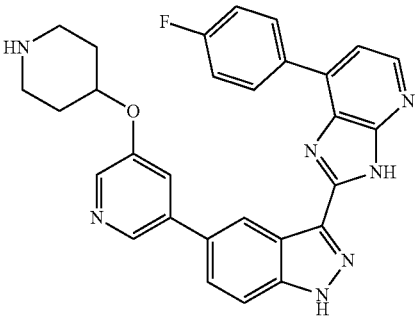
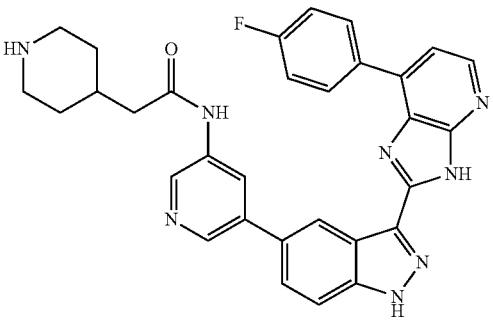
1896	
1897	
1898	
1899	

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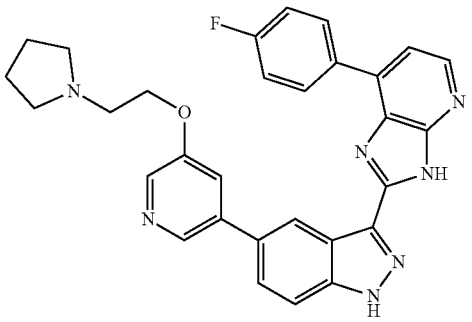
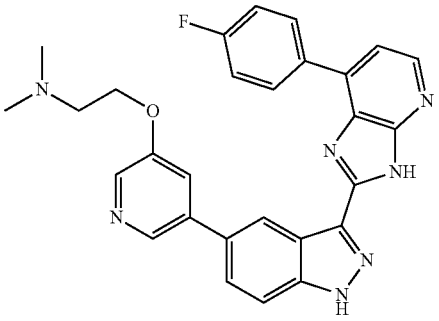
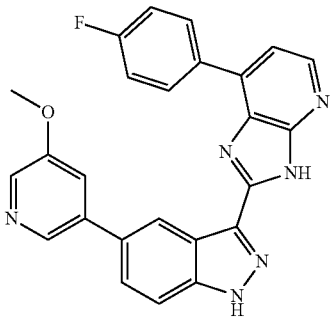
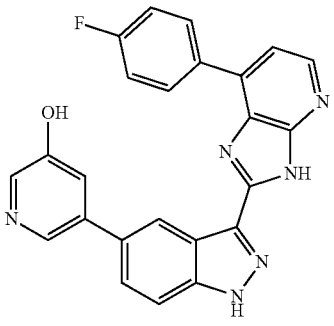
1900	
1901	
1902	
1903	

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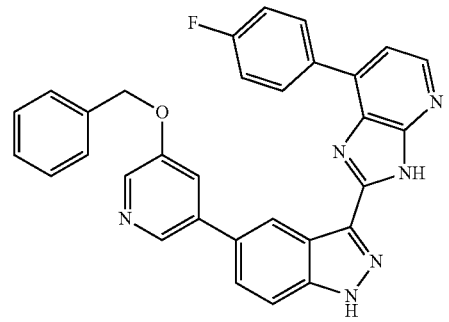
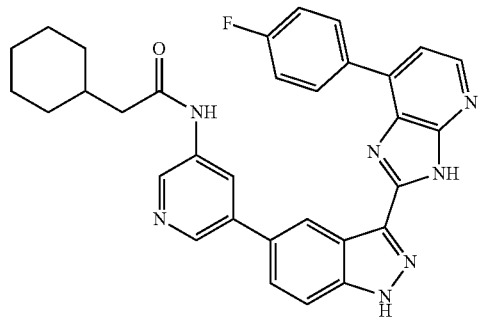
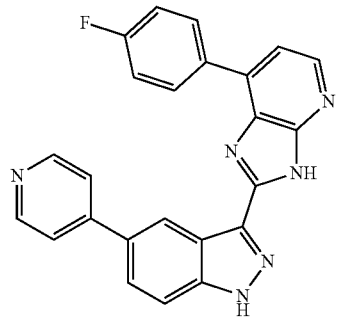
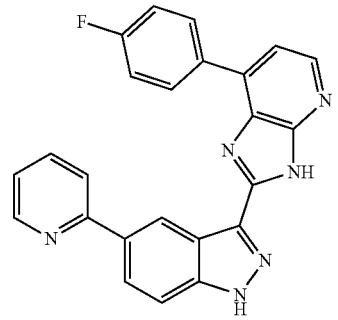
1904	
1905	
1906	
1907	

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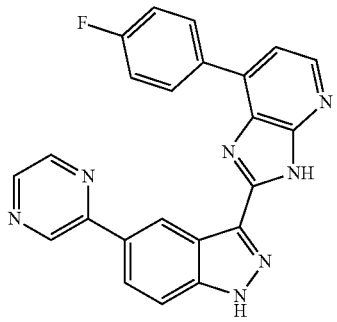
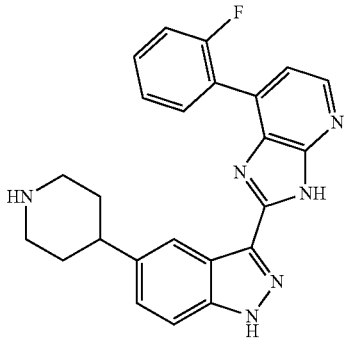
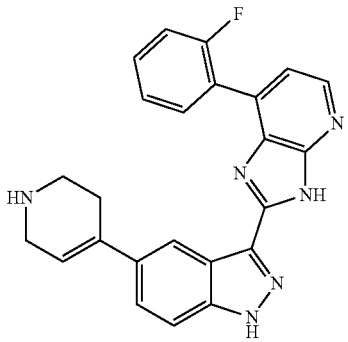
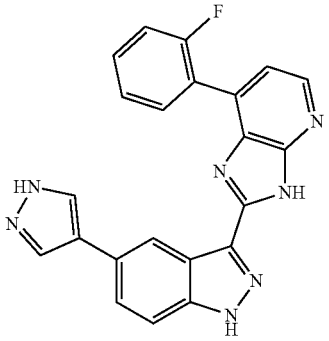
1908	
1909	
1910	
1911	

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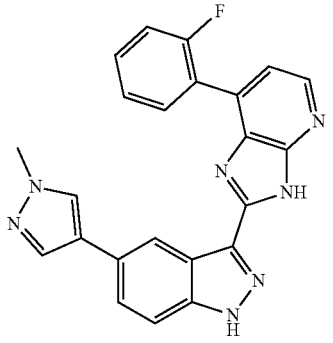
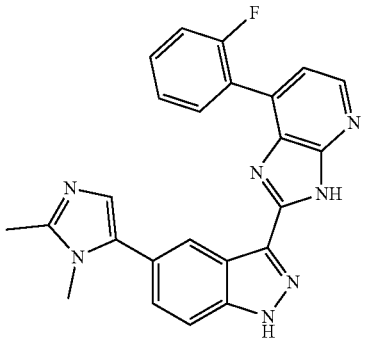
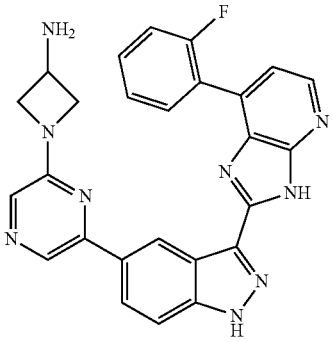
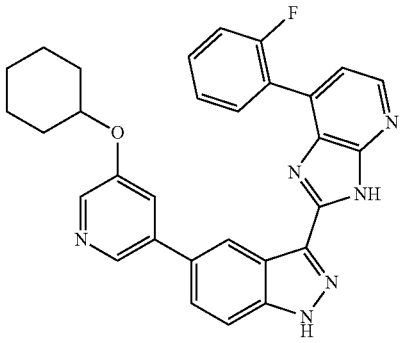
1912	
1913	
1914	
1915	

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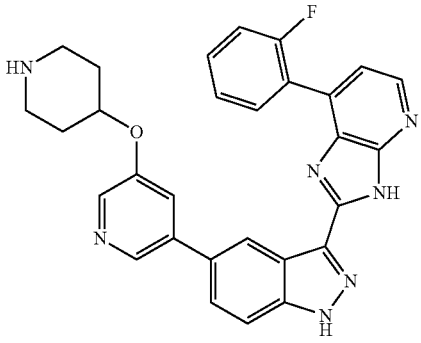
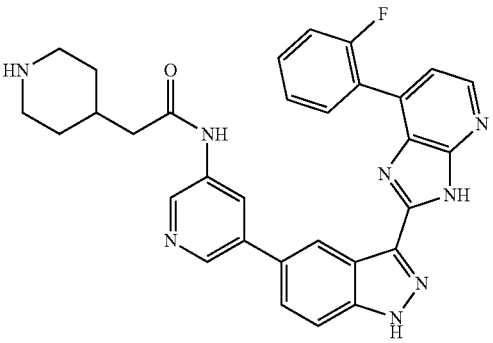
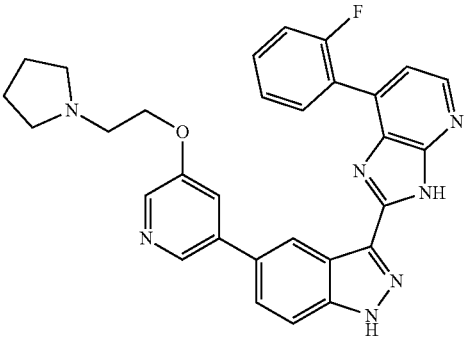
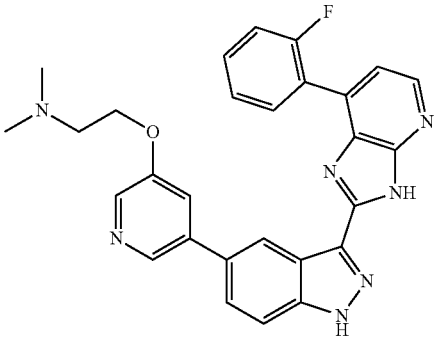
1916	
1917	
1918	
1919	

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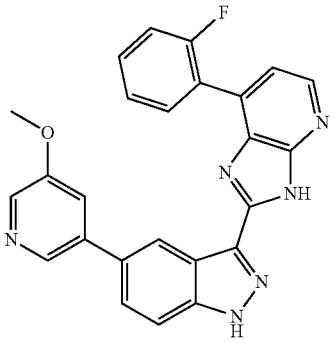
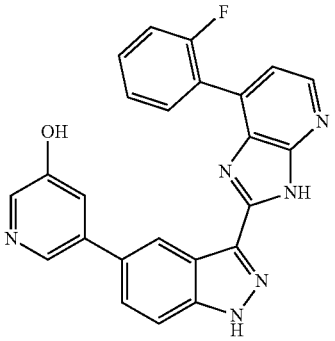
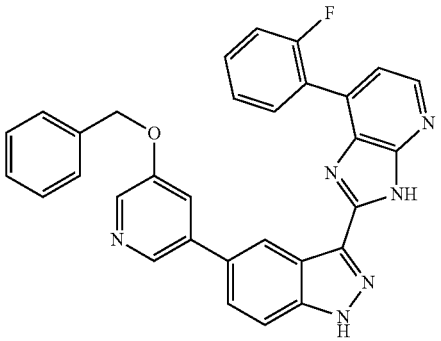
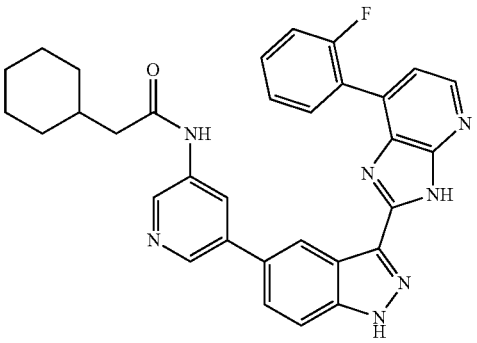
1920	
1921	
1922	
1923	

TABLE 1-continued

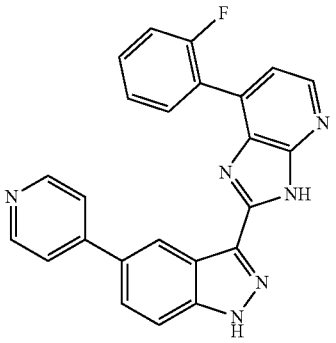
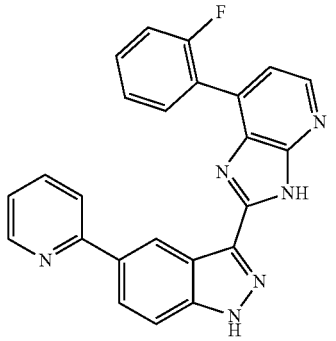
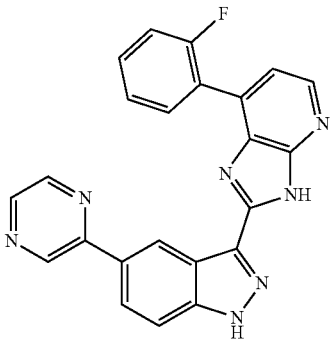
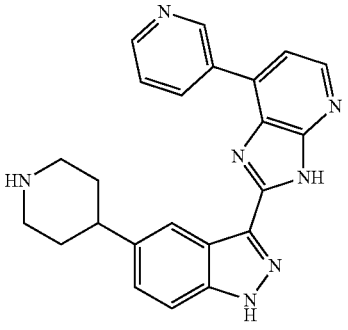
1924	
1925	
1926	
1927	

TABLE 1-continued

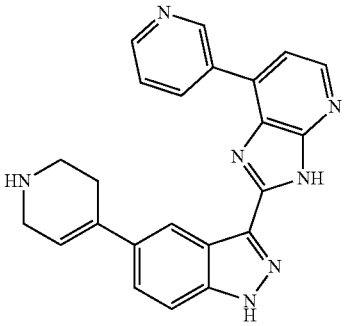
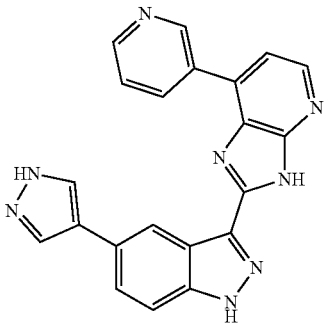
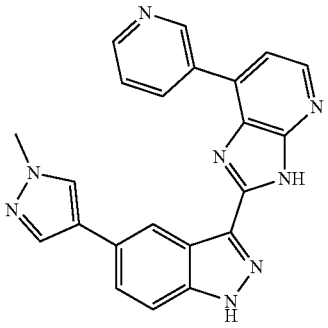
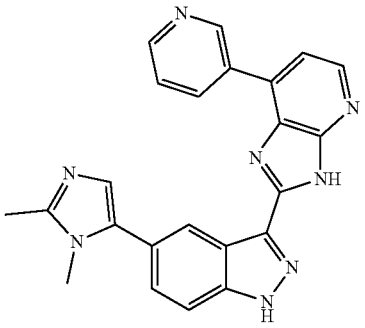
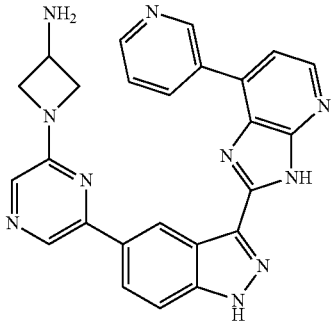
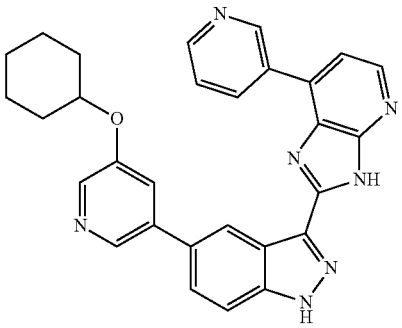
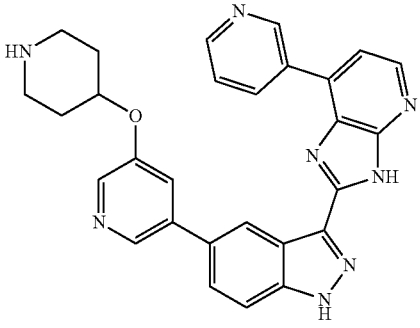
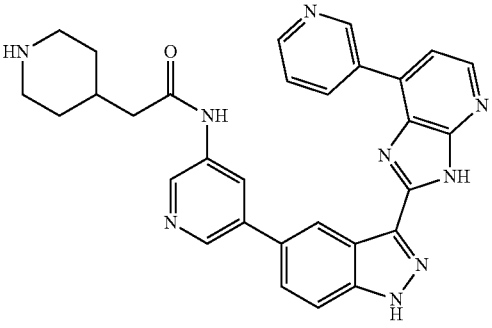
1928	
1929	
1930	
1931	

TABLE 1-continued

1932	
1933	
1934	
1935	

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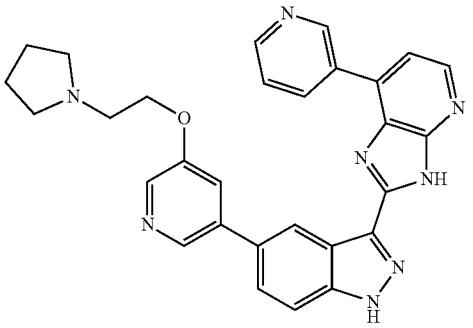
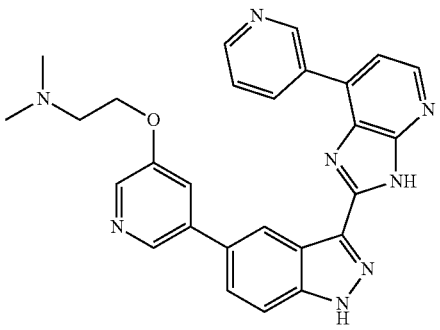
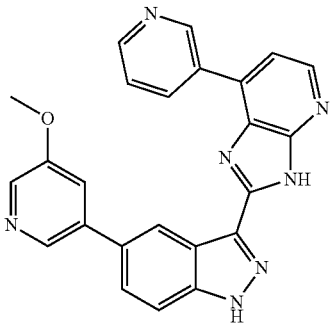
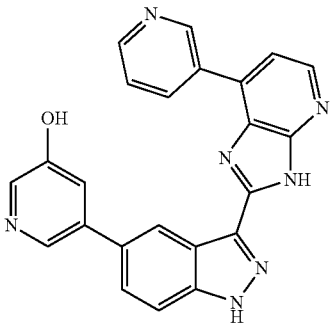
1936	
1937	
1938	
1939	

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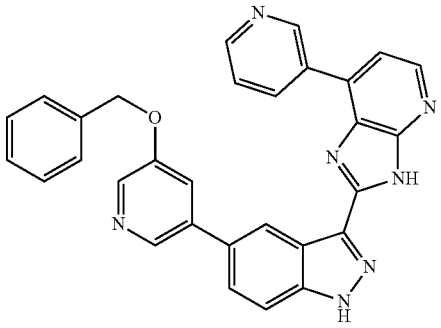
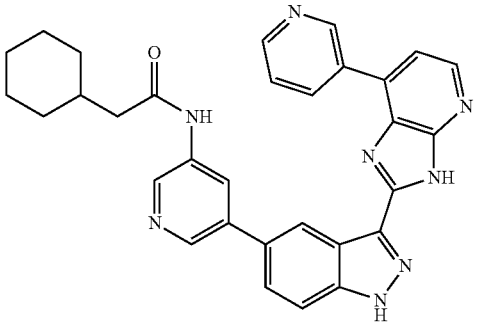
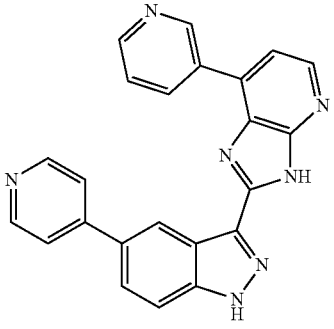
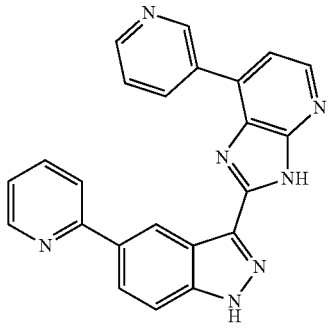
1940	
1941	
1942	
1493	

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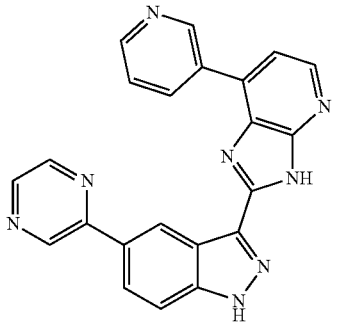

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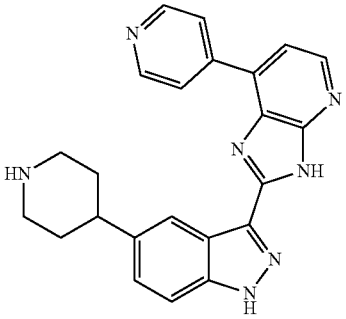

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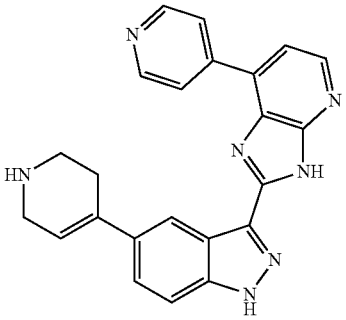

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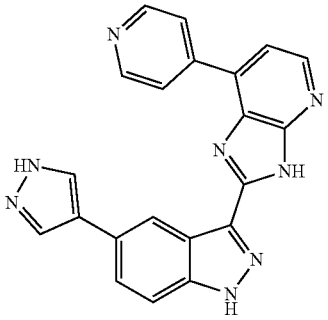

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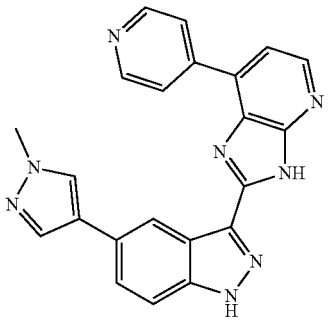

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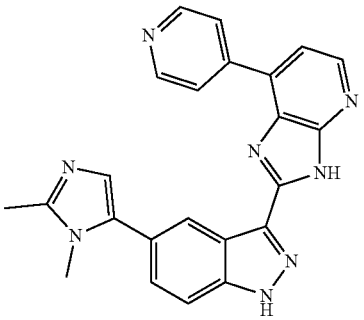

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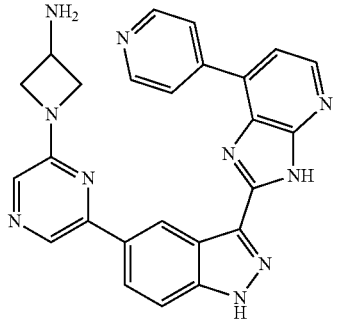

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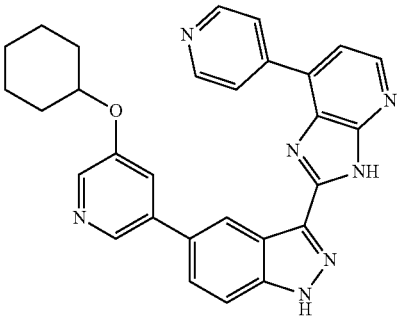

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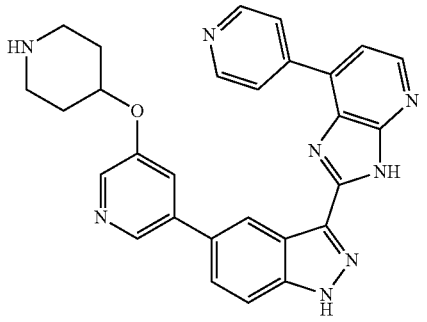

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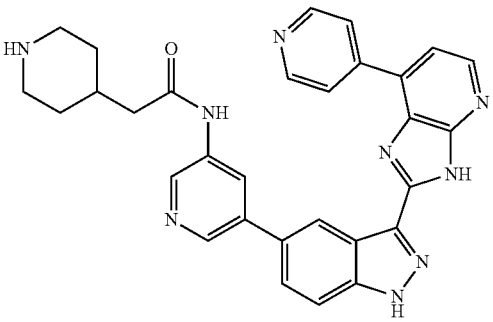

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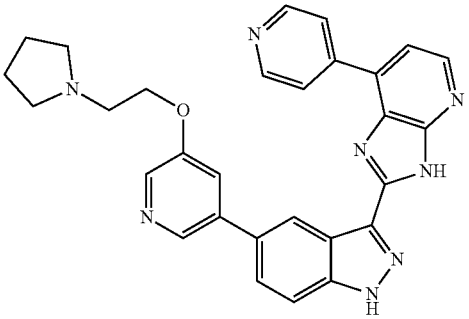

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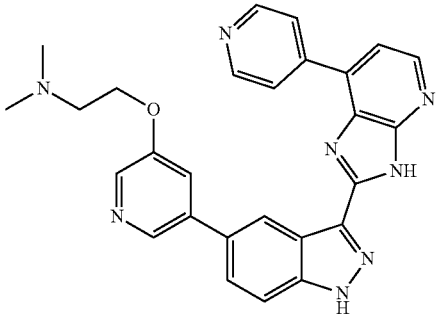

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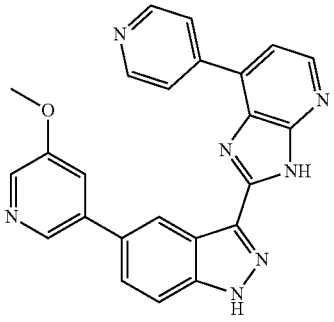

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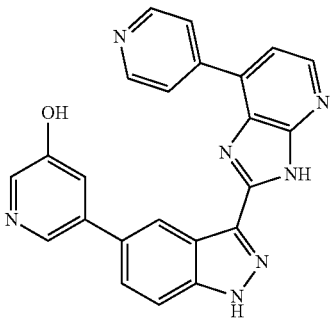

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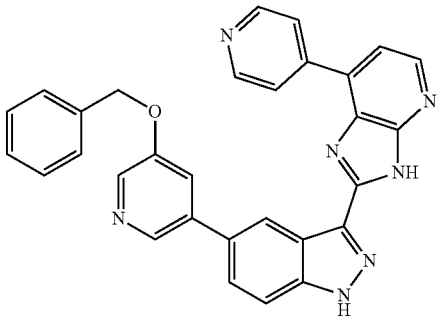

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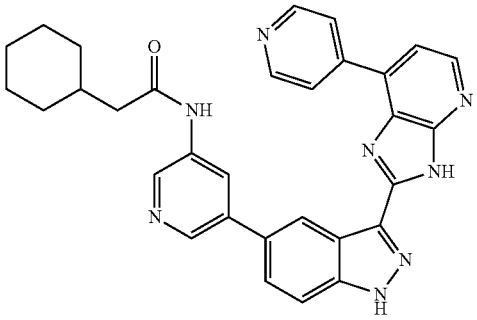

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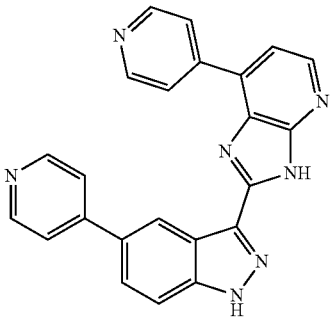
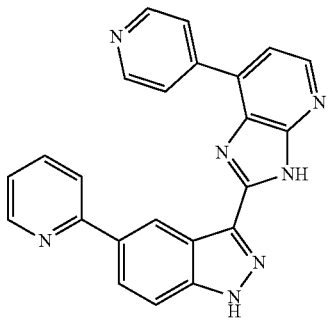
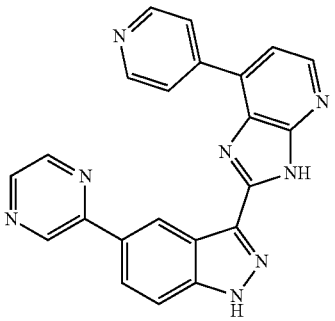
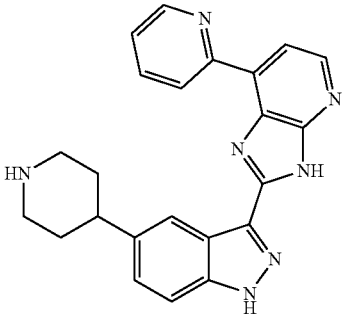
1960	
1961	
1962	
1963	

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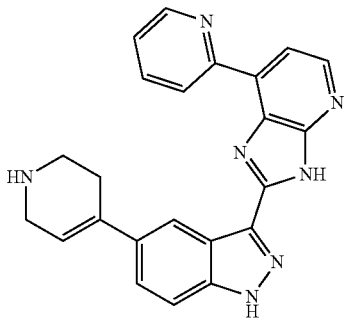
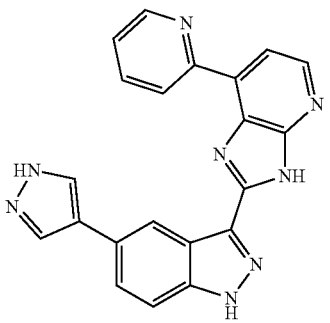
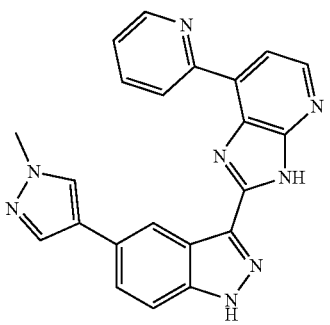
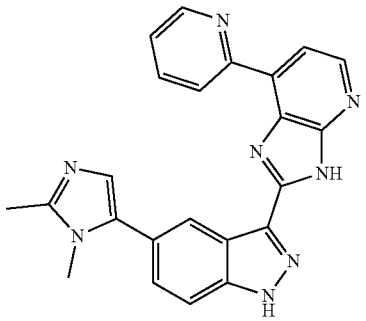
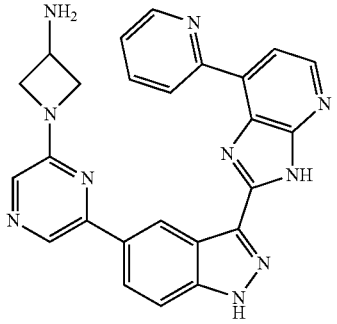
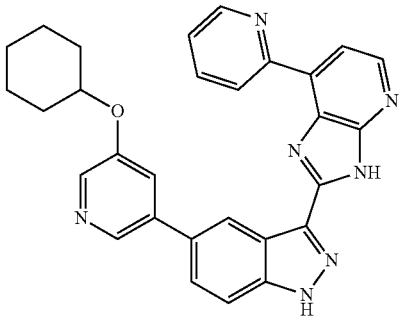
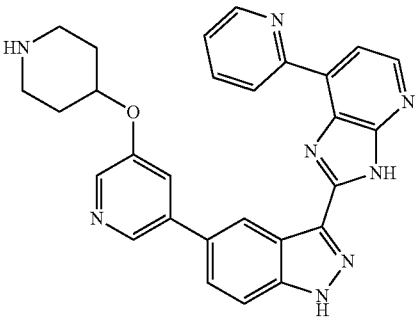
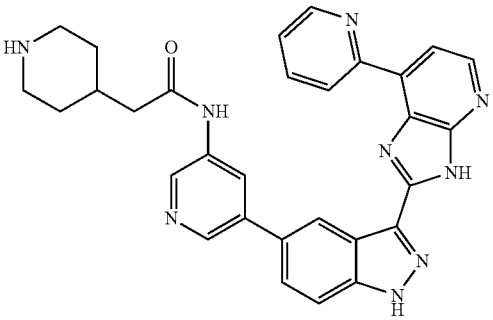
1964	
1965	
1966	
1967	

TABLE 1-continued

1968	
1969	
1970	
1971	

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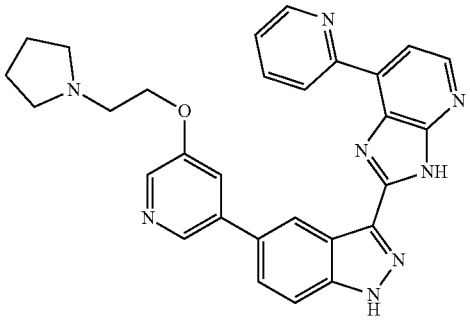
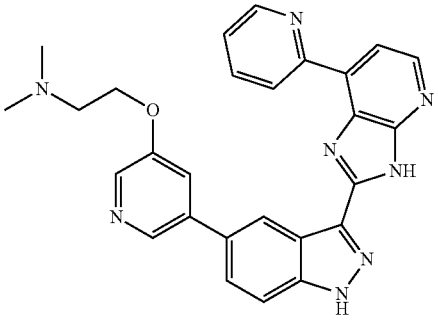
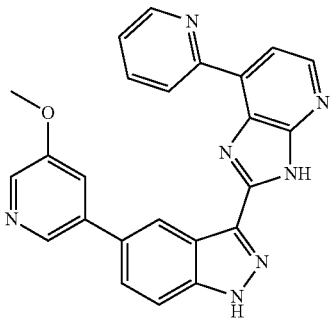
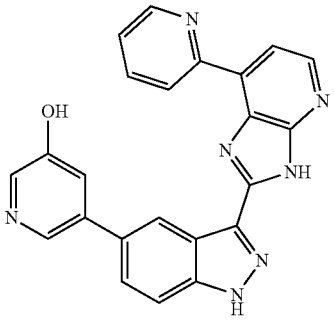
1972	
1973	
1974	
1975	

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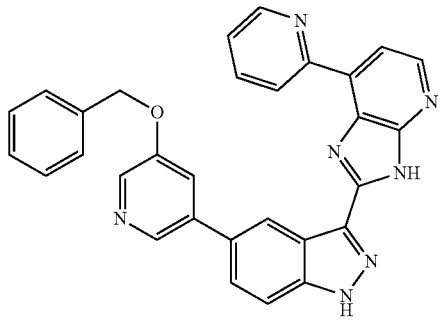
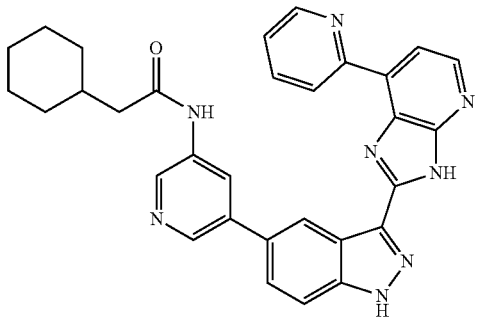
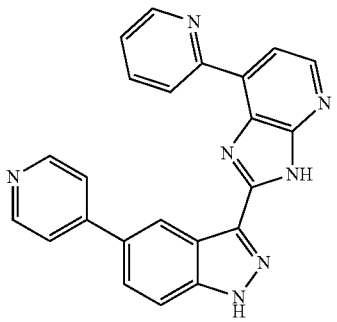
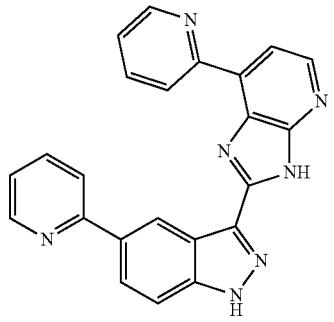
1976	
1977	
1978	
1979	

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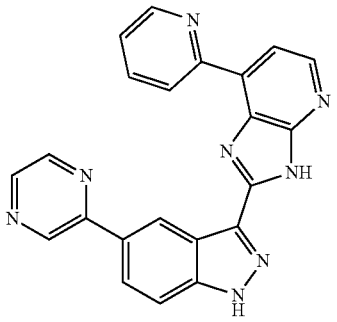
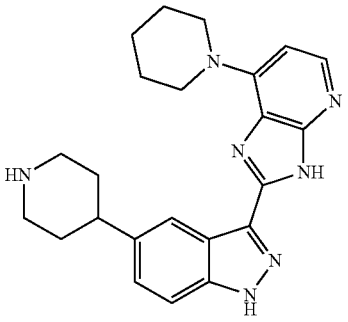
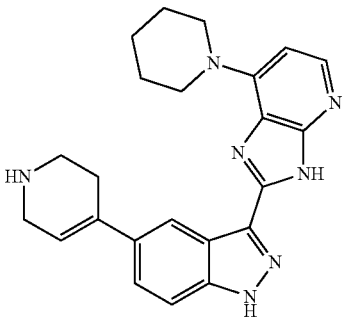
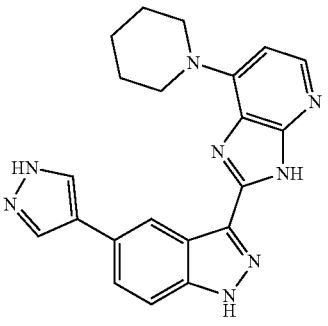
1980	
1981	
1982	
1983	

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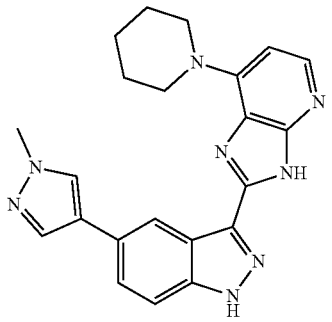
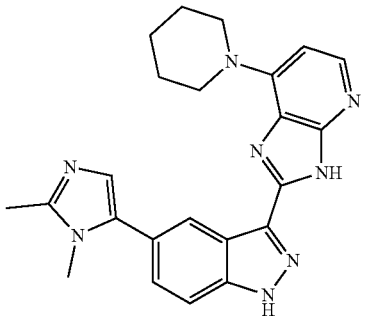
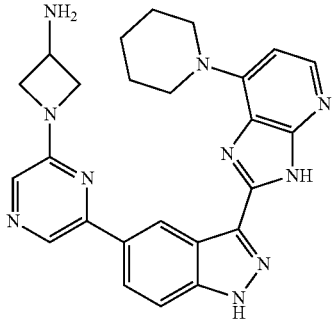
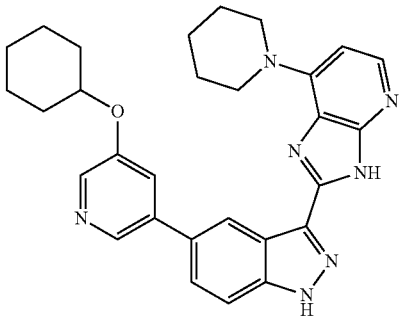
1984	
1985	
1986	
1987	

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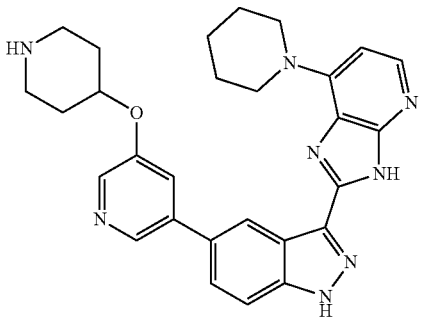
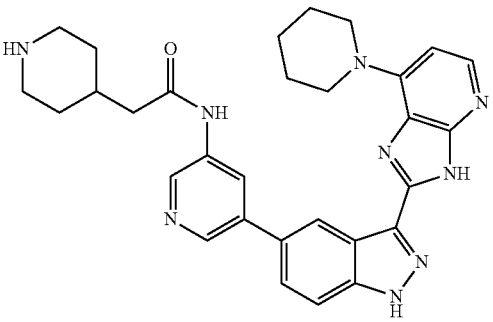
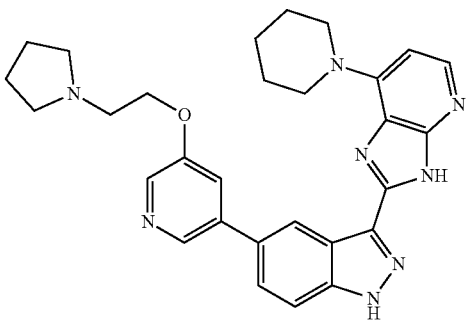
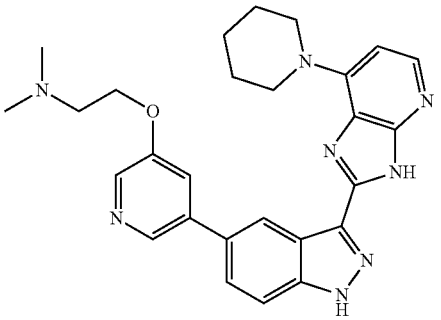
1988	
1989	
1990	
1991	

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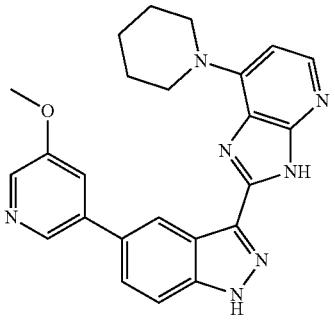
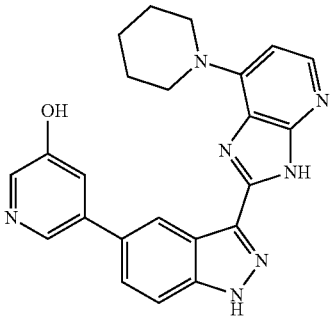
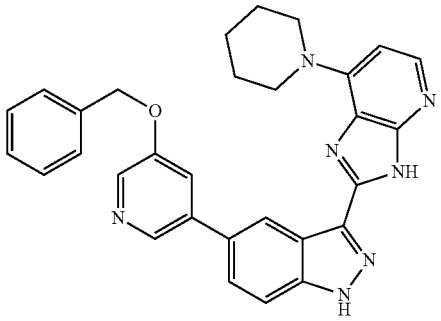
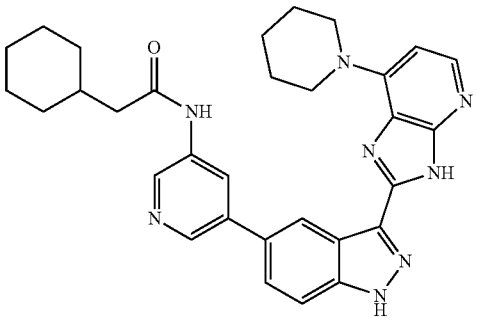
1992	
1993	
1994	
1995	

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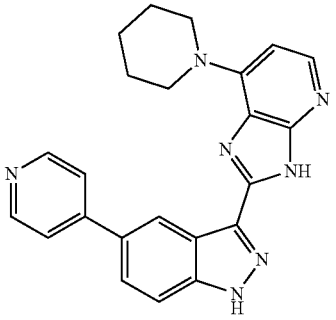
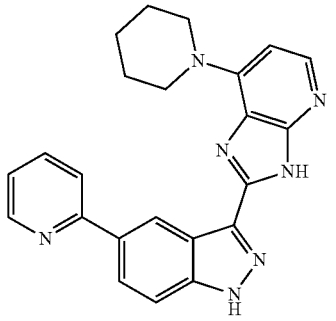
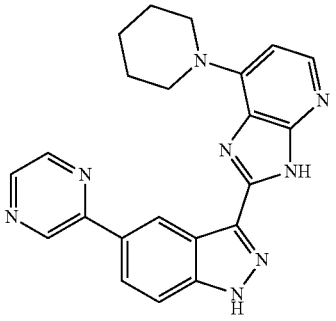
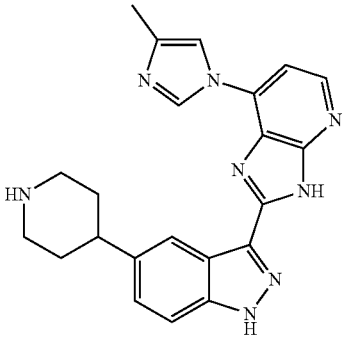
1996	
1997	
1998	
1999	

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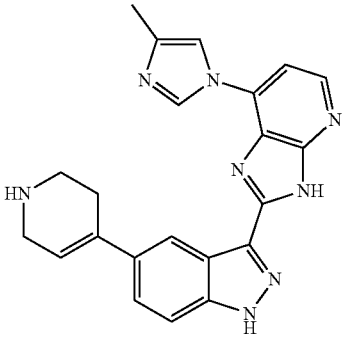
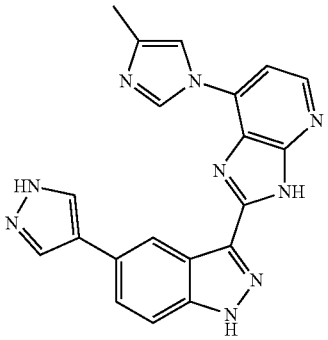
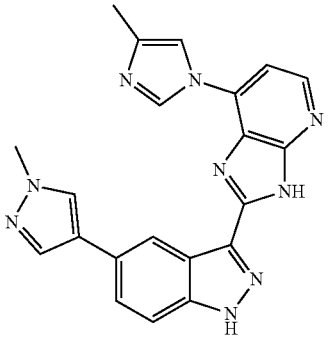
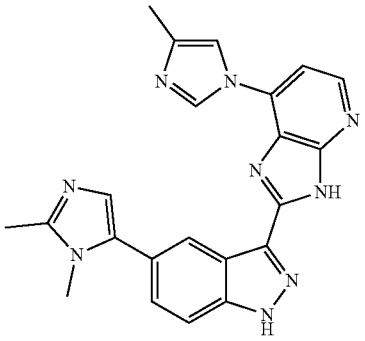
2000	
2001	
2002	
2003	

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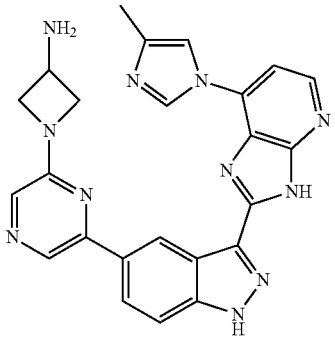
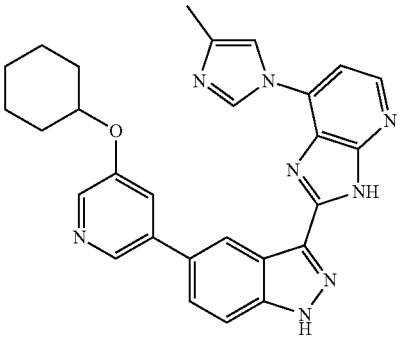
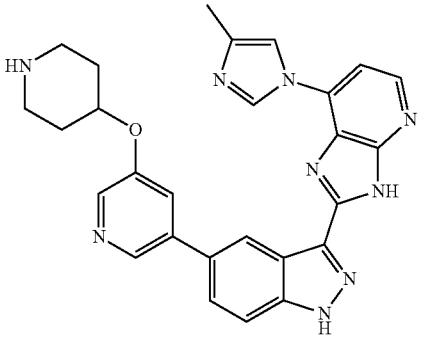
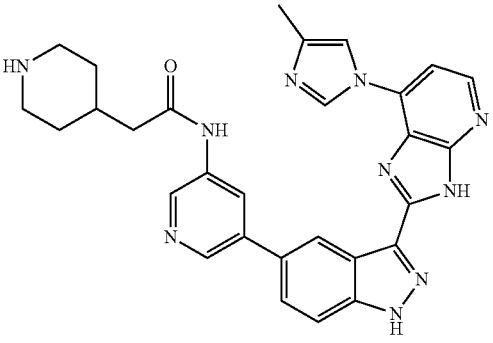
2004	
2005	
2006	
2007	

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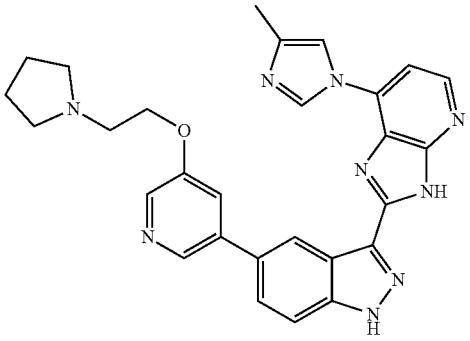
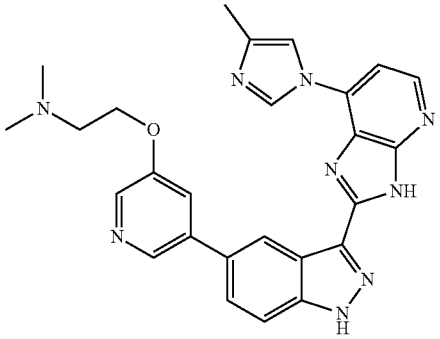
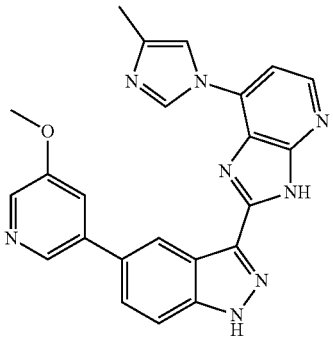
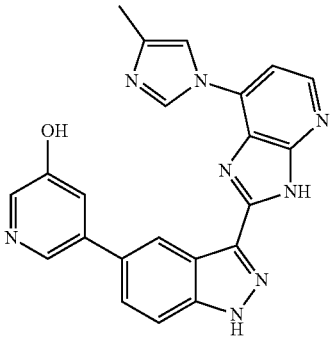
2008	
2009	
2010	
2011	

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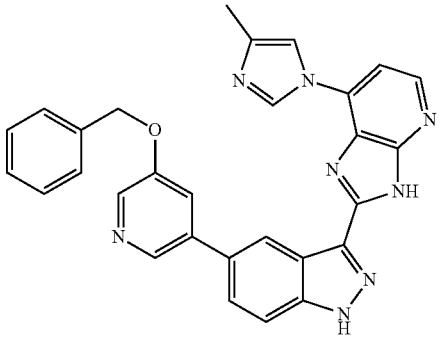
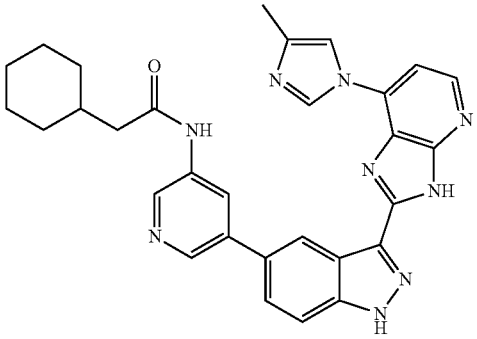
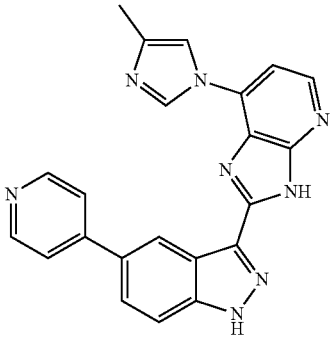
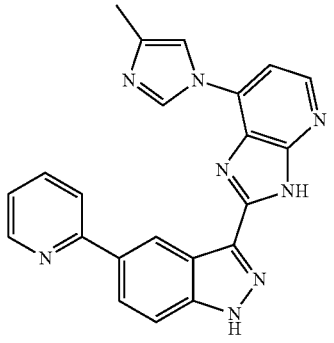
2012	
2013	
2014	
2015	

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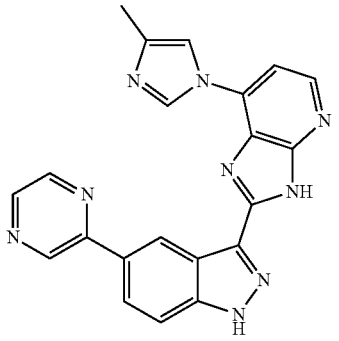
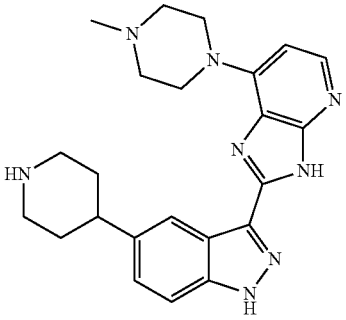
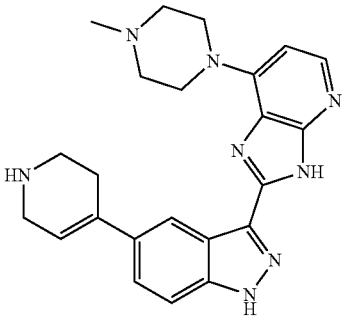
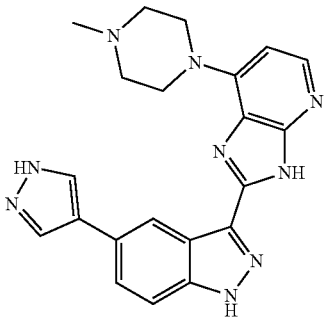
2016	
2017	
2018	
2019	

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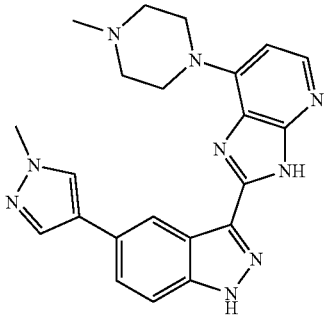
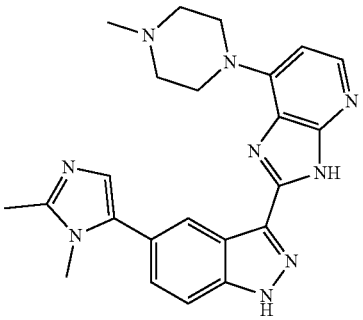
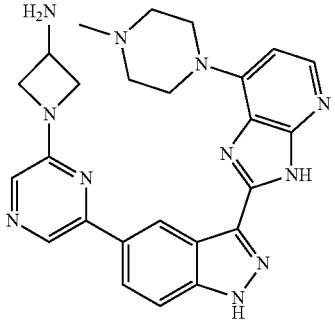
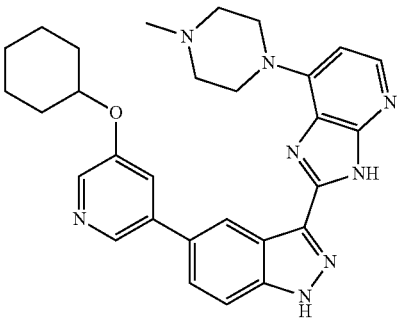
2020	
2021	
2022	
2023	

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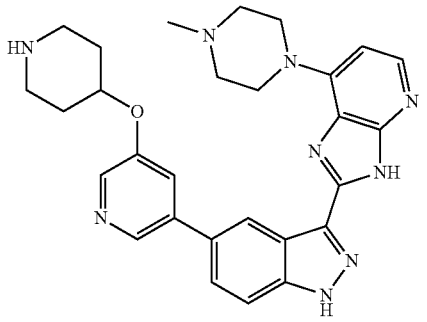
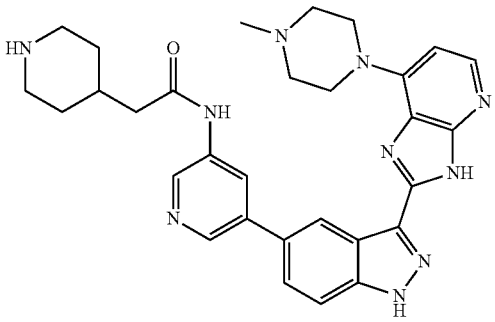
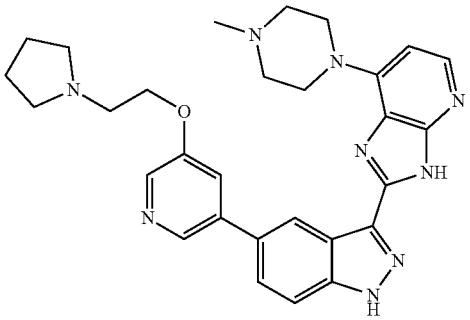
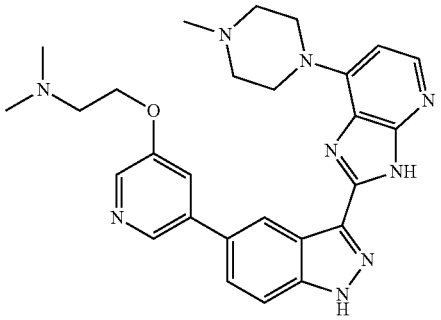
2024	
2025	
2026	
2027	

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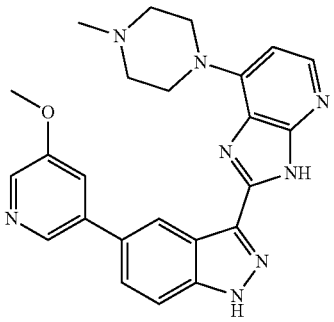
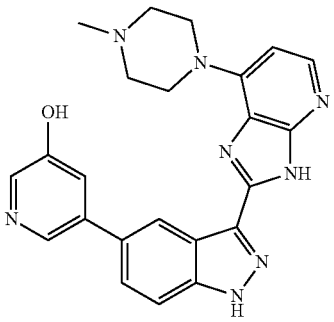
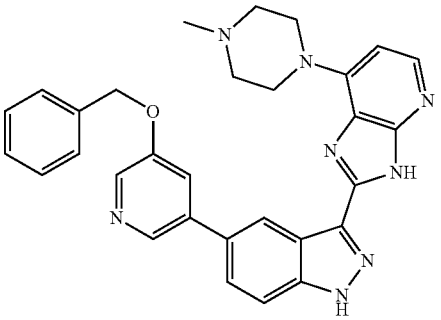
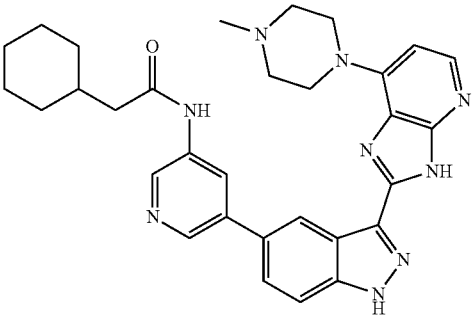
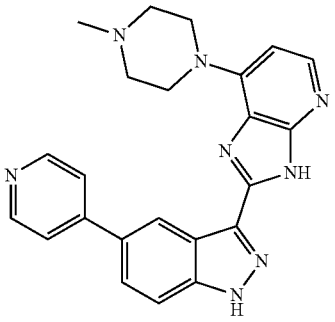
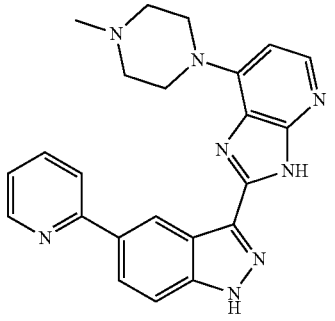
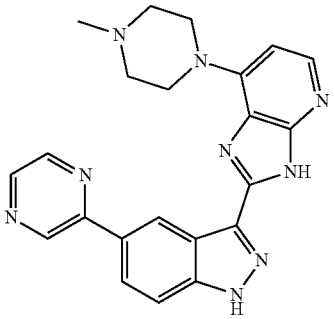
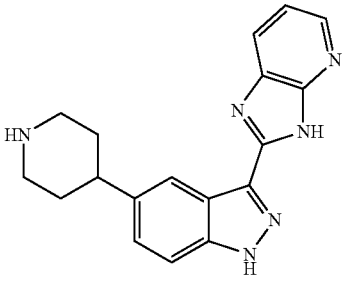
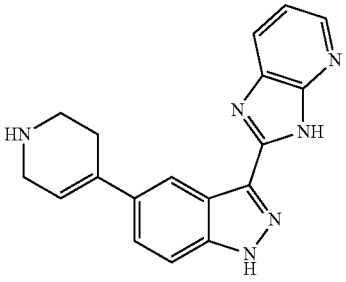
2028	
2029	
2030	
2031	

TABLE 1-continued

2032	
2033	
2034	
2035	
2036	

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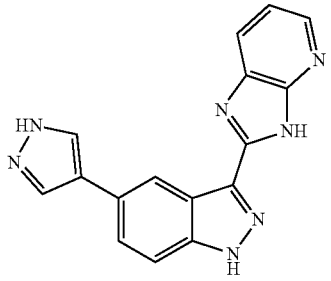
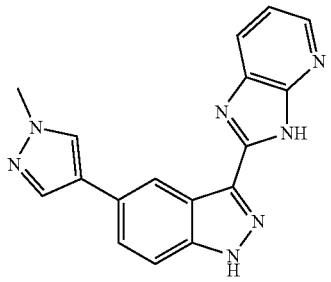
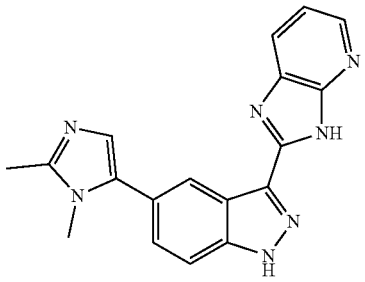
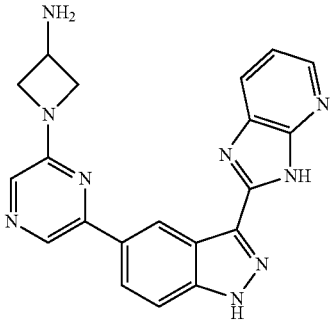
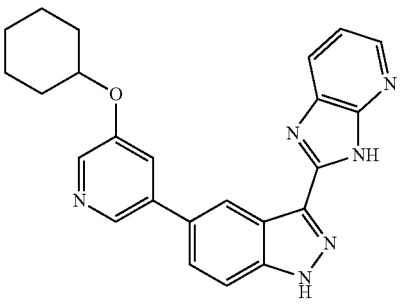
2037	
2038	
2039	
2040	
2041	

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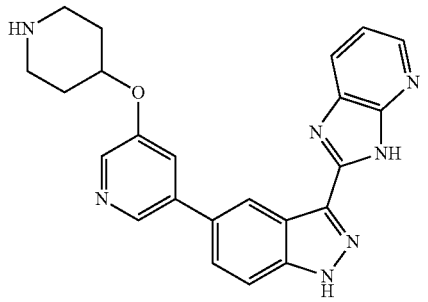
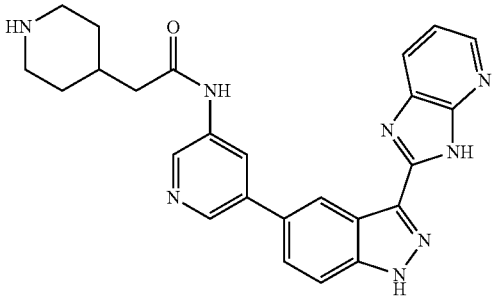
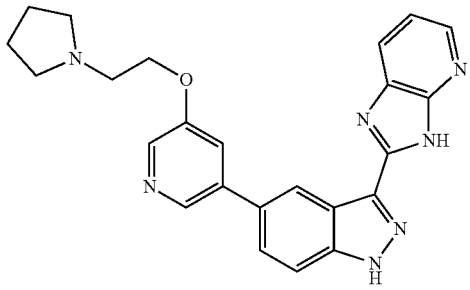
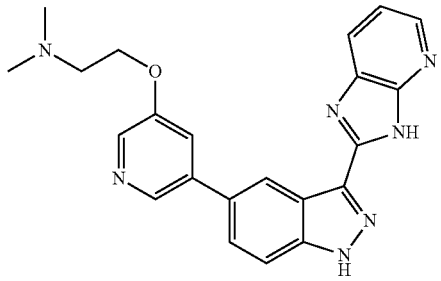
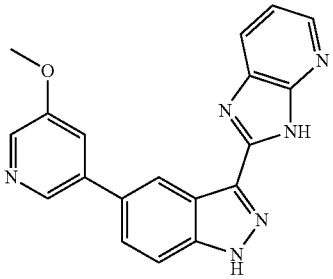
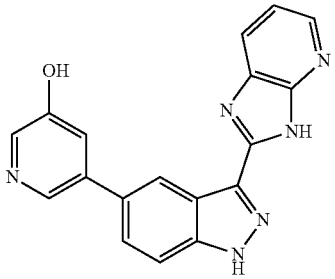
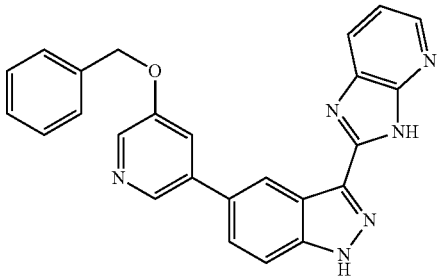
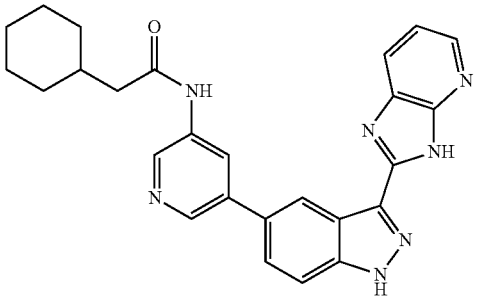
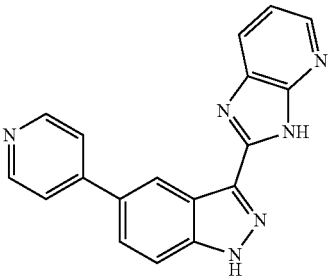
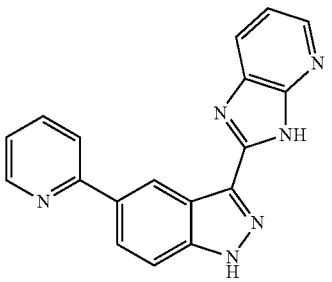
2042	
2043	
2044	
2045	
2046	

TABLE 1-continued

2047	
2048	
2049	
2050	
2051	

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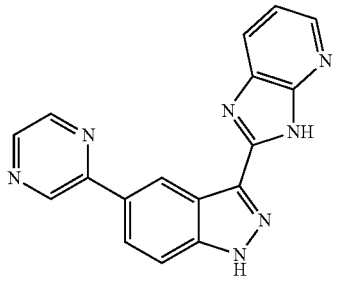
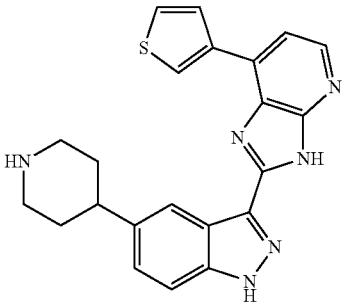
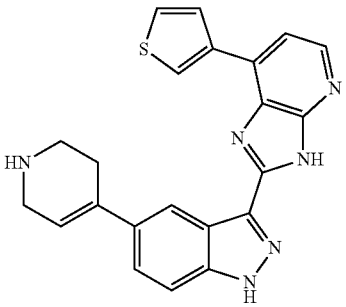
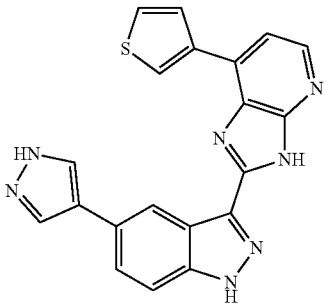
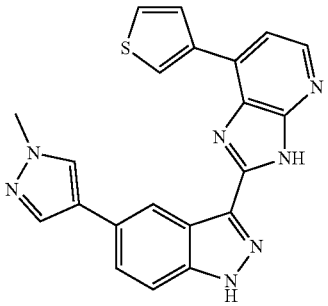
2052	
2053	
2054	
2055	
2056	

TABLE 1-continued

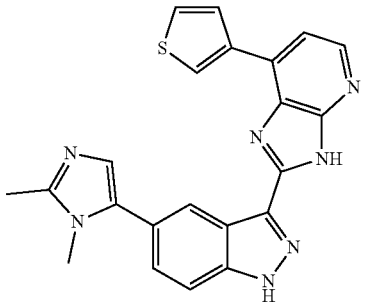
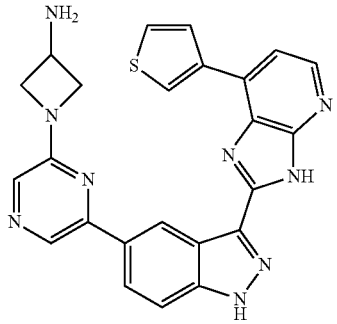
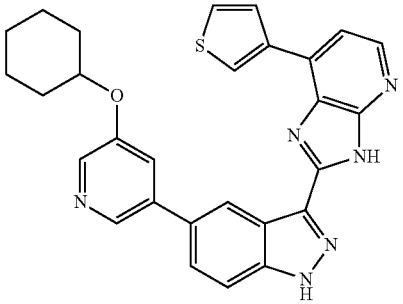
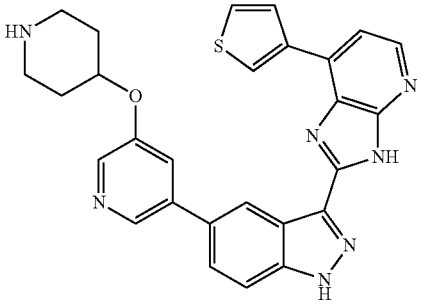
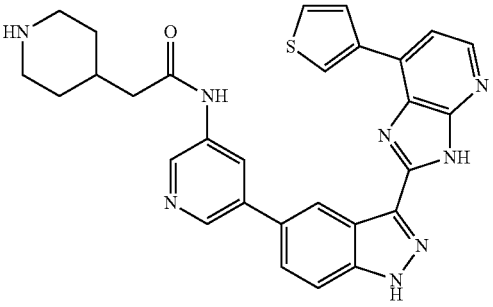
2057	
2058	
2059	
2060	
2061	

TABLE 1-continued

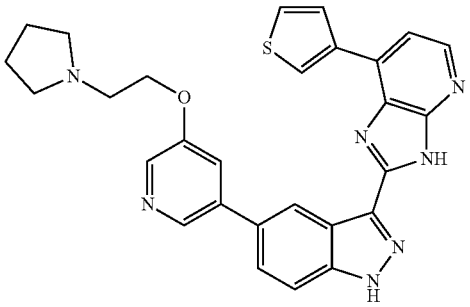
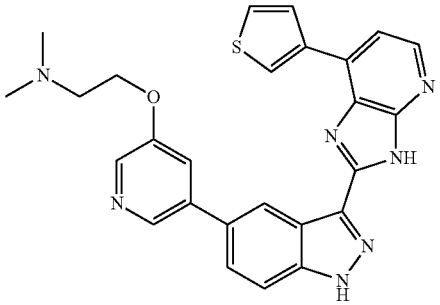
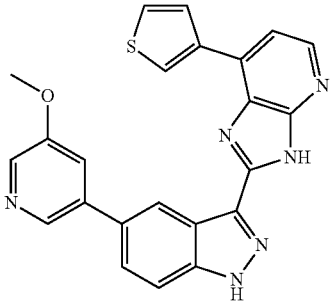
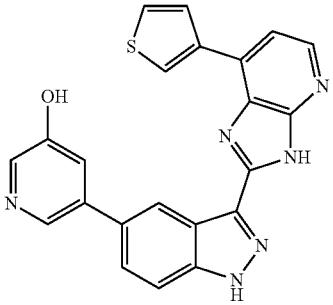
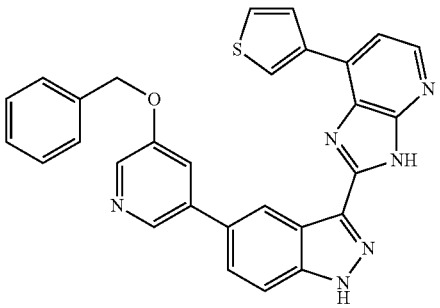
2062	
2063	
2064	
2065	
2066	

TABLE 1-continued

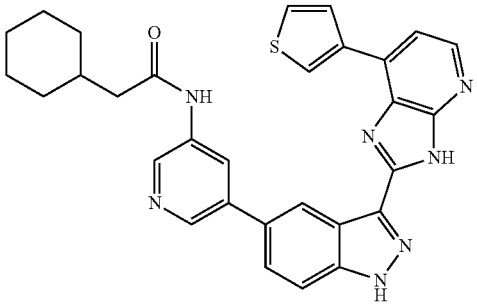
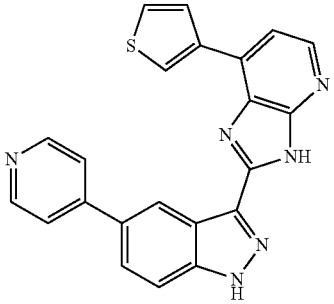
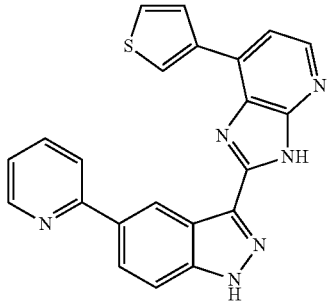
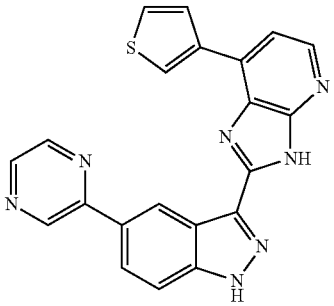
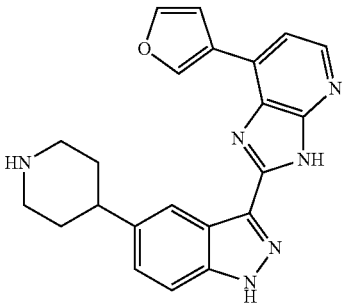
2067	
2068	
2069	
2070	
2071	

TABLE 1-continued

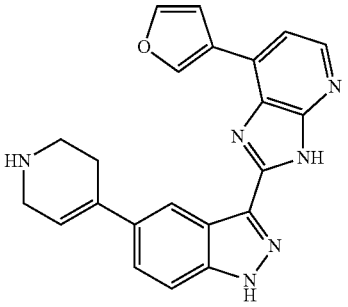
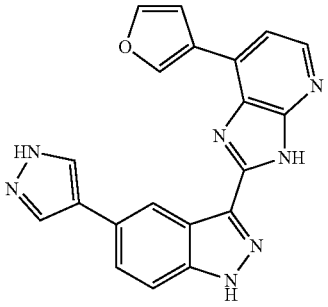
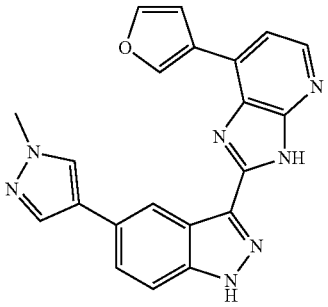
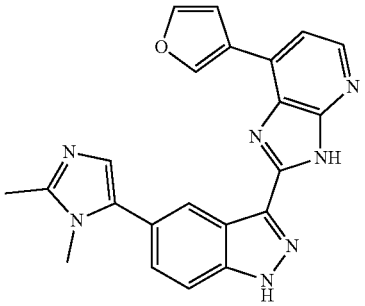
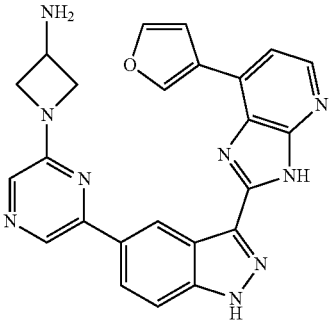
2072	
2073	
2074	
2075	
2076	

TABLE 1-continued

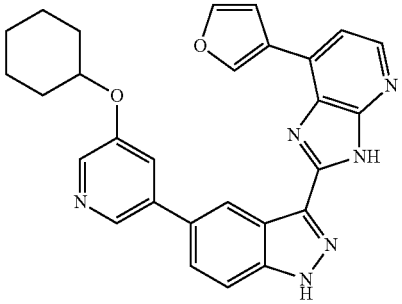
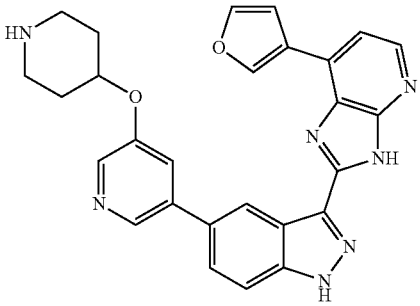
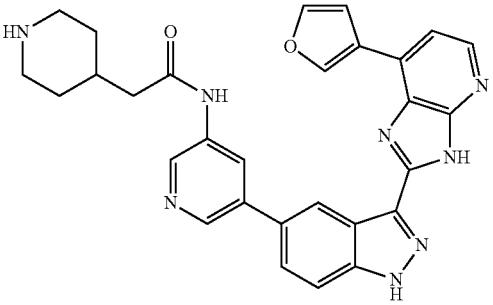
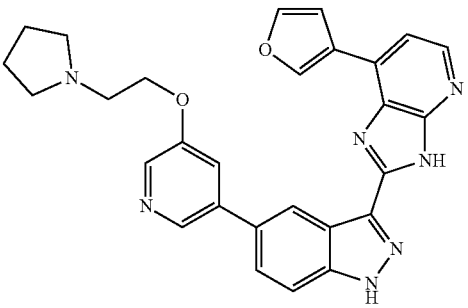
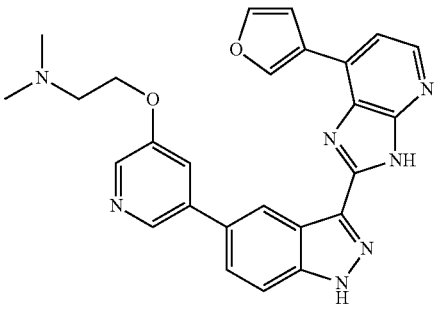
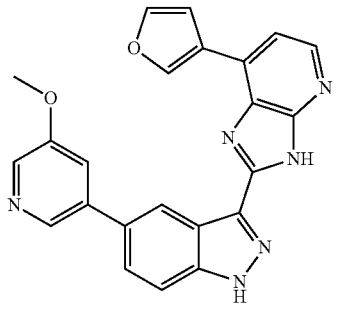
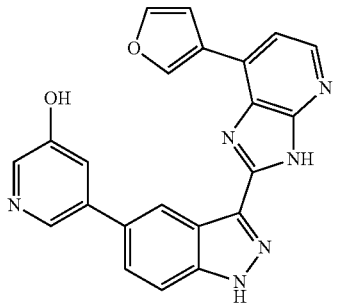
2077	
2078	
2079	
2080	
2081	

TABLE 1-continued

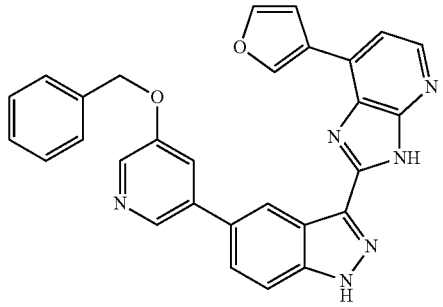
2082



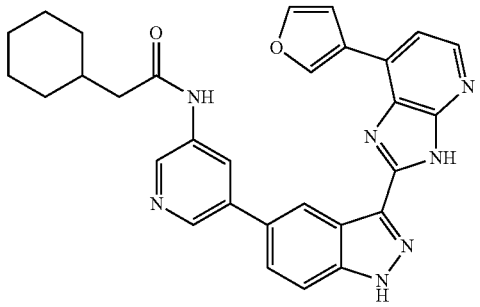
2083



2084



2085



2086

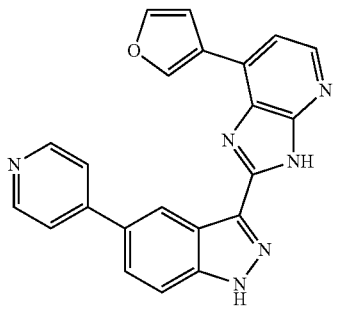
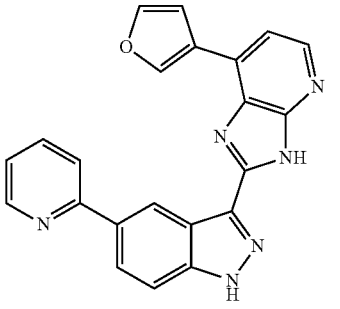


TABLE 1-continued

2087



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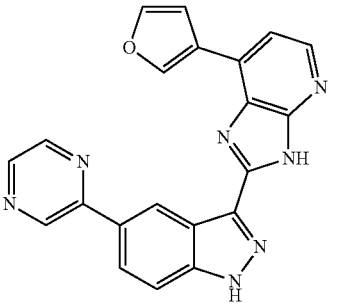
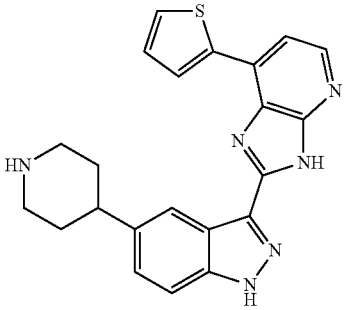
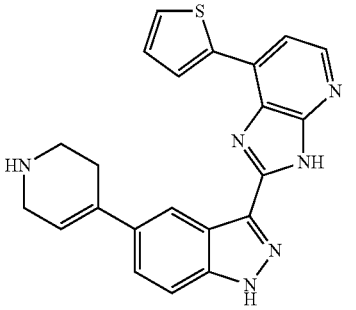


2089



2090



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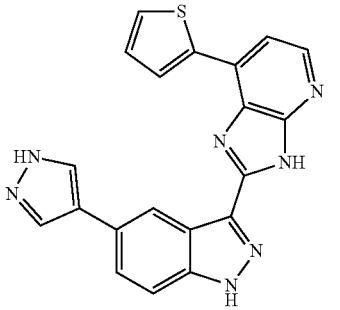


TABLE 1-continued

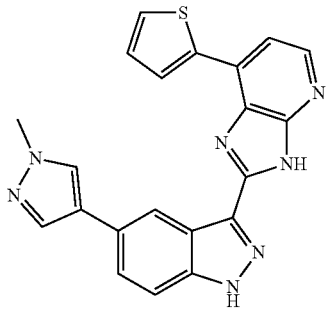
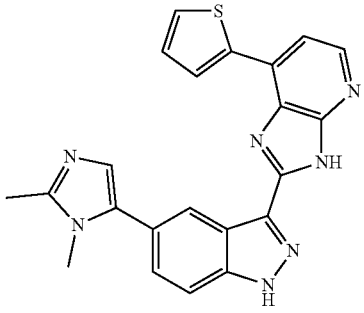
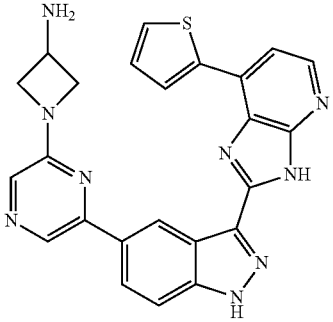
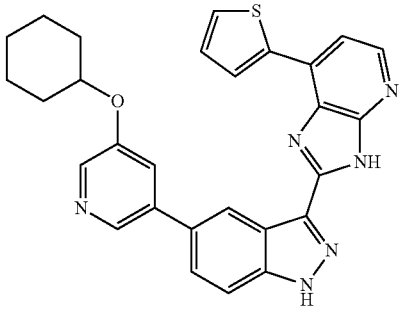
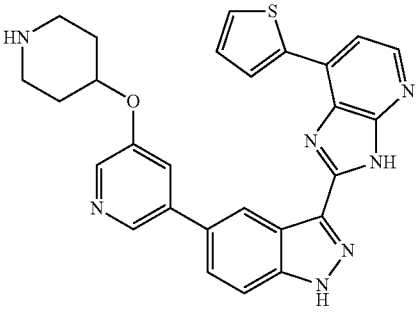
2092	
2093	
2094	
2095	
2096	

TABLE 1-continued

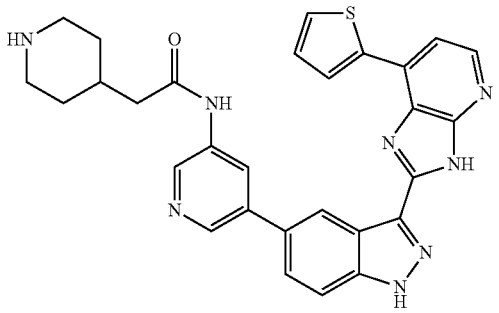
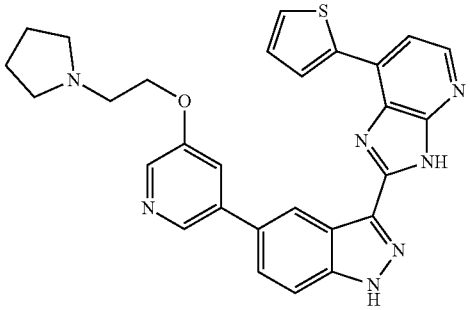
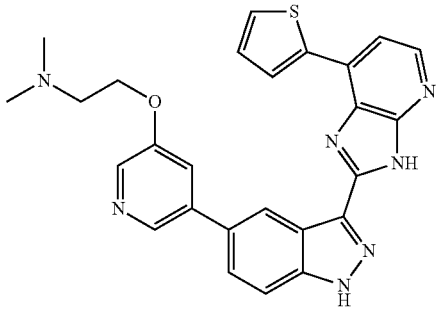
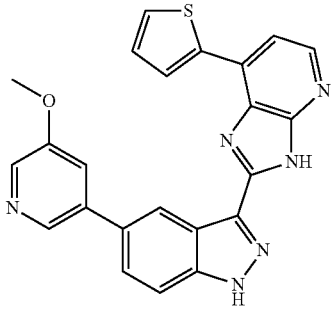
2097	
2098	
2099	
2100	

TABLE 1-continued

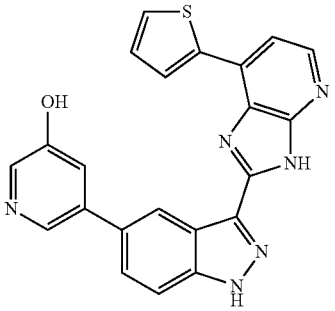
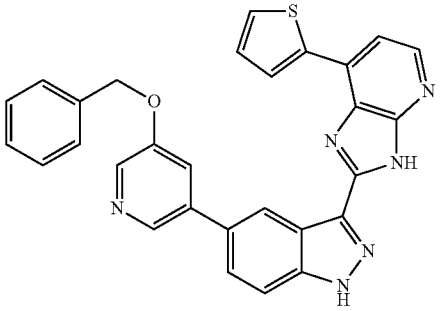
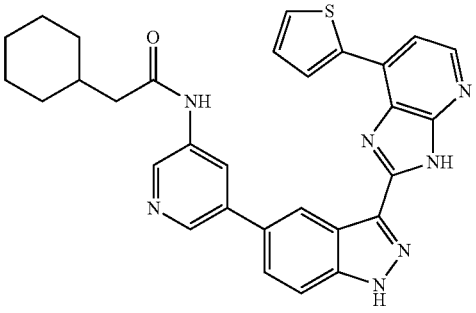
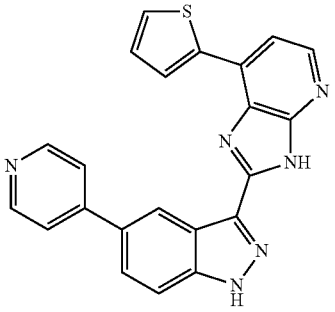
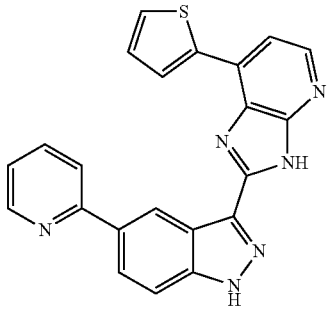
2101	
2102	
2103	
2104	
2105	

TABLE 1-continued

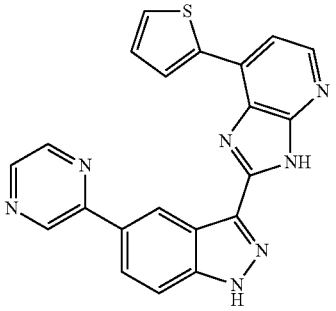
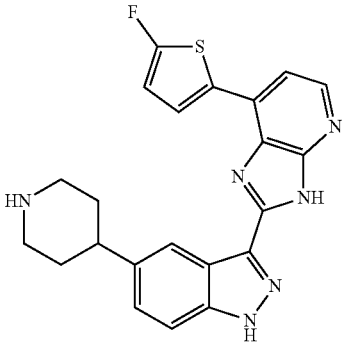
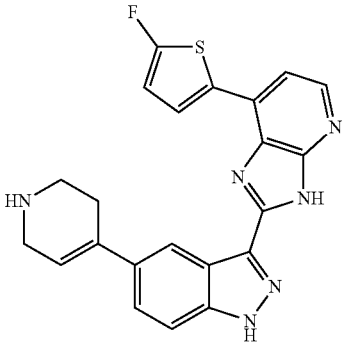
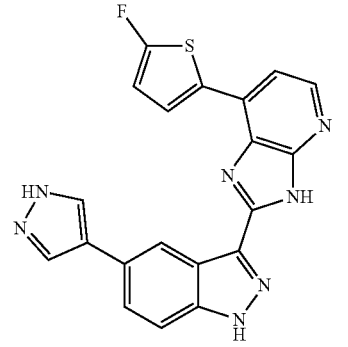
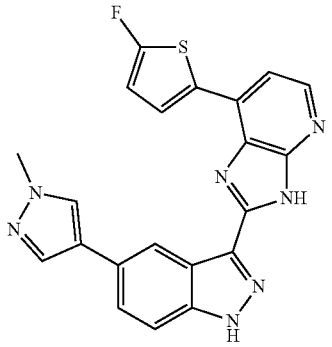
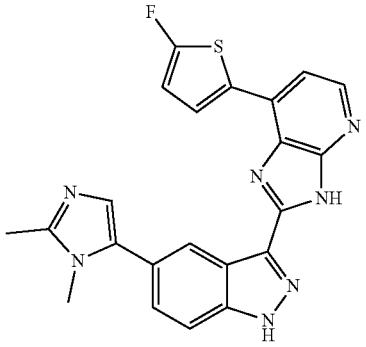
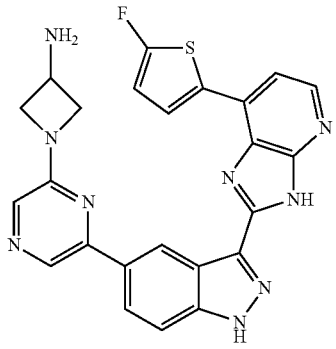
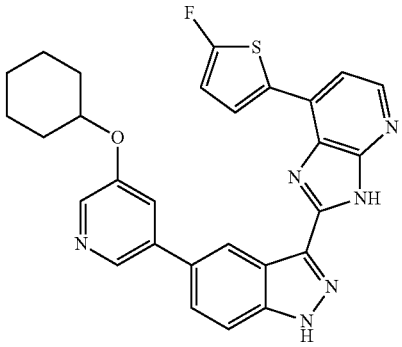
2106	
2107	
2108	
2109	

TABLE 1-continued

2110	
2111	
2112	
2113	

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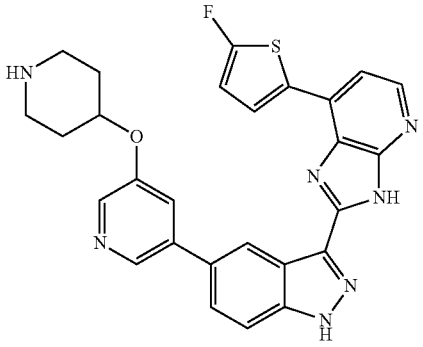
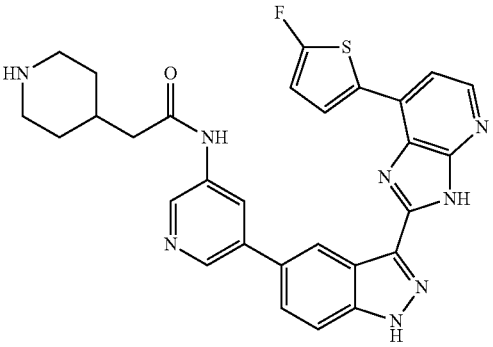
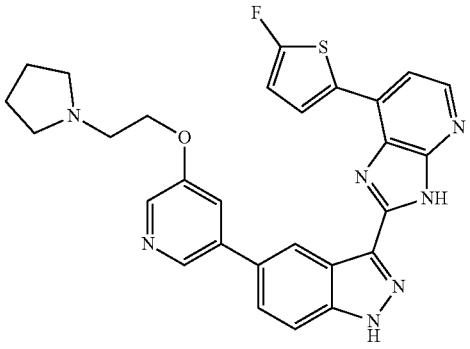
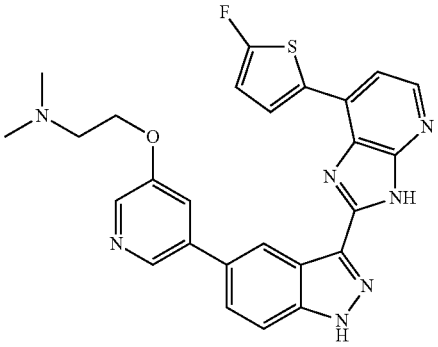
2114	
2115	
2116	
2117	

TABLE 1-continued

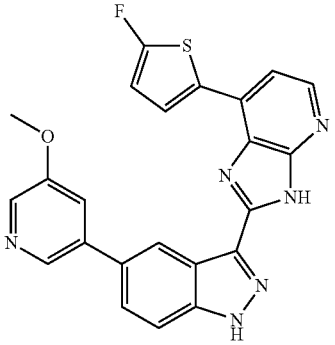
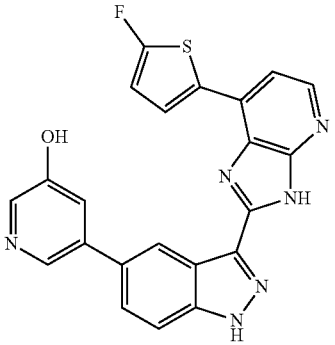
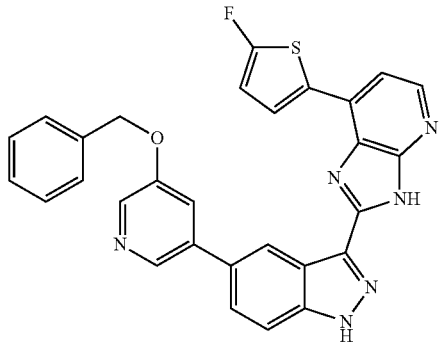
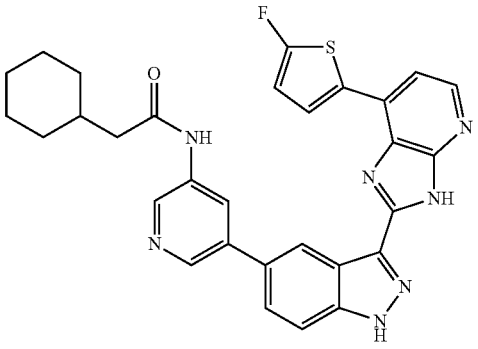
2118	
2119	
2120	
2121	

TABLE 1-continued

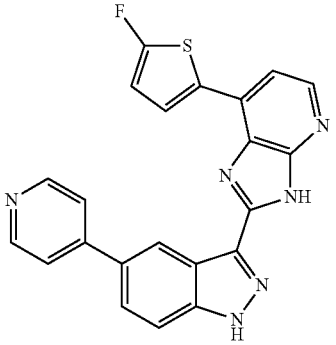
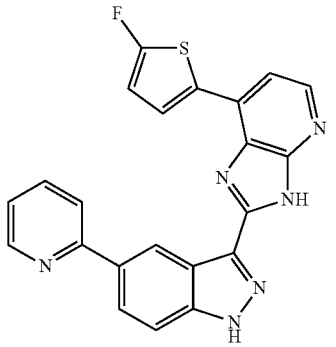
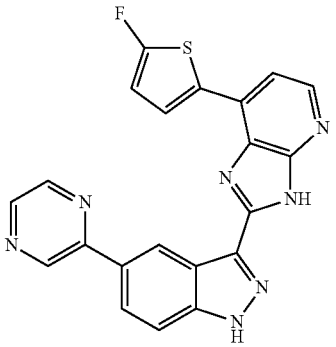
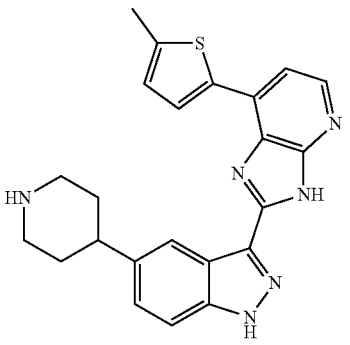
2122	
2123	
2124	
2125	

TABLE 1-continued

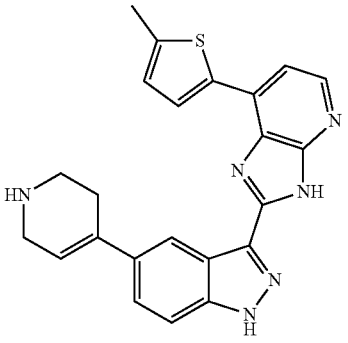
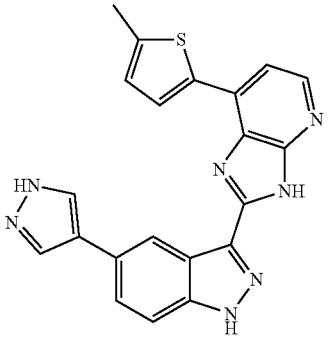
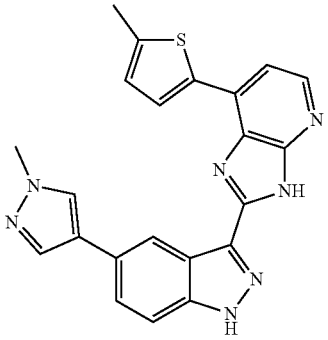
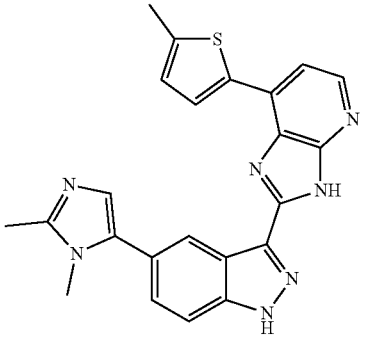
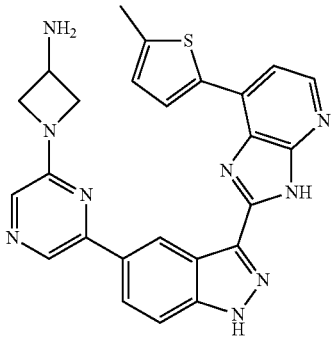
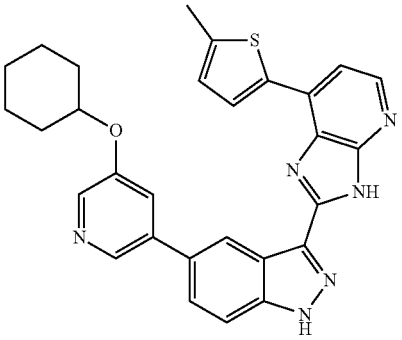
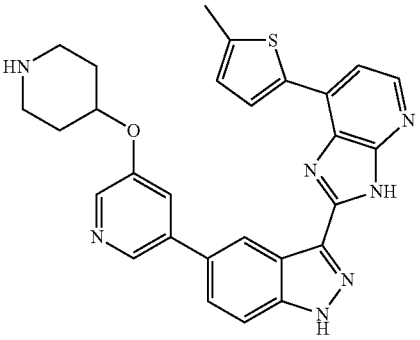
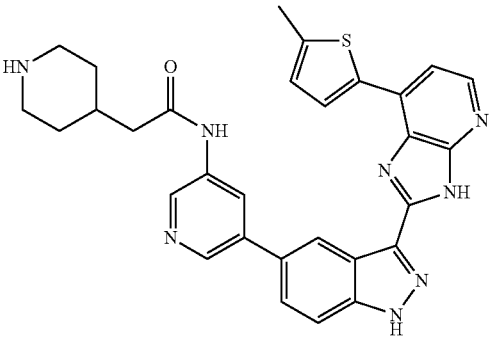
2126	
2127	
2128	
2129	

TABLE 1-continued

2130	
2131	
2132	
2133	

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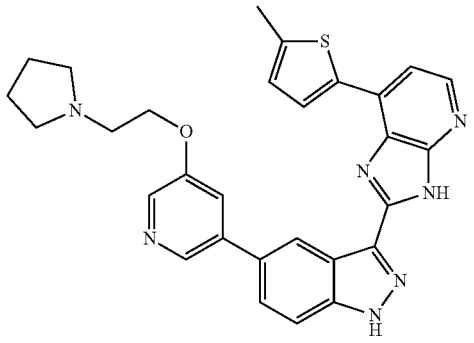
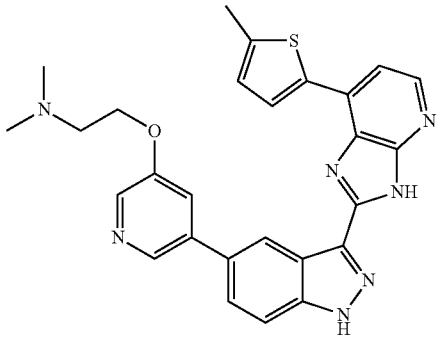
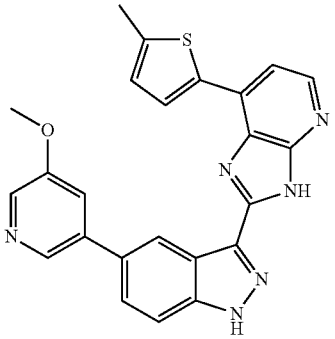
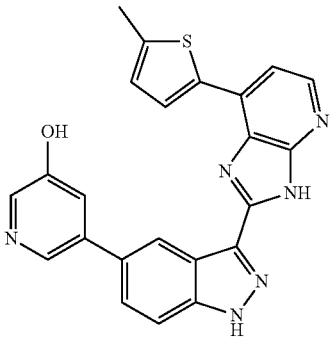
2134	
2135	
2136	
2137	

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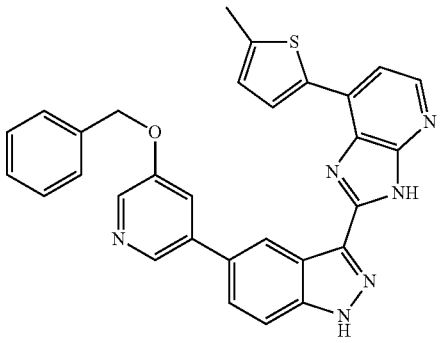
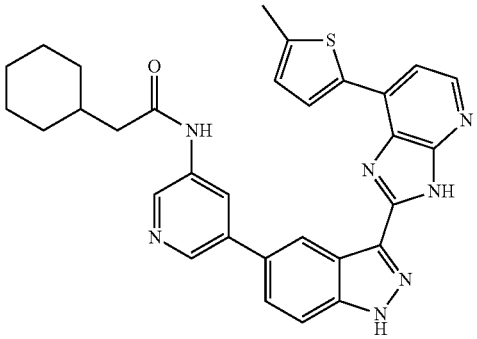
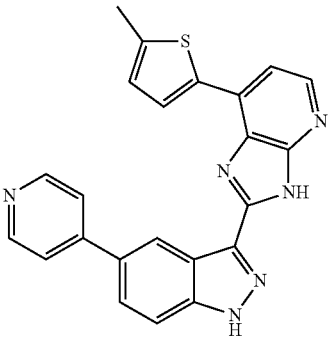
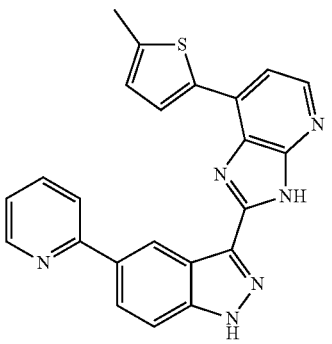
2138	
2139	
2140	
2141	

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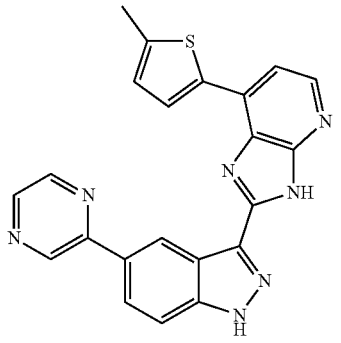
2142



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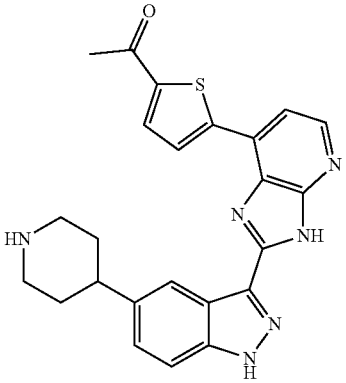
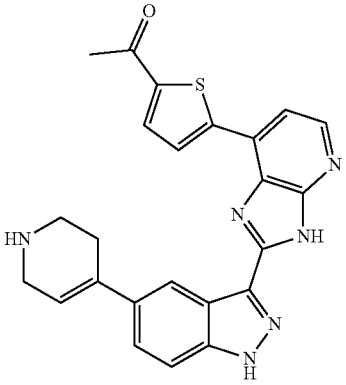


2144



2145

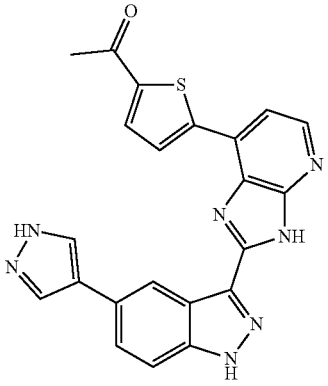
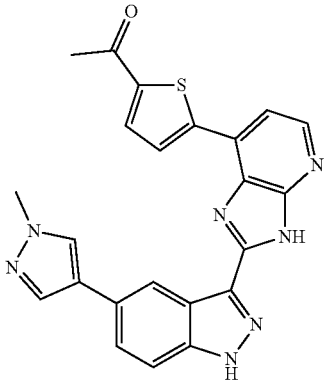
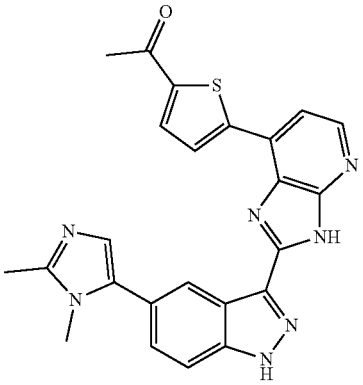


TABLE 1-continued

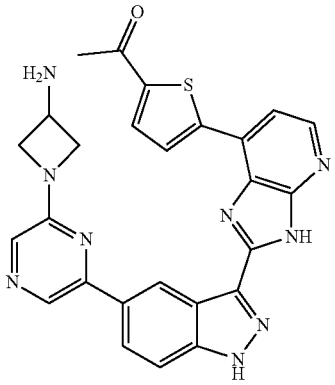
2146



2147



2148



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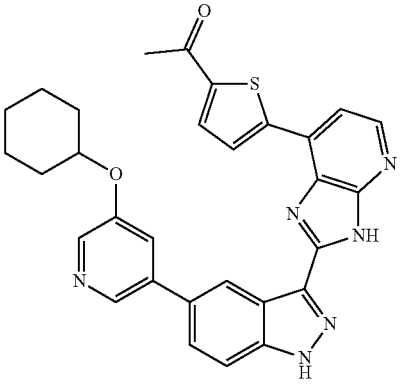
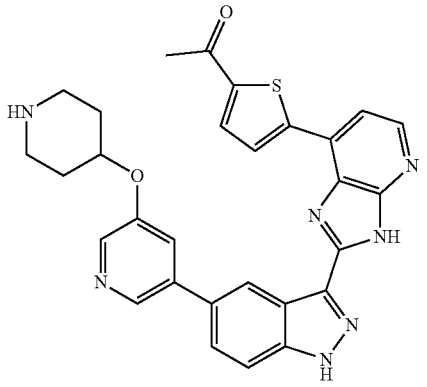


TABLE 1-continued

2150



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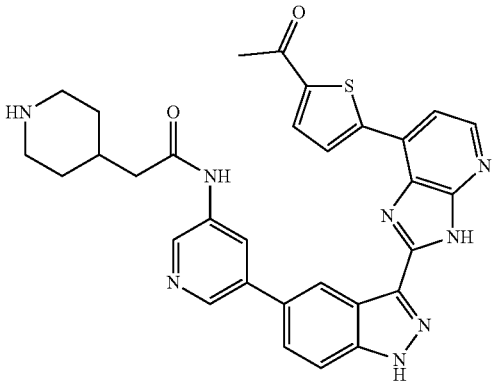
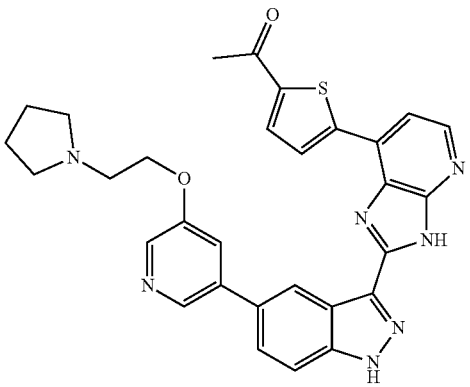


2152



2153

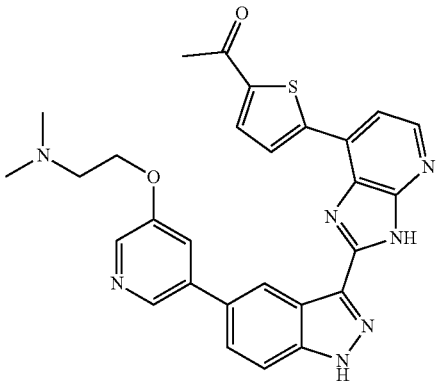
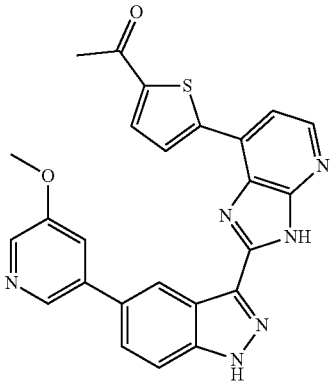
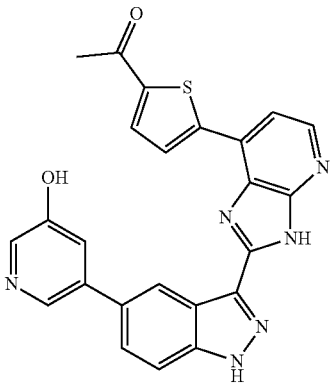


TABLE 1-continued

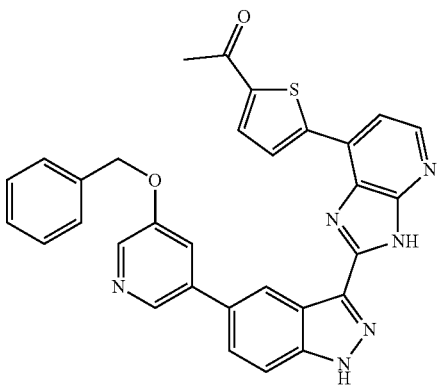
2154



2155



2156



2157

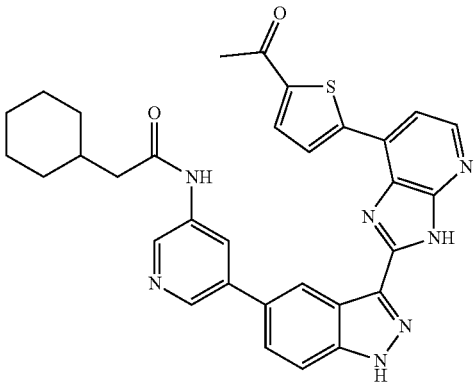


TABLE 1-continued

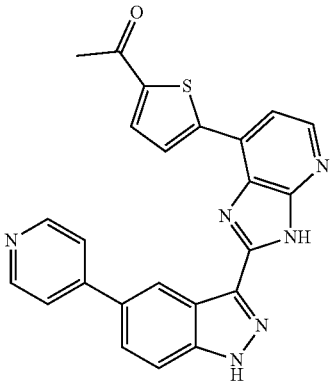
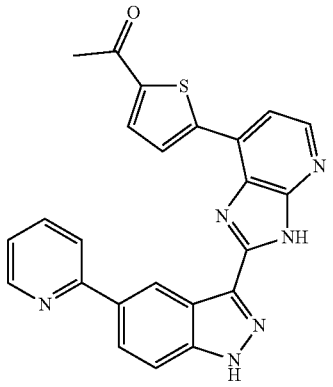
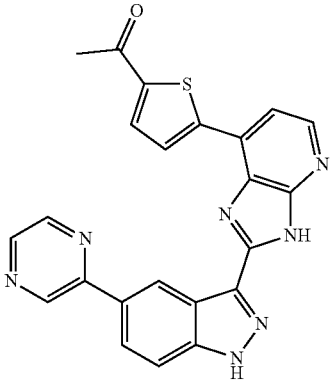
2158	
2159	
2160	

TABLE 1-continued

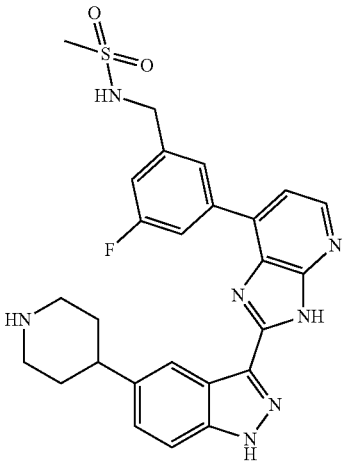
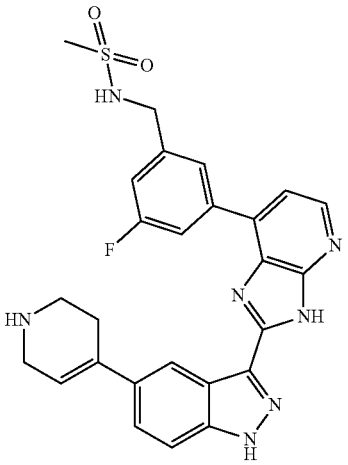
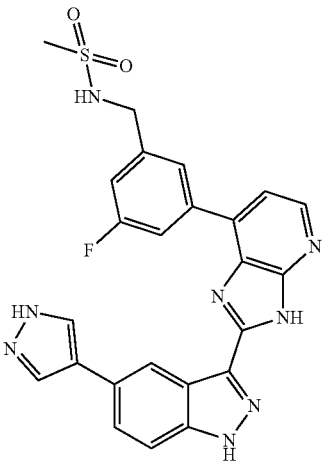
2161	
2162	
2163	

TABLE 1-continued

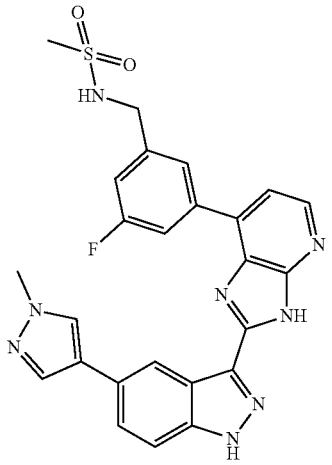
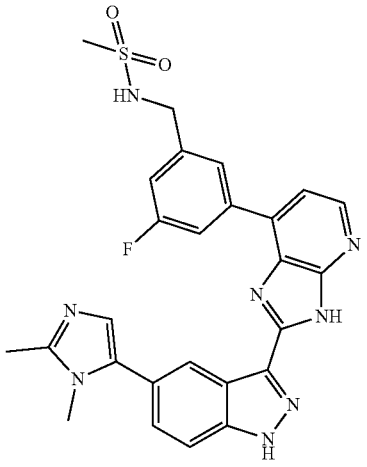
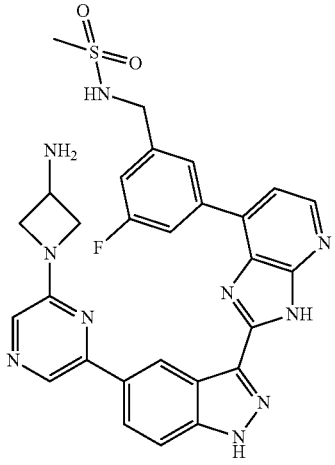
2164	
2165	
2166	

TABLE 1-continued

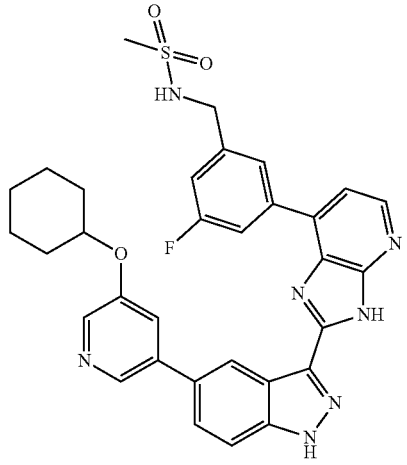
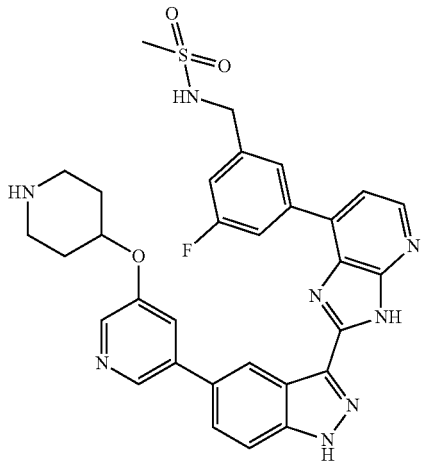
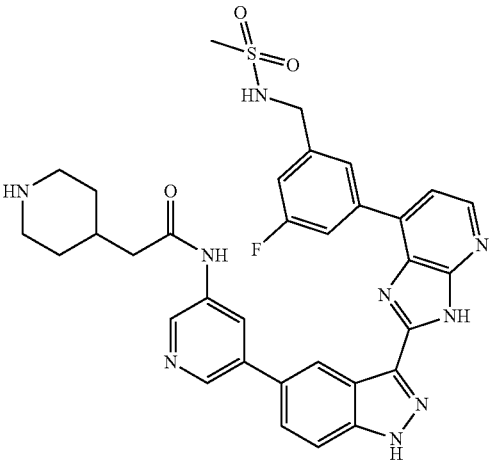
2167	
2168	
2169	

TABLE 1-continued

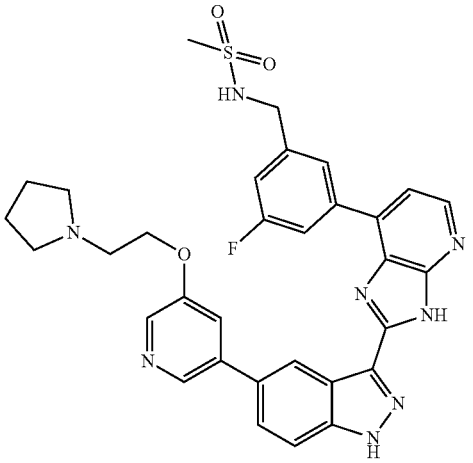
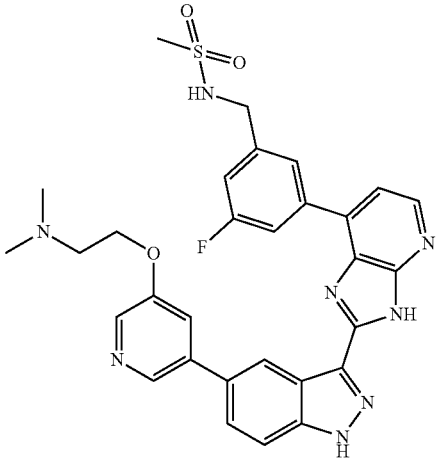
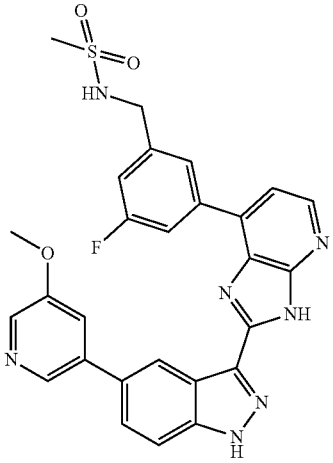
2170	
2171	
2172	

TABLE 1-continued

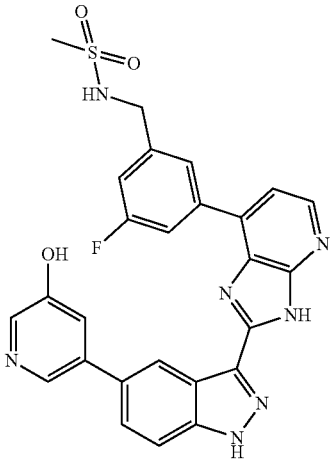
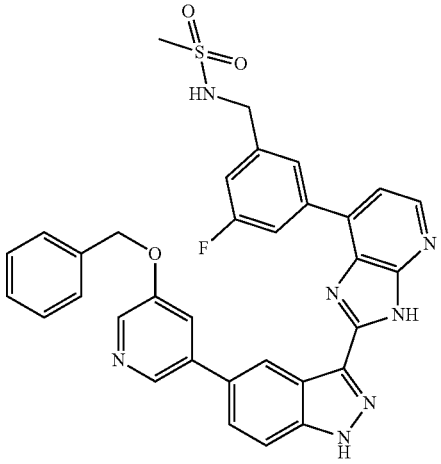
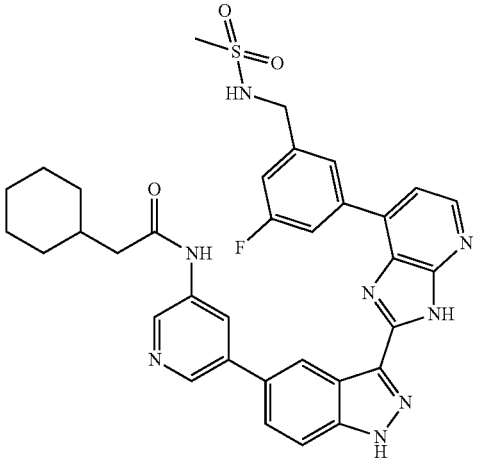
2173	
2174	
2175	

TABLE 1-continued

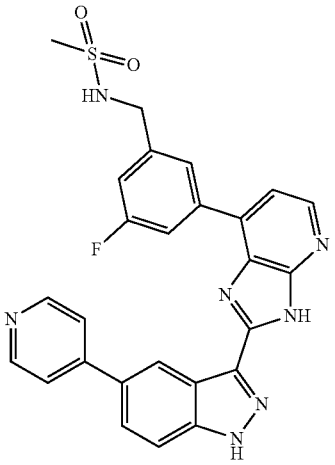
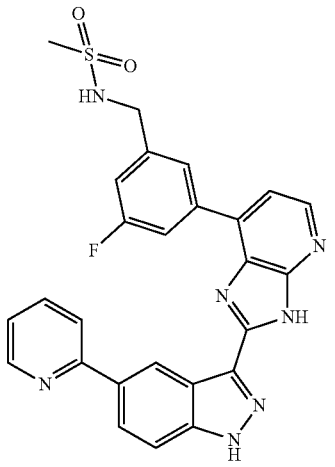
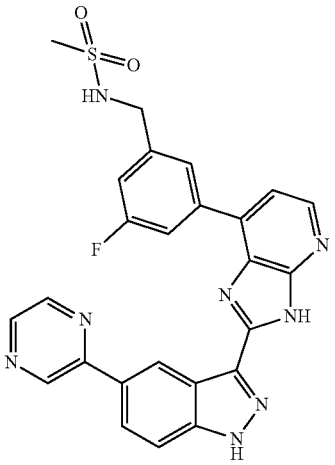
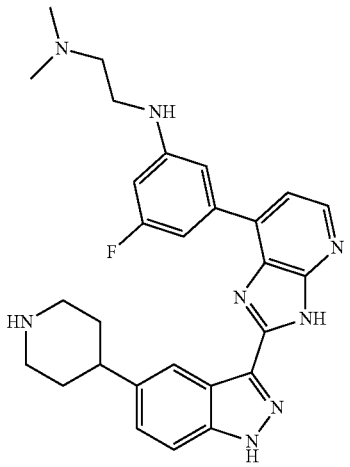
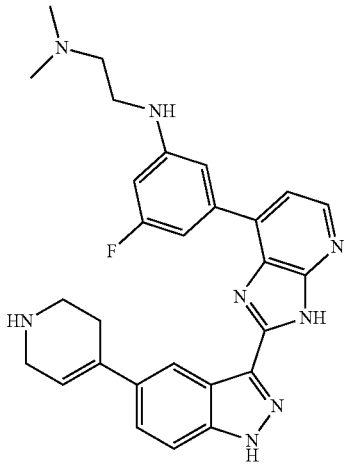
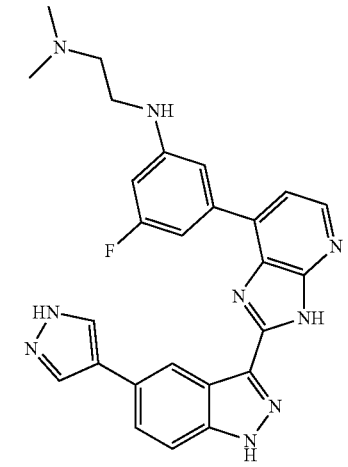
2176	
2177	
2178	

TABLE 1-continued

2179	
2180	
2181	

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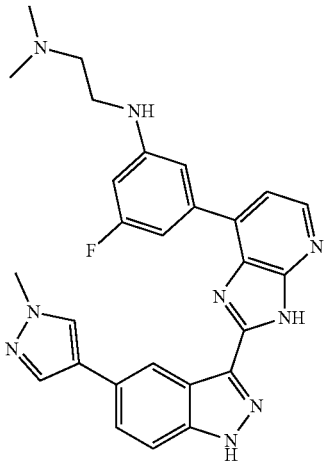
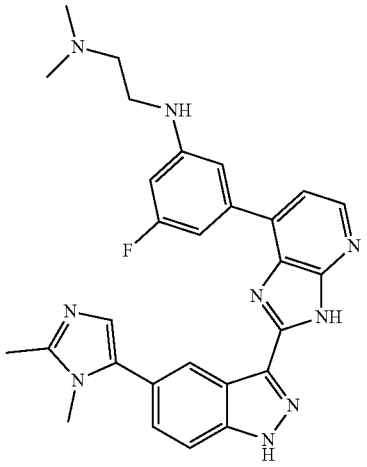
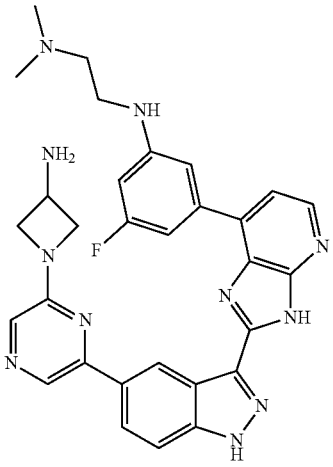
2182	
2183	
2184	

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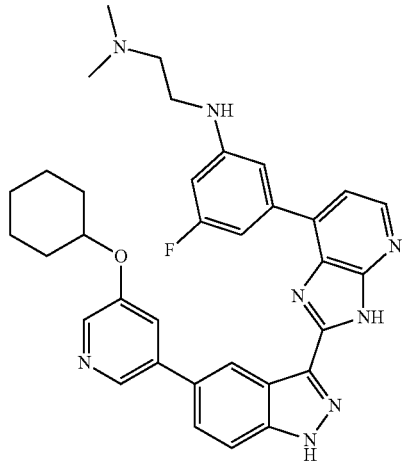
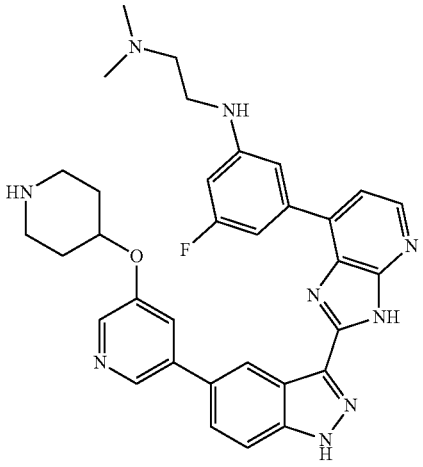
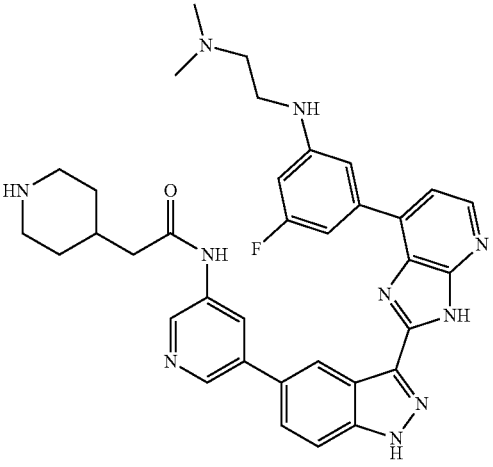
2185	
2186	
2187	

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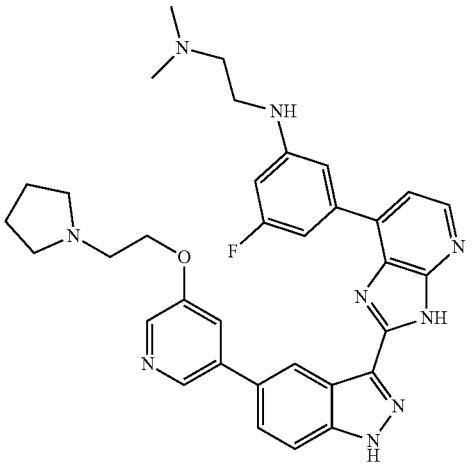
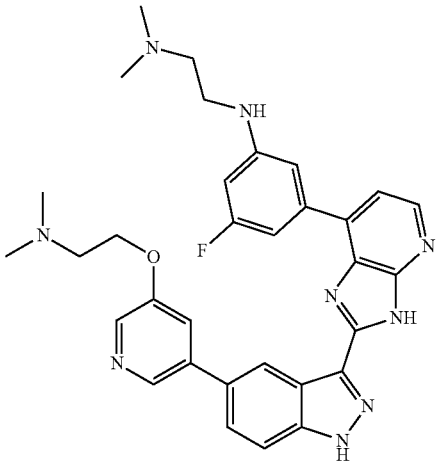
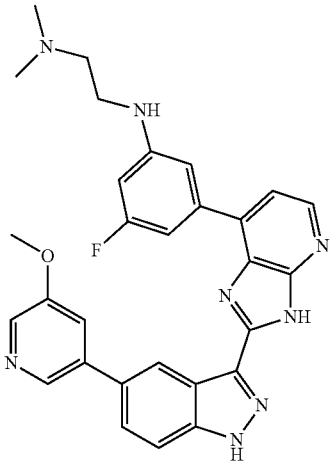
2188	
2189	
2190	

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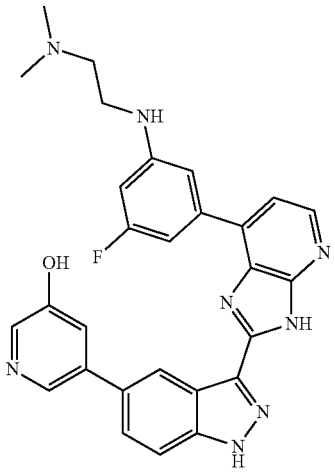
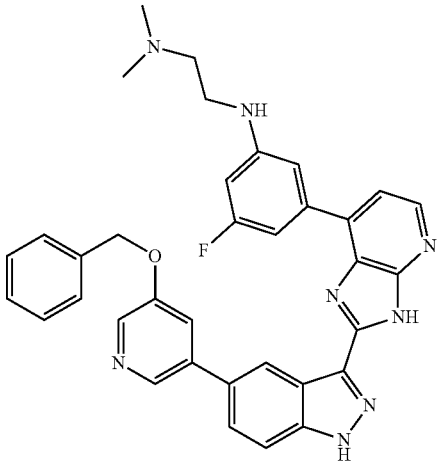
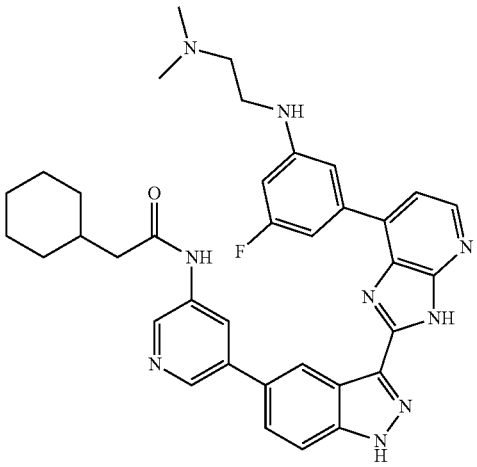
2191	
2192	
2193	

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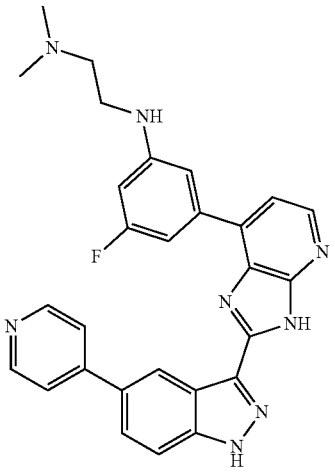
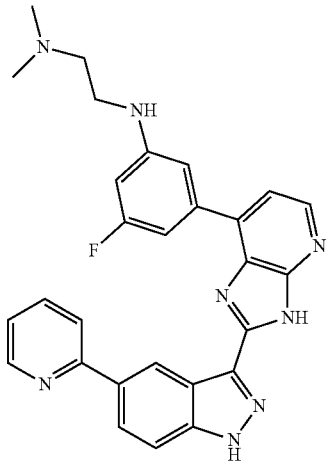
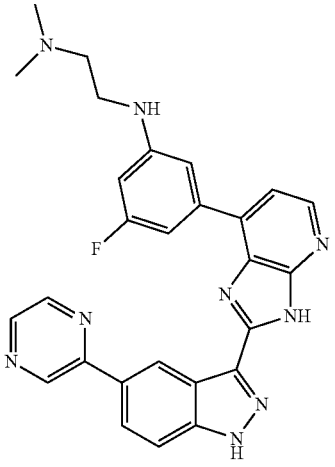
2194	
2195	
2196	

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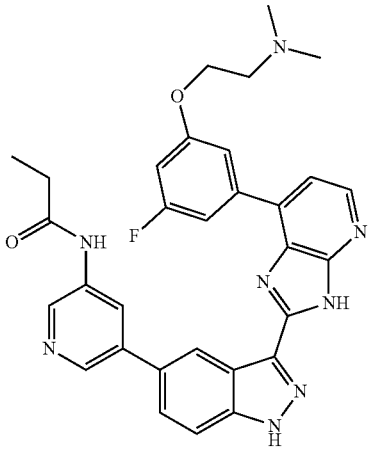
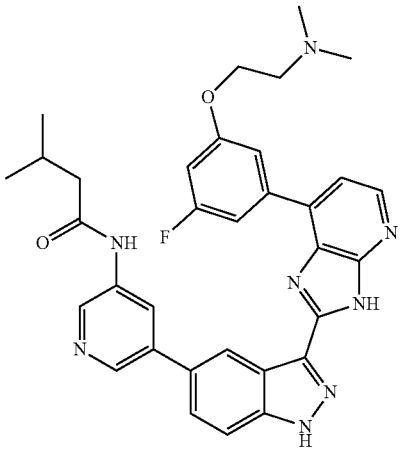
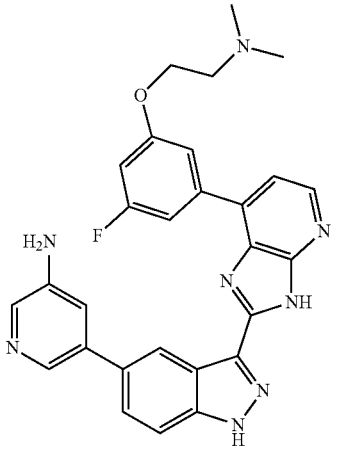
2197	
2198	
2199	

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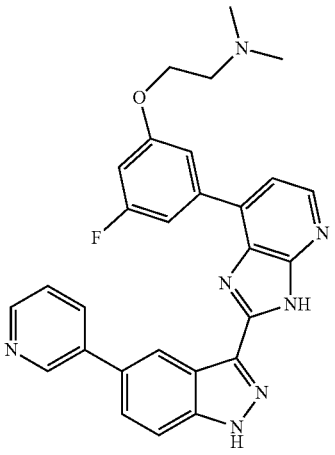
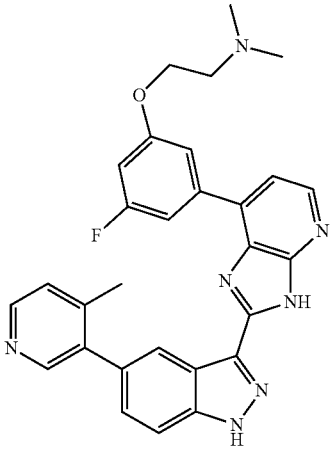
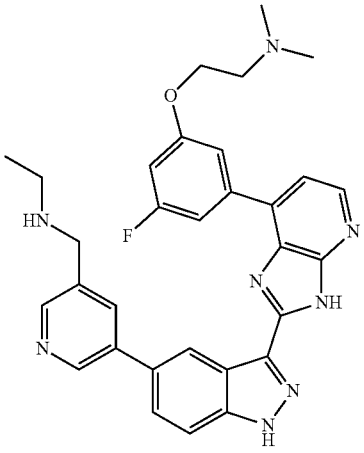
2200	
2201	
2202	

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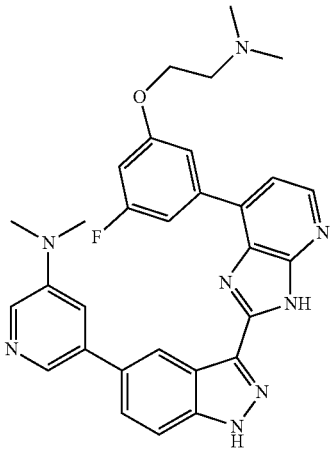
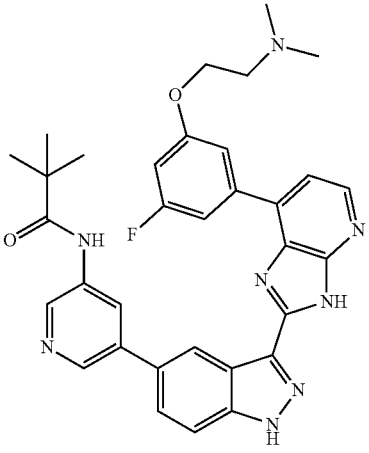
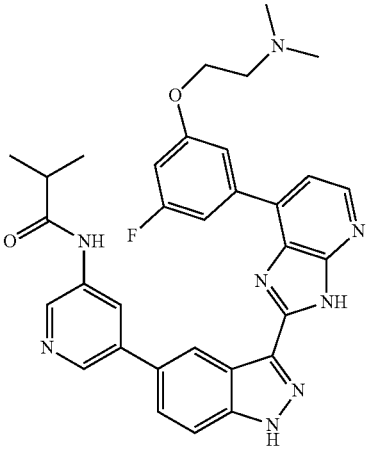
2203	
2204	
2205	

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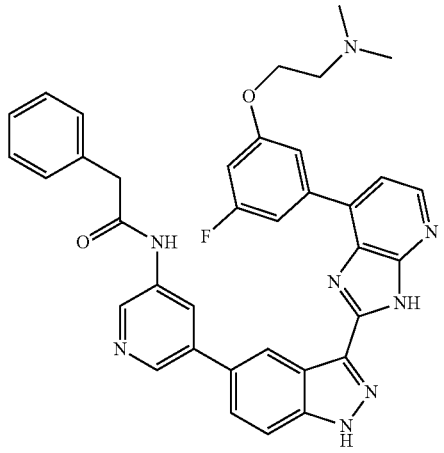
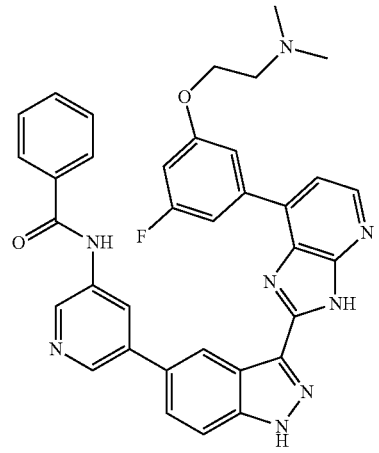
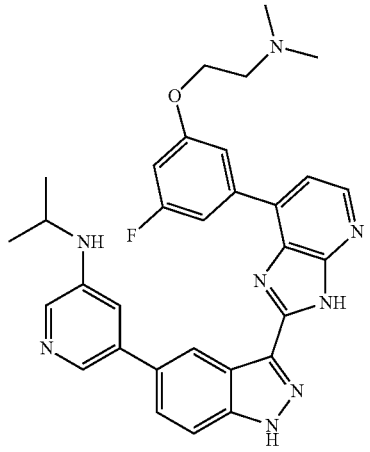
2206	
2207	
2208	

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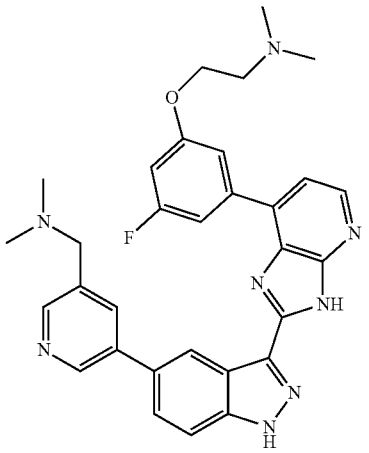
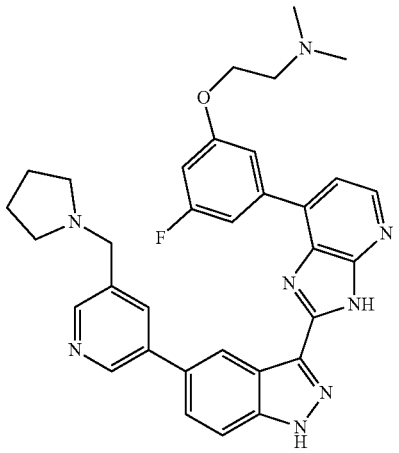
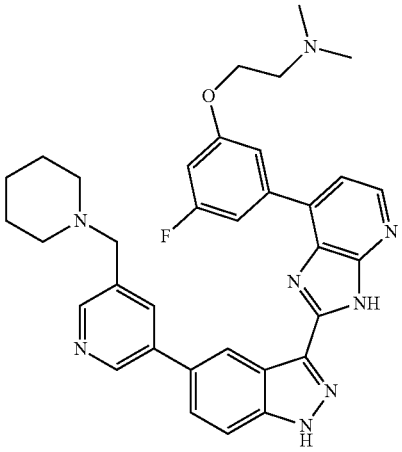
2209	
2210	
2211	

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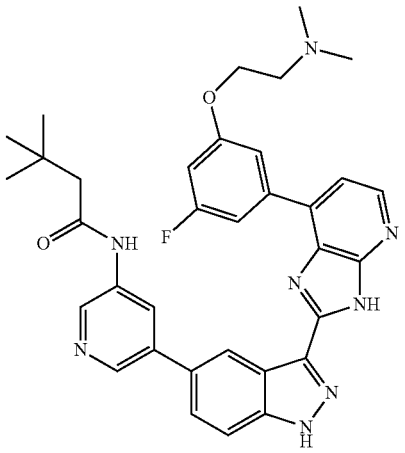

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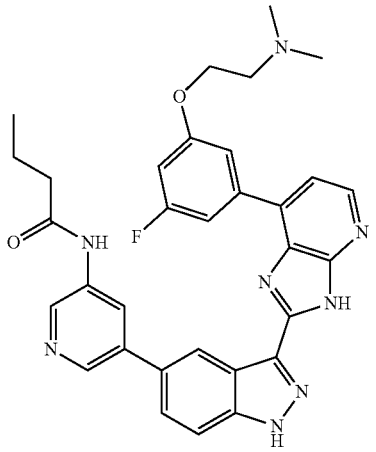

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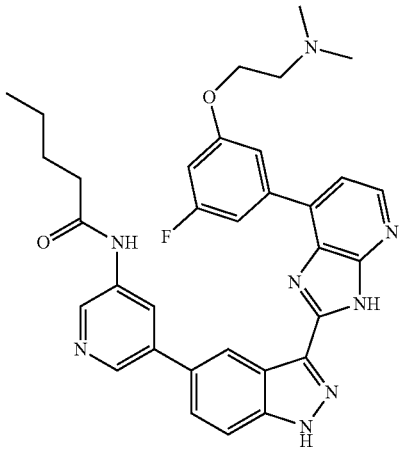

TABLE 1-continued

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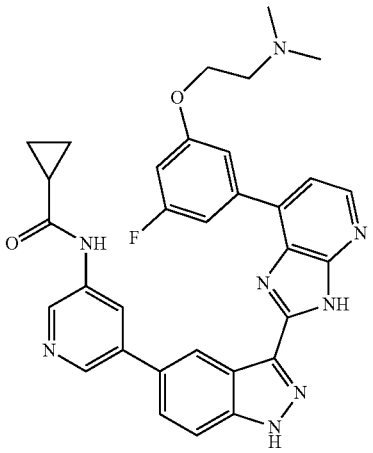

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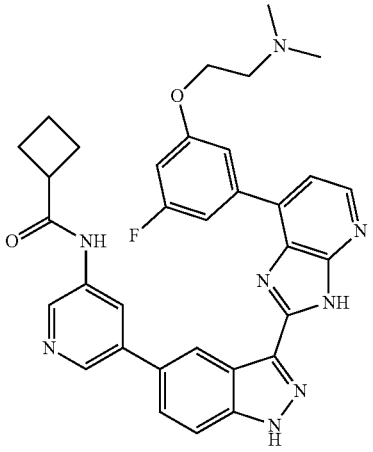

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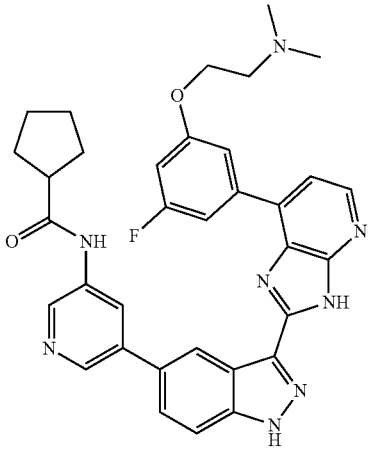

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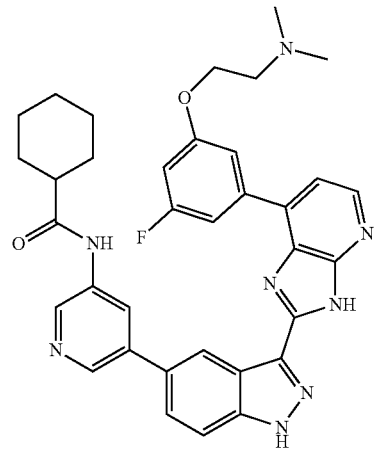
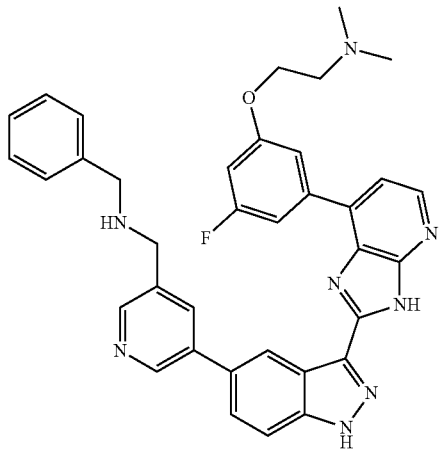
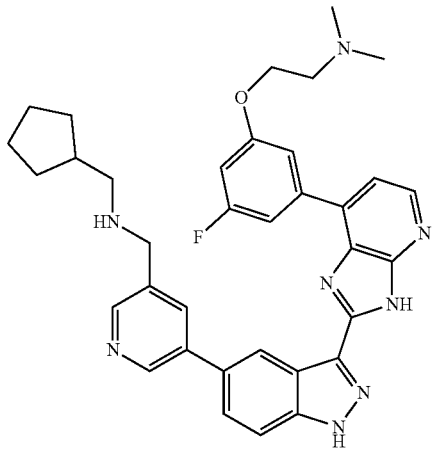
2218	
2219	
2220	

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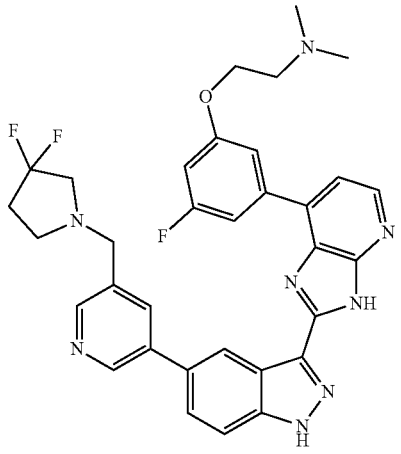
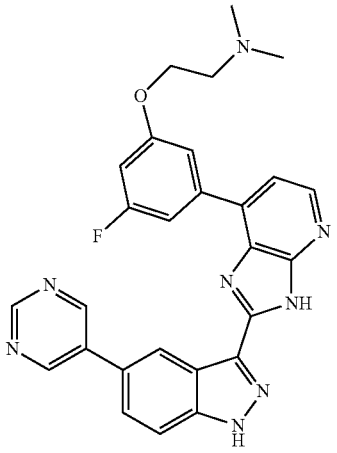
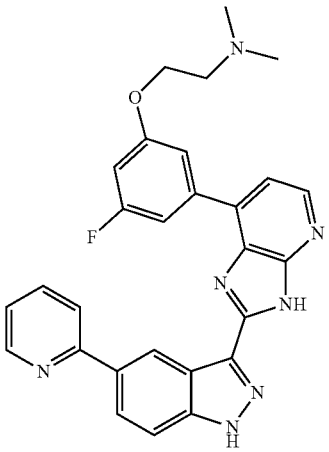
2221	
2222	
2223	

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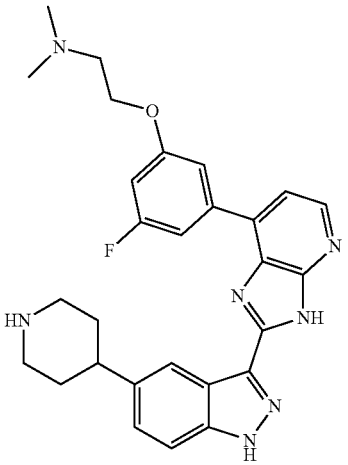
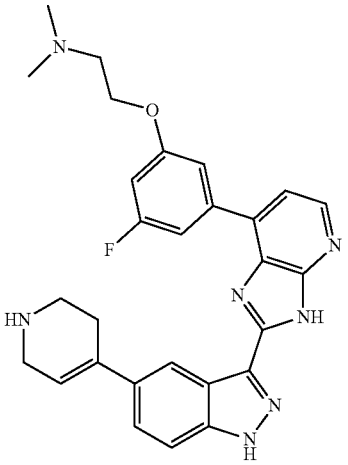
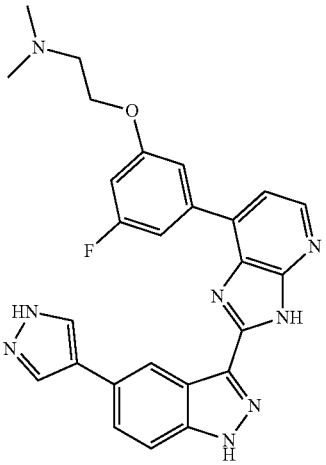
2224	
2225	
2226	

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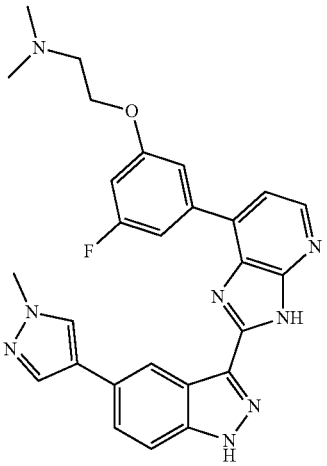
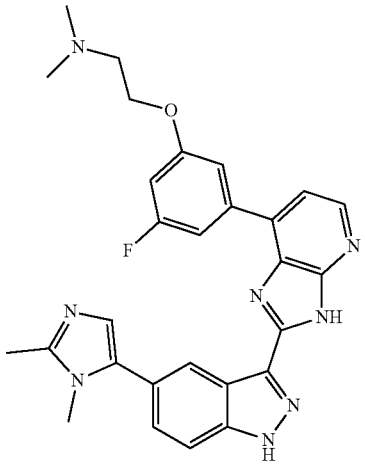
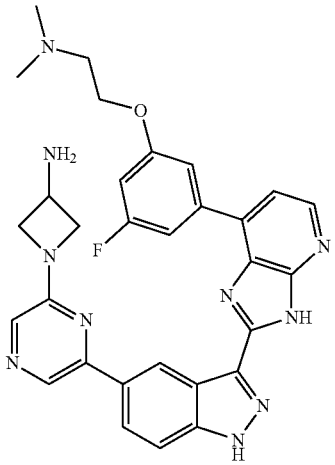
2227	
2228	
2229	

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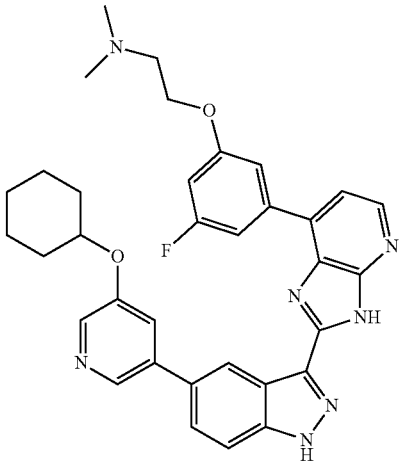
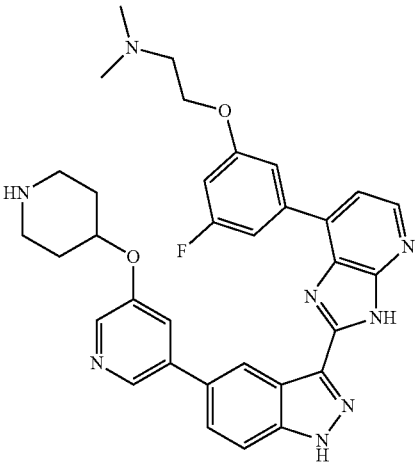
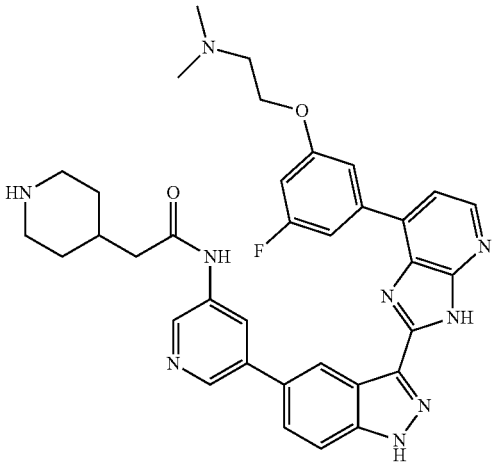
2230	
2231	
2232	

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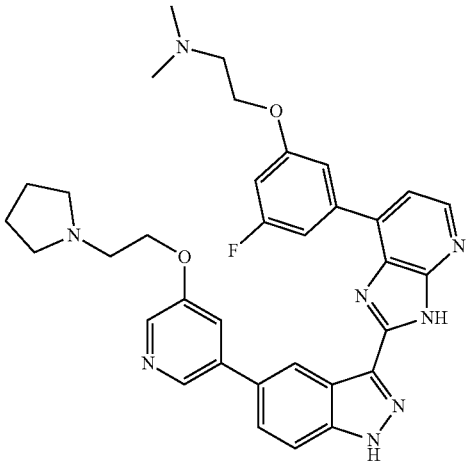
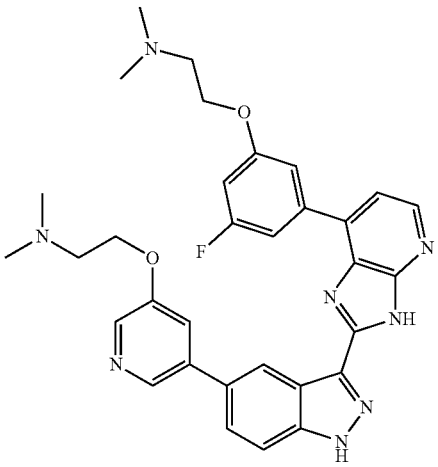
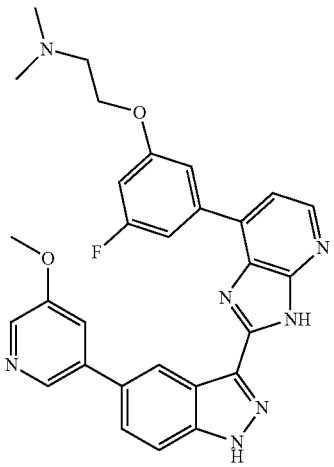
2233	
2234	
2235	

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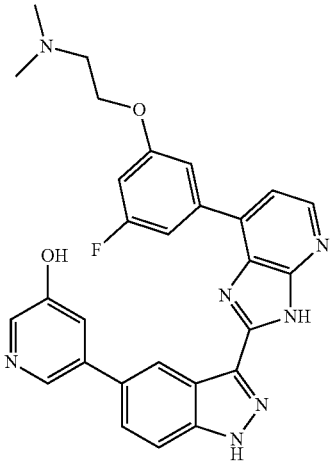

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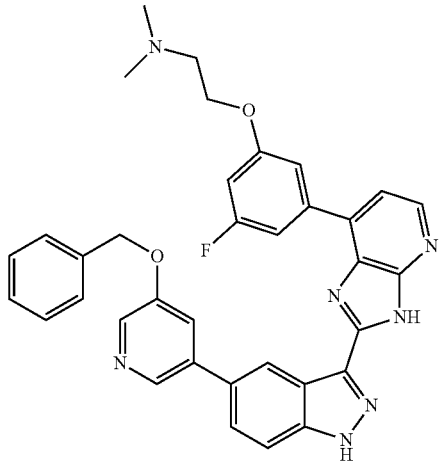

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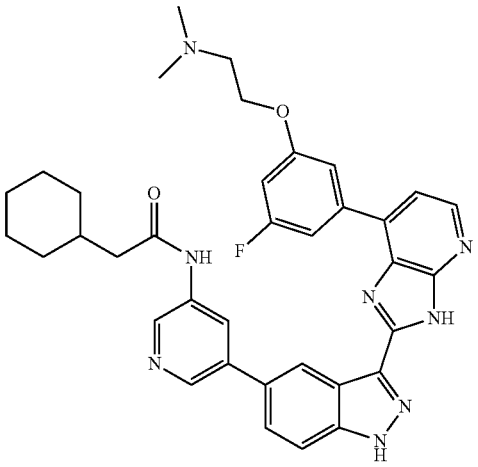

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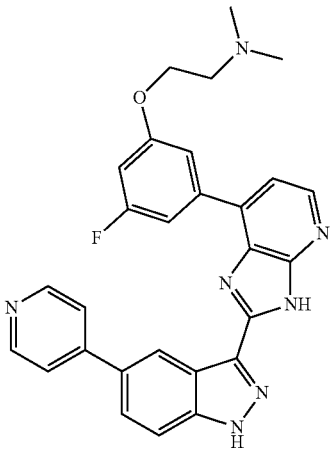

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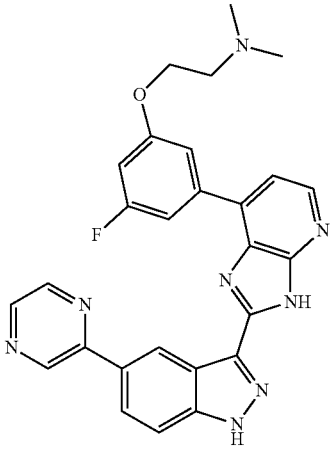

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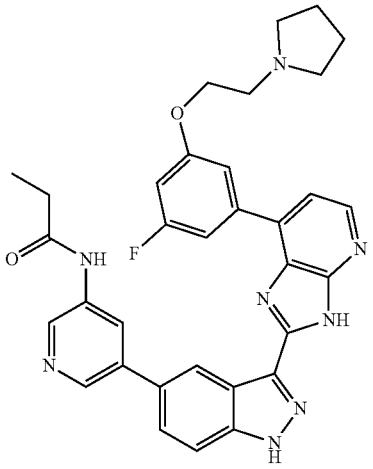

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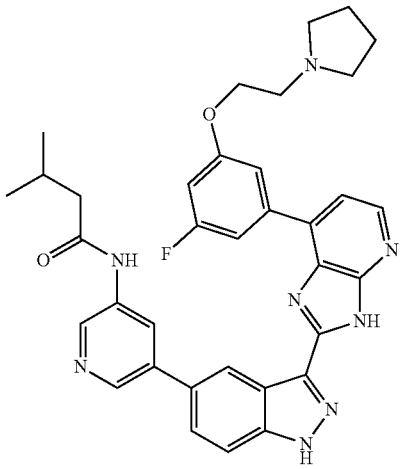
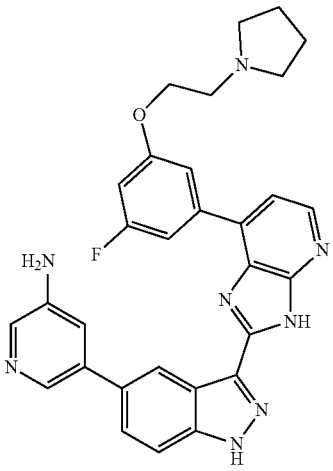
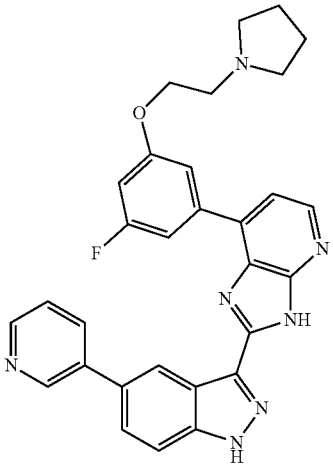
2242	
2243	
2244	

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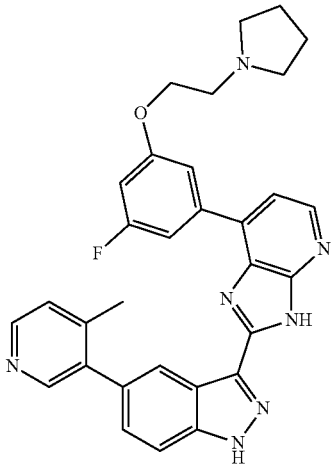
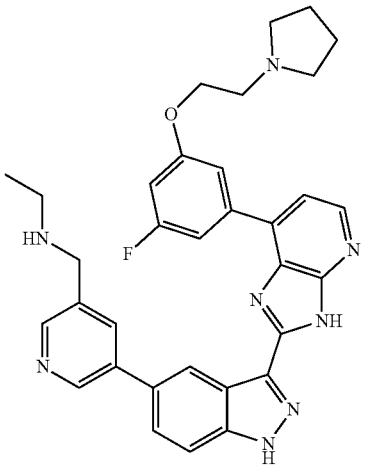
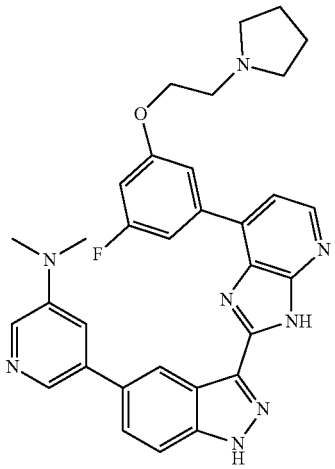
2245	
2246	
2247	

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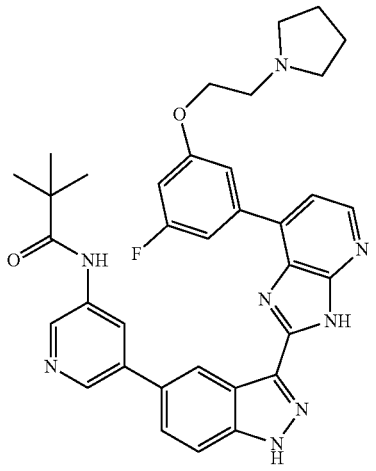
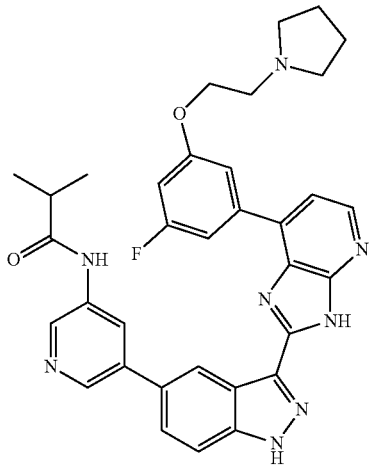
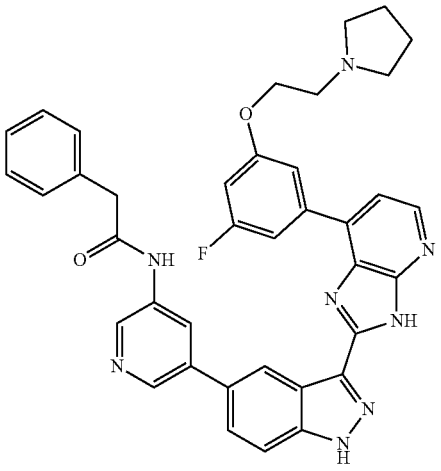
2248	
2249	
2250	

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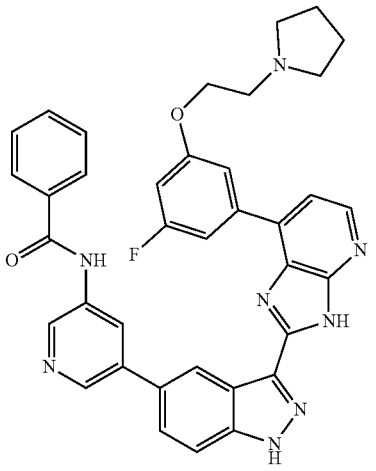
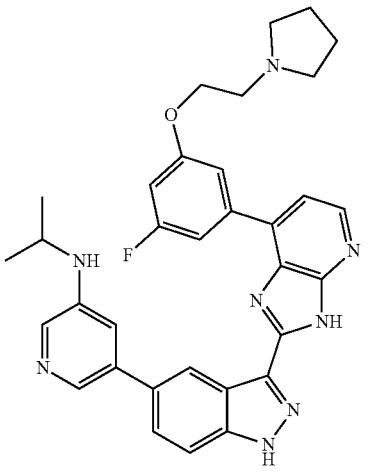
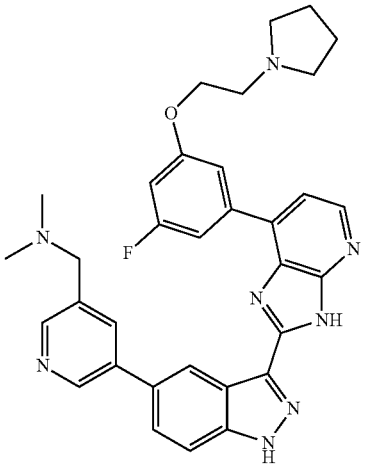
2251	
2252	
2253	

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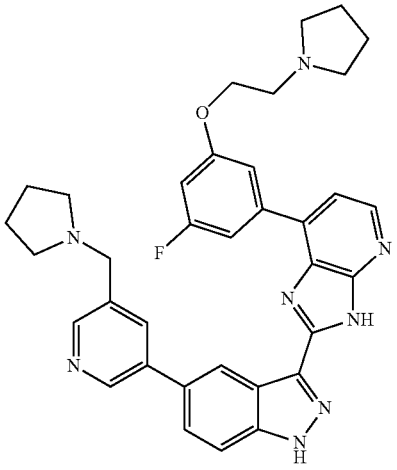
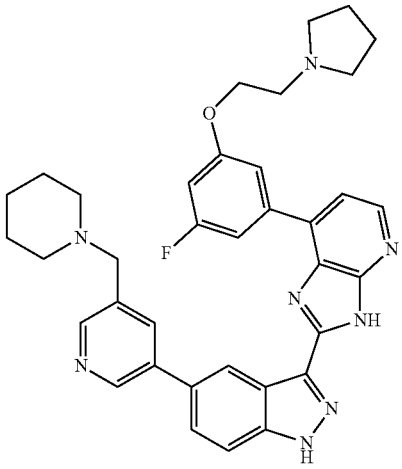
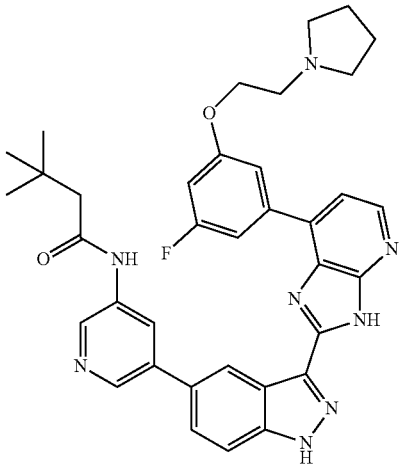
2254	
2255	
2256	

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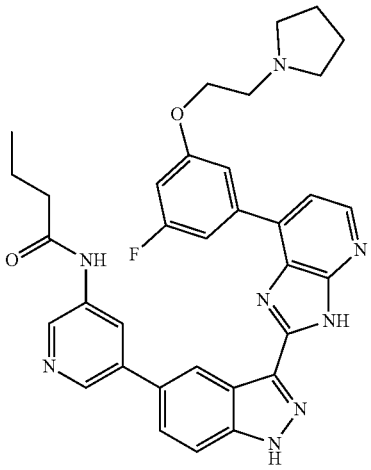
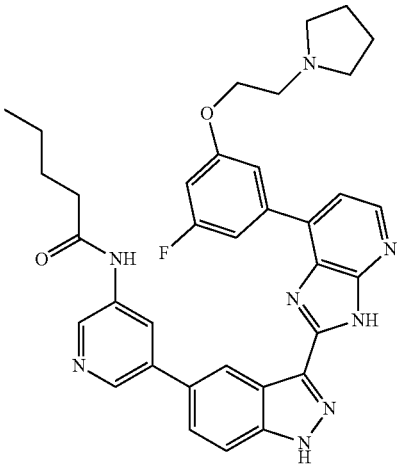
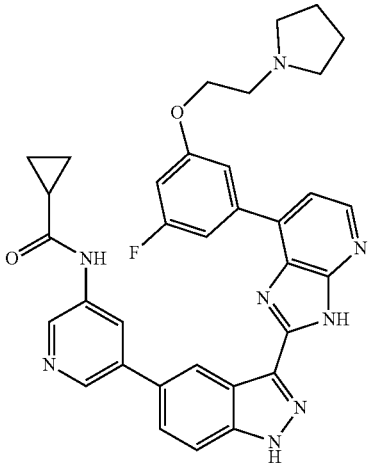
2257	
2258	
2259	

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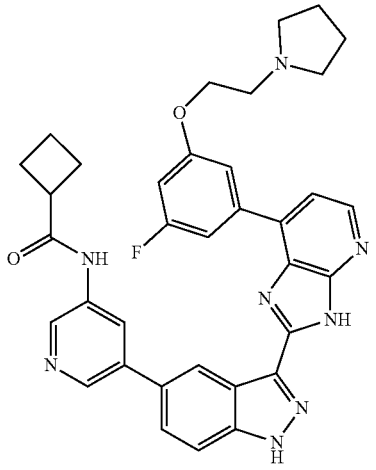

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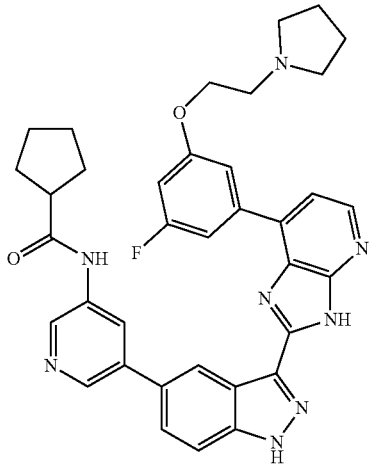

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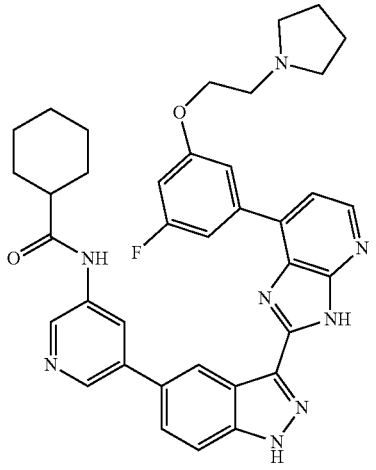

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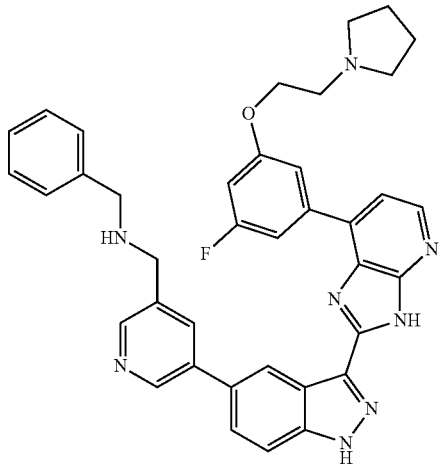

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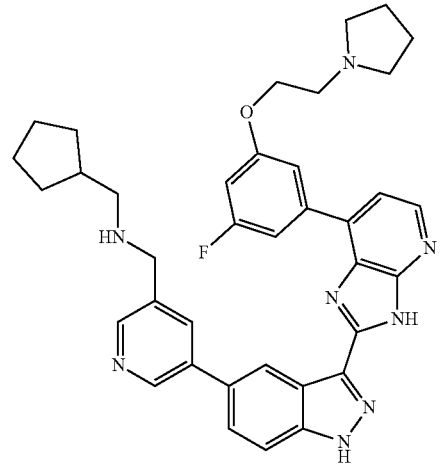

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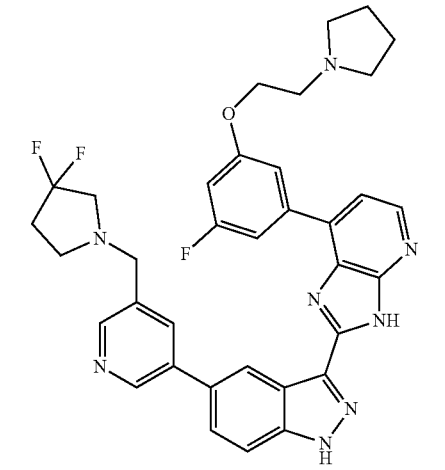

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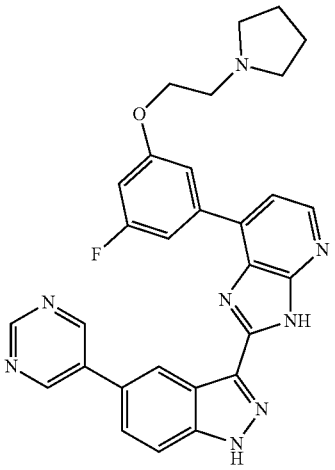

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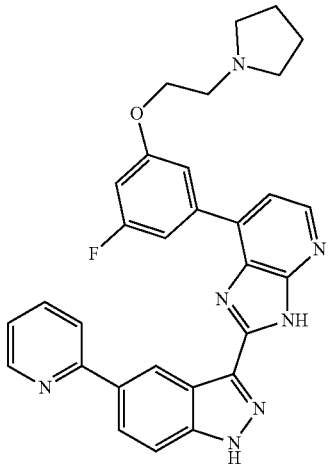

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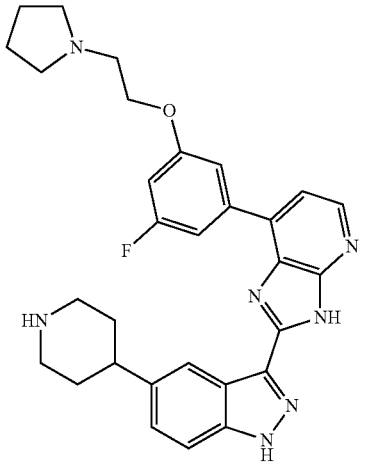

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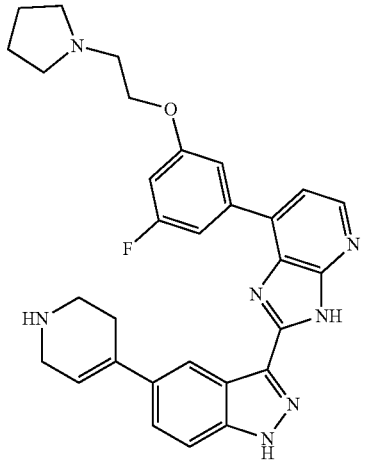

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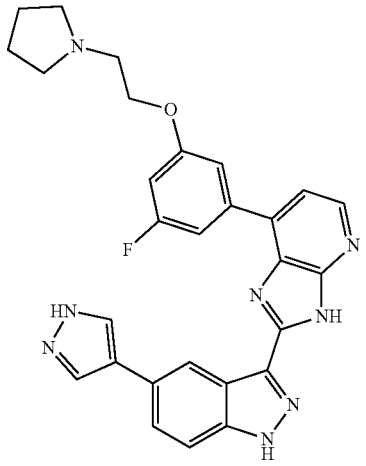

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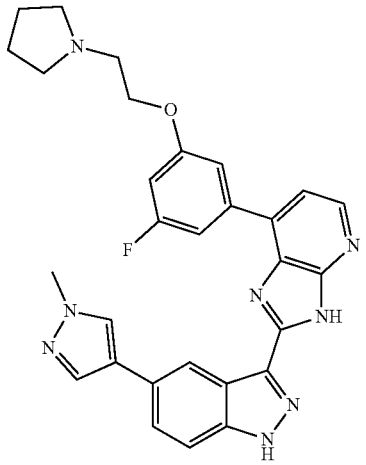

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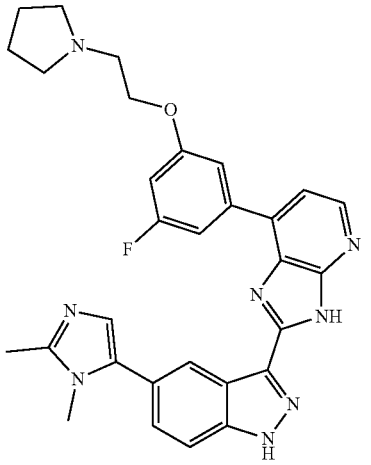
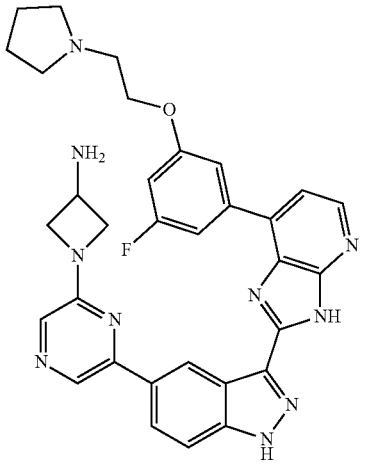
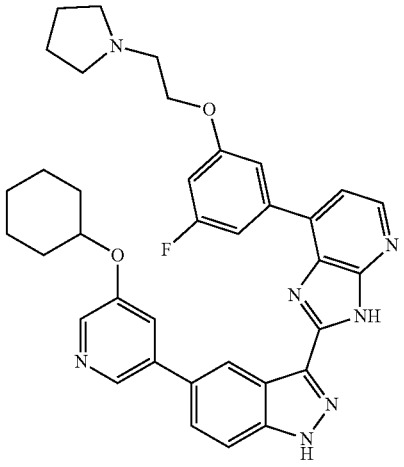
2272	
2273	
2274	

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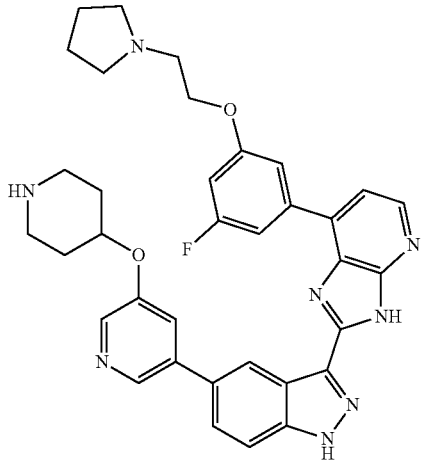
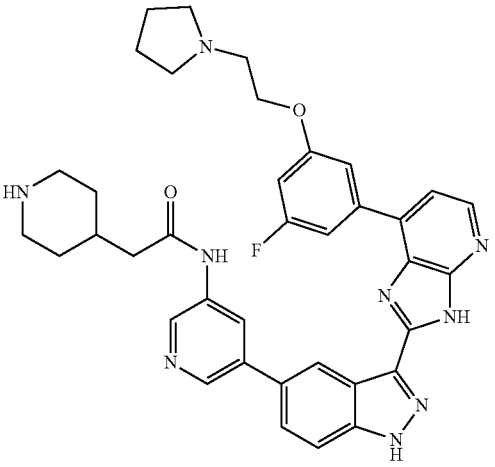
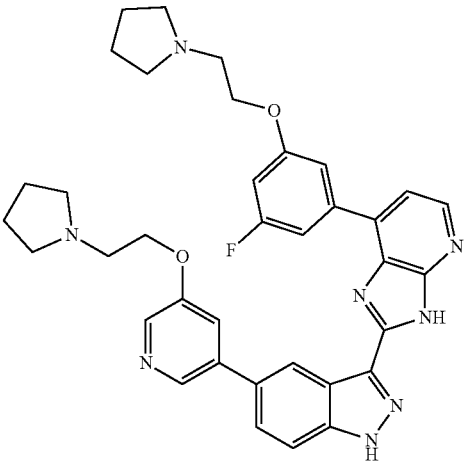
2275	
2276	
2277	

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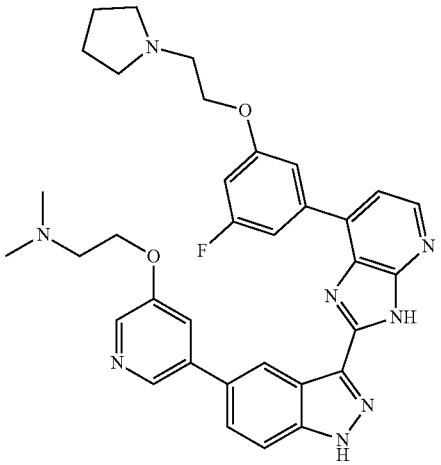
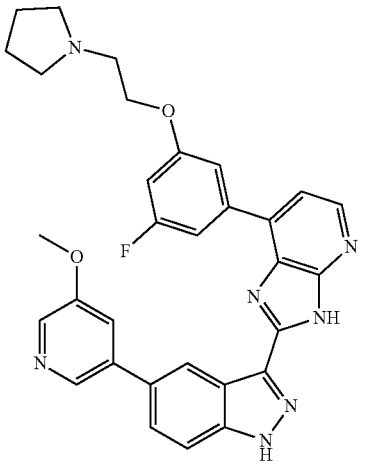
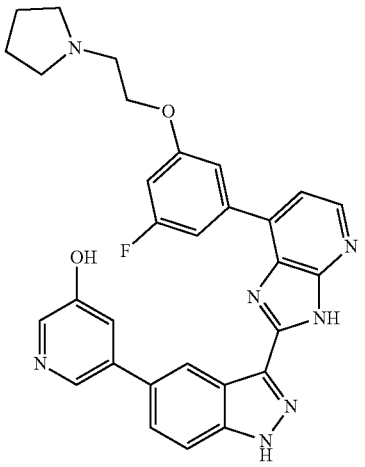
2278	
2279	
2280	

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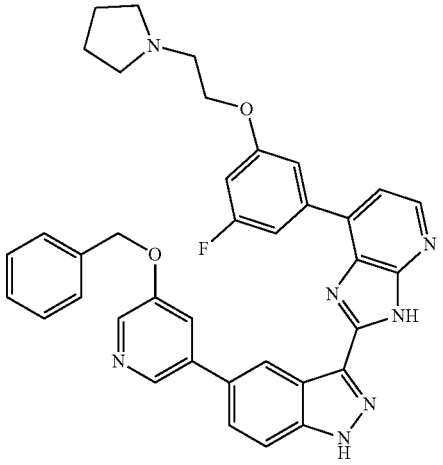
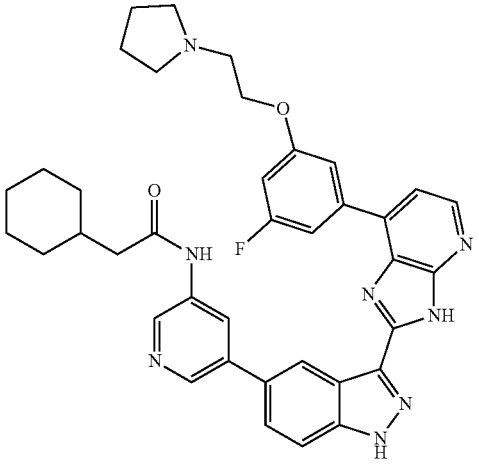
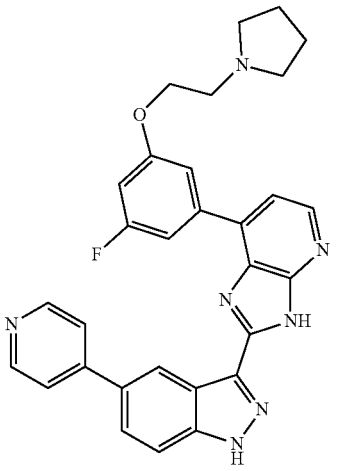
2281	
2282	
2283	

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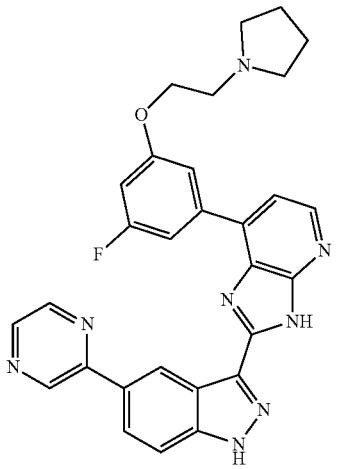
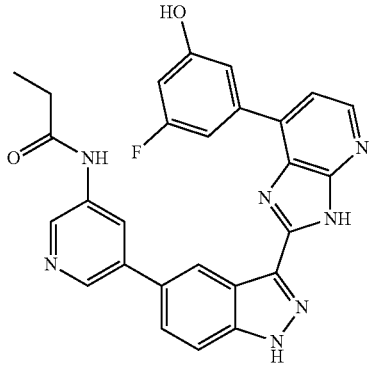
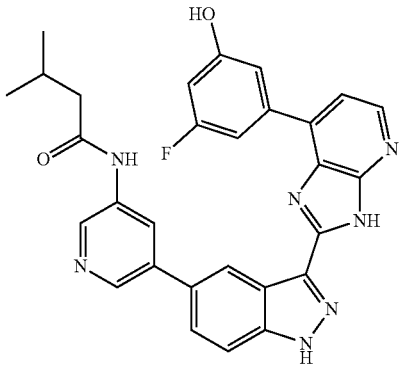
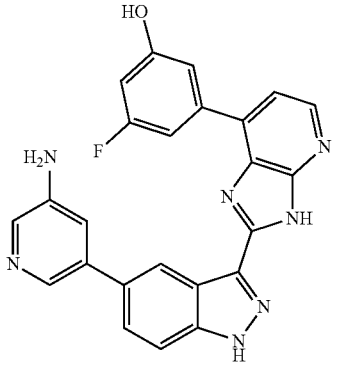
2284	
2285	
2286	
2287	

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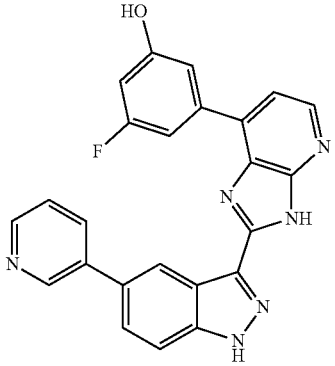
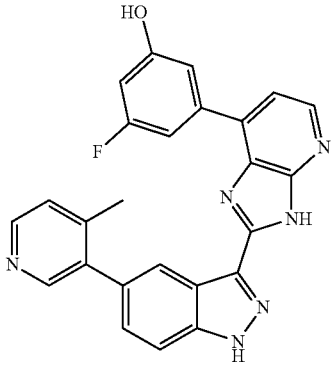
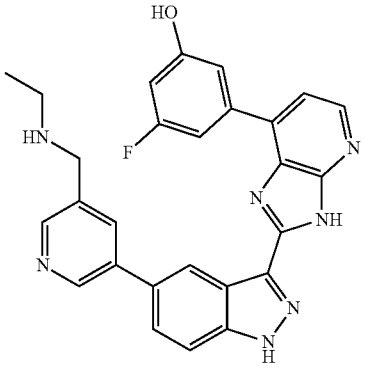
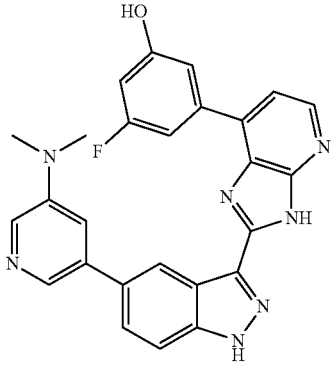
2288	
2289	
2290	
2291	

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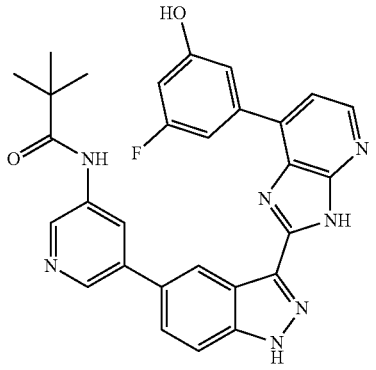
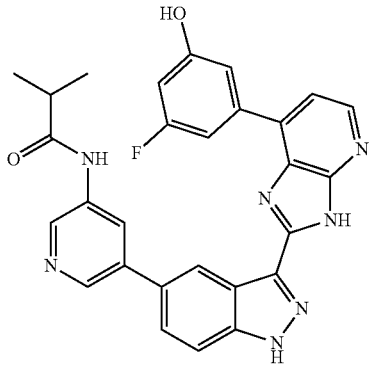
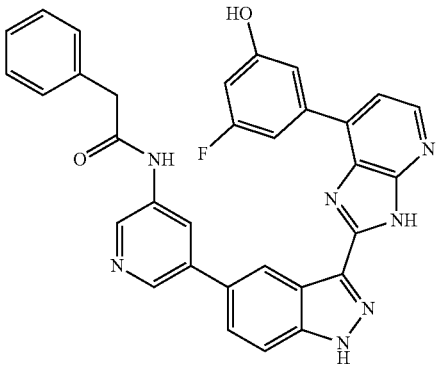
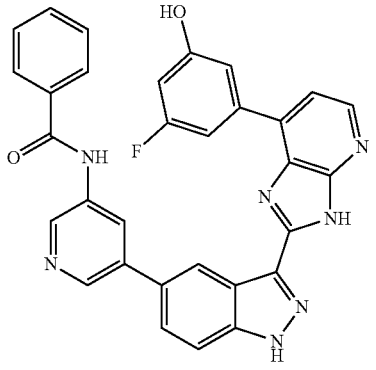
2292	
2293	
2294	
2295	

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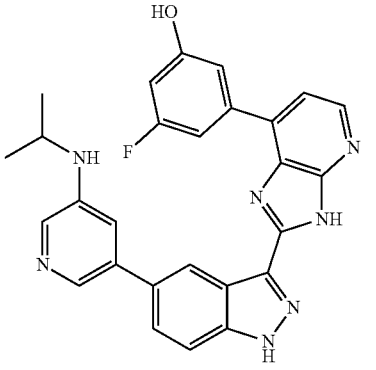
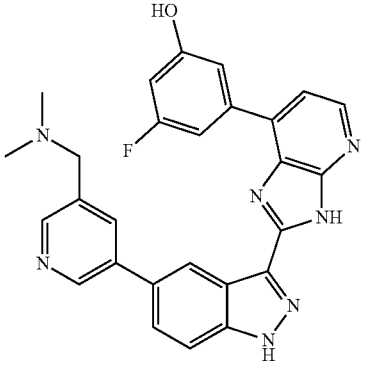
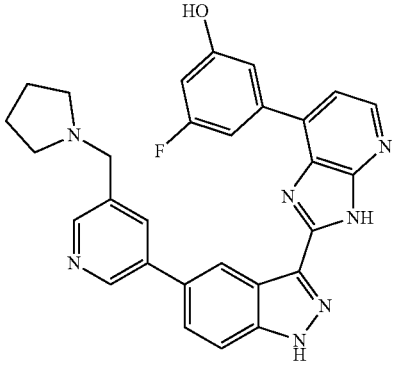
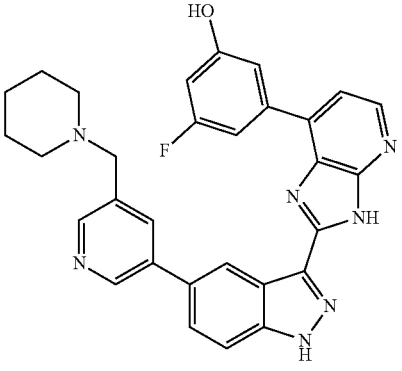
2296	
2297	
2298	
2299	

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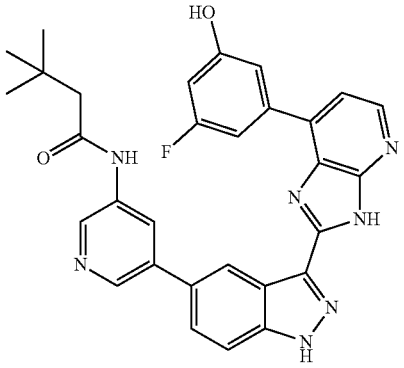
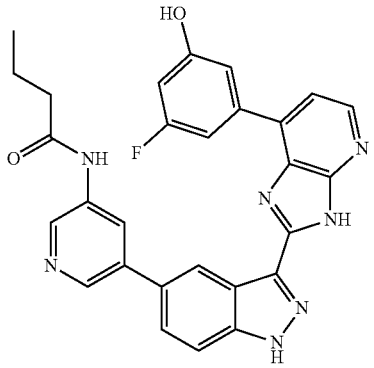
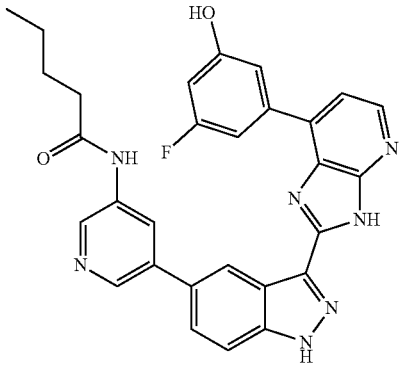
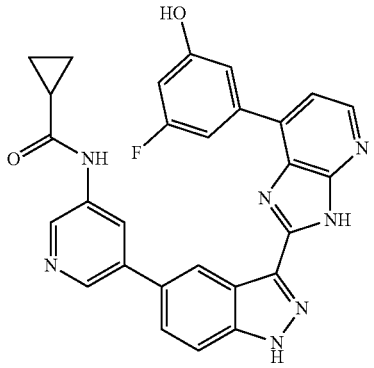
2300	
2301	
2302	
2303	

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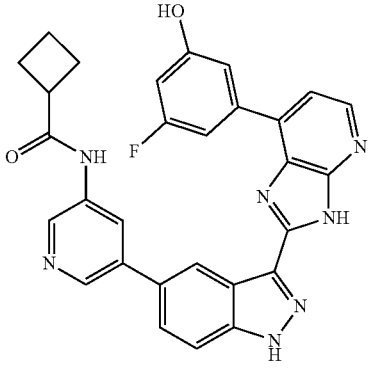
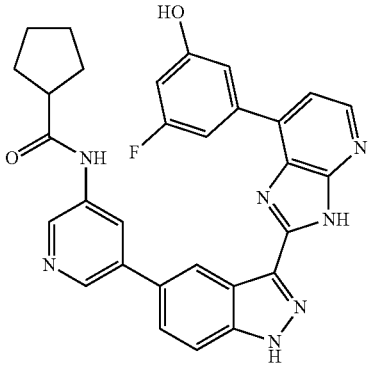
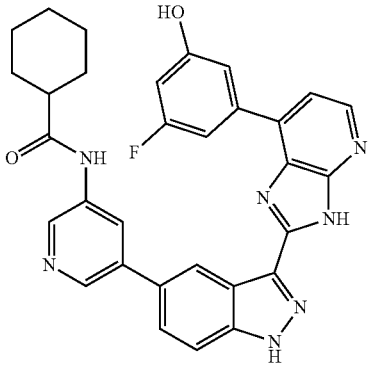
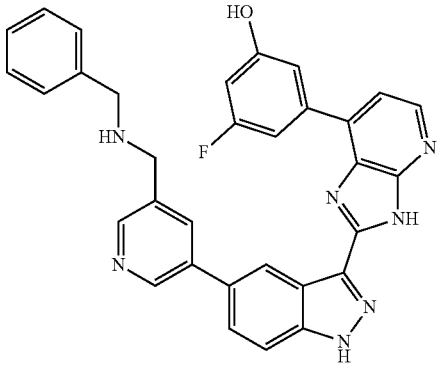
2304	
2305	
2306	
2307	

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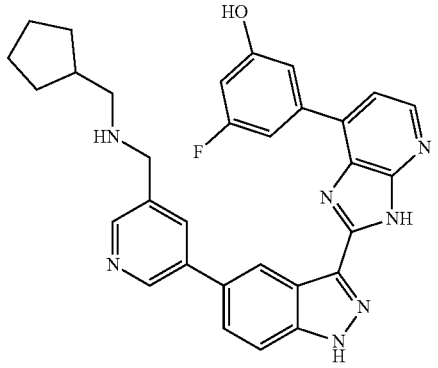
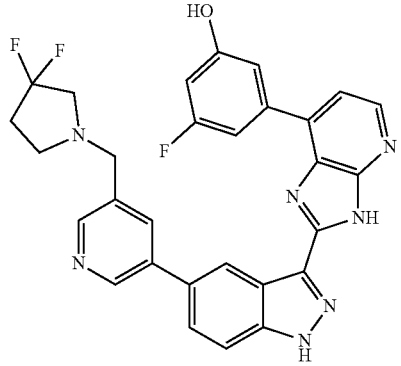
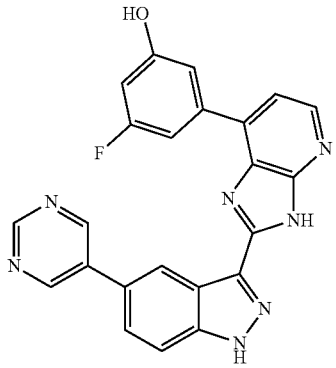
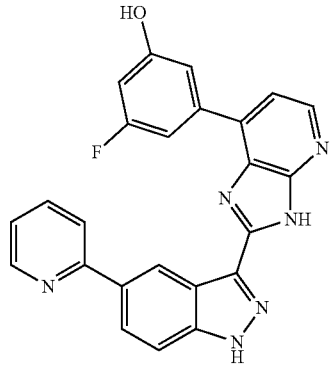
2308	
2309	
2310	
2311	

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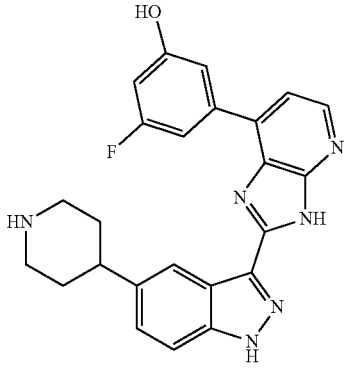
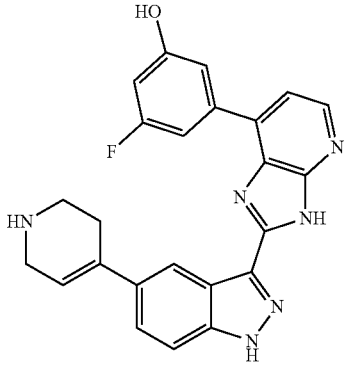
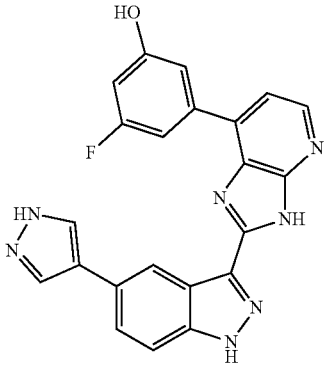
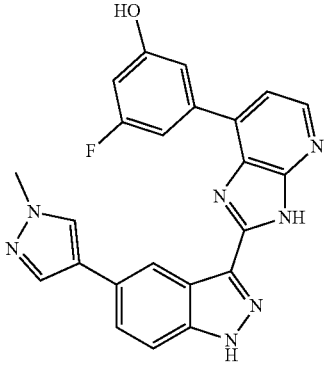
2312	
2313	
2314	
2315	

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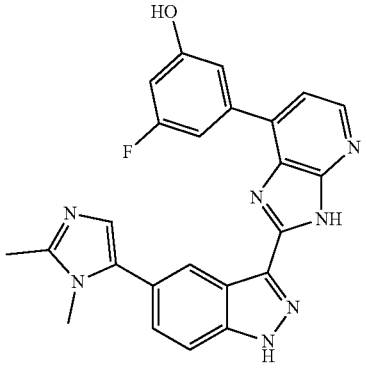
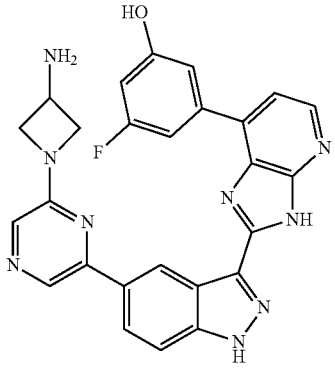
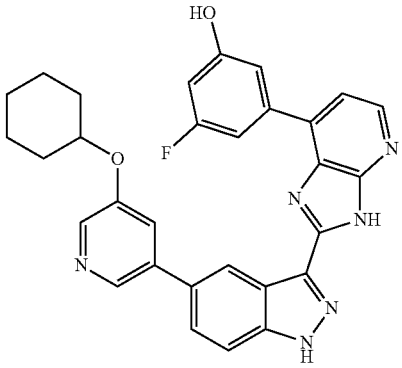
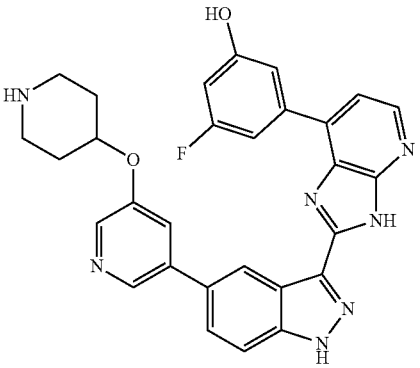
2316	
2317	
2318	
2319	

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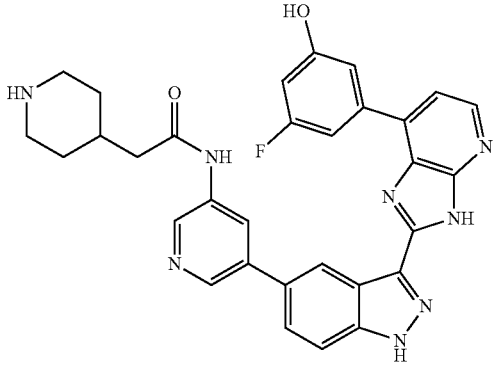
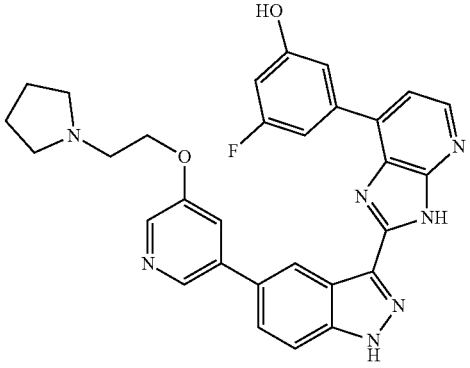
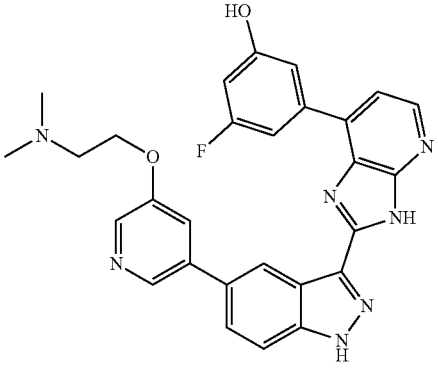
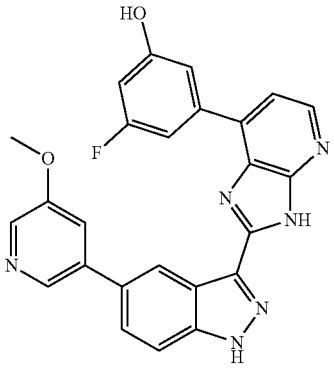
2320	
2321	
2322	
2323	

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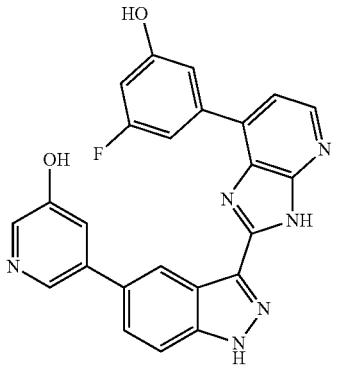
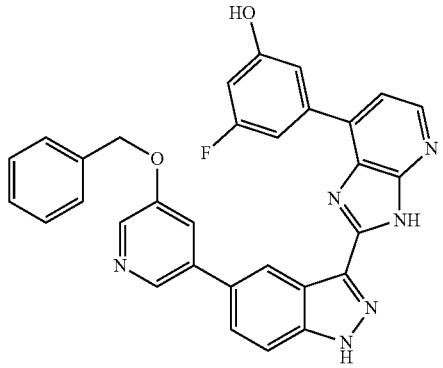
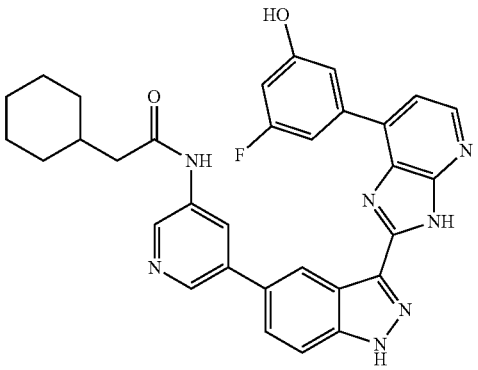
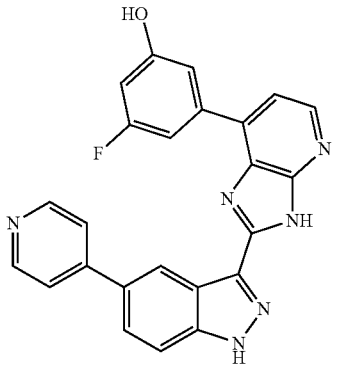
2324	
2325	
2326	
2327	

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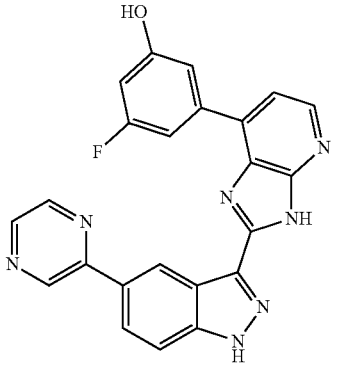
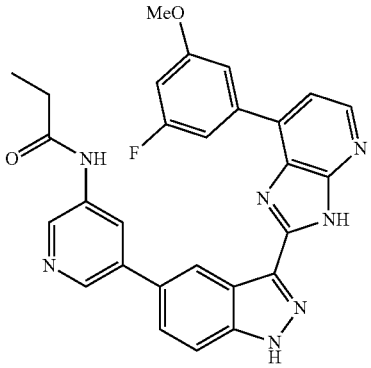
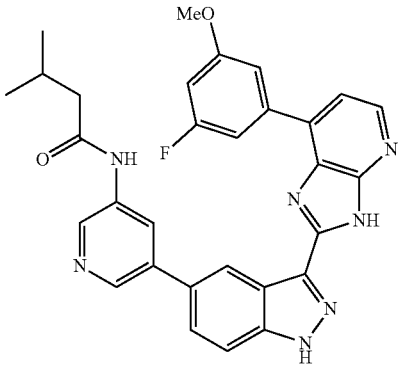
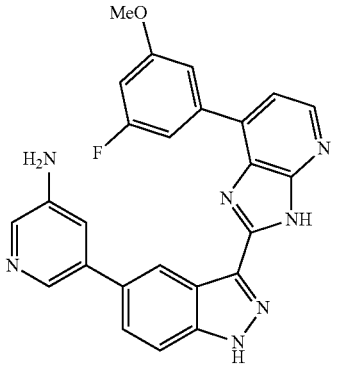
2328	
2329	
2330	
2331	

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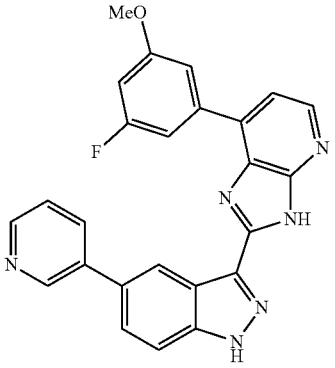
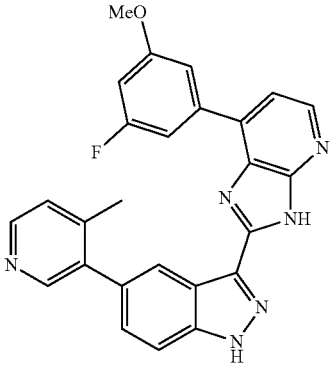
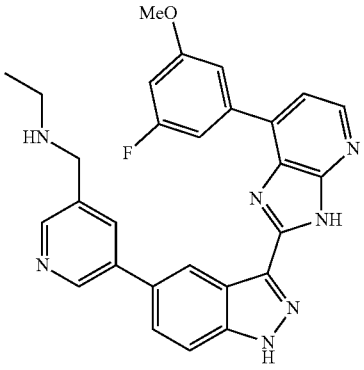
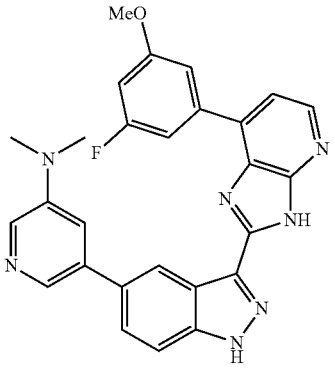
2332	
2333	
2334	
2335	

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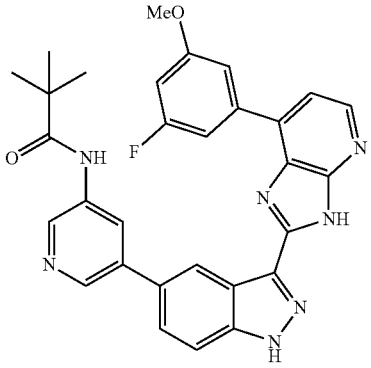
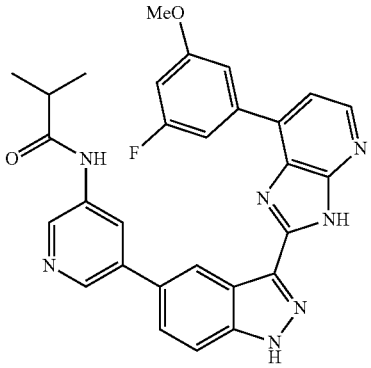
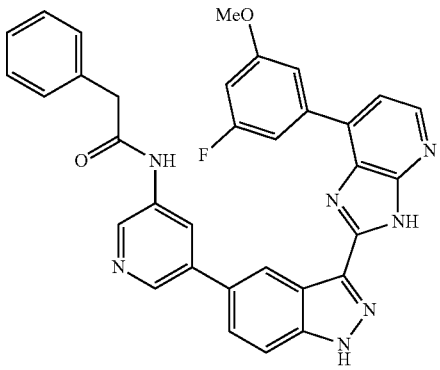
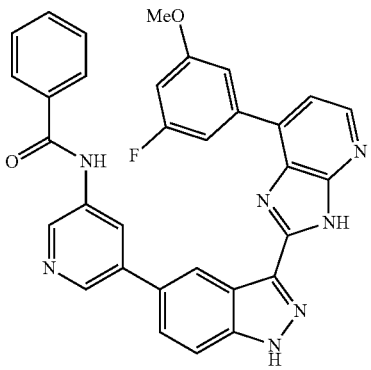
2336	
2337	
2338	
2339	

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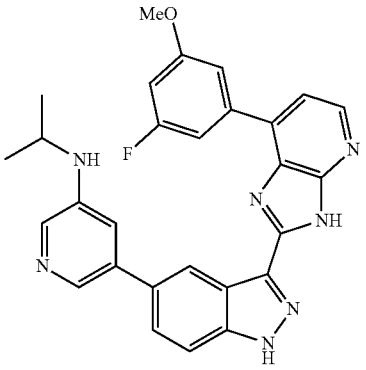
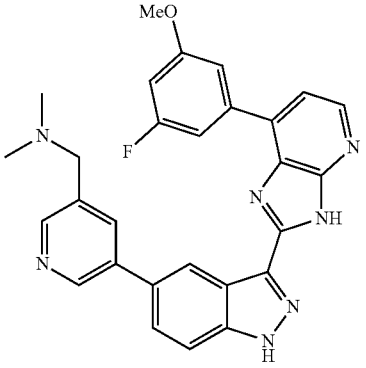
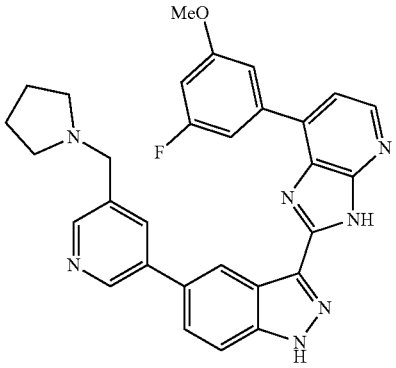
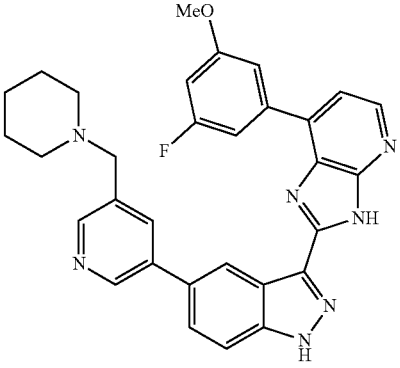
2340	
2341	
2342	
2343	

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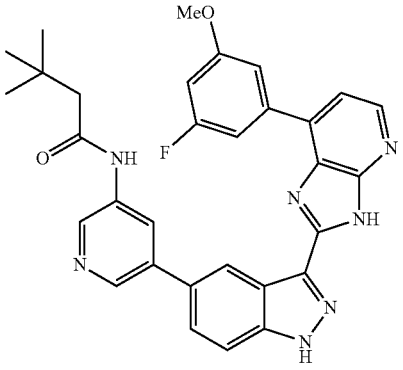
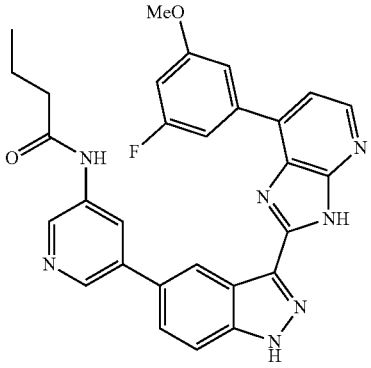
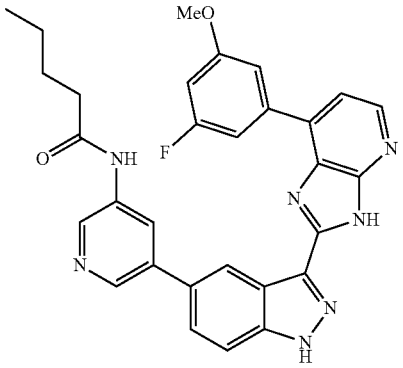
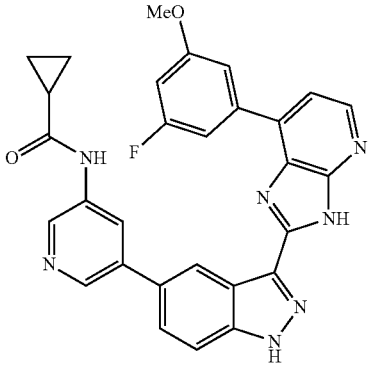
2344	
2345	
2346	
2347	

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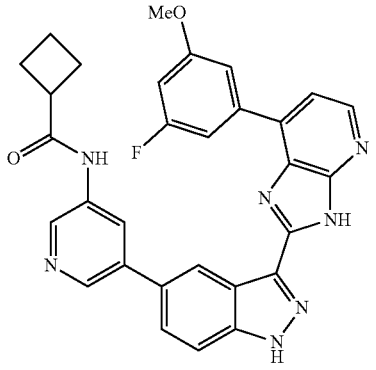
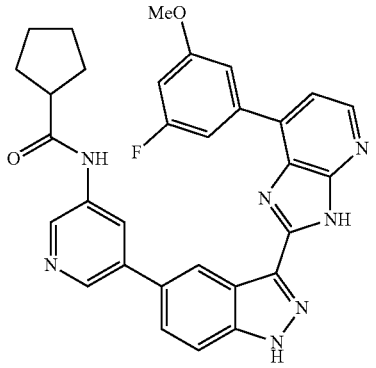
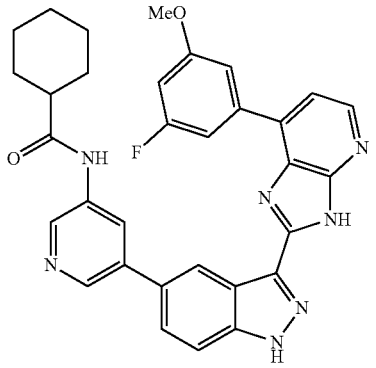
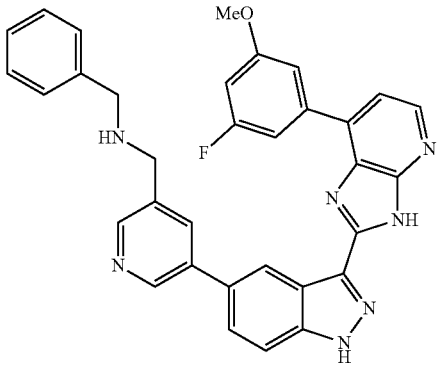
2348	
2349	
2350	
2351	

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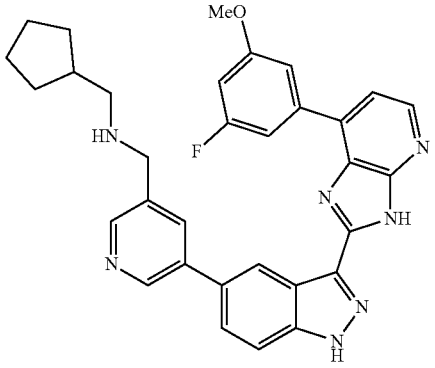
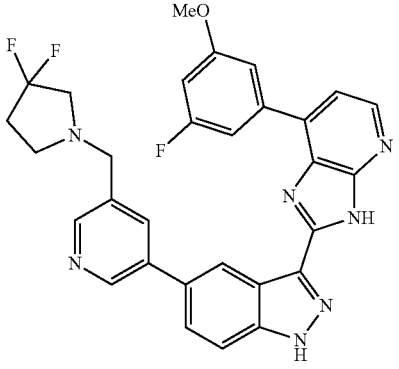
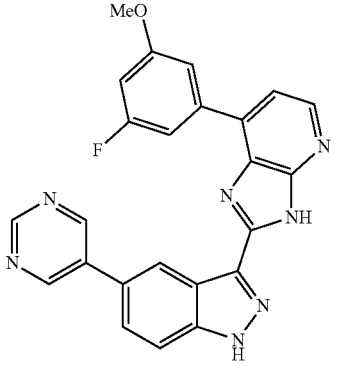
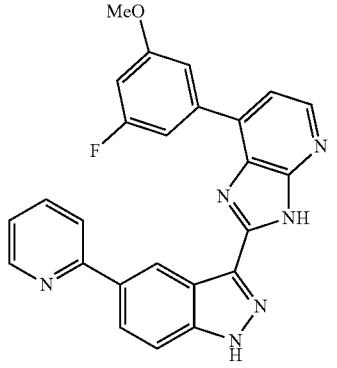
2352	
2353	
2354	
2355	

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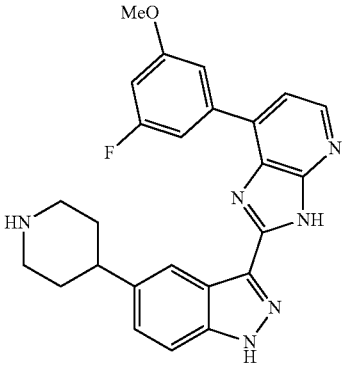
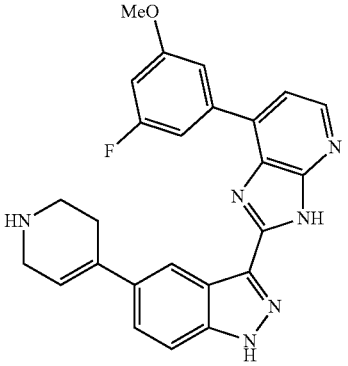
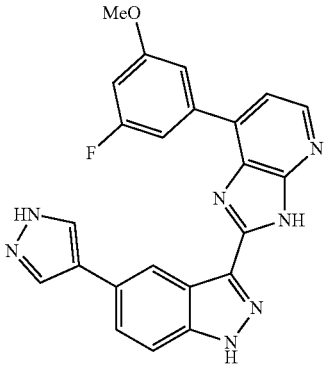
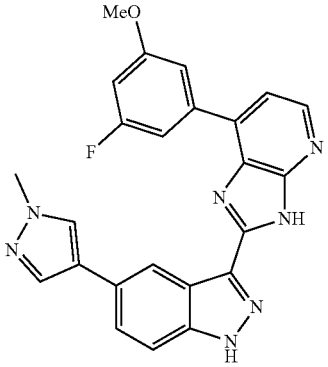
2356	
2357	
2358	
2359	

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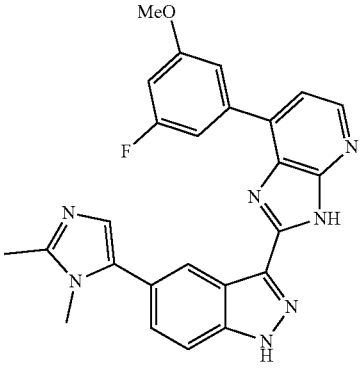
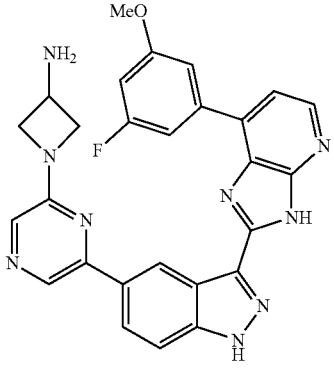
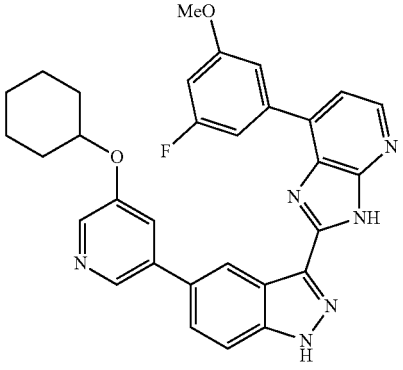
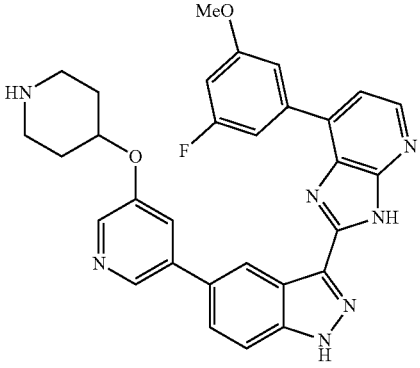
2360	
2361	
2362	
2363	

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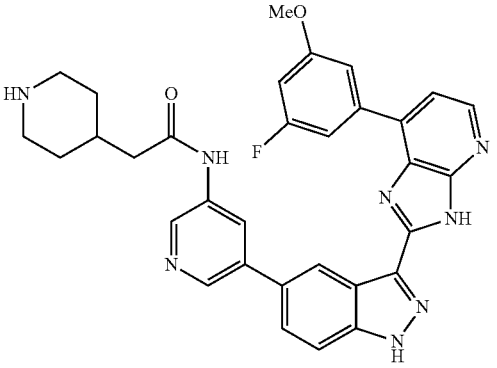

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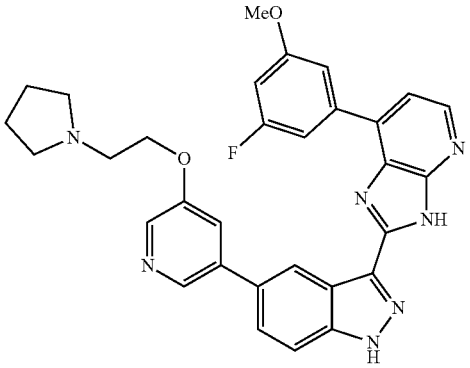

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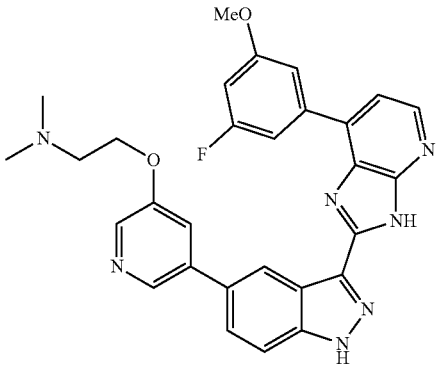

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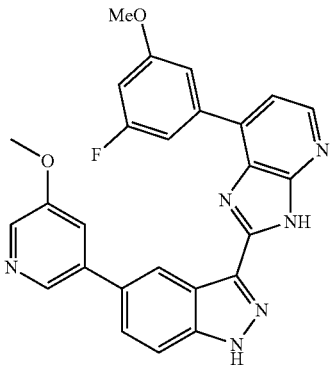

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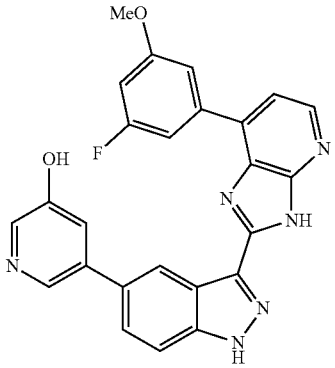

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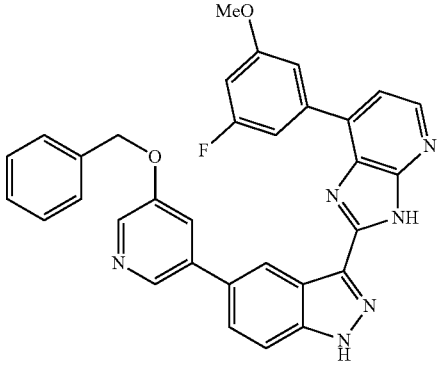

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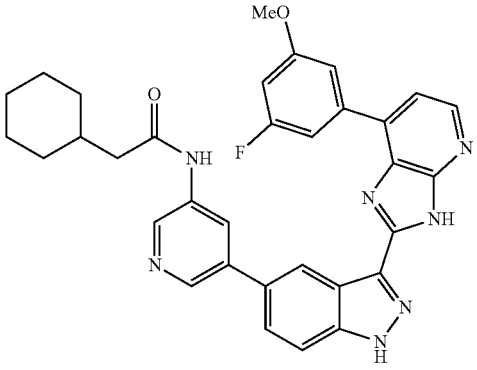

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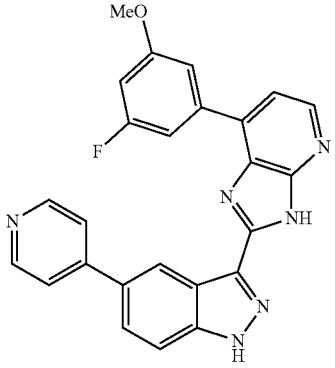

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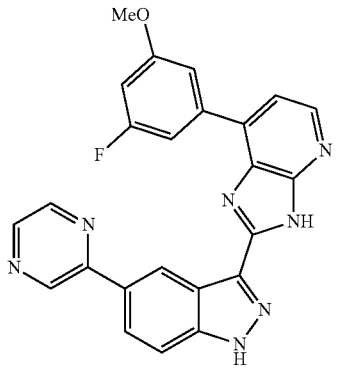

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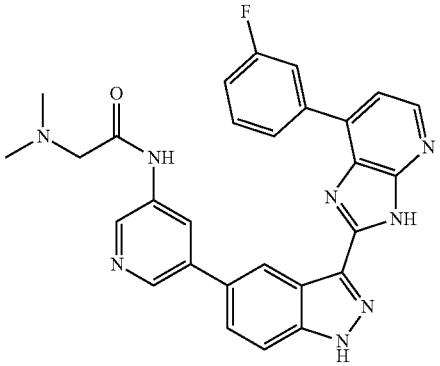

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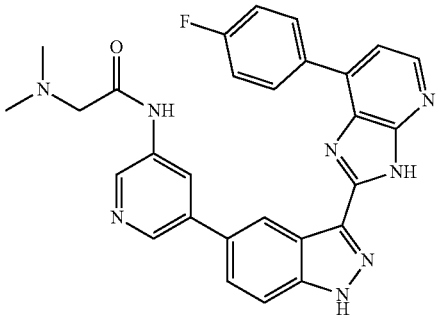

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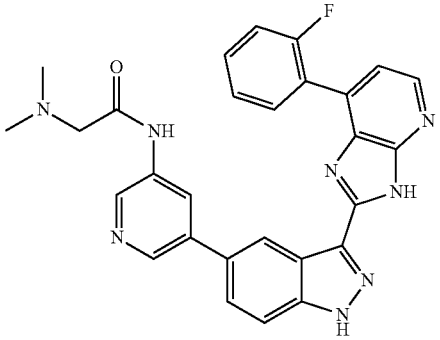

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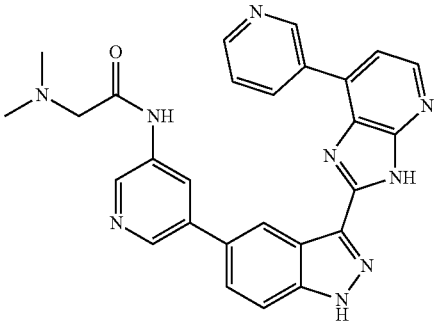

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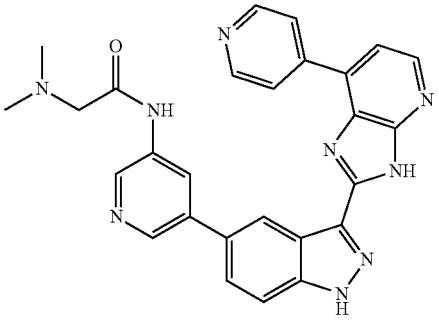

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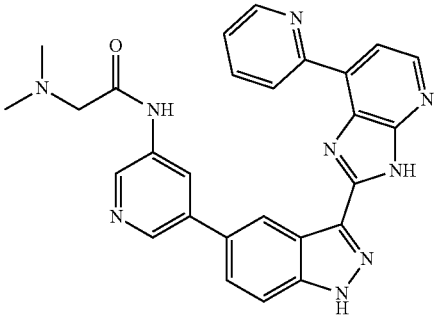

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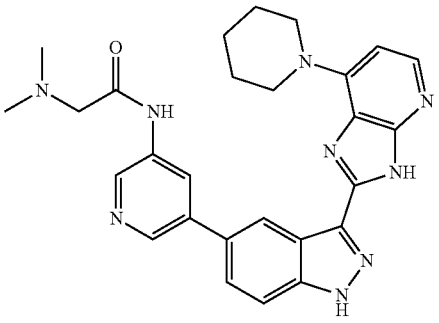

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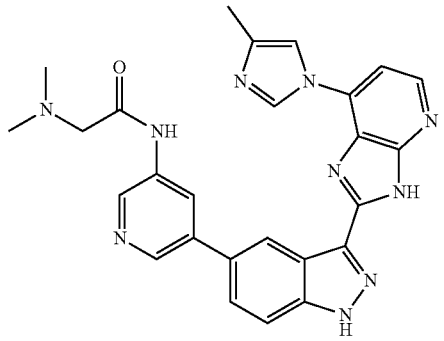
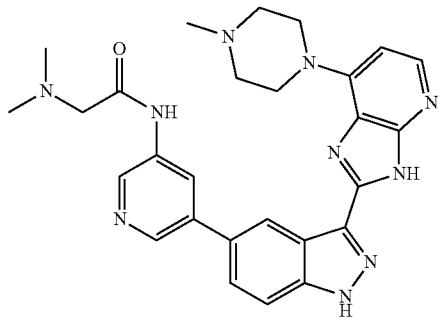
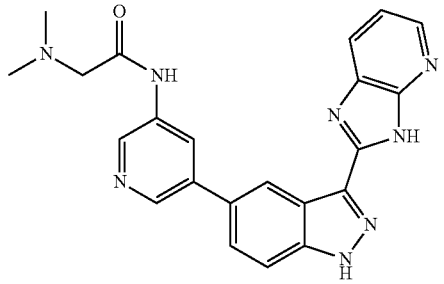
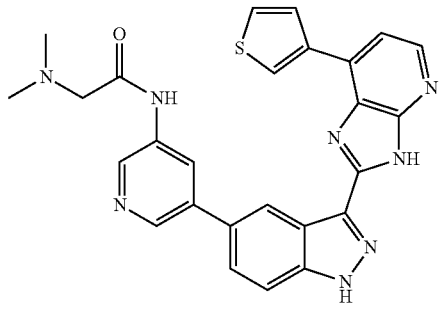
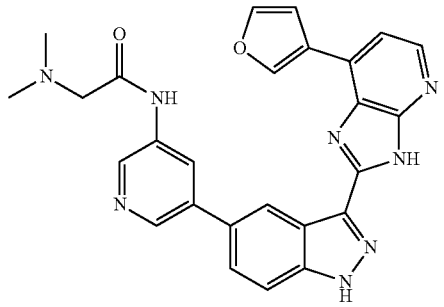
2380	
2381	
2382	
2383	
2384	

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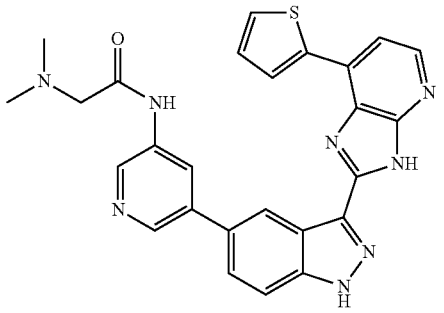
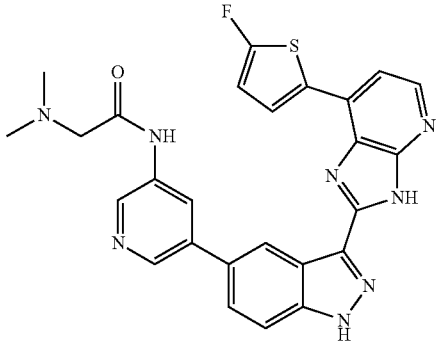
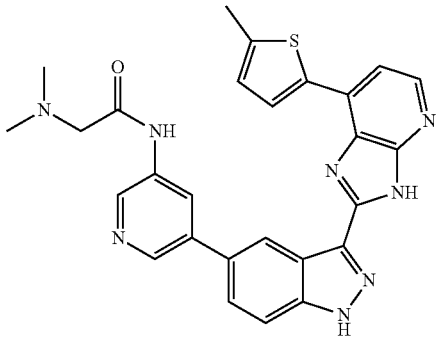
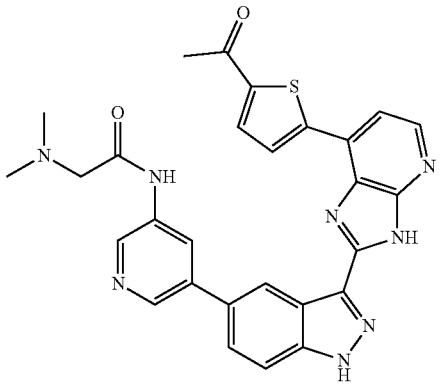
2385	
2386	
2387	
2388	

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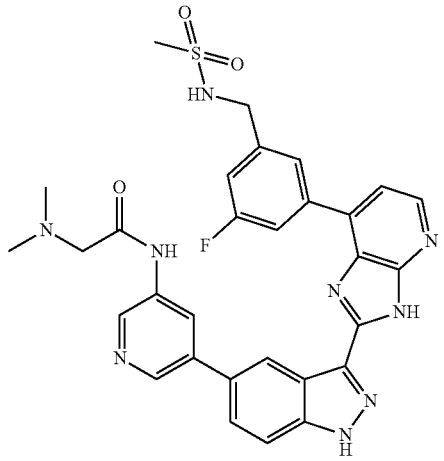

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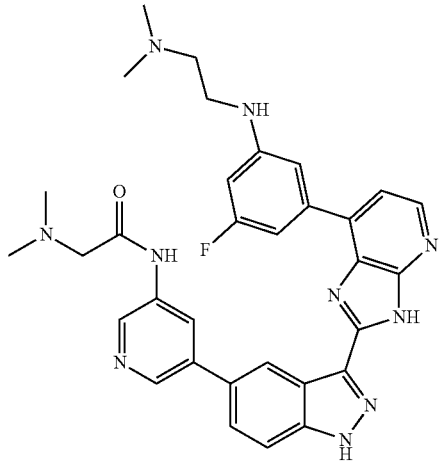

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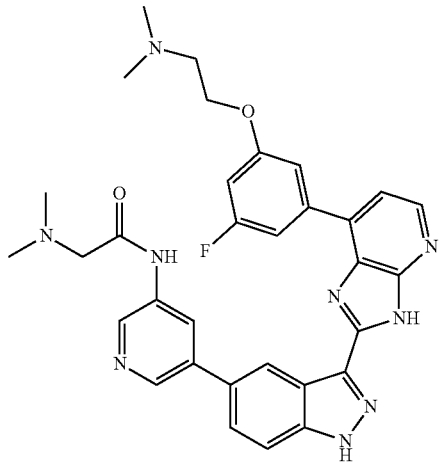

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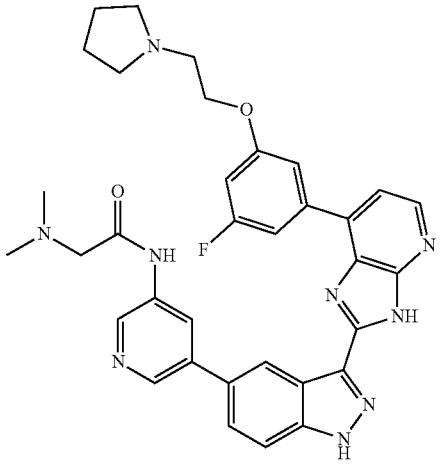

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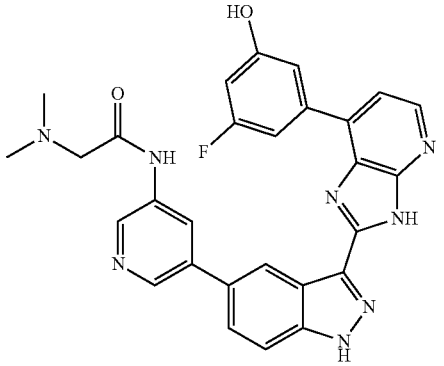

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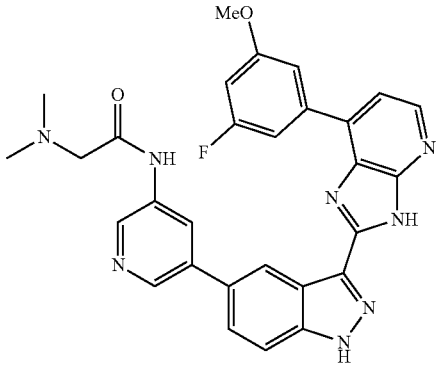

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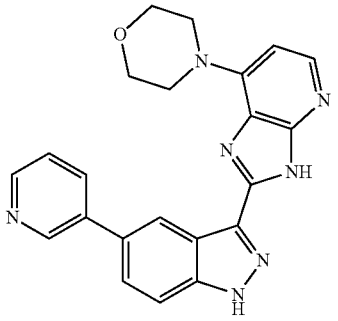

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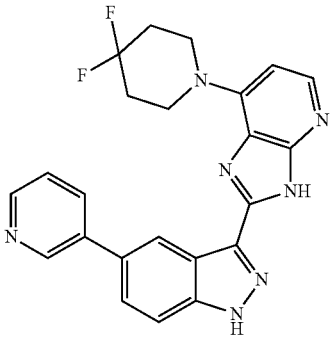
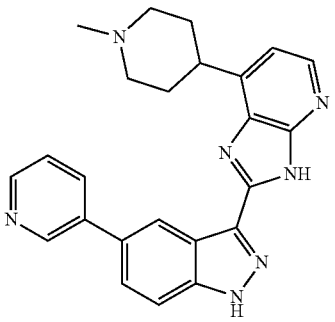
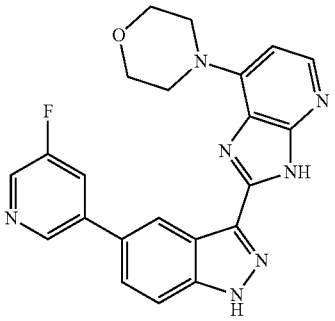
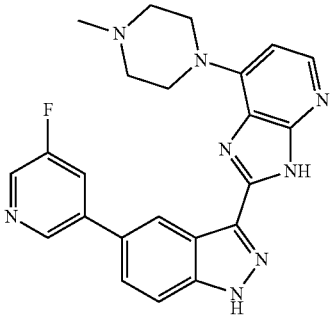
2396	
2397	
2398	
2399	

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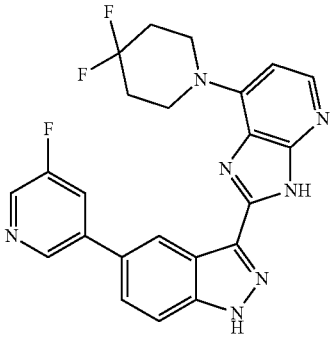
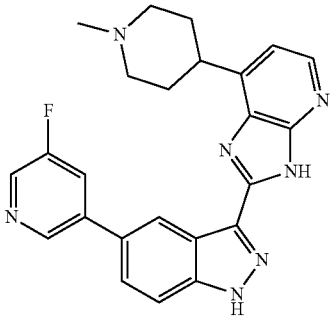
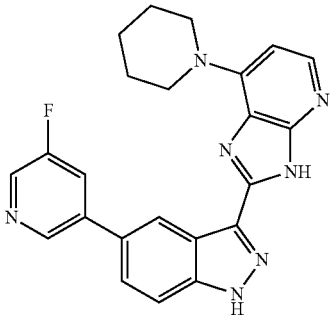
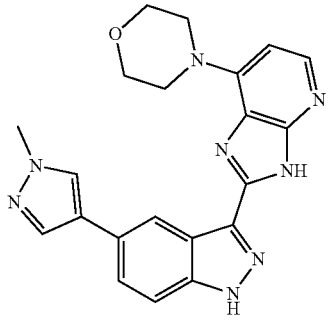
2400	
2401	
2402	
2403	

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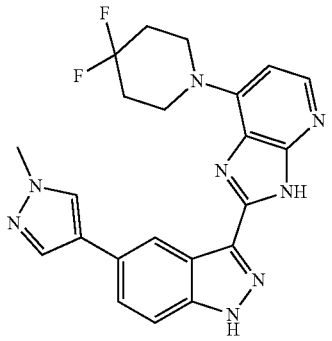
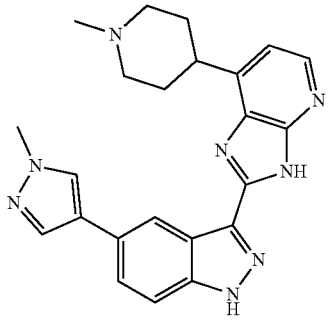
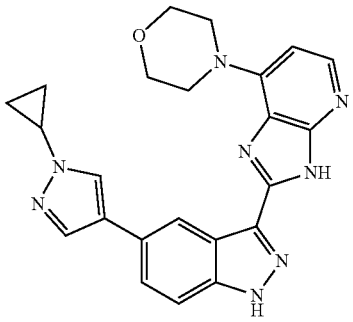
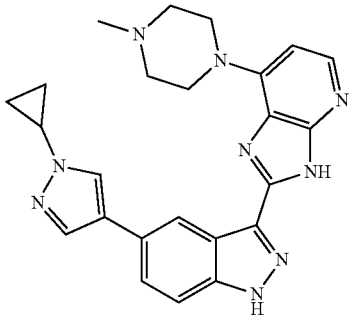
2404	
2405	
2406	
2407	

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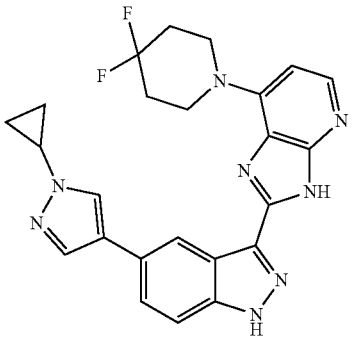
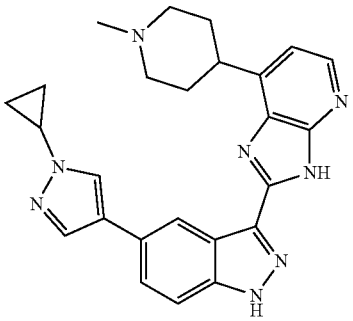
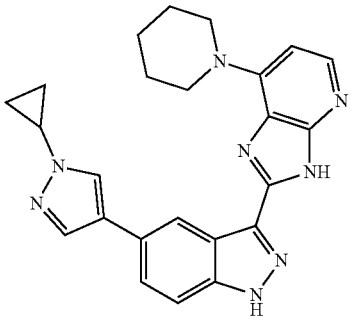
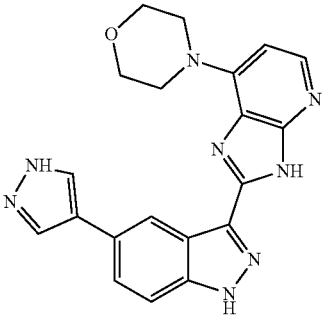
2408	
2409	
2410	
2411	

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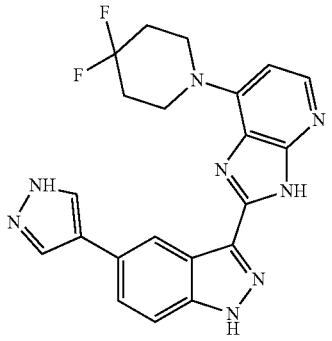
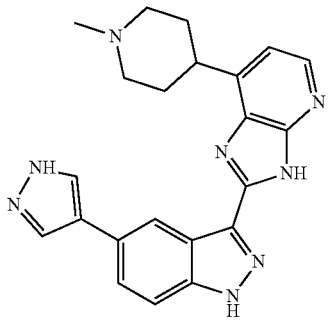
2412	
2413	

Administration and Pharmaceutical Compositions

[0527] Some embodiments include pharmaceutical compositions comprising: (a) a therapeutically effective amount of a compound provided herein, or its corresponding enantiomer, diastereoisomer or tautomer, or pharmaceutically acceptable salt; and (b) a pharmaceutically acceptable carrier.

[0528] The compounds provided herein may also be useful in combination (administered together or sequentially) with other known agents.

[0529] Non-limiting examples of diseases which can be treated with a combination of a compound of Formula (I) and other known agents are colorectal cancer, ovarian cancer, retinitis pigmentosa, macular degeneration, diabetic retinopathy, idiopathic pulmonary fibrosis/pulmonary fibrosis, and osteoarthritis.

[0530] In some embodiments, colorectal cancer can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: 5-Fluorouracil (5-FU), which can be administered with the vitamin-like drug leucovorin (also called folinic acid); capecitabine (XELODA®), irinotecan (CAMPOSTAR®), oxaliplatin (ELOXATIN®). Examples of combinations of these drugs which could be further combined with a compound of Formula (I) are FOLFOX (5-FU, leucovorin, and oxaliplatin), FOLFIRI (5-FU, leucovorin, and irinotecan), FOLFOXIRI (leucovorin, 5-FU, oxaliplatin, and irinotecan) and CapeOx (Capecitabine and oxaliplatin). For rectal cancer, chemo with 5-FU or capecitabine combined with radiation may be given before surgery (neoadjuvant treatment).

[0531] In some embodiments, ovarian cancer can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: Topotecan, Liposomal doxorubicin (DOXIL®), Gemcitabine (GEMZAR®), Cyclophosphamide (CYTOXAN®), Vinorelbine (NAVELBINE®), Ifosfamide (IFEX®), Etoposide (VP-16), Altretamine (HEXALEN®), Capecitabine (XELODA®), Irinotecan (CPT-11, CAMPTOSAR®), Melphalan, Pemetrexed (ALIMTA®) and Albumin bound paclitaxel (nab-paclitaxel, ABRAXANE®). Examples of combinations of these drugs which could be further combined with a compound of Formula (I) are TIP (paclitaxel [Taxol], ifosfamide, and cisplatin), VeIP (vinblastine, ifosfamide, and cisplatin) and VIP (etoposide [VP-16], ifosfamide, and cisplatin).

[0532] In some embodiments, a compound of Formula (I) can be used to treat cancer in combination with any of the following methods: (a) Hormone therapy such as aromatase inhibitors, LHRH [luteinizing hormone-releasing hormone] analogs and inhibitors, and others; (b) Ablation or embolization procedures such as radiofrequency ablation (RFA), ethanol (alcohol) ablation, microwave thermotherapy and cryosurgery (cryotherapy); (c) Chemotherapy using alkylating agents such as cisplatin and carboplatin, oxaliplatin, mechlorethamine, cyclophosphamide, chlorambucil and ifosfamide; (d) Chemotherapy using anti-metabolites such as azathioprine and mercaptopurine; (e) Chemotherapy using plant alkaloids and terpenoids such as vinca alkaloids (i.e. Vincristine, Vinblastine, Vinorelbine and Vindesine) and taxanes; (f) Chemotherapy using podophyllotoxin, etoposide, teniposide and docetaxel; (g) Chemotherapy using topoisomerase inhibitors such as irinotecan, topotecan, amsacrine, etoposide, etoposide phosphate, and teniposide; (h) Chemotherapy using cytotoxic antibiotics such as actinomycin, anthracyclines, doxorubicin, daunorubicin, valrubicin, idarubicin, epirubicin, bleomycin, plicamycin and mitomycin; (i) Chemotherapy using tyrosine-kinase inhibitors such as Imatinib mesylate (GLEEVEC®, also known as STI-571), Gefitinib (Iressa, also known as ZD1839), Erlotinib (marketed as TARCEVA®), Bortezomib (VELCADE®), tamoxifen, tofacitinib, crizotinib, Bcl-2 inhibitors (e.g. obatoclax in clinical trials, ABT-263, and Gossypol), PARP inhibitors (e.g. Iniparib, Olaparib in clinical trials), PI3K inhibitors (eg. perifosine in a phase III trial), VEGF Receptor 2 inhibitors (e.g. Apatinib), AN-152, (AEZS-108), Braf inhibitors (e.g. vemurafenib, dabrafenib and LGX818), MEK inhibitors (e.g. trametinib and MEK162), CDK inhibitors, (e.g. PD-0332991), salinomycin and Sorafenib; (j) Chemotherapy using monoclonal antibodies such as Rituximab (marketed as MABTHERA® or RITUXAN®), Trastuzumab (Herceptin also known as ErbB2), Cetuximab (marketed as ERBITUX®), and Bevacizumab (marketed as AVASTIN®); and (k) radiation therapy.

[0533] In some embodiments, diabetic retinopathy can be treated with a combination of a compound of Formula (I) and one or more of the following natural supplements: Bilberry, Butcher's broom, Ginkgo, Grape seed extract, and Pycnogenol (Pine bark).

[0534] In some embodiments, idiopathic pulmonary fibrosis/pulmonary fibrosis can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: pirfenidone (pirfenidone was approved for use in 2011 in Europe under the brand name Esbriet®), prednisone, azathioprine, N-acetylcysteine, interferon-γ 1b, bosentan (bosentan is currently being studied in patients with IPF, [*The American Journal of Respiratory and Critical Care Medicine* (2011), 184(1), 92-9]), Nintedanib (BIBF 1120

and Vargatef), QAX576 [*British Journal of Pharmacology* (2011), 163(1), 141-172], and anti-inflammatory agents such as corticosteroids.

[0535] In some embodiments, a compound of Formula (I) can be used to treat idiopathic pulmonary fibrosis/pulmonary fibrosis in combination with any of the following methods: oxygen therapy, pulmonary rehabilitation and surgery.

[0536] In some embodiments, a compound of Formula (I) can be used to treat osteoarthritis in combination with any of the following methods: (a) Nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, naproxen, aspirin and acetaminophen; (b) physical therapy; (c) injections of corticosteroid medications; (d) injections of hyaluronic acid derivatives (e.g. Hyalgan, Synvisc); (e) narcotics, like codeine; (f) in combination with braces and/or shoe inserts or any device that can immobilize or support your joint to help you keep pressure off it (e.g., splints, braces, shoe inserts or other medical devices); (g) realigning bones (osteotomy); (h) joint replacement (arthroplasty); and (i) in combination with a chronic pain class.

[0537] In some embodiments, macular degeneration can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: Bevacizumab (Avastin®), Ranibizumab (Lucentis®), Pegaptanib (Macugen), Aflibercept (Eylea®), verteporfin (Visudyne®) in combination with photodynamic therapy (PDT) or with any of the following methods: (a) in combination with laser to destroy abnormal blood vessels (photocoagulation); and (b) in combination with increased vitamin intake of antioxidant vitamins and zinc.

[0538] In some embodiments, retinitis pigmentosa can be treated with a combination of a compound of Formula (I) and one or more of the following drugs: UF-021 (Ocuseva™), vitamin A palmitate and pikachurin or with any of the following methods: (a) with the Argus® II retinal implant; and (b) with stem cell and/or gene therapy.

[0539] Administration of the compounds disclosed herein or the pharmaceutically acceptable salts thereof can be via any of the accepted modes of administration, including, but not limited to, orally, subcutaneously, intravenously, intranasally, topically, transdermally, intraperitoneally, intramuscularly, intrapulmonarilly, vaginally, rectally, ontologically, neuro-otologically, intraocularly, subconjuctivally, via anterior eye chamber injection, intravitreally, intraperitoneally, intrathecally, intracystically, intrapleurally, via wound irrigation, intrabuccally, intra-abdominally, intra-articularly, intra-aurally, intrabronchially, intracapsularly, intrameningeally, via inhalation, via endotracheal or endobronchial instillation, via direct instillation into pulmonary cavities, intraspinally, intrasynovially, intrathoracically, via thoracostomy irrigation, epidurally, intratympanically, intracisternally, intravascularly, intraventricularly, intraosseously, via irrigation of infected bone, or via application as part of any admixture with a prosthetic devices. In some embodiments, the administration method includes oral or parenteral administration.

[0540] Compounds provided herein intended for pharmaceutical use may be administered as crystalline or amorphous products. Pharmaceutically acceptable compositions may include solid, semi-solid, liquid, solutions, colloidal, liposomes, emulsions, suspensions, complexes, coacervates and aerosols. Dosage forms, such as, e.g., tablets, capsules, powders, liquids, suspensions, suppositories, aerosols, implants, controlled release or the like. They may be obtained, for example, as solid plugs, powders, or films by methods such as precipitation, crystallization, milling, grinding, supercritical fluid processing, coacervation, complex coacervation, encapsulation, emulsification, complexation, freeze drying, spray drying, or evaporative drying. Microwave or radio frequency drying may be used for this purpose. The compounds can also be administered in sustained or controlled release dosage forms, including depot injections, osmotic pumps, pills (tablets and or capsules), transdermal (including electrotransport) patches, implants and the like, for prolonged and/or timed, pulsed administration at a predetermined rate.

[0541] The compounds can be administered either alone or in combination with a conventional pharmaceutical carrier, excipient or the like. Pharmaceutically acceptable excipients include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, self-emulsifying drug delivery systems (SEDDS) such as d-α-tocopherol polyethylene glycol 1000 succinate, surfactants used in pharmaceutical dosage forms such as Tweens, poloxamers or other similar polymeric delivery matrices, serum proteins, such as human serum albumin, buffer substances such as phosphates, tris, glycine, sorbic acid, potassium sorbate, partial glyceride mixtures of saturated vegetable fatty acids, water, salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium-chloride, zinc salts, colloidal silica, magnesium trisilicate, polyvinyl pyrrolidone, cellulose-based substances, polyethylene glycol, sodium carboxymethyl cellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, and wool fat. Cyclodextrins such as α-, β, and γ-cyclodextrin, or chemically modified derivatives such as hydroxyalkylcyclodextrins, including 2- and 3-hydroxypropyl-β-cyclodextrins, or other solubilized derivatives can also be used to enhance delivery of compounds described herein. Dosage forms or compositions containing a compound as described herein in the range of 0.005% to 100% with the balance made up from non-toxic carrier may be prepared. The contemplated compositions may contain 0.001%-100% of a compound provided herein, in one embodiment 0.1-95%, in another embodiment 75-85%, in a further embodiment 20-80%. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see *Remington: The Science and Practice of Pharmacy,* 22nd Edition (Pharmaceutical Press, London, U K. 2012).

[0542] In one embodiment, the compositions will take the form of a unit dosage form such as a pill or tablet and thus the composition may contain, along with a compound provided herein, a diluent such as lactose, sucrose, dicalcium phosphate, or the like; a lubricant such as magnesium stearate or the like; and a binder such as starch, gum acacia, polyvinylpyrrolidine, gelatin, cellulose, cellulose derivatives or the like. In another solid dosage form, a powder, marume, solution or suspension (e.g., in propylene carbonate, vegetable oils, PEG's, poloxamer 124 or triglycerides) is encapsulated in a capsule (gelatin or cellulose base capsule). Unit dosage forms in which one or more compounds provided herein or additional active agents are physically separated are also contemplated; e.g., capsules with granules (or tablets in a capsule) of each drug; two-layer tablets; two-compartment gel caps, etc. Enteric coated or delayed release oral dosage forms are also contemplated.

[0543] Liquid pharmaceutically administrable compositions can, for example, be prepared by dissolving, dispersing, etc. a compound provided herein and optional pharmaceutical adjuvants in a carrier (e.g., water, saline, aqueous dextrose, glycerol, glycols, ethanol or the like) to form a solution, colloid, liposome, emulsion, complexes, coacervate or suspension. If desired, the pharmaceutical composition can also contain minor amounts of nontoxic auxiliary substances such as wetting agents, emulsifying agents, cosolvents, solubilizing agents, pH buffering agents and the like (e.g., sodium acetate, sodium citrate, cyclodextrin derivatives, sorbitan monolaurate, triethanolamine acetate, triethanolamine oleate, and the like).

[0544] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.25 mg/Kg to about 50 mg/Kg in humans.

[0545] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.25 mg/Kg to about 20 mg/Kg in humans.

[0546] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.50 mg/Kg to about 19 mg/Kg in humans.

[0547] In some embodiments, the unit dosage of compounds of Formula (I) is about 0.75 mg/Kg to about 18 mg/Kg in humans.

[0548] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.0 mg/Kg to about 17 mg/Kg in humans.

[0549] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.25 mg/Kg to about 16 mg/Kg in humans.

[0550] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.50 mg/Kg to about 15 mg/Kg in humans.

[0551] In some embodiments, the unit dosage of compounds of Formula (I) is about 1.75 mg/Kg to about 14 mg/Kg in humans.

[0552] In some embodiments, the unit dosage of compounds of Formula (I) is about 2.0 mg/Kg to about 13 mg/Kg in humans.

[0553] In some embodiments, the unit dosage of compounds of Formula (I) is about 3.0 mg/Kg to about 12 mg/Kg in humans.

[0554] In some embodiments, the unit dosage of compounds of Formula (I) is about 4.0 mg/Kg to about 11 mg/Kg in humans.

[0555] In some embodiments, the unit dosage of compounds of Formula (I) is about 5.0 mg/Kg to about 10 mg/Kg in humans.

[0556] In some embodiments, the compositions are provided in unit dosage forms suitable for single administration.

[0557] In some embodiments, the compositions are provided in unit dosage forms suitable for twice a day administration.

[0558] In some embodiments, the compositions are provided in unit dosage forms suitable for three times a day administration.

[0559] Injectables can be prepared in conventional forms, either as liquid solutions, colloid, liposomes, complexes, coacervate or suspensions, as emulsions, or in solid forms suitable for reconstitution in liquid prior to injection. The percentage of a compound provided herein contained in such parenteral compositions is highly dependent on the specific nature thereof, as well as the activity of the compound and the needs of the patient. However, percentages of active ingredient of 0.01% to 10% in solution are employable, and could be higher if the composition is a solid or suspension, which could be subsequently diluted to the above percentages.

[0560] In some embodiments, the composition will comprise about 0.1-10% of the active agent in solution.

[0561] In some embodiments, the composition will comprise about 0.1-5% of the active agent in solution.

[0562] In some embodiments, the composition will comprise about 0.1-4% of the active agent in solution.

[0563] In some embodiments, the composition will comprise about 0.15-3% of the active agent in solution.

[0564] In some embodiments, the composition will comprise about 0.2-2% of the active agent in solution.

[0565] In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-96 hours.

[0566] In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-72 hours.

[0567] In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-48 hours.

[0568] In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-24 hours.

[0569] In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-12 hours.

[0570] In some embodiments, the compositions are provided in dosage forms suitable for continuous dosage by intravenous infusion over a period of about 1-6 hours.

[0571] In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 5 mg/m^2 to about 300 mg/m^2.

[0572] In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 5 mg/m^2 to about 200 mg/m^2.

[0573] In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 5 mg/m^2 to about 100 mg/m^2.

[0574] In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 10 mg/m^2 to about 50 mg/m^2.

[0575] In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 50 mg/m^2 to about 200 mg/m^2.

[0576] In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 75 mg/m^2 to about 175 mg/m^2.

[0577] In some embodiments, these compositions can be administered by intravenous infusion to humans at doses of about 100 mg/m^2 to about 150 mg/m^2.

[0578] It is to be noted that concentrations and dosage values may also vary depending on the specific compound and the severity of the condition to be alleviated. It is to be further understood that for any particular patient, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

[0579] In one embodiment, the compositions can be administered to the respiratory tract (including nasal and pulmonary) e.g., through a nebulizer, metered-dose inhalers, atomizer, mister, aerosol, dry powder inhaler, insufflator, liquid instillation or other suitable device or technique.

[0580] In some embodiments, aerosols intended for delivery to the nasal mucosa are provided for inhalation through the nose. For optimal delivery to the nasal cavities, inhaled particle sizes of about 5 to about 100 microns are useful, with particle sizes of about 10 to about 60 microns being preferred. For nasal delivery, a larger inhaled particle size may be desired to maximize impaction on the nasal mucosa and to minimize or prevent pulmonary deposition of the administered formulation. In some embodiments, aerosols intended for delivery to the lung are provided for inhalation through the nose or the mouth. For delivery to the lung, inhaled aerodynamic particle sizes of about less than 10 μm are useful (e.g., about 1 to about 10 microns). Inhaled particles may be defined as liquid droplets containing dissolved drug, liquid droplets containing suspended drug particles (in cases where the drug is insoluble in the suspending medium), dry particles of pure drug substance, drug substance incorporated with excipients, liposomes, emulsions, colloidal systems, coacervates, aggregates of drug nanoparticles, or dry particles of a diluent which contain embedded drug nanoparticles.

[0581] In some embodiments, compounds of Formula (I) disclosed herein intended for respiratory delivery (either systemic or local) can be administered as aqueous formulations, as non-aqueous solutions or suspensions, as suspensions or solutions in halogenated hydrocarbon propellants with or without alcohol, as a colloidal system, as emulsions, coacervates, or as dry powders. Aqueous formulations may be aerosolized by liquid nebulizers employing either hydraulic or ultrasonic atomization or by modified micropump systems (like the soft mist inhalers, the Aerodose® or the AERx® systems). Propellant-based systems may use suitable pressurized metered-dose inhalers (pMDIs). Dry powders may use dry powder inhaler devices (DPIs), which are capable of dispersing the drug substance effectively. A desired particle size and distribution may be obtained by choosing an appropriate device.

[0582] In some embodiments, the compositions of Formula (I) disclosed herein can be administered to the ear by various methods. For example, a round window catheter (e.g., U.S. Pat. Nos. 6,440,102 and 6,648,873) can be used.

[0583] Alternatively, formulations can be incorporated into a wick for use between the outer and middle ear (e.g., U.S. Pat. No. 6,120,484) or absorbed to collagen sponge or other solid support (e.g., U.S. Pat. No. 4,164,559).

[0584] If desired, formulations of the invention can be incorporated into a gel formulation (e.g., U.S. Pat. Nos. 4,474,752 and 6,911,211).

[0585] In some embodiments, compounds of Formula (I) disclosed herein intended for delivery to the ear can be administered via an implanted pump and delivery system through a needle directly into the middle or inner ear (cochlea) or through a cochlear implant stylet electrode channel or alternative prepared drug delivery channel such as but not limited to a needle through temporal bone into the cochlea.

[0586] Other options include delivery via a pump through a thin film coated onto a multichannel electrode or electrode with a specially imbedded drug delivery channel (pathways) carved into the thin film for this purpose. In other embodiments the acidic or basic solid compound of Formula (I) can be delivered from the reservoir of an external or internal implanted pumping system.

[0587] Formulations of the invention also can be administered to the ear by intratympanic injection into the middle ear, inner ear, or cochlea (e.g., U.S. Pat. No. 6,377,849 and Ser. No. 11/337,815).

[0588] Intratympanic injection of therapeutic agents is the technique of injecting a therapeutic agent behind the tympanic membrane into the middle and/or inner ear. In one embodiment, the formulations described herein are administered directly onto the round window membrane via transtympanic injection. In another embodiment, the ion channel modulating agent auris-acceptable formulations described herein are administered onto the round window membrane via a non-transtympanic approach to the inner ear. In additional embodiments, the formulation described herein is administered onto the round window membrane via a surgical approach to the round window membrane comprising modification of the crista fenestrae cochleae.

[0589] In some embodiments, the compounds of Formula (I) are formulated in rectal compositions such as enemas, rectal gels, rectal foams, rectal aerosols, suppositories, jelly suppositories, or retention enemas, containing conventional suppository bases such as cocoa butter or other glycerides, as well as synthetic polymers such as polyvinylpyrrolidone, PEG (like PEG ointments), and the like.

[0590] Suppositories for rectal administration of the drug (either as a solution, colloid, suspension or a complex) can be prepared by mixing a compound provided herein with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt or erode/dissolve in the rectum and release the compound. Such materials include cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, poloxamers, mixtures of polyethylene glycols of various molecular weights and fatty acid esters of polyethylene glycol. In suppository forms of the compositions, a low-melting wax such as, but not limited to, a mixture of fatty acid glycerides, optionally in combination with cocoa butter, is first melted.

[0591] Solid compositions can be provided in various different types of dosage forms, depending on the physicochemical properties of the compound provided herein, the desired dissolution rate, cost considerations, and other criteria. In one of the embodiments, the solid composition is a single unit. This implies that one unit dose of the compound is comprised in a single, physically shaped solid form or article. In other words, the solid composition is coherent, which is in contrast to a multiple unit dosage form, in which the units are incoherent.

[0592] Examples of single units which may be used as dosage forms for the solid composition include tablets, such as compressed tablets, film-like units, foil-like units, wafers, lyophilized matrix units, and the like. In one embodiment, the solid composition is a highly porous lyophilized form. Such lyophilizates, sometimes also called wafers or lyophilized tablets, are particularly useful for their rapid disintegration, which also enables the rapid dissolution of the compound.

[0593] On the other hand, for some applications the solid composition may also be formed as a multiple unit dosage form as defined above. Examples of multiple units are powders, granules, microparticles, pellets, mini-tablets,

beads, lyophilized powders, and the like. In one embodiment, the solid composition is a lyophilized powder. Such a dispersed lyophilized system comprises a multitude of powder particles, and due to the lyophilization process used in the formation of the powder, each particle has an irregular, porous microstructure through which the powder is capable of absorbing water very rapidly, resulting in quick dissolution. Effervescent compositions are also contemplated to aid the quick dispersion and absorption of the compound.

[0594] Another type of multiparticulate system which is also capable of achieving rapid drug dissolution is that of powders, granules, or pellets from water-soluble excipients which are coated with a compound provided herein so that the compound is located at the outer surface of the individual particles. In this type of system, the water-soluble low molecular weight excipient may be useful for preparing the cores of such coated particles, which can be subsequently coated with a coating composition comprising the compound and, for example, one or more additional excipients, such as a binder, a pore former, a saccharide, a sugar alcohol, a film-forming polymer, a plasticizer, or other excipients used in pharmaceutical coating compositions.

[0595] Also provided herein are kits. Typically, a kit includes one or more compounds or compositions as described herein. In certain embodiments, a kit can include one or more delivery systems, e.g., for delivering or administering a compound as provided herein, and directions for use of the kit (e.g., instructions for treating a patient). In another embodiment, the kit can include a compound or composition as described herein and a label that indicates that the contents are to be administered to a patient with cancer. In another embodiment, the kit can include a compound or composition as described herein and a label that indicates that the contents are to be administered to a patient with one or more of hepatocellular carcinoma, colon cancer, leukemia, lymphoma, sarcoma, ovarian cancer, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, sepsis, anklyosing spondylitis, psoriasis, scleroderma, mycotic and viral infections, bone and cartilage diseases, Alzheimer's disease, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, articular cartilage (chondral) defects, degenerative disc disease (or intervertebral disc degeneration), polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects and/or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease, and Rett syndrome.

Methods of Treatment

[0596] The compounds and compositions provided herein can be used as inhibitors and/or modulators of one or more components of the Wnt pathway, which may include one or more Wnt proteins, and thus can be used to treat a variety of disorders and diseases in which aberrant Wnt signaling is implicated, such as cancer and other diseases associated with abnormal angiogenesis, cellular proliferation, and cell cycling. Accordingly, the compounds and compositions provided herein can be used to treat cancer, to reduce or inhibit angiogenesis, to reduce or inhibit cellular proliferation, to correct a genetic disorder, and/or to treat a neurological condition/disorder/disease due to mutations or dysregulation of the Wnt pathway and/or of one or more of Wnt signaling components. Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetic retinopathy, pulmonary fibrosis, rheumatoid arthritis, scleroderma, mycotic and viral infections, bone and cartilage diseases, neurological conditions/diseases such as Alzheimer's disease, amyotrophic lateral sclerosis (ALS), motor neuron disease, multiple sclerosis or autism, lung disease, bone/osteoporotic (wrist, spine, shoulder and hip) fractures, polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects and/or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

[0597] In some embodiments, non-limiting examples of eye diseases which can be treated with the compounds and compositions provided herein include age-related macular degeneration (AMD or ARMD), rod cone dystrophy, retinitis pigmentosa (RP), acute idiopathic blind spot enlargement (AIBSE), acute zonal occult outer retinopathy (AZOOR), acute macular neuroretinopathy (AMN), multiple evanescent white dot syndrome (MEWDS), multifocal choroiditis, opticneuropathy. Further causes of photoreceptor damage that can be treated with the compounds and compositions provided herein include retinal detachment, vascular disturbance, eye tumors or extreme light damage.

[0598] With respect to cancer, the Wnt pathway is known to be constitutively activated in a variety of cancers including, for example, colon cancer, hepatocellular carcinoma, lung cancer, ovarian cancer, prostate cancer, pancreatic cancer and leukemias such as CML, CLL and T-ALL. Accordingly, the compounds and compositions described herein may be used to treat these cancers in which the Wnt pathway is constitutively activated. In certain embodiments, the cancer is chosen from hepatocellular carcinoma, colon cancer, leukemia, lymphoma, sarcoma and ovarian cancer.

[0599] Other cancers can also be treated with the compounds and compositions described herein.

[0600] More particularly, cancers that may be treated by the compounds, compositions and methods described herein include, but are not limited to, the following:

[0601] 1) Breast cancers, including, for example ER^+ breast cancer, ER^- breast cancer, $her2^-$ breast cancer, $her2^+$ breast cancer, stromal tumors such as fibroadenomas, phyllodes tumors, and sarcomas, and epithelial tumors such as

large duct papillomas; carcinomas of the breast including in situ (noninvasive) carcinoma that includes ductal carcinoma in situ (including Paget's disease) and lobular carcinoma in situ, and invasive (infiltrating) carcinoma including, but not limited to, invasive ductal carcinoma, invasive lobular carcinoma, medullary carcinoma, colloid (mucinous) carcinoma, tubular carcinoma, and invasive papillary carcinoma; and miscellaneous malignant neoplasms. Further examples of breast cancers can include luminal A, luminal B, basal A, basal B, and triple negative breast cancer, which is estrogen receptor negative (ER^-), progesterone receptor negative, and her2 negative ($her2^-$). In some embodiments, the breast cancer may have a high risk Oncotype score.

[0602] 2) Cardiac cancers, including, for example sarcoma, e.g., angiosarcoma, fibrosarcoma, rhabdomyosarcoma, and liposarcoma; myxoma; rhabdomyoma; fibroma; lipoma and teratoma.

[0603] 3) Lung cancers, including, for example, bronchogenic carcinoma, e.g., squamous cell, undifferentiated small cell, undifferentiated large cell, and adenocarcinoma; alveolar and bronchiolar carcinoma; bronchial adenoma; sarcoma; lymphoma; chondromatous hamartoma; and mesothelioma.

[0604] 4) Gastrointestinal cancer, including, for example, cancers of the esophagus, e.g., squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, and lymphoma; cancers of the stomach, e.g., carcinoma, lymphoma, and leiomyosarcoma; cancers of the pancreas, e.g., ductal adenocarcinoma, insulinoma, glucagonoma, gastrinoma, carcinoid tumors, and vipoma; cancers of the small bowel, e.g., adenocarcinoma, lymphoma, carcinoid tumors, Kaposi's sarcoma, leiomyoma, hemangioma, lipoma, neurofibroma, and fibroma; cancers of the large bowel, e.g., adenocarcinoma, tubular adenoma, villous adenoma, hamartoma, and leiomyoma.

[0605] 5) Genitourinary tract cancers, including, for example, cancers of the kidney, e.g., adenocarcinoma, Wilm's tumor (nephroblastoma), lymphoma, and leukemia; cancers of the bladder and urethra, e.g., squamous cell carcinoma, transitional cell carcinoma, and adenocarcinoma; cancers of the prostate, e.g., adenocarcinoma, and sarcoma; cancer of the testis, e.g., seminoma, teratoma, embryonal carcinoma, teratocarcinoma, choriocarcinoma, sarcoma, interstitial cell carcinoma, fibroma, fibroadenoma, adenomatoid tumors, and lipoma.

[0606] 6) Liver cancers, including, for example, hepatoma, e.g., hepatocellular carcinoma; cholangiocarcinoma; hepatoblastoma; angiosarcoma; hepatocellular adenoma; and hemangioma.

[0607] 7) Bone cancers, including, for example, osteogenic sarcoma (osteosarcoma), fibrosarcoma, malignant fibrous histiocytoma, chondrosarcoma, Ewing's sarcoma, malignant lymphoma (reticulum cell sarcoma), multiple myeloma, malignant giant cell tumor chordoma, osteochrondroma (osteocartilaginous exostoses), benign chondroma, chondroblastoma, chondromyxofibroma, osteoid osteoma and giant cell tumors.

[0608] 8) Nervous system cancers, including, for example, cancers of the skull, e.g., osteoma, hemangioma, granuloma, xanthoma, and osteitis deformans; cancers of the meninges, e.g., meningioma, meningiosarcoma, and gliomatosis; cancers of the brain, e.g., astrocytoma, medulloblastoma, glioma, ependymoma, germinoma (pinealoma), glioblastoma multiform, oligodendroglioma, schwannoma, retinoblastoma, and congenital tumors; and cancers of the spinal cord, e.g., neurofibroma, meningioma, glioma, and sarcoma.

[0609] 9) Gynecological cancers, including, for example, cancers of the uterus, e.g., endometrial carcinoma; cancers of the cervix, e.g., cervical carcinoma, and pre tumor cervical dysplasia; cancers of the ovaries, e.g., ovarian carcinoma, including serous cystadenocarcinoma, mucinous cystadenocarcinoma, unclassified carcinoma, granulosa theca cell tumors, Sertoli Leydig cell tumors, dysgerminoma, and malignant teratoma; cancers of the vulva, e.g., squamous cell carcinoma, intraepithelial carcinoma, adenocarcinoma, fibrosarcoma, and melanoma; cancers of the vagina, e.g., clear cell carcinoma, squamous cell carcinoma, botryoid sarcoma, and embryonal rhabdomyosarcoma; and cancers of the fallopian tubes, e.g., carcinoma.

[0610] 10) Hematologic cancers, including, for example, cancers of the blood, e.g., acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, and myelodysplastic syndrome, Hodgkin's lymphoma, non-Hodgkin's lymphoma (malignant lymphoma) and Waldenstrom's macroglobulinemia.

[0611] 11) Skin cancers and skin disorders, including, for example, malignant melanoma and metastatic melanoma, basal cell carcinoma, squamous cell carcinoma, Kaposi's sarcoma, moles dysplastic nevi, lipoma, angioma, dermatofibroma, keloids, and scleroderma.

[0612] 12) Adrenal gland cancers, including, for example, neuroblastoma.

[0613] Cancers may be solid tumors that may or may not be metastatic. Cancers may also occur, as in leukemia, as a diffuse tissue. Thus, the term "tumor cell," as provided herein, includes a cell afflicted by any one of the above identified disorders.

[0614] A method of treating cancer using a compound or composition as described herein may be combined with existing methods of treating cancers, for example by chemotherapy, irradiation, or surgery (e.g., oophorectomy). In some embodiments, a compound or composition can be administered before, during, or after another anticancer agent or treatment.

[0615] The compounds and compositions described herein can be used as anti-angiogenesis agents and as agents for modulating and/or inhibiting the activity of protein kinases, thus providing treatments for cancer and other diseases associated with cellular proliferation mediated by protein kinases. For example, the compounds described herein can inhibit the activity of one or more kinases. Accordingly, provided herein is a method of treating cancer or preventing or reducing angiogenesis through kinase inhibition.

[0616] In addition, and including treatment of cancer, the compounds and compositions described herein can function as cell-cycle control agents for treating proliferative disorders in a patient. Disorders associated with excessive proliferation include, for example, cancers, scleroderma, immunological disorders involving undesired proliferation of leukocytes, and restenosis and other smooth muscle disorders. Furthermore, such compounds may be used to prevent de-differentiation of post-mitotic tissue and/or cells.

[0617] Diseases or disorders associated with uncontrolled or abnormal cellular proliferation include, but are not limited to, the following:

[0618] a variety of cancers, including, but not limited to, carcinoma, hematopoietic tumors of lymphoid lin-

eage, hematopoietic tumors of myeloid lineage, tumors of mesenchymal origin, tumors of the central and peripheral nervous system and other tumors including melanoma, seminoma and Kaposi's sarcoma.

[0619] a disease process which features abnormal cellular proliferation, e.g., benign prostatic hyperplasia, familial adenomatosis polyposis, neurofibromatosis, atherosclerosis, arthritis, glomerulonephritis, restenosis following angioplasty or vascular surgery, inflammatory bowel disease, transplantation rejection, endotoxic shock, and fungal infections. Fibrotic disorders such as skin fibrosis; scleroderma; progressive systemic fibrosis; lung fibrosis; muscle fibrosis; kidney fibrosis; glomerulosclerosis; glomerulonephritis; hypertrophic scar formation; uterine fibrosis; renal fibrosis; cirrhosis of the liver, liver fibrosis; fatty liver disease (FLD); adhesions, such as those occurring in the abdomen, pelvis, spine or tendons; chronic obstructive pulmonary disease; fibrosis following myocardial infarction; pulmonary fibrosis; fibrosis and scarring associated with diffuse/interstitial lung disease; central nervous system fibrosis, such as fibrosis following stroke; fibrosis associated with neuro-degenerative disorders such as Alzheimer's Disease or multiple sclerosis; fibrosis associated with proliferative vitreoretinopathy (PVR); restenosis; endometriosis; ischemic disease and radiation fibrosis.

[0620] defective apoptosis-associated conditions, such as cancers (including but not limited to those types mentioned herein), viral infections (including but not limited to herpesvirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus), prevention of AIDS development in HIV-infected individuals, autoimmune diseases (including but not limited to systemic lupus erythematosus, rheumatoid arthritis, sepsis, anklyosing spondylitis, psoriasis, scleroderma, autoimmune mediated glomerulonephritis, inflammatory bowel disease and autoimmune diabetes mellitus), neuro-degenerative disorders (including but not limited to Alzheimer's disease, lung disease, amyotrophic lateral sclerosis, retinitis pigmentosa, Parkinson's disease, AIDS-related dementia, spinal muscular atrophy and cerebellar degeneration), myelodysplastic syndromes, aplastic anemia, ischemic injury associated with myocardial infarctions, stroke and reperfusion injury, arrhythmia, atherosclerosis, toxin-induced or alcohol related liver diseases, hematological diseases (including but not limited to chronic anemia and aplastic anemia), degenerative diseases of the musculoskeletal system (including but not limited to osteoporosis and arthritis), tendinopathies such as tendinitis and tendinosis, aspirin-sensitive rhinosinusitis, cystic fibrosis, multiple sclerosis, kidney diseases and cancer pain.

[0621] genetic diseases due to mutations in Wnt signaling components, such as polyposis coli, bone density and vascular defects in the eye (Osteoporosis-pseudoglioma Syndrome, OPPG) and other eye diseases or syndromes associated with defects and/or damaged photoreceptors, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia, Müllerian-duct regression and virilization, SERKAL syndrome, type II diabetes, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman's syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

[0622] The compounds and compositions described herein can be used to treat neurological conditions, disorders and/or diseases caused by dysfunction in the Wnt signaling pathway. Non-limiting examples of neurological conditions/disorders/diseases which can be treated with the compounds and compositions provided herein include Alzheimer's disease, aphasia, apraxia, arachnoiditis, ataxia telangiectasia, attention deficit hyperactivity disorder, auditory processing disorder, autism, alcoholism, Bell's palsy, bipolar disorder, brachial plexus injury, Canavan disease, carpal tunnel syndrome, causalgia, central pain syndrome, central pontine myelinolysis, centronuclear myopathy, cephalic disorder, cerebral aneurysm, cerebral arteriosclerosis, cerebral atrophy, cerebral gigantism, cerebral palsy, cerebral vasculitis, cervical spinal stenosis, Charcot-Marie-Tooth disease, Chiari malformation, chronic fatigue syndrome, chronic inflammatory demyelinating polyneuropathy (CIDP), chronic pain, Coffin-Lowry syndrome, complex regional pain syndrome, compression neuropathy, congenital facial diplegia, corticobasal degeneration, cranial arteritis, craniosynostosis, Creutzfeldt-Jakob disease, cumulative trauma disorder, Cushing's syndrome, cytomegalic inclusion body disease (CIBD), Dandy-Walker syndrome, Dawson disease, de Morsier's syndrome, Dejerine-Klumpke palsy, Dejerine-Sottas disease, delayed sleep phase syndrome, dementia, dermatomyositis, developmental dyspraxia, diabetic neuropathy, diffuse sclerosis, Dravet syndrome, dysautonomia, dyscalculia, dysgraphia, dyslexia, dystonia, empty sella syndrome, encephalitis, encephalocele, encephalotrigeminal angiomatosis, encopresis, epilepsy, Erb's palsy, erythromelalgia, essential tremor, Fabry's disease, Fahr's syndrome, familial spastic paralysis, febrile seizure, Fisher syndrome, Friedreich's ataxia, fibromyalgia, Foville's syndrome, Gaucher's disease, Gerstmann's syndrome, giant cell arteritis, giant cell inclusion disease, globoid cell leukodystrophy, gray matter heterotopia, Guillain-Barre syndrome, HTLV-1 associated myelopathy, Hallervorden-Spatz disease, hemifacial spasm, hereditary spastic paraplegia, heredopathia atactica polyneuritiformis, herpes zoster oticus, herpes zoster, Hirayama syndrome, holoprosencephaly, Huntington's disease, hydranencephaly, hydrocephalus, hypercortisolism, hypoxia, immune-mediated encephalomyelitis, inclusion body myositis, incontinentia pigmenti, infantile phytanic acid storage disease, infantile Refsum disease, infantile spasms, inflammatory myopathy, intracranial cyst, intracranial hypertension, Joubert syndrome, Karak syndrome, Kearns-Sayre syndrome, Kennedy disease, Kinsbourne syndrome, Klippel Feil syndrome, Krabbe disease, Kugelberg-Welander disease, kuru, Lafora disease, Lambert-Eaton myasthenic syndrome, Landau-Kleffner syndrome, lateral medullary (Wallenberg) syndrome, Leigh's disease, Lennox-Gastaut syndrome, Lesch-Nyhan syndrome, leukodystrophy, Lewy body dementia, lissencephaly, locked-in syndrome, Lou Gehrig's disease, lumbar disc disease, lumbar spinal stenosis, Lyme disease, Machado-Joseph disease (Spinocerebellar ataxia type 3), macrenceph-

aly, macropsia, megalencephaly, Melkersson-Rosenthal syndrome, Meniere's disease, meningitis, Menkes disease, metachromatic leukodystrophy, microcephaly, micropsia, Miller Fisher syndrome, misophonia, mitochondrial myopathy, Mobius syndrome, monomelic amyotrophy, motor neuron disease, motor skills disorder, Moyamoya disease, mucopolysaccharidoses, multi-infarct dementia, multifocal motor neuropathy, multiple sclerosis, multiple system atrophy, muscular dystrophy, myalgic encephalomyelitis, myasthenia gravis, myelinoclastic diffuse sclerosis, myoclonic Encephalopathy of infants, myoclonus, myopathy, myotubular myopathy, myotonia congenital, narcolepsy, neurofibromatosis, neuroleptic malignant syndrome, lupus erythematosus, neuromyotonia, neuronal ceroid lipofuscinosis, Niemann-Pick disease, O'Sullivan-McLeod syndrome, occipital Neuralgia, occult Spinal Dysraphism Sequence, Ohtahara syndrome, olivopontocerebellar atrophy, opsoclonus myoclonus syndrome, optic neuritis, orthostatic hypotension, palinopsia, paresthesia, Parkinson's disease, paramyotonia Congenita, paraneoplastic diseases, paroxysmal attacks, Parry-Romberg syndrome, Pelizaeus-Merzbacher disease, periodic paralyses, peripheral neuropathy, photic sneeze reflex, phytanic acid storage disease, Pick's disease, polymicrogyria (PMG), polymyositis, porencephaly, post-polio syndrome, postherpetic neuralgia (PHN), postural hypotension, Prader-Willi syndrome, primary lateral sclerosis, prion diseases, progressive hemifacial atrophy, progressive multifocal leukoencephalopathy, progressive supranuclear palsy, pseudotumor cerebri, Ramsay Hunt syndrome type I, Ramsay Hunt syndrome type II, Ramsay Hunt syndrome type III, Rasmussen's encephalitis, reflex neurovascular dystrophy, Refsum disease, restless legs syndrome, retrovirus-associated myelopathy, Rett syndrome, Reye's syndrome, rhythmic movement disorder, Romberg syndrome, Saint Vitus dance, Sandhoff disease, schizophrenia, Schilder's disease, schizencephaly, sensory integration dysfunction, septo-optic dysplasia, Shy-Drager syndrome, Sjögren's syndrome, snatiation, Sotos syndrome, spasticity, spina bifida, spinal cord tumors, spinal muscular atrophy, spinocerebellar ataxia, Steele-Richardson-Olszewski syndrome, Stiff-person syndrome, stroke, Sturge-Weber syndrome, subacute sclerosing panencephalitis, subcortical arteriosclerotic encephalopathy, superficial siderosis, Sydenham's chorea, syncope, synesthesia, syringomyelia, tarsal tunnel syndrome, tardive dyskinesia, tardive dysphrenia, Tarlov cyst, Tay-Sachs disease, temporal arteritis, tetanus, tethered spinal cord syndrome, Thomsen disease, thoracic outlet syndrome, tic douloureux, Todd's paralysis, Tourette syndrome, toxic encephalopathy, transient ischemic attack, transmissible spongiform encephalopathies, transverse myelitis, tremor, trigeminal neuralgia, tropical spastic paraparesis, trypanosomiasis, tuberous sclerosis, ubisiosis, Von Hippel-Lindau disease (VHL), Viliuisk Encephalomyelitis (VE), Wallenberg's syndrome, Werdnig, Hoffman disease, west syndrome, Williams syndrome, Wilson's disease and Zellweger syndrome.

[0623] The compounds and compositions may also be useful in the inhibition of the development of invasive cancer, tumor angiogenesis and metastasis.

[0624] In some embodiments, the disclosure provides a method for treating a disease or disorder associated with aberrant cellular proliferation by administering to a patient in need of such treatment an effective amount of one or more of the compounds of Formula (I), in combination (simultaneously or sequentially) with at least one other agent.

[0625] In some embodiments, the disclosure provides a method of treating or ameliorating in a patient a disorder or disease selected from the group consisting of: cancer, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), degenerative disc disease, bone/osteoporotic fractures, bone or cartilage disease, and osteoarthritis, the method comprising administering to the patient a therapeutically effective amount of a compound according to claim **1**, or a pharmaceutically acceptable salt thereof.

[0626] In some embodiments, the pharmaceutical composition comprises a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

[0627] In some embodiments, the method of treats a disorder or disease in which aberrant Wnt signaling is implicated in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound of Formula (I), or a pharmaceutically acceptable salt thereof.

[0628] In some embodiments, the disorder or disease is cancer.

[0629] In some embodiments, the disorder or disease is systemic inflammation.

[0630] In some embodiments, the disorder or disease is metastatic melanoma.

[0631] In some embodiments, the disorder or disease is fatty liver disease.

[0632] In some embodiments, the disorder or disease is liver fibrosis.

[0633] In some embodiments, the disorder or disease is tendonitis.

[0634] In some embodiments, the disorder or disease is damage to a tendon requiring tendon regeneration.

[0635] In some embodiments, the disorder or disease is diabetes.

[0636] In some embodiments, the disorder or disease is degenerative disc disease.

[0637] In some embodiments, the disorder or disease is osteoarthritis.

[0638] In some embodiments, the disorder or disease is diabetic retinopathy.

[0639] In some embodiments, the disorder or disease is pulmonary fibrosis.

[0640] In some embodiments, the disorder or disease is idiopathic pulmonary fibrosis (IPF).

[0641] In some embodiments, the disorder or disease is degenerative disc disease.

[0642] In some embodiments, the disorder or disease is rheumatoid arthritis.

[0643] In some embodiments, the disorder or disease is scleroderma.

[0644] In some embodiments, the disorder or disease is a mycotic or viral infection.

[0645] In some embodiments, the disorder or disease is a bone or cartilage disease.

[0646] In some embodiments, the disorder or disease is Alzheimer's disease.

[0647] In some embodiments, the disorder or disease is osteoarthritis.

[0648] In some embodiments, the disorder or disease is lung disease

[0649] In some embodiments, the disorder or disease is a genetic disease caused by mutations in Wnt signaling components, wherein the genetic disease is selected from: polyposis coli, osteoporosis-pseudoglioma syndrome, familial exudative vitreoretinopathy, retinal angiogenesis, early coronary disease, tetra-amelia syndrome, Müllerian-duct regression and virilization, SERKAL syndrome, diabetes mellitus type 2, Fuhrmann syndrome, Al-Awadi/Raas-Rothschild/Schinzel phocomelia syndrome, odonto-onycho-dermal dysplasia, obesity, split-hand/foot malformation, caudal duplication syndrome, tooth agenesis, Wilms tumor, skeletal dysplasia, focal dermal hypoplasia, autosomal recessive anonychia, neural tube defects, alpha-thalassemia (ATRX) syndrome, fragile X syndrome, ICF syndrome, Angelman syndrome, Prader-Willi syndrome, Beckwith-Wiedemann Syndrome, Norrie disease and Rett syndrome.

[0650] In some embodiments, the patient is a human.

[0651] In some embodiments, the cancer is chosen from: hepatocellular carcinoma, colon cancer, breast cancer, pancreatic cancer, chronic myeloid leukemia (CML), chronic myelomonocytic leukemia, chronic lymphocytic leukemia (CLL), acute myeloid leukemia, acute lymphocytic leukemia, Hodgkin lymphoma, lymphoma, sarcoma and ovarian cancer.

[0652] In some embodiments, the cancer is chosen from: lung cancer—non-small cell, lung cancer—small cell, multiple myeloma, nasopharyngeal cancer, neuroblastoma, osteosarcoma, penile cancer, pituitary tumors, prostate cancer, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, skin cancer—basal and squamous cell, skin cancer—melanoma, small intestine cancer, stomach (gastric) cancers, testicular cancer, thymus cancer, thyroid cancer, uterine sarcoma, vaginal cancer, vulvar cancer, laryngeal or hypopharyngeal cancer, kidney cancer, Kaposi sarcoma, gestational trophoblastic disease, gastrointestinal stromal tumor, gastrointestinal carcinoid tumor, gallbladder cancer, eye cancer (melanoma and lymphoma), Ewing tumor, esophagus cancer, endometrial cancer, colorectal cancer, cervical cancer, brain or spinal cord tumor, bone metastasis, bone cancer, bladder cancer, bile duct cancer, anal cancer and adrenal cortical cancer.

[0653] In some embodiments, the cancer is hepatocellular carcinoma.

[0654] In some embodiments, the cancer is colon cancer.

[0655] In some embodiments, the cancer is colorectal cancer.

[0656] In some embodiments, the cancer is breast cancer.

[0657] In some embodiments, the cancer is pancreatic cancer.

[0658] In some embodiments, the cancer is chronic myeloid leukemia (CML).

[0659] In some embodiments, the cancer is chronic myelomonocytic leukemia.

[0660] In some embodiments, the cancer is chronic lymphocytic leukemia (CLL).

[0661] In some embodiments, the cancer is acute myeloid leukemia.

[0662] In some embodiments, the cancer is acute lymphocytic leukemia.

[0663] In some embodiments, the cancer is Hodgkin lymphoma.

[0664] In some embodiments, the cancer is lymphoma.

[0665] In some embodiments, the cancer is sarcoma.

[0666] In some embodiments, the cancer is ovarian cancer.

[0667] In some embodiments, the cancer is lung cancer—non-small cell.

[0668] In some embodiments, the cancer is lung cancer—small cell.

[0669] In some embodiments, the cancer is multiple myeloma.

[0670] In some embodiments, the cancer is nasopharyngeal cancer.

[0671] In some embodiments, the cancer is neuroblastoma.

[0672] In some embodiments, the cancer is osteosarcoma.

[0673] In some embodiments, the cancer is penile cancer.

[0674] In some embodiments, the cancer is pituitary tumors.

[0675] In some embodiments, the cancer is prostate cancer.

[0676] In some embodiments, the cancer is retinoblastoma.

[0677] In some embodiments, the cancer is rhabdomyosarcoma.

[0678] In some embodiments, the cancer is salivary gland cancer.

[0679] In some embodiments, the cancer is skin cancer—basal and squamous cell.

[0680] In some embodiments, the cancer is skin cancer—melanoma.

[0681] In some embodiments, the cancer is small intestine cancer.

[0682] In some embodiments, the cancer is stomach (gastric) cancers.

[0683] In some embodiments, the cancer is testicular cancer.

[0684] In some embodiments, the cancer is thymus cancer.

[0685] In some embodiments, the cancer is thyroid cancer.

[0686] In some embodiments, the cancer is uterine sarcoma.

[0687] In some embodiments, the cancer is vaginal cancer.

[0688] In some embodiments, the cancer is vulvar cancer.

[0689] In some embodiments, the cancer is Wilms tumor.

[0690] In some embodiments, the cancer is laryngeal or hypopharyngeal cancer.

[0691] In some embodiments, the cancer is kidney cancer.

[0692] In some embodiments, the cancer is Kaposi sarcoma.

[0693] In some embodiments, the cancer is gestational trophoblastic disease.

[0694] In some embodiments, the cancer is gastrointestinal stromal tumor.

[0695] In some embodiments, the cancer is gastrointestinal carcinoid tumor.

[0696] In some embodiments, the cancer is gallbladder cancer.

[0697] In some embodiments, the cancer is eye cancer (melanoma and lymphoma).

[0698] In some embodiments, the cancer is Ewing tumor.

[0699] In some embodiments, the cancer is esophagus cancer.

[0700] In some embodiments, the cancer is endometrial cancer.

[0701] In some embodiments, the cancer is colorectal cancer.

[0702] In some embodiments, the cancer is cervical cancer.

[0703] In some embodiments, the cancer is brain or spinal cord tumor.

[0704] In some embodiments, the cancer is bone metastasis.

[0705] In some embodiments, the cancer is bone cancer.

[0706] In some embodiments, the cancer is bladder cancer.

[0707] In some embodiments, the cancer is bile duct cancer.

[0708] In some embodiments, the cancer is anal cancer.

[0709] In some embodiments, the cancer is adrenal cortical cancer.

[0710] In some embodiments, the disorder or disease is a neurological condition, disorder or disease, wherein the neurological condition/disorder/disease is selected from: Alzheimer's disease, frontotemporal dementias, dementia with lewy bodies, prion diseases, Parkinson's disease, Huntington's disease, progressive supranuclear palsy, corticobasal degeneration, multiple system atrophy, amyotrophic lateral sclerosis (ALS), inclusion body myositis, autism, degenerative myopathies, diabetic neuropathy, other metabolic neuropathies, endocrine neuropathies, orthostatic hypotension, multiple sclerosis and Charcot-Marie-Tooth disease.

[0711] In some embodiments, the compound of Formula (I) inhibits one or more proteins in the Wnt pathway.

[0712] In some embodiments, the compound of Formula (I) inhibits signaling induced by one or more Wnt proteins.

[0713] In some embodiments, the Wnt proteins are chosen from: WNT1, WNT2, WNT2B, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, and WNT16.

[0714] In some embodiments, the method inhibits one or more proteins in the Wnt pathway, the method comprises contacting a cell with an effective amount of a compound of Formula (I).

[0715] In some embodiments, the cell is a human cell.

[0716] In some embodiments, the human cell is a cancerous cell.

[0717] In some embodiments, the cancerous cell is a colon cancer cell.

[0718] In some embodiments, the contacting is in vitro.

[0719] In some embodiments, the compound of Formula (I) inhibits a kinase activity.

[0720] In some embodiments, the method treats a disease or disorder mediated by the Wnt pathway in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

[0721] In some embodiments, the compound of Formula (I) inhibits one or more Wnt proteins.

[0722] In some embodiments, the method treats a disease or disorder mediated by kinase activity in a patient, the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

[0723] In some embodiments, the disease or disorder comprises tumor growth, cell proliferation, or angiogenesis.

[0724] In some embodiments, the method inhibits the activity of a protein kinase receptor, the method comprises contacting the receptor with an effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

[0725] In some embodiments, the method treats a disease or disorder associated with aberrant cellular proliferation in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

[0726] In some embodiments, the method prevents or reduces angiogenesis in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

[0727] In some embodiments, the method prevents or reduces abnormal cellular proliferation in a patient; the method comprises administering to the patient a therapeutically effective amount of a compound (or compounds) of Formula (I), or a pharmaceutically acceptable salt thereof.

[0728] In some embodiments, the method treats a disease or disorder associated with aberrant cellular proliferation in a patient, the method comprises administering to the patient a pharmaceutical composition comprising one or more of the compounds of claim **1** in combination with a pharmaceutically acceptable carrier and one or more other agents.

[0729] Moreover, the compounds and compositions, for example, as inhibitors of the cyclin-dependent kinases (CDKs), can modulate the level of cellular RNA and DNA synthesis and therefore are expected to be useful in the treatment of viral infections such as HIV, human papilloma virus, herpes virus, Epstein-Barr virus, adenovirus, Sindbis virus, pox virus and the like.

[0730] Compounds and compositions described herein can inhibit the kinase activity of, for example, CDK/cyclin complexes, such as those active in the G_0. or G_1 stage of the cell cycle, e.g., CDK2, CDK4, and/or CDK6 complexes.

Evaluation of Biological Activity

[0731] The biological activity of the compounds described herein can be tested using any suitable assay known to those of skill in the art, see, e.g., WO 2001/053268 and WO 2005/009997. For example, the activity of a compound may be tested using one or more of the test methods outlined below.

[0732] In one example, tumor cells may be screened for Wnt independent growth. In such a method, tumor cells of interest are contacted with a compound (i.e. inhibitor) of interest, and the proliferation of the cells, e.g. by uptake of tritiated thymidine, is monitored. In some embodiments, tumor cells may be isolated from a candidate patient who has been screened for the presence of a cancer that is associated with a mutation in the Wnt signaling pathway. Candidate cancers include, without limitation, those listed above.

[0733] In another example, one may utilize in vitro assays for Wnt biological activity, e.g. stabilization of β-catenin and promoting growth of stem cells. Assays for biological activity of Wnt include stabilization of β-catenin, which can be measured, for example, by serial dilutions of a candidate inhibitor composition. An exemplary assay for Wnt biological activity contacts a candidate inhibitor with cells containing constitutively active Wnt/β-catenin signaling. The cells are cultured for a period of time sufficient to stabilize β-catenin, usually at least about 1 hour, and lysed. The cell lysate is resolved by SDS PAGE, then transferred to nitrocellulose and probed with antibodies specific for β-catenin.

[0734] In a further example, the activity of a candidate compound can be measured in a *Xenopus* secondary axis bioassay (Leyns, L. et al. *Cell* (1997), 88(6), 747-756).

[0735] To further illustrate this invention, the following examples are included. The examples should not, of course, be construed as specifically limiting the invention. Variations of these examples within the scope of the claims are within the purview of one skilled in the art and are considered to fall within the scope of the invention as described, and claimed herein. The reader will recognize that the skilled artisan, armed with the present disclosure, and skill in the art is able to prepare and use the invention without exhaustive examples.

EXAMPLES

Compound Preparation

[0736] The starting materials used in preparing the compounds of the invention are known, made by known methods, or are commercially available. It will be apparent to the skilled artisan that methods for preparing precursors and functionality related to the compounds claimed herein are generally described in the literature. The skilled artisan given the literature and this disclosure is well equipped to prepare any of the compounds.

[0737] It is recognized that the skilled artisan in the art of organic chemistry can readily carry out manipulations without further direction, that is, it is well within the scope and practice of the skilled artisan to carry out these manipulations. These include reduction of carbonyl compounds to their corresponding alcohols, oxidations, acylations, aromatic substitutions, both electrophilic and nucleophilic, etherifications, esterification and saponification and the like. These manipulations are discussed in standard texts such as *March's Advanced Organic Chemistry*: Reactions, Mechanisms, and Structure 7th Ed., John Wiley & Sons (2013), Carey and Sundberg, *Advanced Organic Chemistry* 5th Ed., Springer (2007), *Comprehensive Organic Transformations: A Guide to Functional Group Transformations,* 2nd Ed., John Wiley & Sons (1999) (incorporated herein by reference in its entirety) and the like.

[0738] The skilled artisan will readily appreciate that certain reactions are best carried out when other functionality is masked or protected in the molecule, thus avoiding any undesirable side reactions and/or increasing the yield of the reaction. Often the skilled artisan utilizes protecting groups to accomplish such increased yields or to avoid the undesired reactions. These reactions are found in the literature and are also well within the scope of the skilled artisan. Examples of many of these manipulations can be found for example in T. Greene and P. Wuts *Protective Groups in Organic Synthesis,* 4th Ed., John Wiley & Sons (2007), incorporated herein by reference in its entirety.

[0739] Trademarks used herein are examples only and reflect illustrative materials used at the time of the invention. The skilled artisan will recognize that variations in lot, manufacturing processes, and the like, are expected. Hence the examples, and the trademarks used in them are non-limiting, and they are not intended to be limiting, but are merely an illustration of how a skilled artisan may choose to perform one or more of the embodiments of the invention.

[0740] (^{1}H) nuclear magnetic resonance spectra (NMR) were measured in the indicated solvents on a Bruker NMR spectrometer (Avance TM DRX300, 300 MHz for ^{1}H or Avance™ DRX500, 500 MHz for ^{1}H) or Varian NMR spectrometer (Mercury 400BB, 400 MHz for ^{1}H). Peak positions are expressed in parts per million (ppm) downfield from tetramethylsilane. The peak multiplicities are denoted as follows, s, singlet; d, doublet; t, triplet; q, quartet; ABq, AB quartet; quin, quintet; sex, sextet; sep, septet; non, nonet; dd, doublet of doublets; ddd, doublet of doublets of doublets; d/ABq, doublet of AB quartet; dt, doublet of triplets; td, triplet of doublets; dq, doublet of quartets; m, multiplet.

[0741] The following abbreviations have the indicated meanings:

[0742] BH_3-Me_2S=borane dimethyl sulfide complex

[0743] $(Boc)_2O$=di-tert-butyl dicarbonate

[0744] brine=saturated aqueous sodium chloride

[0745] $CDCl_3$=deuterated chloroform

[0746] CD_3OD=deuterated methanol

[0747] DCAD=di-(4-chlorobenzyl)azodicarboxylate

[0748] DCE=dichloroethane

[0749] DCM=dichloromethane

[0750] DEAD=diethyl azodicarboxylate

[0751] DHP=dihydropyran

[0752] DMAP=4-dimethylaminopyridine

[0753] DMF=N,N-dimethylformamide

[0754] DMSO-d_6=deuterated dimethylsulfoxide

[0755] ESIMS=electron spray mass spectrometry

[0756] EtOAc=ethyl acetate

[0757] EtOH=ethanol

[0758] HCl=hydrochloric acid

[0759] HOAc=acetic acid

[0760] K_2CO_3=potassium carbonate

[0761] KOAc=potassium acetate

[0762] LC/MS=liquid chromatography-mass spectrometry

[0763] MeOH=methanol

[0764] $MgSO_4$=magnesium sulfate

[0765] MsCl=methanesulfonyl chloride or mesyl chloride

[0766] MW=microwave

[0767] $NaBH_4$=sodium borohydride

[0768] $NaBH(OAc)_3$=sodium triacetoxyborohydride

[0769] $NaCNBH_3$=sodium cyanoborohydride

[0770] $NaHCO_3$=sodium bicarbonate

[0771] NaOH=sodium hydroxide

[0772] $Na_2S_2O_5$=sodium metabisulfite or sodium pyrosulfite

[0773] NBS=N-bromosuccinimide

[0774] NH_4OH=ammonium hydroxide

[0775] NMR=nuclear magnetic resonance

[0776] ON=overnight

[0777] Pd/C=palladium(0) on carbon

[0778] $Pd(dppf)Cl_2$=1,1'-bis(diphenylphosphino)ferrocene]palladium(II) chloride

[0779] $Pd(PPh_3)_4$=tetrakis(triphenylphosphine)palladium (0)

[0780] $Pd(PPh_3)_2Cl_2$=bis(triphenylphosphine)palladium (II) dichloride

[0781] PE=petroleum ether

[0782] Pin_2B_2=bis(pinacolato)diboron

[0783] PPh_3=triphenylphosphine

[0784] PPTS=pyridinium p-toluenesulfonate

[0785] r.t.=room temperature

[0786] SEM-Cl=2-(trimethylsilyl)ethoxymethyl chloride

[0787] TBME=methyl tert-butyl ether

[0788] TEA=triethylamine

[0789] TFA=trifluoroacetic acid

[0790] THF=tetrahydrofuran

[0791] THP=tetrahydropyran

[0792] TLC=thin layer chromatography

[0793] p-TsOH=p-toluenesulfonic acid

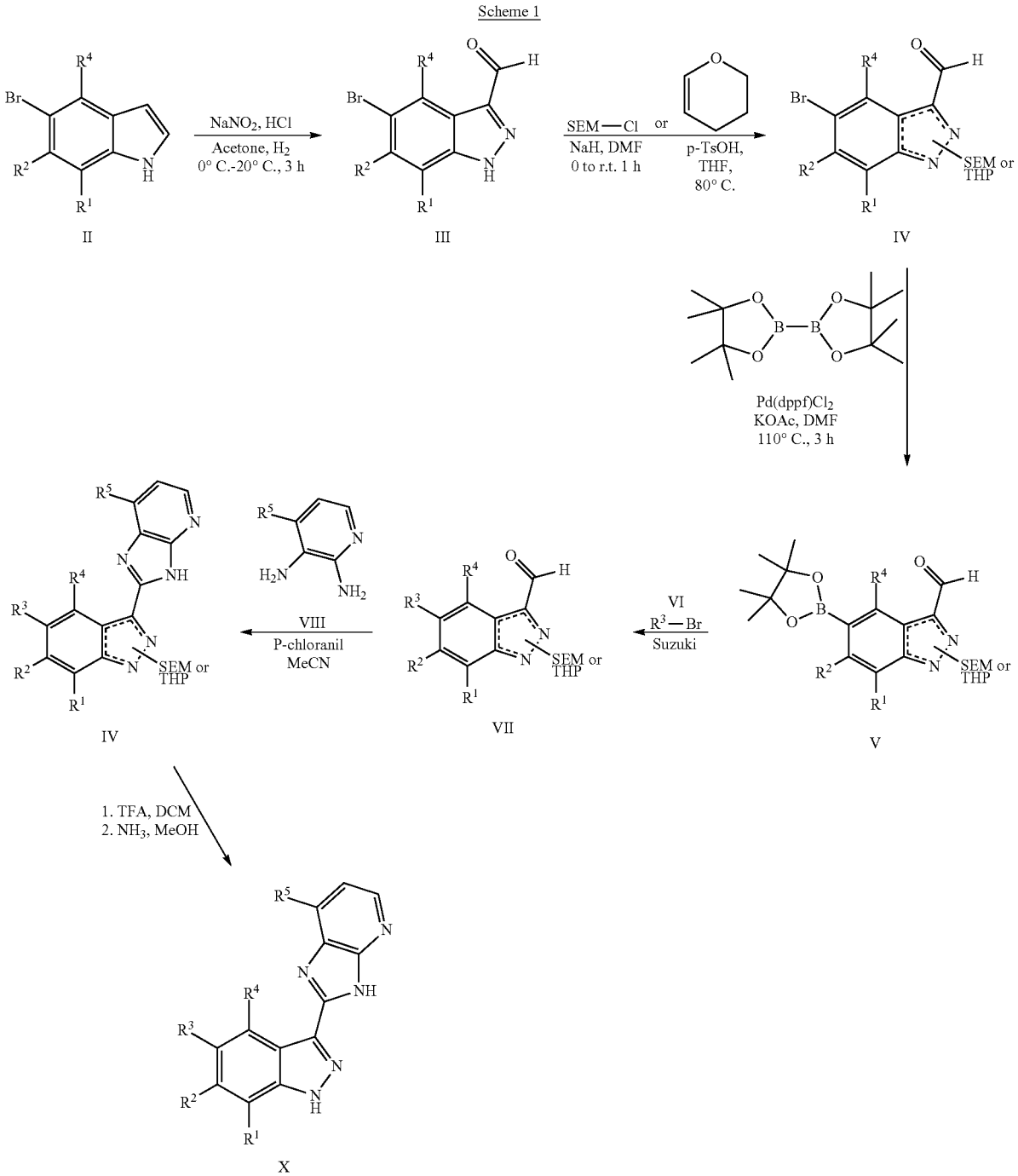
[0794] The following example schemes are provided for the guidance of the reader, and collectively represent an example method for making the compounds provided herein. Furthermore, other methods for preparing com-

pounds of the invention will be readily apparent to the person of ordinary skill in the art in light of the following reaction schemes and examples. The skilled artisan is thoroughly equipped to prepare these compounds by those methods given the literature and this disclosure. The compound numberings used in the synthetic schemes depicted below are meant for those specific schemes only, and should not be construed as or confused with same numberings in other sections of the application. Unless otherwise indicated, all variables are as defined above.

General Procedure

[0795] Compounds of Formula (I) of the present invention can be prepared as depicted in Scheme 1.

Scheme 1

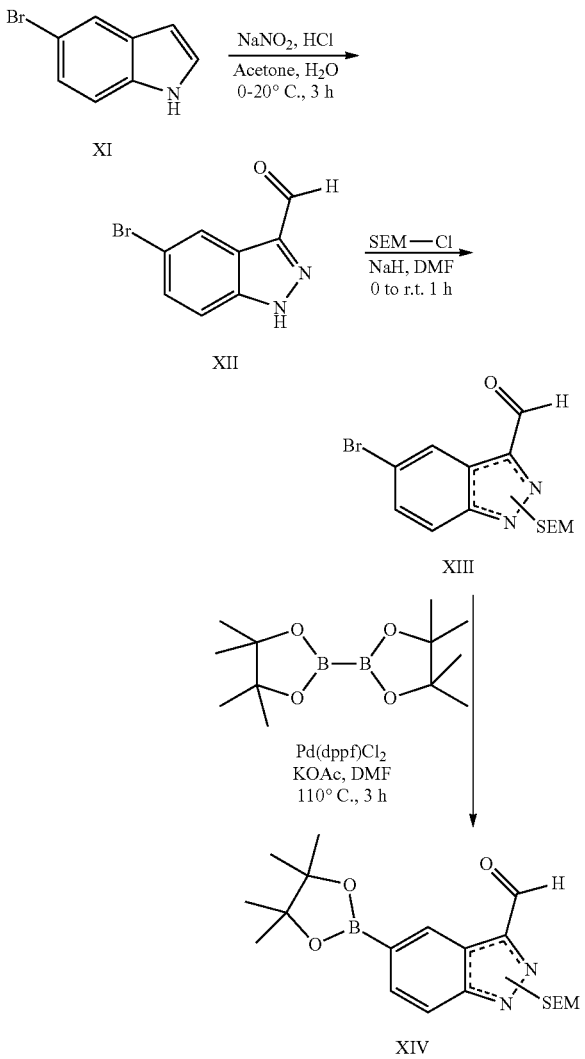


[0796] Scheme 1 describes an alternative method for preparation of indazole derivatives (X) by first formylating 5-bromo-1H-indole (II) to produce 5-bromo-1H-indazole-3-carbaldehyde (III) followed by protection with either SEM-Cl or DHP to give the protected aldehyde (IV). Aldehyde (IV) is then reacted with bis(pinacolato)diboron to form the borate ester (V). Suzuki coupling with various bromides (VI) yields indazole derivatives (VII). Aldehyde (VII) is reacted with various 1,2-diamines (VIII) to produce (IX). Final deprotection of the pyrazole nitrogen yields the desired indazole derivatives (X).

Illustrative Compound Examples

[0797] Preparation of SEM protected intermediate (XIV) is depicted below in Scheme 2.

Scheme 2



Step 1

[0798] A solution of $NaNO_2$ (110.4 g, 1.6 mol, 8 eq) in water (200 mL) was added dropwise to a solution of 5-bromoindole (XI) (39.2 g, 0.2 mol, 1 eq) in acetone (1000 mL) stirred at −10→0° C., while adding $NaNO_2$ the solution temperature was maintained below 20° C. An aqueous 2N HCl solution (480 mL) was added slowly to the solution with vigorously stirring while keeping the internal temperature between 0 and 20° C. The solution was further stirred at 20° C. for 3 h after the addition. The solution was concentrated under reduced pressure to remove acetone while keeping the temperature below 35° C. The solid was collected by filtration and transferred to a flask. Cold (−10° C.) DCM (200 mL) was added and stirred for 30 min at −5° C., the solids were filtered and dried under vacuum at 40° C. to get 5-bromo-1H-indazole-3-carbaldehyde (XII) (34.0 g, 151 mmol, 76% yield) as a brown solid. ESIMS found for $C_8H_5BrN_2O$ m/z 225 (M+H).

Step 2

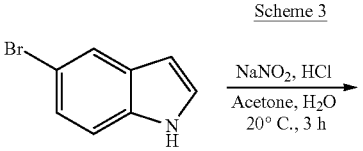
[0799] To a suspension of NaH (6.6 g, 166 mmol, 1.10 eq) in DMF (500 mL) was added a solution of 5-bromo-1H-indazole-3-carbaldehyde (XII) (34.0 g, 151 mmol, 1.0 eq) in DMF (50 mL) dropwise at 0° C. over a period of 30 min. The mixture was stirred at room temperature for 2 h, then SEM-Cl (26.4 g, 159 mmol, 1.08 eq) was added dropwise and the mixture was stirred at room temperature for another 3 h. Then the mixture was poured into an ice-water mixture (1000 mL) and extracted with EtOAc (300 mL×3), the organic phases were combined, dried over Na_2SO_4, filtered and concentrated in vacuo, the resultant residue was purified by flash chromatography on silica gel (PE:EtOAc=20:1→10:1) to afford 5-bromo-1-((2-(trimethylsilyl)ethoxy) methyl)-1H-indazole-3-carbaldehyde (XIII) as a mixture of regioisomers (53.0 g, 151 mmol, 100% yield) as a yellow oil. ESIMS found for $C_{14}H_{19}BrN_2O_2Si$ m/z 355 (M+H).

Step 3

[0800] To a solution of the mixed 5-bromo-1-((2-(trimethylsilyl)ethoxy) methyl)-1H-indazole-3-carbaldehyde (XIII) (53.0 g, 151 mmol, 1.0 eq), bis(pinacolato)diboron (38.0 g, 150 mmol, 1.0 eq) and KOAc (44.0 g, 450 mmol, 3.0 eq) in DMF (1000 mL) was added $Pd(dppf)Cl_2$ (7.7 g, 10.5 mmol, 0.07 eq). The mixture was stirred at 90° C. under nitrogen for 10 h. The mixture was filtered; the filtrate was poured onto water (1000 mL) and extracted with EtOAc (500 mL×3). The combined organic phases were dried, filtered and concentrated in vacuo. The resultant residue was purified by flash chromatography on silica gel (PE:EtOAc=10:1→1:1) to give the 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-H-indazole-3-carbaldehyde (XIV) as a mixture of regioisomers (42.9 g, 106 mmol, 71% yield) as a yellow oil. ESIMS found for $C_{20}H_{31}BN_2O_4Si$ m/z 403 (M+H).

[0801] Preparation of THP protected intermediate (XV) is depicted below in Scheme 3.

Scheme 3



XI

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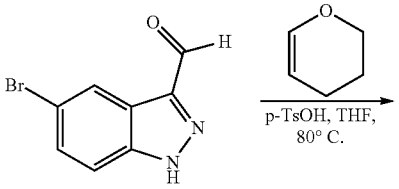
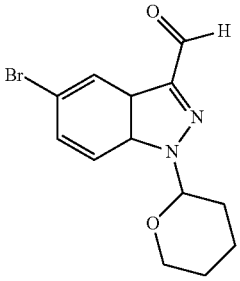


XII



XV

Step 1

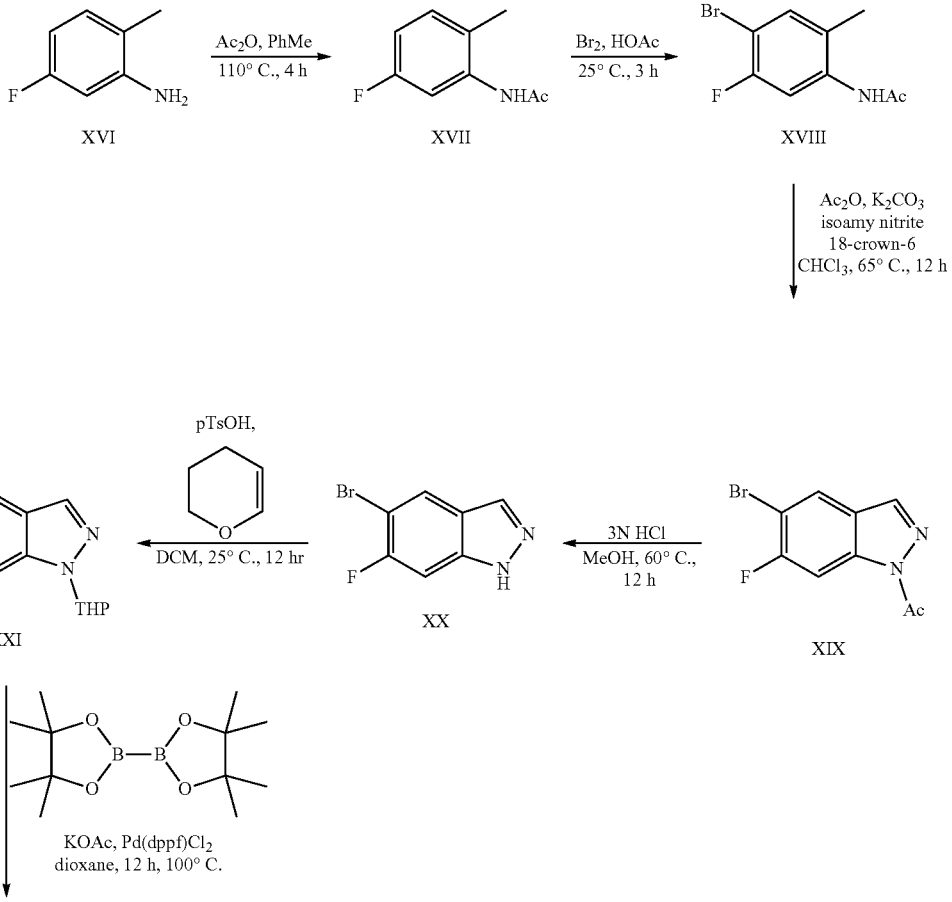
[0802] Procedure can be found in Scheme 2, Step 1.

Step 2

[0803] A mixture of 5-bromo-1H-indazole-3-carbaldehyde (XII) (29.9 g, 133 mmol), 3,4-dihydro-2H-pyran (27.4 mL, 300 mmol) and PPTS (352 mg, 1.4 mmol) in DCM was heated to reflux for 5 hours. The solution was poured into a saturated $NaHCO_3$ solution, the layers were separated, and the aqueous layer was extracted with DCM. The combined organic layers were washed with 5% aqueous citric acid and brine, dried over $MgSO_4$, and concentrated. The crude product was purified on a silica gel column (100% EtOAc→3:97 MeOH:DCM) to provide 5-bromo-1-(tetrahydro-2H-pyran-2-yl)-3a,7a-dihydro-1H-indazole-3-carbaldehyde (XV) was isolated as a white solid (16.4 g, 52.7 mmol, 39.6% yield). ^1H NMR (DMSO-d_6, 500 MHz) δ ppm 1.57-1.65 (m, 2H), 1.72-1.83 (m, 1H), 2.02-2.11 (m, 2H), 2.33-2.44 (m 1H), 3.76-3.83 (m, 1H), 3.84-3.93 (m, 1H), 6.08 (dd, J=2.5 Hz, 9 Hz, 1H), 7.72 (dd, J=1.5 Hz, J=8.5 Hz, 1H), 7.92 (d, J=9 Hz, 1H), 8.28 (d, J=2 Hz, 1H), 10.17 (s, 1H); ESIMS found $C_{13}H_{15}BrN_2O_2$ m/z 311.0 (M+H).

[0804] Preparation of 6-fluoro-substituted indazole intermediate (XXII) is depicted below in Scheme 4.

Scheme 4



XVI XVII XVIII

XXI XX XIX

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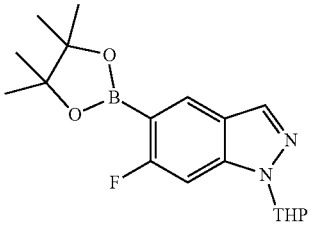


XXII

Step 1

[0805] A solution of 5-fluoro-2-methylaniline (XVI) (100 g, 799 mmol, 1.0 eq) and Ac_2O (89 g, 879 mmol, 1.1 eq) in toluene (4.0 L) was stirred at 110° C. for 4 h. TLC (PE:EtOAc=2:1) showed (XVI) was consumed. The reaction mixture was cooled to 25° C. The precipitated solid was filtered, washed with petro ether. The solid was dried in vacuo to give N-(5-fluoro-2-methylphenyl)acetamide (XVII) as a white solid (120 g, 717.8 mmol, 89.8% yield), which was used in step 2 without further purification. ESIMS found $C_9H_{10}FNO$ m/z 168.1 (M+1).

Step 2

[0806] To a solution of N-(5-fluoro-2-methylphenyl)acetamide (XVII) (120 g, 717 mmol, 1.0 eq) in HOAc (3 L) was added a solution of Br_2 (140 g, 876 mmol, 1.2 eq) in HOAc (1 L) dropwise. The mixture was stirred at 25° C. for 3 h. LC/MS showed compound 2 was (XVII) completely consumed. The reaction mixture was quenched with water (8 L). The solid was filtered, washed with water and petroleum ether. The solid was dried in vacuo to give N-(4-bromo-5-fluoro-2-methylphenyl)acetamide (XVIII) as a white solid (155 g, 629.9 mmol, 87.8% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 2.20 (s, 6H), 7.07 (brs, 1H), 7.32 (d, J=7.2 Hz, 1H), 7.85 (d, J 10.8 Hz, 1H); ESIMS found C_9H_9BrFNO m/z 247.2 (M+1).

Step 3

[0807] A solution of N-(4-bromo-5-fluoro-2-methylphenyl)acetamide (XVIII) (155 g, 629.9 mmol, 1.0 eq), Ac_2O (192 g, 1.8 mol, 3.0 eq), KOAc (123 g, 1.26 mol, 2.0 eq), 18-CROWN-6 (8.3 g, 31 mmol, 0.05 eq) and isoamyl nitrite (147 g, 1.2 mol, 2.0 eq) in $CHCl_3$ (7.0 L) was stirred at 65° C. for 12 h. TLC (PE:EtOAc=5:1, Rf=0.2) showed (XVIII) was consumed completely. The solvent was removed under reduced pressure. The residue was extracted with EtOAc (1.5 L) and water (1.5 L). The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure to give 1-(5-bromo-6-fluoro-1H-indazol-1-yl)ethan-1-one (XIX) as a white solid (170 g, crude, quantitative yield), which was used in step 4 without further purification. ESIMS found $C_9H_6BrFN_2O$ m/z 258.1 (M+1).

Step 4

[0808] A solution of 1-(5-bromo-6-fluoro-1H-indazol-1-yl)ethan-1-one (XIX) (170 g, 629.9 mmol, 1.0 eq) in 3 N HCl (6.6 mol, 10 eq) and MeOH (900 mL) was stirred at 60° C. for 12 h. TLC (PE:EtOAc=5:1, Rf=0.8) showed (XIX) was consumed completely. The reaction mixture was cooled to room temperature and basified with 1N aq. NaOH to pH=10. The precipitated solid was filtered and dried in vacuo to afford 5-bromo-6-fluoro-1H-indazole (XX) as a yellow solid (100 g, 465.1 mmol, 73.8% yield). ESIMS found $C_7H_4BrFN_2$ m/z 215.1 (M+1).

Step 5

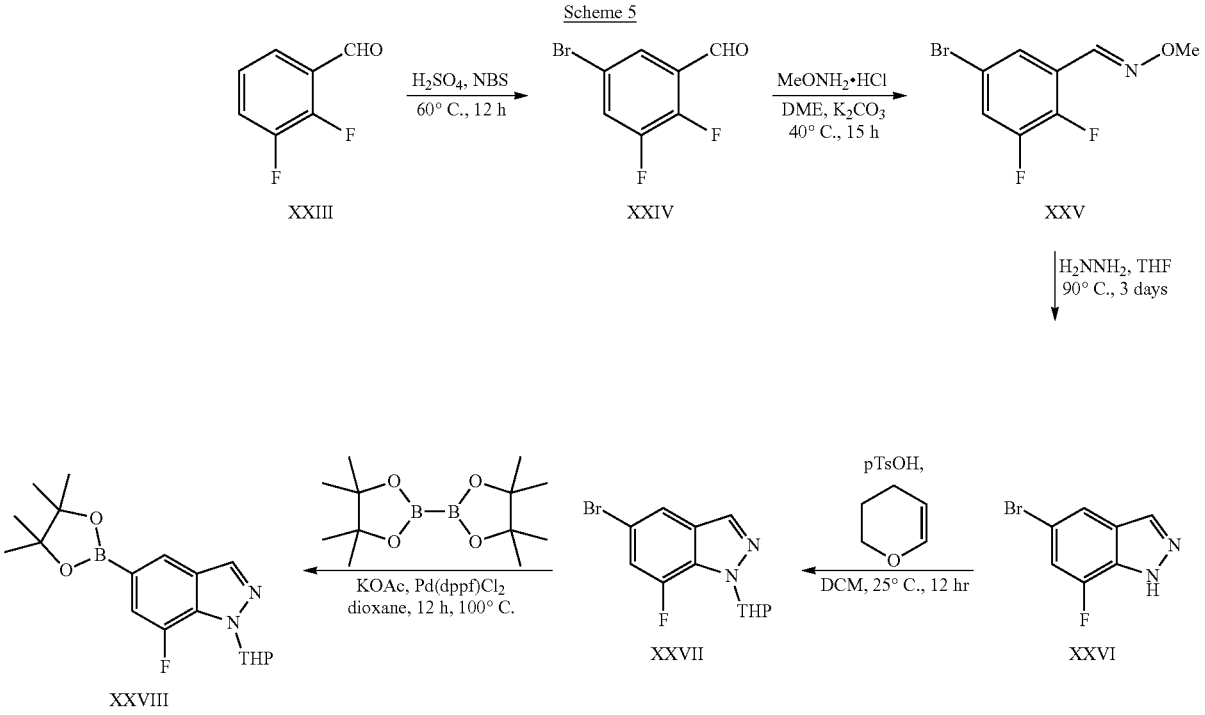
[0809] To solution of a mixture of 5-bromo-6-fluoro-1H-indazole (XX) (90 g, 418 mmol, 1.0 eq) and 3,4-dihydro-2H-pyran (70 g, 837 mmol, 2.0 eq) in DCM (2.0 L) was added p-TsOH (3.6 g, 20 mmol, 0.05 eq) at 25° C. The resulting mixture was stirred at 25° C. for 12 h. TLC (PE:EtOAc=5:1, Rf=0.7) showed (XX) was completely consumed. To the reaction mixture was added saturated aqueous $NaHCO_3$ (4 L). The organic layer was separated, dried over Na_2SO_4, concentrated in vacuo to give a residue, which was further purified by silica gel column (EtOAc:PE=20:1) to give 5-bromo-6-fluoro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (XXI) as a brown oil (120 g, 401.1 mmol, 96.0% yield), which was used in step 6 without further purification. ESIMS found $C_{12}H_{12}BrFN_2O$ m/z 299.2 (M+1).

Step 6

[0810] A solution of 5-bromo-6-fluoro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (XXI) (30 g, 100 mmol, 1.0 eq), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (25 g, 100 mmol, 1.0 eq), $Pd(dppf)Cl_2$ (3.6 g, 5.0 mmol, 0.05 eq), KOAc (19.6 g, 200 mmol, 2.0 eq) in dioxane (550 mL) was stirred at 100° C. for 12 h under N_2. LC/MS showed (XXI) was completely consumed. The reaction mixture was concentrated and then extracted with EtOAc (300 mL) and water (100 mL). The mixture was filtered and separated. The organic layer was dried over anhydrous Na_2SO_4, concentrated to give crude product, which was further purified by silica gel column (EtOAc:PE=20/1) to give 6-fluoro-1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (XXII) as a green solid (13 g, 37.5 mmol, 37.4% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.37 (s, 12H), 1.73-1.43 (m, 3H), 2.58-2.50 (m, 1H), 3.79-3.73 (m, 1H), 4.06-4.04 (m, 1H), 5.66-5.63 (m, 1H), 7.28-7.21 (m, 1H), 8.00 (s, 1H), 8.19 (d, J=5.6 Hz, 1H); ESIMS found $C_{18}H_{24}BFN_2O_3$ m/z 347.2 (M+1).

[0811] Preparation of 7-fluoro-substituted indazole intermediate (XXVIII) is depicted below in Scheme 5.

Scheme 5



Step 1

[0812] To a stirred solution of 2,3-difluorobenzaldehyde (XXIII) (75.0 g, 528 mmol, 1.0 eq) in H_2SO_4 (565 mL) was added NBS (113 g, 633 mmol, 1.2 eq) in portions at 60° C. The resulting mixture was stirred at 60° C. for 12 hr. LC/MS showed the reaction was completed. The reaction mixture was poured into ice water and petroleum ether (500 mL) and stirred for 10 min, the organic layer was separated and concentrated under vacuum to give crude product. The residue was purified column chromatography silica gel (100% petroleum ether) to give 5-bromo-2,3-difluorobenzaldehyde (XXIV) (120 g, 543.0 mmol, quantitative yield). ESIMS found $C_7H_3BrF_2O$ m/z 221.1 (M+1).

Step 2

[0813] To a solution of 5-bromo-2,3-difluorobenzaldehyde (XXIV) (115 g, 520 mmol, 1.0 eq), $MeONH_2$—HCl (47.8 g, 572 mmol, 1.1 eq) and K_2CO_3 (86.3 g, 624 mmol, 1.20 eq) was in DME (1.30 L) was heated to 40° C. for 15 h. TLC (petroleum ether) showed (XXIV) was consumed. The reaction was filtered and the filtrate was concentrated under vacuum to give crude product. The residue was purified by column chromatography on silica gel (100% petroleum ether) to give (E)-5-bromo-2,3-difluorobenzaldehyde O-methyl oxime (XXV) (74 g, 56.9% yield). ^{1}'H NMR ($CDCl_3$, 400 MHz) δ ppm 4.04 (s, 3H), 7.37-7.32 (m, 1H), 7.77 (s, 1H), 8.23 (s, 1H); ESIMS found $C_8H_6BrF_2NO$ m/z 250.2 (M+1).

Step 3

[0814] A solution of (E)-5-bromo-2,3-difluorobenzaldehyde O-methyl oxime (XXV) (150 g, 600 mmol, 1.0 eq), $NH_2NH_2H_2O$ (600 mL) in dry THF (600 mL) was heated to 90° C. for 84 h. LC/MS showed the reaction was completed. The solvent was evaporated and the resulting mixture was diluted with EtOAc, washed with water, dried over Na_2SO_4 and concentrated under vacuum to give crude product. The residue was purified by column chromatography on silica gel (PE:EtOAc=10:1) to give 5-bromo-7-fluoro-1H-indazole (XXVI) as a white solid (78 g, 362.7 mmol, 60.5% yield). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.44 (d, J=9.6 Hz, 1H), 7.87 (d, J=1.6 Hz, 1H), 8.17 (s, 1H), 13.90 (s, 1H); ESIMS found $C_7H_4BrFN_2$ m/z 215 (M+1).

Step 4

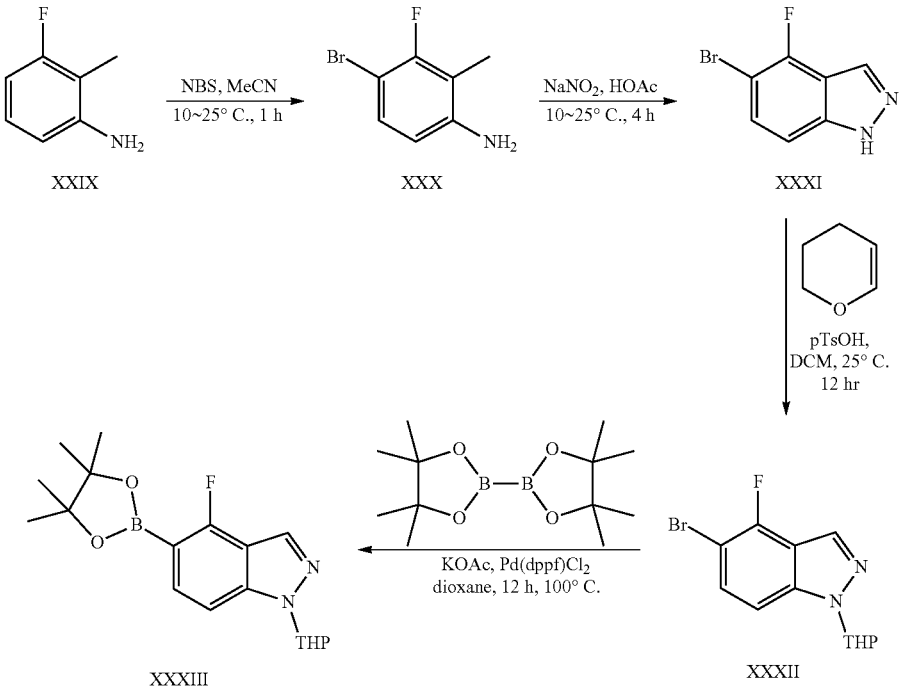
[0815] Preparation of 5-bromo-7-fluoro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (XXVII) was performed following the procedure listed in Scheme 4, Step 5. Light yellow solid (98 g, 327.6 mmol, 93.9% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 1.78-1.62 (m, 3H), 2.17-2.09 (m, 2H), 2.63-2.58 (m, 1H), 3.76 (t, J=11.6 Hz, 1H), 4.05 (d, J=9.6 Hz, 1H), 5.85 (d, J=9.6 Hz, 1H), 7.22 (d, J=12.0 Hz, 1H), 7.65 (s, 1H), 8.00 (s, 1H); ESIMS found $C_{12}H_{12}BrFN_2O$ m/z 299.2 (M+1).

Step 5

[0816] Preparation of 7-fluoro-1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (XXVIII) was performed following the procedure listed in Scheme 4, Step 6. White solid (45 g, 130.0 mmol, 86.7% yield). ESIMS found $C_{18}H_{24}BFN_2O_3$ m/z 347.1 (M+1).

[0817] Preparation of 4-fluoro-substituted indazole intermediate (XXXIII) is depicted below in Scheme 6.

Scheme 6



XXIX XXX XXXI XXXII XXXIII

Step 1

[0818] To a stirred solution of 3-fluoro-2-methylaniline (XXIX) (50 g, 399 mmol, 1.0 eq) in CH_3CN (1.2 L) was added NBS (78 g, 439 mmol, 1.1 eq) in portions at 10° C., the resulting mixture was stirred at 25° C. for 1 h. LC/MS showed the reaction was completed. Saturated $Na_2S_2O_3$ (1.2 L) was then added slowly to the reaction mixture at 10° C., extracted with EtOAc (2 L) and the organic layer was concentrated under vacuum to give crude product. The residue was washed with PE (1 L), the solid was filtered, washed again with PE (500 mL) and dried under vacuum to give 4-bromo-3-fluoro-2-methylaniline (XXX) as a white solid (163.0 g, 798.9 mmol, 66.7% yield). ESIMS found C_7H_7BrFN m/z 204.1 (M+1).

Step 2

[0819] To a stirred solution of 4-bromo-3-fluoro-2-methylaniline (XXX) (40 g, 196 mmol, 1.0 eq) in HOAc (1.2 L) was added $NaNO_2$ (16 g, 235 mmol, 1.2 eq) in portions at 10° C., the resulting mixture was stirred at 25° C. for 4 h. LC/MS showed the reaction was completed. Upon completion, aqueous NaOH (50%) was added to the reaction mixture until pH 7-8, then the mixture was extracted with EtOAc (1.6 L), the organic layer was dried over Na_2SO_4, filtered; filtrate was concentrated under vacuum to give crude 5-bromo-4-fluoro-1H-indazole (XXXI) (40 g, 186.0 mmol, 94.9% yield), which was used in step 3 without further purification. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 7.47-7.42 (m, 1H), 7.56-7.53 (m, 1H), 8.23 (s, 1H); ESIMS found $C_7H_4BrFN_2$ m/z 215 (M+1).

Step 3

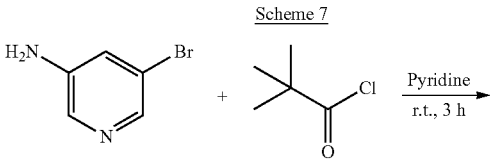
[0820] Preparation of 5-bromo-4-fluoro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole (XXXII) was performed following the procedure listed in Scheme 4, Step 5. Brown oil (9.9 g, 33.1 mmol, 71.9% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.75-1.67 (m, 3H), 2.10-1.76 (m, 2H), 2.52-2.14 (m, 1H), 3.76-3.71 (m, 1H), 4.01-3.97 (m, 1H), 5.70-5.69 (m, 1H), 7.30-7.26 (m, 1H), 7.47-7.45 (m, 1H), 8.06 (s, 1H); ESIMS found $C_{12}H_{12}BrFN_2O$ m/z 299 (M+1).

Step 4

[0821] Preparation of 4-fluoro-1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (XXXIII) was performed following the procedure listed in Scheme 4, Step 6. Red oil (25 g, 72.2 mmol, 72.2% yield). ^1H NMR (CD_3OD, 400 MHz) δ ppm 1.72 (s, 12H), 2.12-1.74 (m, 5H), 2.52-2.16 (m, 1H), 3.85-3.80 (m, 1H), 4.12-4.00 (m, 1H), 5.84-5.81 (m, 1H), 7.48 (d, J=8.0 Hz, 1H), 7.71-7.67 (m, 1H), 8.15 (s, 1H); ESIMS found $C_{18}H_{24}BFN_2O_3$ m/z 347 (M+1).

[0822] Preparation of intermediate N-(5-bromopyridin-3-yl)pivalamide (XXXVI) is depicted below in Scheme 7.

Scheme 7



XXXIV XXXV

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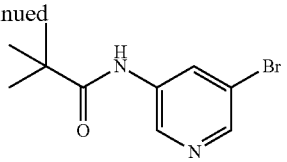


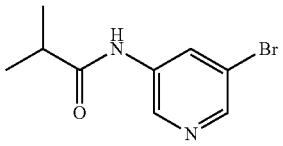
XXXVI

Step 1

[0823] To a solution of 3-amino-5-bromo pyridine (XXXIV) (1.0 g, 5.78 mmol) in dry pyridine (10 mL) was added pivaloyl chloride (XXXV) (769 mg, 6.38 mmol). The reaction mixture was stirred at room temperature for 3 h. The reaction was poured into an ice water/saturated aqueous $NaHCO_3$ mixture and stirred for 30 min. The precipitate was filtered, washed with cold water and dried at room temperature to yield N-(5-bromopyridin-3-yl)pivalamide (XXXVI) as an off-white solid (1.082 g, 4.22 mmol, 73.1% yield). ^1H NMR (DMSO-d_6, 500 MHz) δ ppm 1.23 (s, 9H), 8.37 (d, J=2 Hz, 1H), 8.39 (t, J=2 Hz, 1H), 8.80 (d, J=2 Hz, 1H), 9.58 (brs, 1H); ESIMS found $C_{10}H_3BrN_2O$ m/z 258.9 ($Br^{81}M+H$).

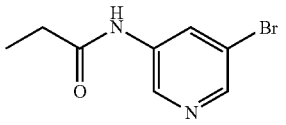
[0824] The following intermediates were prepared in accordance with the procedure described in the above Scheme 7.

XXXVII



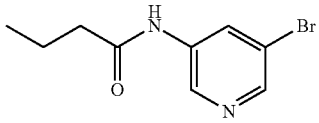
[0825] N-(5-Bromopyridin-3-yl)isobutyramide (XXXVII): Off-white solid, (71% yield). ^1H NMR ($CDCl_3$) δ ppm 8.55-8.35 (m, 3H), 7.32 (s, 1H), 2.59-2.48 (m, 1H), 1.28-1.27 (d, 6H); ESIMS found $C_9H_{11}BrN_2O$ m/z 242.9 ($Br^{79}M+H$).

XXXVIII



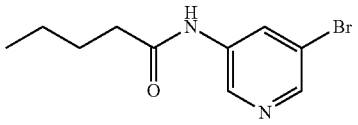
[0826] N-(5-Bromopyridin-3-yl)propionamide (XXXVIII): Off white solid (92% yield). ^1H NMR (DMSO-d_6) δ ppm 1.09 (t, J=7.54 Hz, 3H), 2.36 (q, J=7.54 Hz, 2H), 8.36 (m, 2H), 8.65 (d, J=2.07 Hz, 1H), 10.26 (s, 1H); ESIMS found $C_8H_9BrN_2O$ m/z 231.1 ($Br^{81}M+H$).

XXXIX



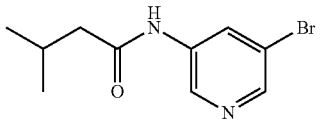
[0827] N-(5-Bromopyridin-3-yl)butyramide (XXXIX): Yellow solid (2.1 g, 8.64 mmol, 88.8% yield). ^1H NMR (CD_3OD, 400 MHz) δ ppm 1.02 (t, J=7.2 Hz, 3H), 1.74 (sxt, J=7.2 Hz, 2H), 2.40 (t, J=7.2 Hz, 2H), 8.35 (d, J=2 Hz, 1H), 8.46 (t, J=2 Hz, 1H), 8.63 (d, J=2 Hz, 1H); ESIMS found $C_9H_{11}BrN_2O$ m/z 243.1 ($Br^{79}M+H$).

XL



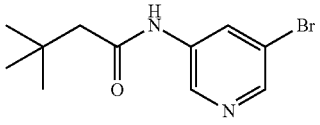
[0828] N-(5-Bromopyridin-3-yl)pentanamide (XL): Yellow solid (2.0 g, 7.78 mmol, 85.3% yield). ^1H NMR (CD_3OD, 400 MHz) δ ppm 0.98 (t, J=7.4 Hz, 3H), 1.43 (sxt, J=7.4 Hz, 2H), 1.70 (quin, J=7.4 Hz, 2H), 2.43 (t, J=7.6 Hz, 2H), 8.35 (s, 1H), 8.45 (d, J=2 Hz, 1H), 8.64 (d, J=2 Hz, 1H); ESIMS found $C_{10}H_{13}BrN_2O$ m/z 256.9 ($Br^{79}M+H$).

XLI



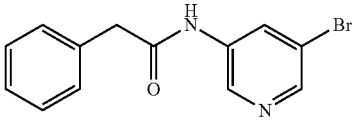
[0829] N-(5-Bromopyridin-3-yl)-3-methylbutanamide (XLI): Off white solid, (67% yield), ^1H NMR ($CDCl_3$, 500 MHz) δ ppm 8.55-8.42 (m, 3H), 7.62 (s, 1H), 2.31-2.18 (m, 3H), 1.02-1.01 (d, J=6 Hz, 6H); ESIMS found $C_{10}H_{13}BrN_2O$ m/z 258.9 ($Br^{81}M+H$).

XLII



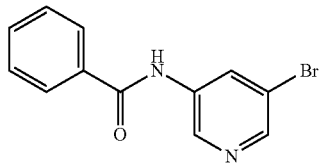
[0830] N-(5-Bromopyridin-3-yl)-3,3-dimethylbutanamide (XLII): Yellow solid (1.7 g, 6.27 mmol, 78.6% yield). ^1H NMR (CD_3OD, 400 MHz) δ ppm 1.10 (s, 9H), 2.29 (s, 2H), 8.36 (d, J=1.6 Hz, 1H), 8.46 (d, J=2.0 Hz, 1H), 8.64 (d, J=2.0 Hz, 1H); ESIMS found $C_{11}H_{15}BrN_2O$ m/z 273.1 (($Br^{81}M+H$).

XLIII



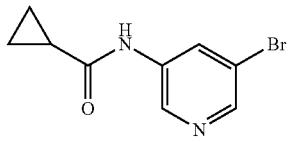
[0831] N-(5-Bromopyridin-3-yl)-2-phenylacetamide (XLIII): White solid (2.5 g, 8.59 mmol, 77.9% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 3.76 (s, 2H), 7.26-7.45 (m, 5H), 7.57 (brs, 1H), 8.33 (s, 1H), 8.37 (s, 2H); ESIMS found $C_{13}H_{11}BrN_2O$ m/z 292.8 ($Br^{81}M+H$).

XLIV



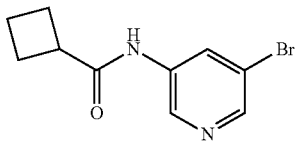
[0832] N-(5-Bromopyridin-3-yl)benzamide (XLIV): White solid (2.7 g, 9.74 mmol, 60% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 7.40-7.52 (m, 2H), 7.52-7.62 (m, 1H), 7.86 (d, J=7.2 Hz, 2H), 8.39 (d, J=1.6 Hz, 1H), 8.46 (s, 1H), 8.55 (d, J=1.6 Hz, 1H), 8.57 (d, J=2.0 Hz, 1H); ESIMS found $C_{12}H_9BrN_2O$ m/z 278.8 ($Br^{81}M+H$).

XLV



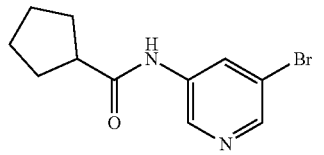
[0833] N-(5-Bromopyridin-3-yl)cyclopropanecarboxamide (XLV): Off-white solid, (83% yield), ^{1}H NMR ($CDCl_3$, 500 MHz) δ ppm 8.46-8.39 (m, 3H), 7.54 (bs, 1H), 1.56-1.50 (m, 1H), 1.13-1.07 (m, 2H), 0.96-0.90 (m, 2H); ESIMS found for $C_9H_9BrN_2O$ m/z 240.9 ($Br^{79}M+H$).

XLVI



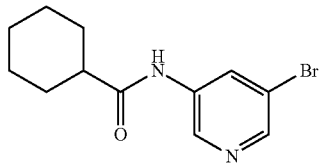
[0834] N-(5-Bromopyridin-3-yl)cyclobutanecarboxamide (XLVI): Yellow solid (2.1 g, 6.27 mmol, 86.6% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.80-1.99 (m, 1H), 1.99-2.15 (m, 1H), 2.16-2.30 (m, 2H), 2.30-2.45 (m, 2H), 3.25-3.35 (m, 1H), 8.34 (d, J=2.0 Hz, 1H), 8.47 (s, 1H), 8.64 (d, J=2.0 Hz, 1H); ESIMS found $C_{10}H_{11}BrN_2O$ m/z 257.1 ($Br^{81}M+H$).

XLVII



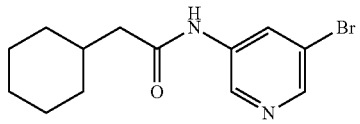
[0835] N-(5-Bromopyridin-3-yl)cyclopentanecarboxamide (XLVII): Yellow solid (1.9 g, 7.06 mmol, 80.2% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.57-1.74 (m, 2H), 1.74-1.91 (m, 4H), 1.91-2.07 (m, 2H), 2.77-2.92 (m, 1H), 8.34 (d, J=1.6 Hz, 1H), 8.45 (s, 1H), 8.65 (d, J=2.0 Hz, 1H); ESIMS found $C_{11}H_{13}BrN_2O$ m/z 271.1 ($Br^{81}M+H$).

XLVIII



[0836] N-(5-bromopyridin-3-yl)cyclohexanecarboxamide (XLVIII): Yellow solid (2.0 g, 7.06 mmol, 84.3% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.19-1.46 (m, 3H), 1.46-1.63 (m, 2H), 1.74 (d, J=11.6 Hz, 1H), 1.88 (t, J=14.0 Hz, 4H), 2.40 (tt, J=11.6 Hz, J=3.6 Hz, 1H), 8.34 (d, J=2.0 Hz, 1H), 8.44 (t, J=2.0 Hz, 1H), 8.64 (d, J=2.0 Hz, 1H); ESIMS found $C_{12}H_{15}BrN_2O$ m/z 285.1 ($Br^{81}M+H$).

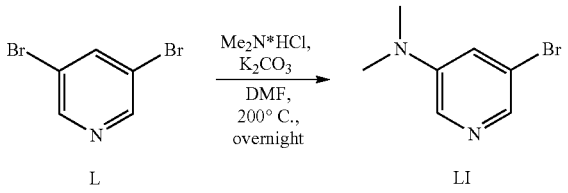
XLIX



[0837] N-(5-bromopyridin-3-yl)-2-cyclohexylacetamide (XLIX): Yellow solid (261 mg, 0.878 mmol, 84.4% yield). ESIMS found $C_{13}H_{17}BrN_2O$ m/z 297.1 ($Br^{s8}M+H$).

[0838] Preparation of intermediate 5-bromo-N,N-dimethylpyridin-3-amine (LI) is depicted below in Scheme 8.

Scheme 8



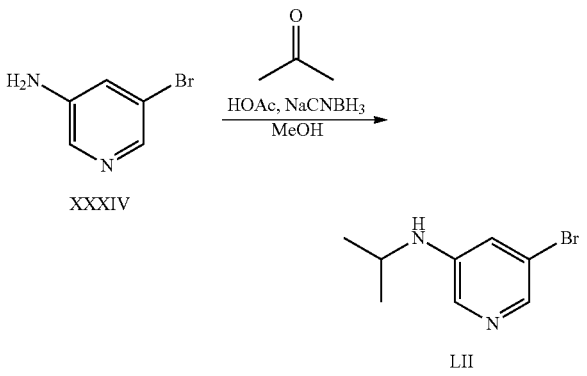
L LI

Step 1

[0839] To a solution of 3,5-dibromopyridine (L) (2.37 g, 10.0 mmol) in dry DMF (20.0 mL) was added K_2CO_3 (4.5 g, 33 mmol) and dimethylamino hydrochloride (1.79 g, 22 mmol). The mixture was heated overnight at 200° C. in a sealed tube. The solution was cooled to room temperature and excess DMF was removed under vacuum. The residue was partitioned between EtOAc and water. The organic phase was separated. The aqueous phase was washed with EtOAc and the combined organic phases were dried over $MgSO_4$, and concentrated to afford 5-bromo-N,N-dimethylpyridin-3-amine (LI) as an off-white solid (1.78 g, 8.85 mmol, 88% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.94 (s, 6H), 7.25 (t, J=2 Hz, 1H), 7.91 (d, J=2 Hz, 1H), 8.07 (d, J=2 Hz, 1H); ESIMS found $C_7H_9BrN_2$ m/z 201.1 (M+H).

[0840] Preparation of intermediate 5-bromo-N-isopropylpyridin-3-amine (LII) is depicted below in Scheme 9.

Scheme 9

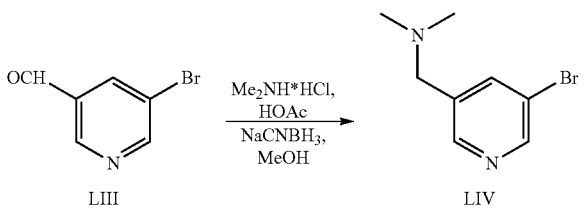


Steps 1

[0841] To a solution of 5-bromopyridin-3-amine (XXXIV) (535 mg, 3.09 mmol) in MeOH (62 mL) was added acetone (296 μL, 4.02 mL). The pH was adjusted to 4 using HOAc and stirred for 30 min. $NaCNBH_3$ (272 mg, 4.33 mmol) was added and stirred at room temperature overnight. The MeOH was removed under vacuum and the residue was partitioned between EtOAc and saturated aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated under vacuum. The crude product was purified on a silica gel column (100% hexane→90:10 hexane:EtOAc) to produce 5-bromo-N-isopropylpyridin-3-amine (LII) as an oil which slowly solidified into an off-white solid (309 mg, 1.44 mmol, 47% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.12 (d, J=6.3 Hz, 6H), 3.55-3.59 (m, 1H), 6.03 (d, J=7.9 Hz, 1H), 7.05-7.06 (m, 1H), 7.75 (d, J=2 Hz, 1H), 7.90 (d, J=2 Hz, 1H); ESIMS found $C_8H_{11}BrN_2$ m/z 215.1 (M+H).

[0842] Preparation of intermediate 1-(5-bromopyridin-3-yl)-N,N-dimethylmethanamine (LIV) is depicted below in Scheme 10.

Scheme 10

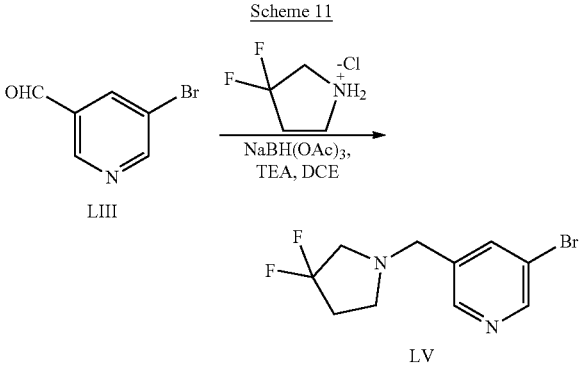


Steps 1

[0843] Preparation of 1-(5-bromopyridin-3-yl)-N,N-dimethylmethanamine (LIV) was performed following the procedure listed in Scheme 9, Step 1. Brown oil (1.20 g, 5.59 mmol, 45% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.15 (s, 6H), 3.43 (s, 2H), 7.94 (s, 1H), 8.47 (d, J=1.1 Hz, 1H), 8.59 (d, J=2.2 Hz, 1H); ESIMS found $C_8H_{11}BrN_2$ m/z 215 (M^{Br79}+H) and 217 (M^{B81}+H).

[0844] Preparation of intermediate 3-bromo-5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridine (LV) is depicted below in Scheme 11.

Scheme 11

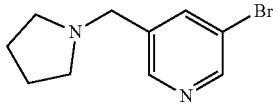


Steps 1

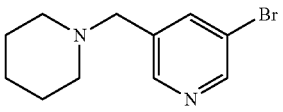
[0845] To a mixture of 5-bromopyridine-3-carbaldehyde (LIII) (6.00 g, 32.26 mmol, 1.0 eq), 3,3-difluoropyrrolidine (5.56 g, 38.71 mmol, 1.20 eq) and TEA (5.39 mL, 38.71 mmol, 1.2 Eq) in DCE (200 mL) was stirred at room temperature for 30 min, then added sodium triacetoxyborohydride (10.25 g, 48.38 mmol, 1.50 eq) in one portion at room temperature under N_2. The mixture was stirred at room temperature for 6 hours. TLC showed the reaction was complete. The reaction was quenched with 1N NaOH (100 mL), extracted with DCE (100 mL×2). The combined organic layers were washed with brine (100 mL), dried and concentrated. The residue was purified by silica gel chromatography (column height: 50 mm, diameter: 50 mm, 300-400 mesh silica gel, DCM/MeOH=30/1→20/1) to give 3-bromo-5-((3,3-difluoropyrrolidin-1-yl)methyl) pyridine (LV): Yellow oil (8.00 g, 28.9 mmol, 89.5% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 2.30 (spt, J=7.2 Hz. 2H), 2.75 (t, J=6.8 Hz, 2H), 2.91 (t, J=13.2 Hz, 2H), 7.85 (s, 1H), 8.45 (s, 1H), 8.59 (d, J=2 Hz, 1H); ESIMS found for $C_{10}H_{11}BrF_2N_2$ m/z 277.0 (M+H).

[0846] The following intermediates were prepared in accordance with the procedure described in the above Scheme 10 or Scheme 11.

LVI

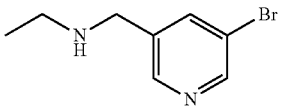


[0847] 3-Bromo-5-(pyrrolidin-1-ylmethyl)pyridine (LVI): Golden liquid (1.35 g, 97% yield). ^{1}H NMR (DMSO-d_6) 1.68-1.71 (m, 4H), 2.42-2.44 (m, 4H), 3.60 (s, 2H), 7.96 (s, 1H), 8.48 (d, J=2 Hz, 1H), 8.58 (d, J=3 Hz, 1H); ESIMS found for $C_{10}H_{13}BrN_2$ m/z 242.2 (M+H).



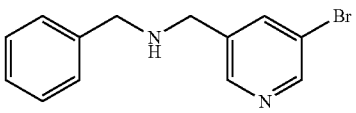
LVII

[0848] 3-Bromo-5-(piperidin-1-ylmethyl)pyridine (LVII): Brown liquid (13.1 g, 94% yield). ^{1}H NMR (DMSO-d_6) 1.36-1.39 (m, 2H), 1.46-1.51 (m, 4H), 2.31-2.32 (m, 4H), 3.46 (s, 2H), 7.94 (s, 1H), 8.47 (d, J=2 Hz, 1H), 8.58 (d, J=3 Hz, 1H); ESIMS found for $C_{11}H_{15}BrN_2$ m/z 257.0 (M+H).



LVIII

[0849] N-((5-Bromopyridin-3-yl)methyl)ethanamine (LVIII): Golden liquid (1.29 g, 6.00 mmol, 60% yield). ^{1}HNMR ($CDCl_3$, 400 MHz) δ ppm 1.14 (t, J=7.2 Hz, 3H), 2.67 (q, J=7.2 Hz, 2H), 3.79 (s, 2H), 7.85 (t, J=2 Hz, 1H), 8.46 (d, J=1.6 Hz, 1H), 8.56 (d, J=2.4 Hz, 1H); ESIMS found for $C_8H_{11}BrN_2$ m/z 215.1 (M+H).

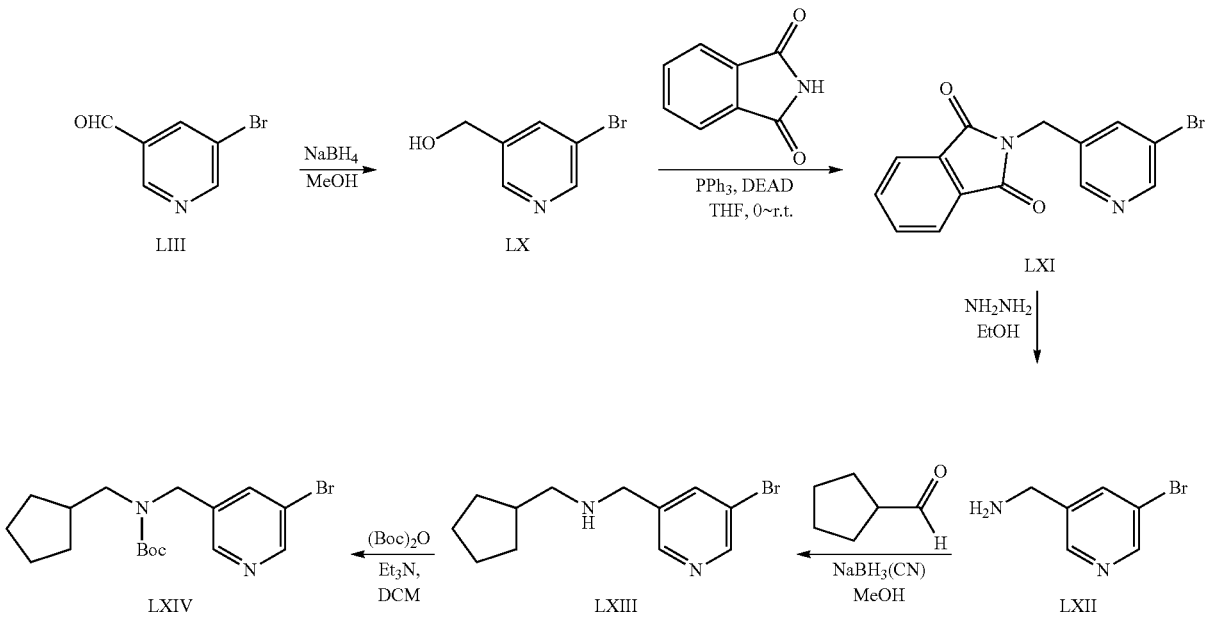


LIX

[0850] N-Benzyl-1-(5-bromopyridin-3-yl)methanamine (LIX): Yellow oil (8.0 g, 28.9 mmol, 89.5% yield). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.71 (s, 2H), 3.74 (s, 2H), 7.18-7.28 (m, 1H), 7.28-7.40 (m, 4H), 8.04 (s, 1H), 8.52 (s, 1H), 8.58 (s, 1H); ESIMS found for $C_{13}H_{13}BrN_2$ m/z 277.1 (M+H).

[0851] Preparation of intermediate tert-butyl (5-bromopyridin-3-yl)methyl (cyclopentylmethyl)carbamate (LXIV) is depicted below in Scheme 12.

Scheme 12



Step 1

[0852] To a solution of 5-bromonicotinaldehyde (LIII) (2.0 g, 10.8 mmol, 1 eq) in MeOH (20 mL) was added $NaBH_4$ (2.4 g, 64.9 mmol, 6 eq) and the reaction mixture was stirred at room temperature for 3 h. The mixture was concentrated in vacuo and the residue was diluted in water (15 mL), the aqueous phase was extracted with DCM (10 mL×3). The combined organic layers were dried over $MgSO_4$, filtered and concentrated in vacuo to afford (5-bromopyridin-3-yl)methanol (LX) (1.8 g, 9.57 mmol, 90.0% yield) as a colorless oil. ^{1}H NMR (CDC_3, 500 MHz) δ ppm 4.73 (s, 2H), 7.90 (s, 1H), 8.47 (s, 1H), 8.57 (s, 1H). ESIMS found for C_6H_6BrNO m/z 188.0 (M+H).

Step 2

[0853] To a stirred solution of (5-bromopyridin-3-yl) methanol (LX) (1.60 g, 8.5 mmol, 1 eq), phthalimide (1.24 g, 8.5 mmol, 1 eq) and PPh_3 (3.33 g, 12.75 mmol, 1.5 eq) in anhydrous THF (15 mL) was added DEAD (2.21 g, 12.75 mmol, 1.5 eq) dropwise at 0° C. under N_2. Then the reaction mixture was stirred at room temperature for 6 h. The mixture was washed with saturated $NaHCO_3$ solution (15 mL), water (15 mL) and brine (15 mL) subsequently. The organic layers were dried over $MgSO_4$, concentrated under reduced pressure, the resultant residue was purified by flash chromatog-

raphy on silica gel (PE:EtOAc=4:1) to give 2-((5-bromopyridin-3-yl)methyl)isoindoline-1,3-dione (LXI) (2.5 g, 7.88 mmol, 82.3% yield) as a white solid. ESIMS found for $C_{14}H_9BrN_2O_2$ m/z 317.1 (M+H).

Step 3

[0854] A solution of 2-((5-bromopyridin-3-yl)methyl) isoindoline-1,3-dione (LXI) (1.9 g, 6.0 mmol, 1 eq) and hydrazine hydrate (2.0 g, 40 mmol, 6 eq) in EtOH (20 mL) was heated at 70° C. for 3 h. The mixture was filtered through a Celite® pad and the filtrate was concentrated in vacuo, the crude product was dissolved in 1N HCl solution (15 mL) and concentrated to dryness, then it was washed with acetone (10 mL×3), the precipitate was collected by filtration, dried in vacuo to give (5-bromopyridin-3-yl)methanamine (LXII) (1.3 g, 6.95 mmol, 97.7% yield) as a white solid. ^{1}H NMR (D_2O, 500 MHz) δ ppm 4.34 (s, 2H), 8.56 (s, 1H), 8.75 (d, J=1.2 Hz, 1H), 8.91 (d, J=1.6 Hz, 1H). ESIMS found for $C_6H_7BrN_2$ m/z 187.0 (M+H).

Step 4

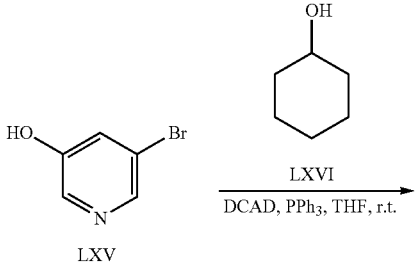
[0855] A solution of (5-bromopyridin-3-yl)methanamine (LXII) (1.30 g, 5.8 mmol, 1.0 eq), cyclopentanecarbaldehyde (0.57 g, 5.8 mmol, 1.0 eq) and TEA (0.60 g, 5.8 mmol, 1.0 eq) in MeOH (15 mL) was stirred at room temperature for 2 h. Then $NaBH_3CN$ (1.98 g, 34.6 mmol, 6.0 eq) was added and the mixture was stirred at the same temperature for another 3 h. The solvent was removed under reduced pressure and the residue was diluted in water (20 mL) and extracted with DCM (10 mL×3), combined organic layers were dried over $MgSO_4$ and concentrated in vacuo to give 1-(5-bromopyridin-3-yl)-N-(cyclopentylmethyl)methanamine (LXIII) (1.23 g, 4.57 mmol, 79.3% yield) as a yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 1.07-1.23 (m, 2H), 1.47-1.67 (m, 4H), 1.70-1.84 (m, 2H), 2.02 (spt, J=7.6 Hz. 1H), 2.53 (d, J=7.2 Hz, 2H), 3.80 (s, 2H), 7.86 (s, 1H), 8.47 (s, 1H), 8.56 (d, J=2.0 Hz, 1H); ESIMS found for $C_{12}H_{17}BrN_2$ m/z 269.1 (M+H).

Step 5

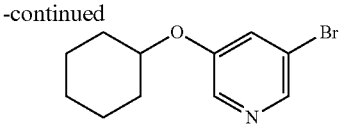
[0856] To a solution of 1-(5-bromopyridin-3-yl)-N-(cyclopentylmethyl) methanamine (LXIII) (1.00 g, 3.7 mmol, 1 eq) and TEA (0.93 g, 9.2 mmol, 2.5 eq) in DCM (20 mL) was added portionwise $(Boc)_2O$ (0.85 g, 4.0 mmol, 1.1 eq) at 0° C., the reaction mixture was stirred at room temperature for 1 h. The mixture was washed with water (10 mL), brine (10 mL), the organic layer was separated, dried over $MgSO_4$ and concentrated in vacuo to give tert-butyl (5-bromopyridin-3-yl)methyl (cyclopentylmethyl)carbamate (LXIV) (1.25 g, 3.38 mmol, 91.9% yield) as a white solid. ESIMS found for $C_{17}H_{25}BrN_2O_2$ m/z 369.1 (M+H).

[0857] Preparation of intermediate 3-bromo-5-(cyclohexyloxy)pyridine (LXVII) is depicted below in Scheme 13.

Scheme 13



-continued



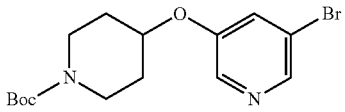
LXVII

Step 1

[0858] To a solution of 5-bromopyridin-3-ol (LXV) (523 mg, 3.01 mmol) in THF (30 mL) cooled to 0° C. were added triphenylphosphine (867 mg, 3.31 mmol) and cyclohexanol (LXVI) (331 mg, 3.31 mmol) followed by (E)-bis(4-chlorobenzyl) diazene-1,2-dicarboxylate (1.21 g, 3.31 mmol), added portionwise. The reaction mixture was then stirred at 25° C. overnight. The reaction was worked-up with a EtOAc—$NaHCO_3$ extraction and the solid filtered off. The solvent was removed and the residue was purified by Isco (20% EtOAc-Hexanes) to give 3-bromo-5-(cyclohexyloxy) pyridine (LXVII) (209 mg, 0.82 mmol, 27.2% yield) as a yellow oil. ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.21-1.31 (m, 1H) 1.34-1.48 (m, 4H) 1.49-1.57 (m, 1H) 1.70 (br dd, J=9.74, 4.25 Hz, 2H) 1.88-1.96 (m, 2H) 2.50 (dt, J=3.70, 1.72 Hz, 5H) 4.46-4.54 (m, 1H) 7.72 (t, J=2.20 Hz, 1H) 8.24 (d, J=1.92 Hz, 1H) 8.27 (d, J=2.47 Hz, 1H).

[0859] The following intermediate was prepared in accordance with the procedure described in the above Scheme 13.

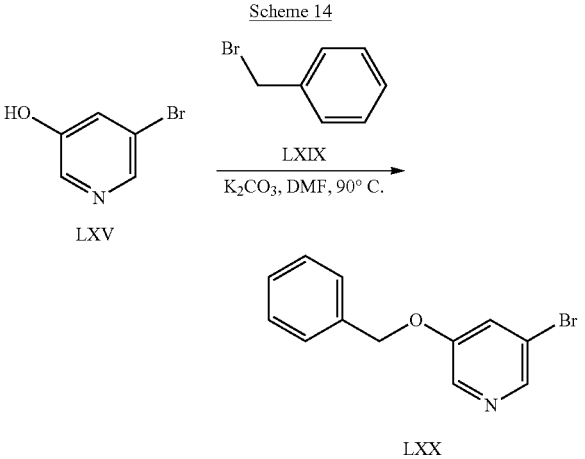
LXVIII



[0860] tert-Butyl 4-((5-bromopyridin-3-yl)oxy)piperidine-1-carboxylate (LXVIII): Yellow oil (244 mg, 0.683 mmol, 23.2% yield). ESIMS found for $C_{15}H_{21}BrN_2O_3$ m/z 358.3 (M+H).

[0861] Preparation of intermediate 3-(benzyloxy)-5-bromopyridine (LXX) is depicted below in Scheme 14.

Scheme 14

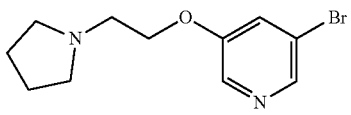


Step 1

[0862] To a solution of 5-bromopyridin-3-ol (LXV) (174 mg, 1.0 mmol) in DMF (3 mL) was added potassium carbonate (415 mg, 3.0 mmol). The slurry was heated at 90° C. for 1 hour and then cooled to 25° C. The (bromomethyl) benzene (LXIX) (171 mg, 1.0 mmol) was added and the mixture was stirred at 25° C. overnight. The reaction was worked-up using a saturated sodium bicarbonate and ethyl acetate extraction. The product was purified by ISCO column eluted with 40-100% EtOAc-Hexanes. The 3-(benzyloxy)-5-bromopyridine (LXX) (105 mg, 0.398 mmol, 39.8% yield) was obtained as yellow oil. MS: 266.1. ESIMS found for $C_{12}H_{10}BrNO$ m/z 266.1 (M+H).

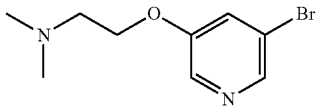
[0863] The following intermediates were prepared in accordance with the procedure described in the above Scheme 14.

LXXI



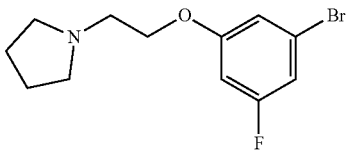
[0864] 3-Bomo-5-(2-(pyrrolidin-1-yl)ethoxy)pyridine (LXXI): Yellow oil ((97 mg, 0.358 mmol, 15.56% yield). ESIMS found for $C_{11}H_{15}BrN_2O$ m/z 272.2 (M+H).

LXXII



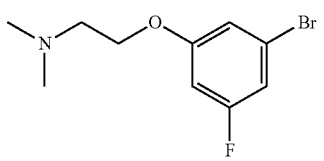
[0865] 2-((5-bromopyridin-3-yl)oxy)-N,N-dimethylethan-1-amine (LXXII): Yellow oil (97 mg, 0.396 mmol, 28.9% yield). ESIMS found for $C_9H_{13}BrN_2O$ m/z 245.1 (M+H).

LXXIII



[0866] 1-(2-(3-bromo-5-fluorophenoxy)ethyl)pyrrolidine (LXXIII): Yellow oil (370 mg, 1.284 mmol, 85.8% yield). ESIMS found for $C_{12}H_{15}BrFNO$ m/z 289.0 (M+H).

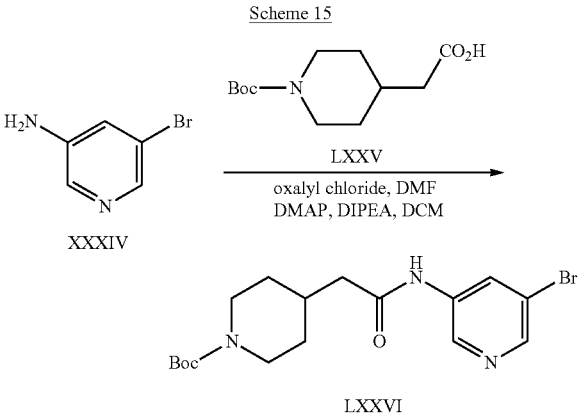
LXXIV



[0867] 2-(3-bromo-5-fluorophenoxy)-N,N-dimethylethan-1-amine (LXXIV): Yellow oil (364 mg, 1.389 mmol, 50.2% yield). ESIMS found for $C_{10}H_{13}BrFNO$ m/z 263.9 (M+H).

[0868] Preparation of intermediate tert-butyl 4-(2-((5-bromopyridin-3-yl)amino)-2-oxoethyl)piperidine-1-carboxylate (LXXVI) is depicted below in Scheme 15.

Scheme 15



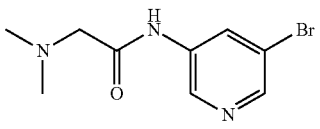
LXXVI

[0869] Step 1

[0870] To a solution of 2-(1-(tert-butoxycarbonyl)piperidin-4-yl)acetic acid (LXXV) (3.4 g, 13.97 mmol) in DCM (10 mL) was added DMF (1 mL). The solution was cooled in ice-water to 0° C. Oxalyl chloride (1.835 mL, 20.96 mmol) was then added dropwise. The mixture was stirred for one hour at 25° C. The organic volatile was then removed under vacuum. The residue was dissolved in DCM (10 mL). DMAP (0.171 g, 1.397 mmol) and 5-bromopyridin-3-amine (XXXIV) (2.418 g, 13.97 mmol) were added to the solution and cooled to 0° C. DIEA (4.88 ml, 27.9 mmol) was then added dropwise and the mixture was stirred for 2 hours at 25° C. The reaction was worked-up with DCM and saturated NaHCO3. The product was purified by ISCO eluted with 0-100% EtOAc-Hexanes. The tert-butyl 4-(2-((5-bromopyridin-3-yl)amino)-2-oxoethyl)piperidine-1-carboxylate (LXXVI) (2.82 g, 7.08 mmol, 50.7% yield) was obtained as yellow oil. ESIMS found for $C_{17}H_{24}BrN_3O_3$ m/z 343.1 (M−56).

[0871] The following intermediate was prepared in accordance with the procedure described in the above Scheme 15.

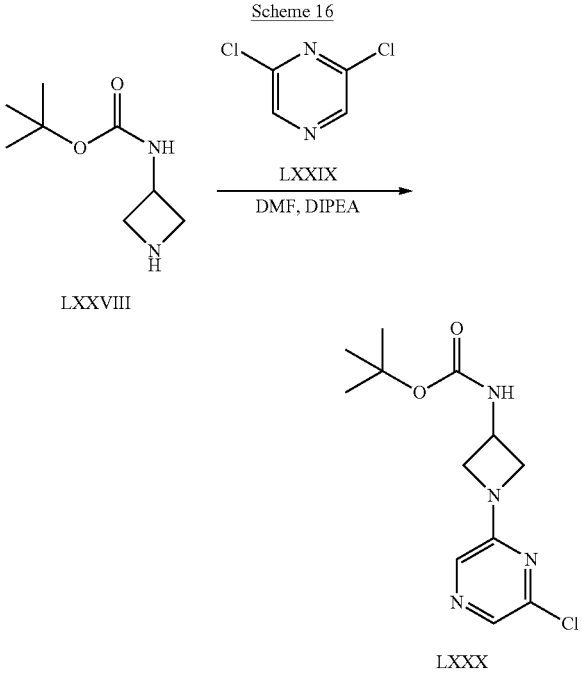
LXXVII



[0872] N-(5-Bromopyridin-3-yl)-2-(dimethylamino)acetamide (LXXVII): Yellow oil (528 mg, 2.05 mmol, 19.0% yield). ESIMS found for $C_9H_{12}BrN_3O$ m/z 259.3 (M+H).

[0873] Preparation of tert-butyl (1-(6-chloropyrazin-2-yl) azetidin-3-yl)carbamate (LXXX) is depicted below in Scheme 16.

Scheme 16



LXXVIII

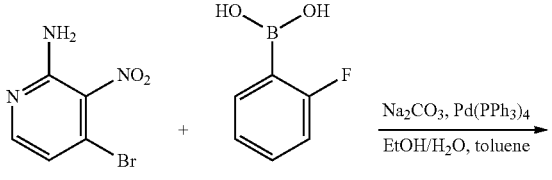
LXXX

Step 1

[0874] To a solution of tert-butyl azetidin-3-ylcarbamate hydrochloride (LXXVIII) (2 g, 9.58 mmol) in dry DMF (19.2 mL) was added DIPEA (8.37 ml, 47.9 mmol). To this mixture was added 2,6-dichloropyrazine (LXXIX) (1.428 g, 9.58 mmol) and the reaction was stirred at 95° C. for 3 hours. The reaction was quenched with water (20 mL) and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by silica gel column chromatography (40 g) (100% hexanes→hexanes:EtOAc 1:1) to yield tert-butyl (1-(6-chloropyrazin-2-yl)azetidin-3-yl)carbamate (LXXX) (2.2882 g, 8.04 mmol, 84% yield) as a white solid. ESIMS found for $C_{12}H_{17}ClN_4O_2$ m/z 285.1 (M+H).

[0875] Preparation of intermediate 4-(2-fluorophenyl)-3-nitropyridin-2-amine (LXXXIV) is depicted below in Scheme 17.

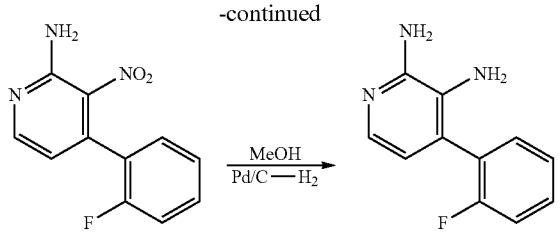
Scheme 17



LXXXI

LXXXII

-continued



LXXXIII

LXXXIV

Step 1

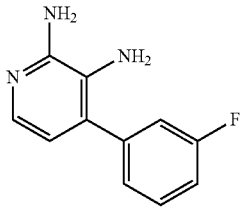
[0876] A solution of 4-bromo-3-nitropyridin-2-amine (LXXXI) (5.00 g, 22.9 mmol, 1.00 eq), (2-fluorophenyl) boronic acid (LXXXII) (3.82 g, 27.5 mmol, 1.20 eq), $Pd(PPh_3)_4$ (1.32 g, 1.14 mmol, 0.05 eq), and Na_2CO_3 (4.85 g, 45.8 mmol, 2 eq) in a mixture of toluene (25 mL), H_2O (9 mL) and EtOH (6 mL) was stirred at 75° C. for 15 h under nitrogen atmosphere. The reaction mixture was the washed with brine (50 mL) and dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resultant residue was purified by chromatography on silica gel (PE:EtOAc=3:1) to give 4-(2-fluorophenyl)-3-nitropyridin-2-amine (LXXXIII) (4.0 g, 17.15 mmol, 74.9%) as a yellow solid. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 6.29 (brs, 2H), 6.68 (d, J=4.8 Hz, 1H), 7.14 (t, J=5.2 Hz, 1H), 7.23-7.50 (m, 3H), 8.32 (d, J=4.8 Hz, 1H); ESIMS found $C_{11}H_8FN_3O_2$ m/z 234.2 (M+H).

Step 2

[0877] A mixture of 4-(2-fluorophenyl)-3-nitropyridin-2-amine (LXXXIII) (2.8 g, 12.0 mmol, 1 eq) and Pd/C (0.2 g) in MeOH (200 mL) was stirred under 50 psi of H_2 at room temperature overnight. The reaction was monitored by TLC. The mixture was filtered and the filtrate was concentrated in vacuo to produce 4-(2-fluorophenyl)pyridine-2,3-diamine (LXXXIV) (1.55 g, 7.63 mmol, 63.6% yield) as a black solid. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 3.38 (brs, 2H), 4.40 (brs, 2H), 6.64 (d, J=4.8 Hz, 1H), 7.11-7.53 (m, 4H), 7.72 (d, J=4.8 Hz, 1H); ESIMS found $C_{11}H_{10}FN_3$ m/z 204.2 (M+H).

[0878] The following intermediates were prepared in accordance with the procedure described in the above Scheme 17.

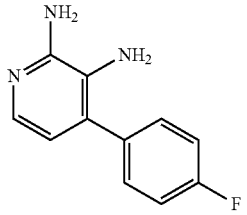
LXXXV



[0879] 4-(3-Fluorophenyl)pyridine-2,3-diamine (LXXXV): Grey solid, (1.55 g, 7.63 mmol, 86.0% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 3.50 (brs, 2H), 4.36 (brs,

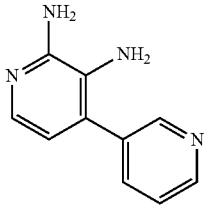
2H), 6.63 (d, J=3.6 Hz, 1H), 7.3-7.37 (m, 3H), 7.47 (d, J=6 Hz, 1H), 7.72 (d, J=3.6 Hz, 1H); ESIMS found $C_{11}H_{10}FN_3$ m/z 204.2 (M+H).

LXXXVI



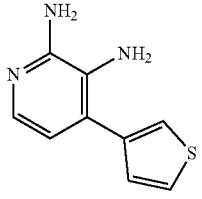
[0880] 4-(4-Fluorophenyl)pyridine-2,3-diamine (LXXXVI): Grey solid, (1.55 g, 7.63 mmol, 60.0% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 3.46 (brs, 2H), 4.36 (brs, 2H), 6.62 (s, 1H), 7.19 (s, 2H), 7.43 (s, 2H), 7.70 (d, J=3.2 Hz, 1H); ESIMS found $C_{11}H_{10}FN_3$ m/z 204.1 (M+H).

LXXXVII



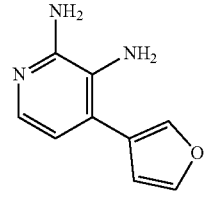
[0881] 4-(4-Fluorophenyl)pyridine-2,3-diamine (LXXXVII): Grey solid, (1.55 g, 7.63 mmol, 60.0% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 3.46 (brs, 2H), 4.36 (brs, 2H), 6.62 (s, 1H), 7.19 (s, 2H), 7.43 (s, 2H), 7.70 (d, J=3.2 Hz, 1H); ESIMS found $C_{11}H_{10}FN_3$ m/z 204.1 (M+H).

LXXXVIII



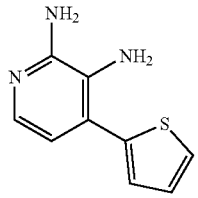
[0882] 4-(Thiophen-3-yl)pyridine-2,3-diamine (LXXXVIII): Yellow solid, (1.9 g, 9.94 mmol, 84.9% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 3.80 (brs, 2H), 4.34 (brs, 2H), 6.77 (s, 1H), 7.18 (s, 1H), 7.27 (s, 2H), 7.44 (s, 1H), 7.68 (s, 1H); ESIMS found $C_9H_9N_3S$ m/z 192.2 (M+H).

LXXXIX



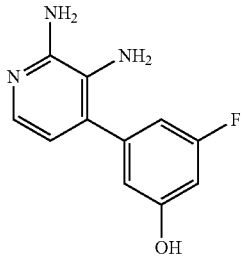
[0883] 4-(Furan-3-yl)pyridine-2,3-diamine (LXXXIX): Black solid, (1.9 g, 10.84 mmol, 89.0% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 3.64 (brs, 2H), 4.32 (brs, 2H), 6.65 (s, 1H), 6.69 (d, J=4.8 Hz, 1H), 7.58 (s, 1H), 7.67 (d, J=4.8 Hz, 1H), 7.71 (s, 1H); ESIMS found $C_9H_9N_3O$ m/z 176.3 (M+H).

XC



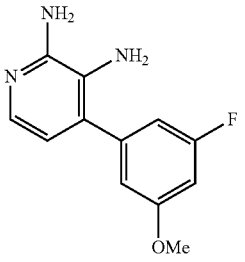
[0884] 4-(Thiophen-2-yl)pyridine-2,3-diamine (XC): Yellow solid, (0.90 g, 4.71 mmol, 96.5% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 3.63 (brs, 2H), 4.35 (brs, 2H), 6.71 (s, 1H), 7.27 (s, 1H), 7.45 (s, 1H), 7.49 (s, 1H), 7.69 (s, 1H); ESIMS found $C_9H_9N_3S$ m/z 192.1 (M+H).

XCI



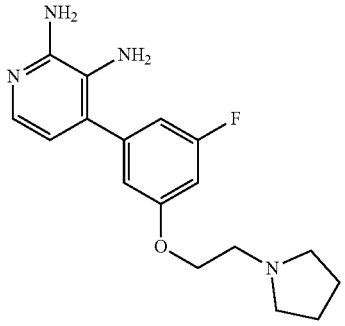
[0885] 3-(2,3-Diaminopyridin-4-yl)-5-fluorophenol (XCI): White solid (303 mg, 1.38 mmol, 84.4% yield). ESIMS found for $C_{11}H_{10}FN_3O$ m/z 220.1 (M+H).

XCII



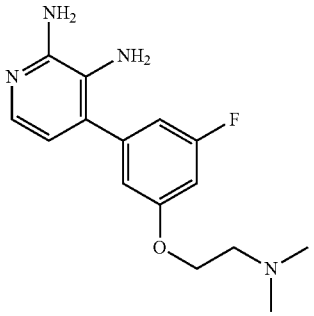
[0886] 4-(3-Fluoro-5-methoxyphenyl)pyridine-2,3-diamine (XCII): White solid (404 mg, 1.73 mmol, 75.1% yield). ESIMS found for $C_{12}H_{12}FN_3O$ m/z 234.1 (M+H).

XCIII



[0887] 4-(3-Fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl) pyridine-2,3-diamine (XCIII): Black oil (368 mg, 1.163 mmol, 95.0% yield). ESIMS found for $C_{17}H_{21}FN_4O$ m/z 317.1 (M+H).

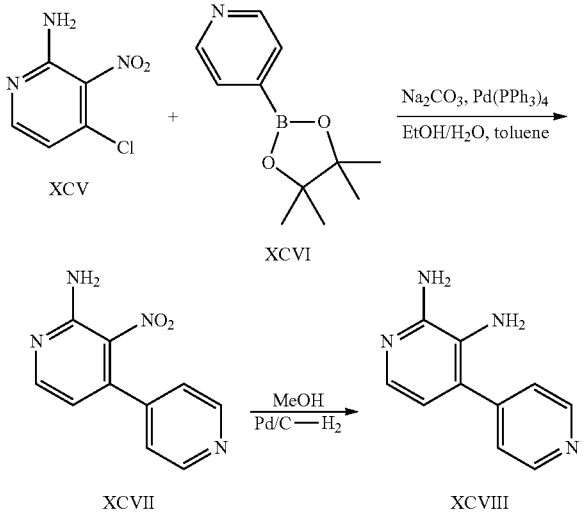
XCIV



[0888] 4-(3-(2-(Dimethylamino)ethoxy)-5-fluorophenyl) pyridine-2,3-diamine (XCIV): Black oil (352 mg, 1.212 mmol, 83.6% yield). ESIMS found for $C_{15}H_{19}FN_4O$ m/z 291.1 (M+H).

[0889] Preparation of intermediate 3-nitro-[4,4'-bipyridin]-2-amine (XCVIII) is depicted below in Scheme 18.

Scheme 18



Step 1

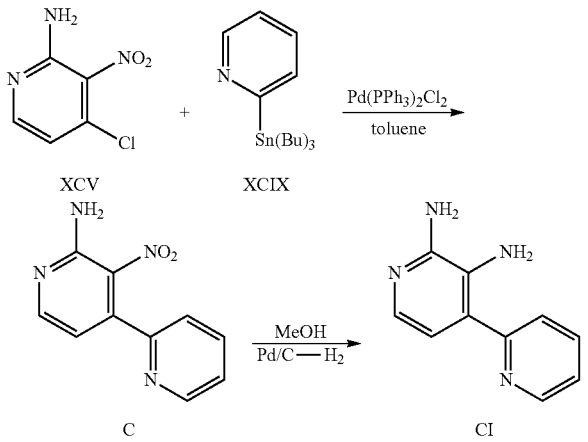
[0890] To a solution of 4-chloro-3-nitropyridin-2-amine (XCV) (5.00 g, 28.9 mmol, 1.00 eq) and 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (XCVI) (7.1 g, 34.6 mmol, 1.20 eq) in a mixture of toluene (30 mL), H_2O (18 mL) and EtOH (6 mL) was added $Pd(PPh_3)_4$ (1.0 g, 0.87 mmol, 0.03 eq) and Na_2CO_3 (6.1 g, 57.6 mmol, 2 eq). The mixture was stirred at 75° C. for 15 h under a nitrogen atmosphere. The reaction mixture was then poured into brine (100 mL) and extracted with EtOAc (30 mL×3), the combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resultant residue was purified by chromatography on silica gel (PE:EtOAc=5:1→1:1) to afford 3-nitro-[4,4'-bipyridin]-2-amine (XCVII) (1.80 g, 8.33 mmol, 28.8% yield) as a yellow solid. ESIMS found $C_{10}H_8N_4O_2$ m/z 217.1 (M+H).

Step 2

[0891] To a solution of 3-nitro-[4,4'-bipyridin]-2-amine (XCVII) (1.80 g, 8.33 mol, 1 eq) in MeOH (50 mL) was added Pd/C (0.5 g) under a nitrogen atmosphere. The mixture was stirred under 50 psi of H_2 for 6 h at room temperature. Then the mixture was filtered through a Celite pad and the filtrate was concentrated in vacuo to afford [4,4'-bipyridine]-2,3-diamine (XCVIII) (1.4 g, 7.52 mmol, 90.4% yield) as a black solid. ESIMS found $C_{10}H_{10}N_4$ m/z 186.0 (M+H).

[0892] Preparation of intermediate 3-nitro-[4,4'-bipyridin]-2-amine (CI) is depicted below in Scheme 19.

Scheme 19



Step 1

[0893] A solution of 4-chloro-3-nitropyridin-2-amine (XCV) (5.00 g, 28.9 mmol, 1.00 eq), 2-(tributylstannyl) pyridine (XCIX) (15.9 g, 43.4 mmol, 1.50 eq), and $Pd(PPh_3)_2Cl_2$ (1.05 g, 1.44 mmol, 0.05 eq) in a mixture of toluene (25 mL) and H_2O (9 mL) was stirred at 75° C. for 16 h under a nitrogen atmosphere. The reaction mixture was then poured into brine (80 mL) and extracted with EtOAc (30 mL×3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The resultant residue was purified by chromatography on silica gel (PE:

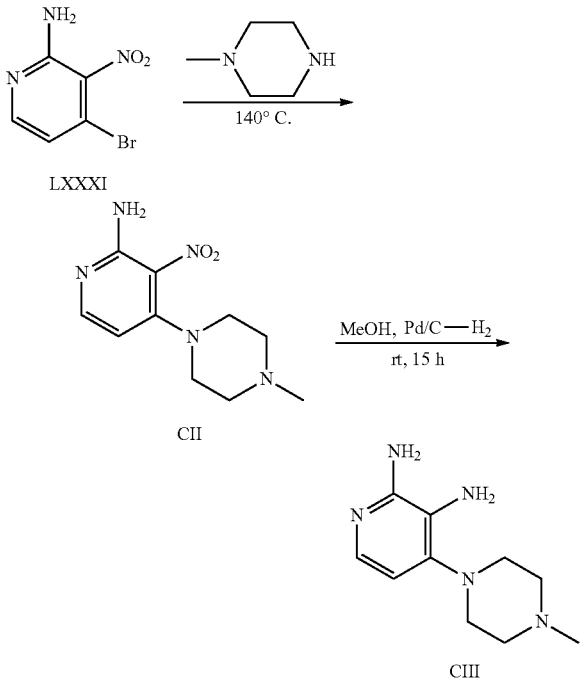
EtOAc=5:1→1:1) to afford 3'-nitro-[2,4'-bipyridin]-2'-amine (C) (1.6 g, 7.40 mmol, 25.6% yield) as a yellow solid. ESIMS found $C_{10}H_8N_4O_2$ m/z 217.1 (M+H).

Step 2

[0894] To a solution of compound 3'-nitro-[2,4'-bipyridin]-2'-amine (C) (1.6 g, 7.4 mmol, 1.0 eq) in MeOH (50 mL) was added Pd/C (0.5 g) under a nitrogen atmosphere. The mixture was stirred under 50 psi of H_2 for 6 h at room temperature. The mixture was then filtered and concentrated in vacuo to afford [2,4'-bipyridine]-2',3'-diamine (CI) (1.1 g, 5.91 mmol, 79.8%) as a black solid. ESIMS found $C_{10}H_{11}N_4$ m/z 186.1 (M+H).

[0895] Preparation of intermediate 4-(4-methylpiperazin-1-yl)pyridine-2,3-diamine (CIII) is depicted below in Scheme 20.

Scheme 20



Step 1

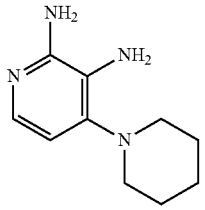
[0896] A solution of 4-bromo-3-nitropyridin-2-amine (LXXXI) (2.50 g, 11.47 mmol) in 1-methylpiperazine (4 mL, 34.5 mmol) was heated at 140° C. overnight. The reaction was poured into an EtOAc/H_2O mixture; the organic layer was separated, dried over $MgSO_4$ and concentrated under vacuum. The crude product was purified on a silica gel column (100% $CHCl_3$→3:97 MeOH (7N NH_3): $CHCl_3$) to give 4-(4-methylpiperazin-1-yl)-3-nitropyridin-2-amine (CII) as a yellow solid (1.80 g, 7.59 mmol, 66.1% yield). ^{1}H NMR ($CDCl_3$, 400 MHz) δ ppm 2.36 (s, 3H), 2.54 (t, J=4.8 Hz, 4H), 3.25 (t, J=5 Hz, 4H), 6.18 (s, 2H), 6.22 (d, J=6 Hz, 1H), 7.85 (d, J=6 Hz, 1H); ESIMS found $C_{10}H_{15}N_5O_2$ m/z 238.0 (M+H).

Step 2

[0897] To a solution of 4-(4-methylpiperazin-1-yl)-3-nitropyridin-2-amine (CII) (1.80 g, 7.59 mmol) in MeOH (52 mL) was added 10% Pd/C (0.5 g). The solution was purged with hydrogen and stirred at room temperature under hydrogen for 4 h. The suspension was filtered through Celite® and the concentrated under vacuum to produce 4-(4-methylpiperazin-1-yl)pyridine-2,3-diamine (CIII) as black solid (1.4 g, 6.75 mmol, 89.0% yield). ^{1}H NMR ($CDCl_3$, 400 MHz): δ ppm 2.38 (s, 3H), 2.60 (brs, 4H), 2.99 (s, 4H), 3.49 (brs, 2H), 4.12 (brs, 2H), 6.52 (d, J=5.6 Hz, 1H), 7.64 (d, J=5.6 Hz, 1H); ESIMS found $C_{10}H_{17}N_5$ m/z 208.1 (M+H).

[0898] The following intermediate was prepared in accordance with the procedure described in the above Scheme 20.

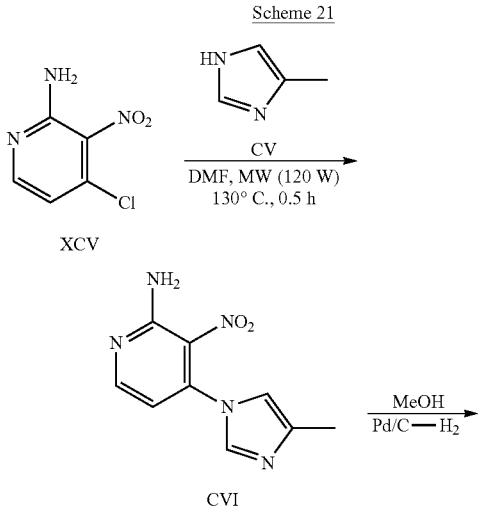
CIV



[0899] 4-(Piperidin-1-yl)pyridine-2,3-diamine (CIV): Black solid, (2.40 g, 12.48 mmol, 92.5% yield). ^{1}HNMR ($CDCl_3$, 400 MHz): δ ppm 1.61 (brs, 2H), 1.73 (s, 4H), 2.88 (s, 4H), 3.48 (brs, 2H), 4.13 (brs, 2H), 6.50 (d, J=5.2 Hz, 1H), 7.63 (d, J=4.8 Hz, 1H); ESIMS found $C_{10}H_{16}N_4$ m/z 193.1 (M+H).

[0900] Preparation of intermediate 4-(2-fluorophenyl)-3-nitropyridin-2-amine (CVII) is depicted below in Scheme 21.

Scheme 21



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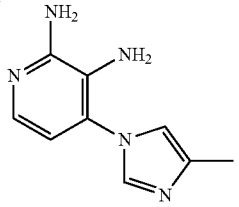


CVII

Step 1

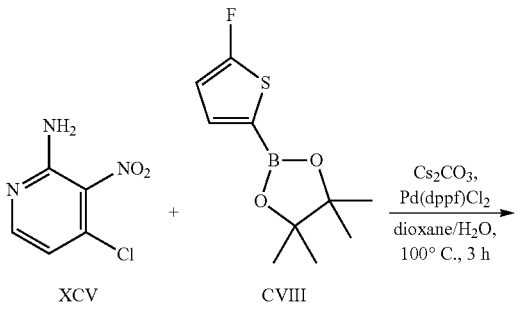
[0901] 4-Chloro-3-nitro-pyridin-2-amine (XCV) (3.00 g, 17.3 mmol, 1.0 eq) and 4-methyl-1H-imidazole (CV) (2.84 g, 34.6 mmol, 2.0 eq) were taken up into a microwave tube in DMF (20 mL). The sealed tube was heated at 130° C. for 30 min under microwave. TLC showed the starting material was consumed, LC/MS showed the desired product was found. 10% NH_4Cl (60 mL) were added. The aqueous layer was extracted with DCM (2×100 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, concentrated in vacuum. The residue was purified by chromatography on silica gel (PE:THF=1:1) to give the product 4-(4-methylimidazol-1-yl)-3-nitro-pyridin-2-amine (CVI) (1.20 g, 5.47 mmol, 31.6% yield) as a yellow solid. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 2.30 (d, J=0.75 Hz, 3H), 5.96-6.26 (m, 2H), 6.68 (d, J=5.02 Hz, 1H), 6.72-6.75 (m, 1H), 7.57 (d, J=1.0 Hz, 1H), 8.32 (d, J=5.14 Hz, 1H); ESIMS found $C_9H_9N_5O_2$ m/z 219.1 (M+H).

Step 2

[0902] To a solution of 4-(4-methylimidazol-1-yl)-3-nitro-pyridin-2-amine (CVI) (900.0 mg, 4.11 mmol, 1.0 eq) in MeOH (50 mL) was added Pd/C (100.0 mg, 4.11 mmol, 1.0 eq) at room temperature. The mixture was stirred at 20° C. under H_2 for 2 hr. TLC (DCM:MeOH=20:1) showed that starting the material was consumed completely. The mixture was filtered and concentrated to afford 4-(4-methyl-1H-imidazol-1-yl)pyridine-2,3-diamine (CVII) (750.0 mg, 3.96 mmol, 96.4% yield) as a brown solid. ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 2.17 (s, 3H), 4.58 (brs, 2H), 5.85 (brs, 2H), 6.36 (d, J=5.4 Hz, 1H), 7.06 (s, 1H), 7.34 (s, 1H), 7.34 (s, 1H), 7.69 (d, J=0.88 Hz, 1H); ESIMS found $C_9H_{11}N_5$ m/z 190.1 (M+H).

[0903] Preparation of intermediate 4-(5-fluorothiophen-2-yl)pyridine-2,3-diamine (CX) is depicted below in Scheme 22.

Scheme 22



XCV CVIII

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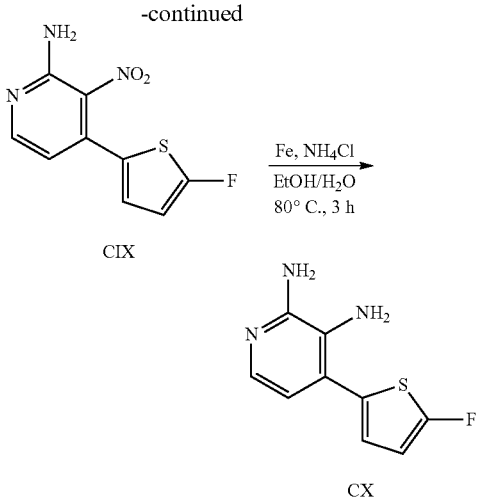


CIX CX

Step 1

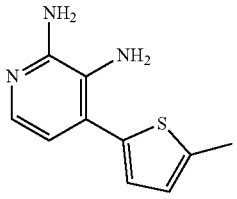
[0904] A solution of 2-chloro-3-nitro-pyridin-4-amine (XCV) (1.5 g, 8.64 mmol), 2-(5-fluorothiophen-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (CVIII) (2.96 g, 12.96 mmol), $Pd(dppf)Cl_2$ (632 mg, 0.86 mmol) and Cs_2CO_3 (5.63 g, 17.29 mmol) in dioxane (30 mL) and H_2O (5 mL) was de-gassed and then heated to 100° C. under N^2 for 3 h. TLC (PE:EtOAc=1:1) showed the starting material was consumed completely. The mixture was concentrated in vacuum to give a residue, which was purified by column chromatography to afford 4-(5-fluorothiophen-2-yl)-3-nitropyridin-2-amine (CIX) (800 mg, 3.34 mmol, 38.7% yield). ESIMS found $C_9H_6FN_3O_2S$ m/z 240.1 (M+H).

Step 2

[0905] A solution of 4-(5-fluorothiophen-2-yl)-3-nitropyridin-2-amine (CIX) (700 mg, 2.93 mmol), Fe (817 mg, 14.63 mmol) and NH_4Cl (939 mg, 17.56 mmol) in EtOH (18 mL) and H_2O (6 mL) was heated to 80° C. for 2 h. TLC (PE:EtOAc=1:1) showed the starting material was consumed completely. The mixture was filtered, washed with HCl/EtOH, concentrated, basified to pH=7~8, extracted with EtOAc and H_2O, the organic layer was concentrated to give 4-(5-fluorothiophen-2-yl)pyridine-2,3-diamine (CX) (550 mg, 2.63 mmol, 89.7% yield). ESIMS found $C_9H_8FN_3S$ m/z 210.0 (M+H).

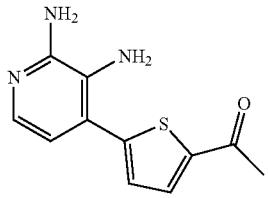
[0906] The following intermediates were prepared in accordance with the procedure described in the above Scheme 22.

CXI



[0907] 4-(5-Methylthiophen-2-yl)pyridine-2,3-diamine (CXI): Brown solid, (1.20 g, 5.85 mmol, 86.0% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 2.54 (s, 3H), 6.63 (d, J=4.8 Hz, 1H), 6.85 (s, 1H), 7.12 (s, 1H), 7.38 (d, J=5.2 Hz, 1H); ESIMS found $C_{10}H_{11}N_3S$ m/z 206.2 (M+H).

CXII



[0908] 1-(5-(2,3-Diaminopyridin-4-yl)thiophen-2-yl) ethan-1-one (CXII): Brown solid, (500 mg, 2.14 mmol, 56.4% yield). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.55 (s, 3H), 4.89 (brs, 2H), 5.80 (brs, 2H), 6.52 (d, J=5.2 Hz, 1H), 7.33 (d, J=5.2 Hz, 1H), 7.46 (d, J=4.0 Hz, 1H), 7.96 (d, J=4.0 Hz, 1H); ESIMS found $C_{11}H_{11}N_3OS$ m/z 234 (M+H).

[0909] Preparation of intermediate 4-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)pyridine-2,3-diamine (CXVII) is depicted below in Scheme 23.

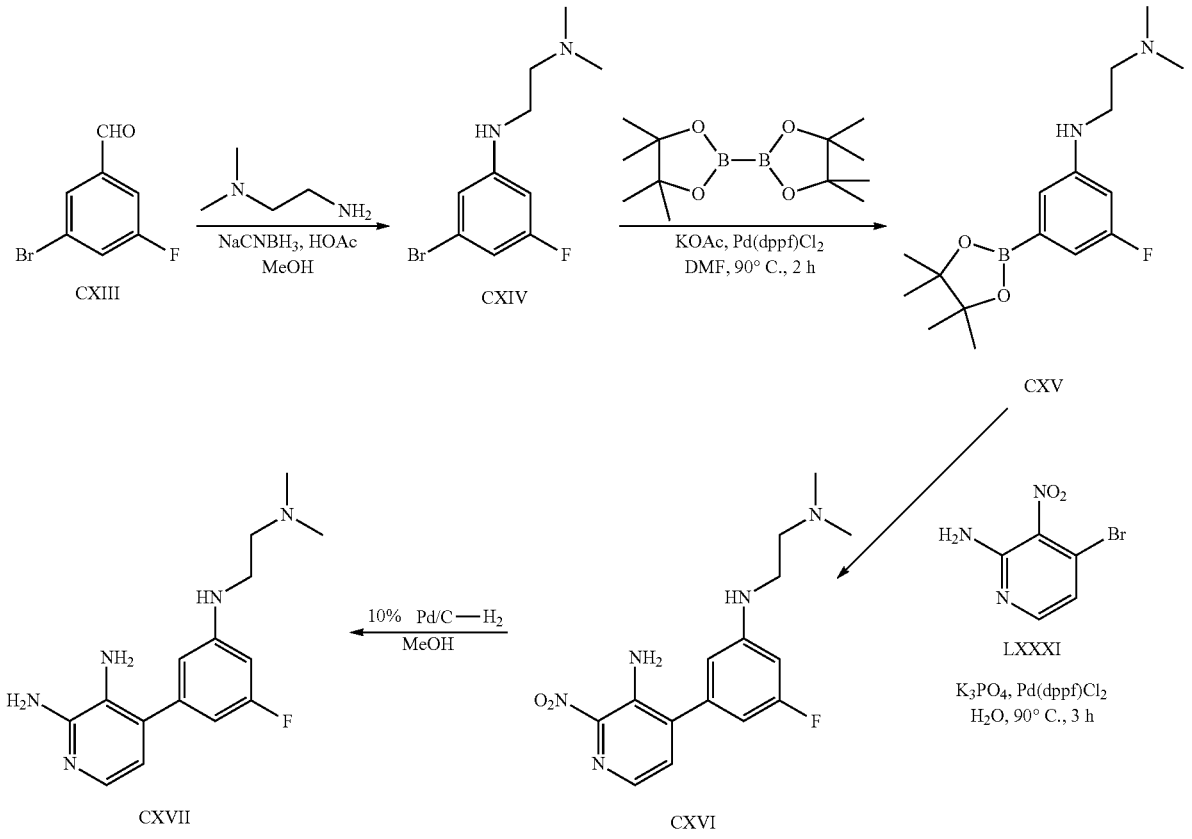
Step 1

[0910] A solution of3-bromo-5-fluorobenzaldehyde (CXIII) (20.0 g, 98.2 mmol, 1.0 eq) in MeOH (1.8 L) was added N^1,N^1-dimethylethane-1,2-diamine (21.5 mL, 196.4 mmol, 2.0 eq). The pH was adjusted to 6 using HOAc and stirred for 1 h. $NaCNBH_3$ (8.6 g, 137.5 mmol, 1.4 eq) was added and stirred at room temperature overnight. The MeOH was removed under vacuum and the residue was partitioned between $CHCl_3$ and saturated aqueous $NaHCO_3$. The organic layer was dried over $MgSO_4$ and evaporated under vacuum. The crude product was purified on a silica gel column (100% $CHCl_3$→3:97 MeOH[7N NH_3]:$CHCl_3$) to produce N^1-(3-bromo-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CXIV) as a yellow oil (13.0 g, 49.9 mmol, 51% yield). ESIMS found $C_{10}H_{14}BrFN_2$ m/z 261.0 (M+H).

Step 2

[0911] A solution of N^1-(3-bromo-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CXIV) (13.0 g, 49.9 mmol, 1.0 eq), bis(pinacolato)diboron (12.6 g, 59.9 mmol, 1.2 eq), KOAc (12.1 g, 124.3 mmol, 2.5 eq) and dioxane (600 mL) was purged with argon. $Pd(dppf)Cl_2$ (2.0 g, 2.47 mmol, 0.05 eq) was added to the reaction and purged again with argon. The solution was heated at 90° C. for 2 h. Once TLC showed the disappearance of (CXIV), the solution was cooled to

Scheme 23



room temperature and then concentrated under reduced pressure to produce crude N^1-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine (CXV) (7.4 g, 24.0 mmol, 48.2% yield).

Step 3

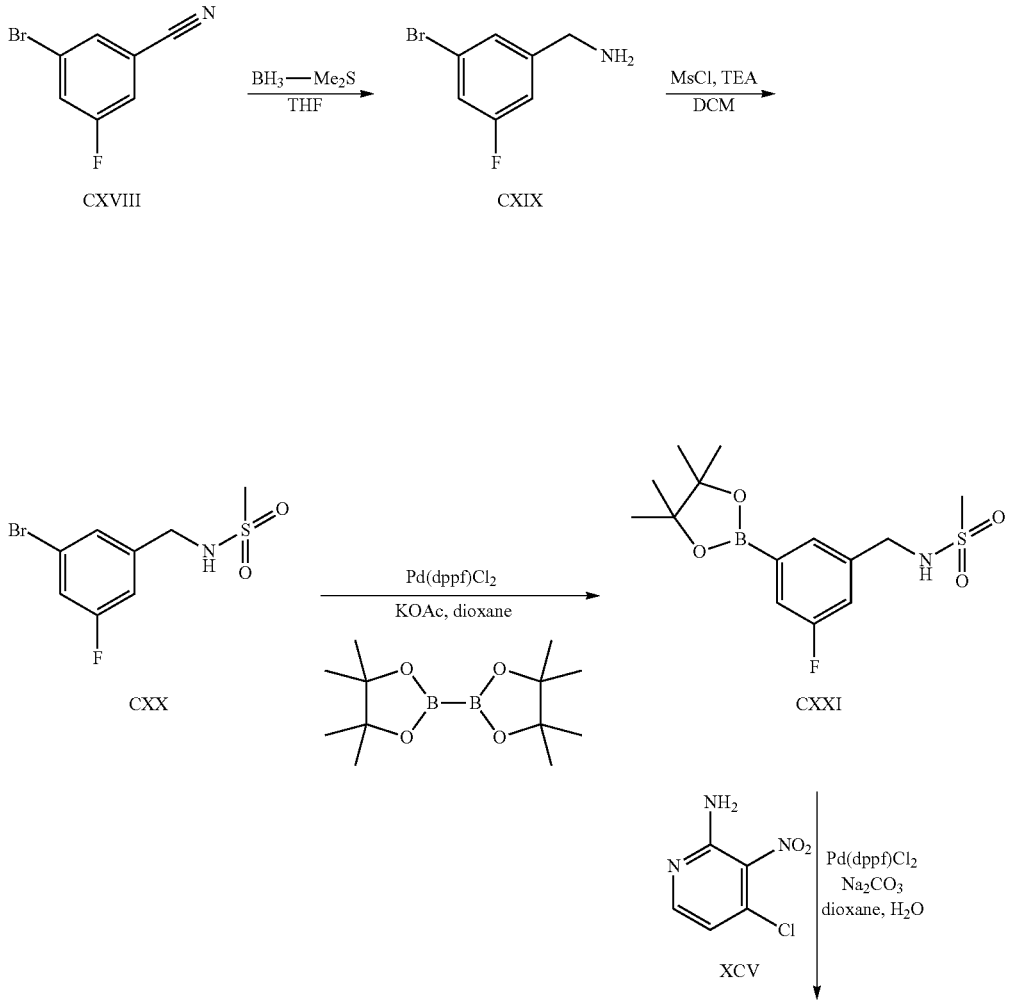
[0912] To a solution of N^1-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine (CXV) (5.0 g, 16.22 mmol, 1.2 eq) in water (25 mL) was added K_2CO_3 (448 mg, 3.24 mmol, 2.0 eq), 4-bromo-3-nitropyridin-2-amine (LXXXI) (3.5 g, 16.22 mmol, 1.0 eq) and Pd(dppf)Cl_2 (1.0 g, 81.0 μmol, 0.05 eq). The solution was purged with argon and heated at 100° C. for 48 h. The solution was cooled to room temperature and then concentrated under reduced pressure. The residue was purified on a silica gel column (100% $CHCl_3$→2:98 MeOH [7N NH_3]:$CHCl_3$) to give N^1-(3-(2-amino-3-nitropyridin-4-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CXVI) as a yellow amorphous solid (4.5 g, 14.1 mmol, 86.9% yield). ESIMS found for $C_{15}H_{18}FN_5O_2$ m/z 220.1 (M+H).

Step 4

[0913] To a solution of N^1-(3-(2-amino-3-nitropyridin-4-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine (CXVI) (4.50 g, 10.43 mmol, 1.0 eq) in MeOH (15 mL) was added 10% Pd/C (540 mg, 15% by wt). The solution was purged with hydrogen and stirred for 48 h at room temperature under hydrogen (15 psi). The suspension was filtered through Celite® and concentrated under vacuum and purified by silica gel chromatography (MeOH:DCM=10:1) to produce 4-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl) pyridine-2,3-diamine (CXVII) as a tan solid (750.0 mg, 2.59 mmol, 24.9% yield). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 2.32 (s, 6H), 2.60 (t, J=6.8 Hz, 2H), 3.26 (t, J=6.8 Hz, 2H), 6.34-6.43 (m, 2H), 6.47 (d, J=5.6 Hz, 1H), 7.58 (s, 1H), 7.75 (s, 1H); ESIMS found $C_{15}H_{20}FN_5$ m/z 290.1 (M+H).

[0914] Preparation of intermediate N-(3-(2,3-diaminopyridin-4-yl)-5-fluorobenzyl)methanesulfonamide (CXXIII) is depicted below in Scheme 24.

Scheme 24



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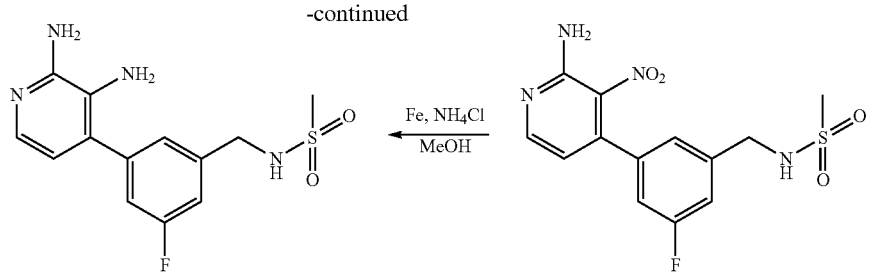


CXXIII CXXII

Step 1

[0915] A solution of 3-bromo-5-fluorobenzonitrile (CXVIII) (44.0 g, 220.0 mmol, 1.0 eq) was dissolved in THF (30 mL). BH_3-Me_2S (33.43 g, 440.0 mmol, 2.0 eq) was added to the solution at 20° C. Then it was stirred at 80° C. for 2 h, HCl (6 N, 100 mL) was added to the mixture slowly at 20° C. The mixture was stirred at 80° C. for 1 h, then it was washed with EtOAc (300 ml). The water phase was basified with 50% aqueous NaOH and it was extracted with EtOAc (300 mL×3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in vacuo to produce (3-bromo-5-fluoro-phenyl)methanamine (CXIX) (24.0 g, 117.62 mmol, 53.5% yield). ^{1}HNMR ($CDCl_3$, 300 MHz) 3.86 (s, 2H), 7.01 (d, J=8 Hz, 1H), 7.12 (d, J=8 Hz, 1H), 7.28 (s, 1H); ESIMS found C_7H_7BrFN m/z 203.9 (Br^{79}M+H).

Step 2

[0916] A solution of (3-bromo-5-fluoro-phenyl)methanamine (CXIX) (23.0 g, 112.7 mmol, 1.0 eq) was dissolved in DCM (15 mL), TEA (34.22 g, 338.2 mmol, 3.0 eq) was added to the mixture. Then MsCl (13.44 g, 117.3 mmol, 1.04 eq) was added slowly to the solution at 0° C. It was stirred at 0-30° C. for 2 h. The reaction was washed with water and extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated to give N-(3-bromo-5-fluorobenzyl)methanesulfonamide (CXX) (34.0 g, 102.44 mmol, 90.9% yield, 85% purity) as an oil. ^{1}H NMR ($CDCl_3$, 300 MHz) 2.88 (s, 3H), 4.24 (d, J=4.5 Hz, 2H), 6.99 (d, J=9 Hz, 1H), 7.13 (dt, J=8.1 Hz, J=2 Hz, 1H), 7.25 (s, 1H); ESIMS found $C_8H_9BrFNO_2S$ m/z 282.0 (Br^{79}M+H).

Step 3

[0917] A solution of N-(3-bromo-5-fluorobenzyl)methanesulfonamide (CXX) (34.0 g, 102.4 mmol, 1.0 eq) and 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (52.02 g, 204.9 mmol, 2.0 eq), KOAc (20.11 g, 204.9 mmol, 2.0 eq) was dissolved in dioxane (20 mL). Then Pd(dppf)Cl_2 (7.60 g, 10.2 mmol, 0.1 eq) was added to the mixture. It was stirred at 90° C. for 2 h. Then the solvent was removed to get the residue which was purified by silica gel column (PE:EtOAc=10:1-100% EtOAc) to get N-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzyl)methanesulfonamide (CXXI) (30.0 g, crude). ^{1}H NMR ($CDCl_3$, 400 MHz) 1.37 (s, 12H), 2.92 (s, 3H), 4.34 (d, J=6.3 Hz, 2H), 7.19 (dt, J=9.3 Hz, J=2.1 Hz, 1H), 7.44 (dd, J=8.7 Hz, J=2.4 Hz, 1H), 7.54 (s, 1H); ESIMS found $C_{14}H_{21}BFNO_4S$ m/z 330.1 (M+H).

Step 4

[0918] A solution of N-(3-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) benzyl)methanesulfonamide (CXXI) (6.83 g, 20.75 mmol, 1.2 eq), 4-chloro-3-nitropyridin-2-amine (XCV) (3.0 g, 17.29 mmol, 1.0 eq), Na_2CO_3 (6.41 g, 60.52 mmol) and Pd(dppf)Cl_2 (641.27 mg, 864.50 μmol) in dioxane (40 mL) and H_2O (8 mL) was de-gassed and then heated to 80° C. overnight under N_2. TLC (PE:EtOAc=1:1) showed the starting material was consumed completely. The reaction mixture was poured into H_2O (300 mL). The mixture was extracted with EtOAc (3×250 mL). The organic phase was washed with saturated brine (300 mL), dried over anhydrous $NaSO_4$, concentrated in vacuum to give a residue. The crude product was purified by silica gel chromatography (PE:EtOAc=10:1) to give N-(3-(2-amino-3-nitropyridin-4-yl)-5-fluorobenzyl) methanesulfonamide (CXXII) (2.2 g, 6.46 mmol, 37.4% yield) as brown solid. ESIMS found $C_{13}H_{13}FN_4O_4S$ m/z 341.1 (M+H).

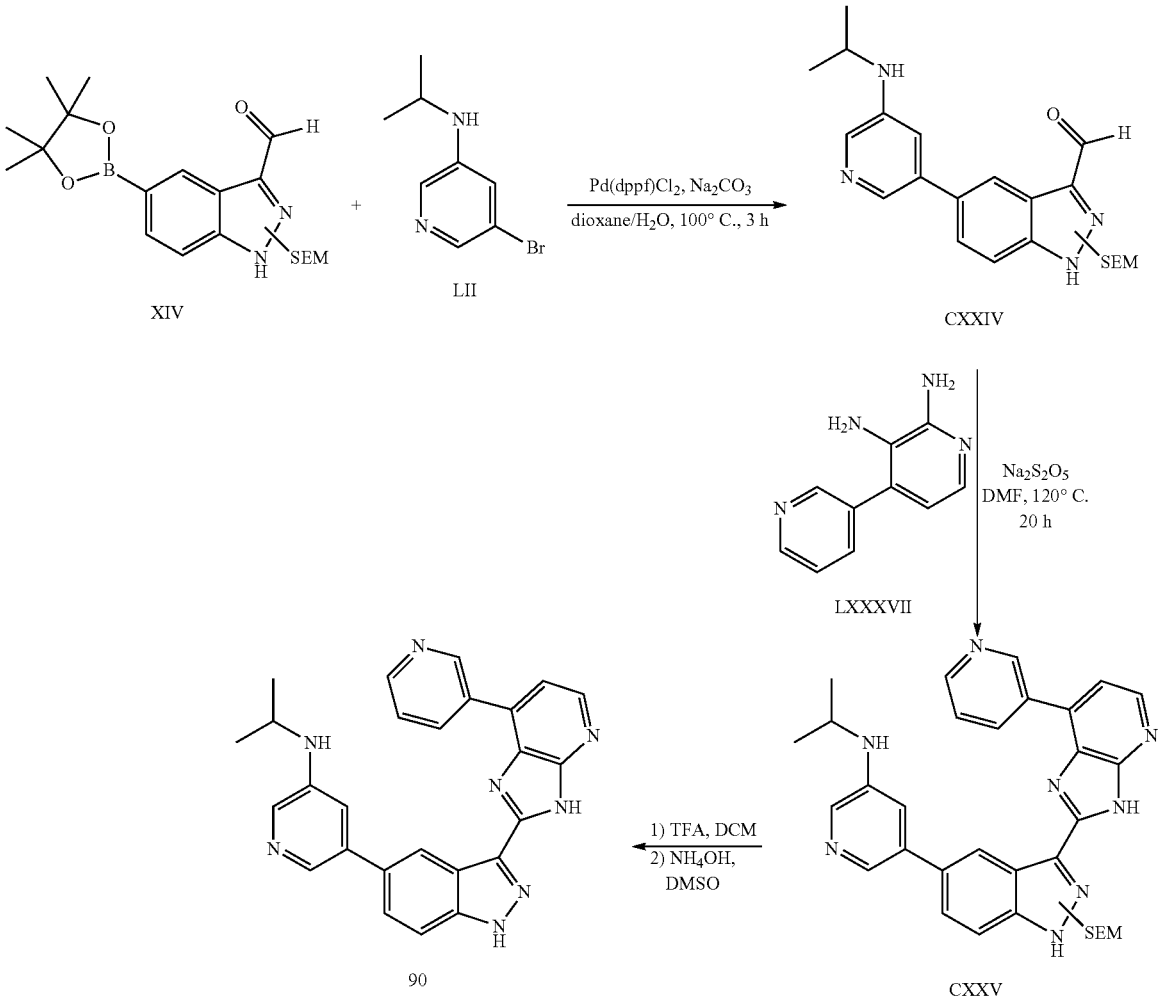
Step 5

[0919] A solution of N-[[3-(4-amino-3-nitro-2-pyridyl)-5-fluoro-phenyl]methyl]methanesulfonamide (CXXII) (2.2 g, 6.46 mmol, 1.0 eq), Fe (1.44 g, 25.84 mmol, 4.0 eq) and NH_4Cl (2.8 g, 51.68 mmol, 8.0 eq) was dissolved in MeOH (30 mL). The mixture was stirred at 80° C. for 16 h. The mixture was cooled to room temperature and concentrated in reduced pressure at 60° C. The combined organic phase was washed with saturated brine (100 mL×2), dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to get crude N-(3-(3,4-diaminopyridin-2-yl)-5-fluorobenzyl) methanesulfonamide (CXXIII) (1.60 g, 5.16 mmol, 79.8% yield) as brown solid. ^{1}H NMR (CD_3OD, 400 MHz) 2.96 (s, 3H), 3.37 (s, 2H), 6.53 (d, J=4 Hz, 1H), 7.13 (d, J=8.8 Hz, 1H), 7.20 (d, J=9.2 Hz, 1H), 7.31 (s, 1H), 7.44 (d, J=4 Hz, 1H); ESIMS found $C_{13}H_{15}FN_4O_2S$ m/z 311.1 (M+H).

Example 1

[0920] Preparation of N-isopropyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine (90) is depicted below in Scheme 25.

Scheme 25



Step 1

[0921] To a solution of 5-bromo-N-isopropylpyridin-3-amine (LII) (1.0 g, 4.65 mmol, 1.0 eq) and 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-((2-(trimethylsilyl) ethoxy)methyl)-1H-indazole-3-carbaldehyde (XIV) (2.25 g, 5.58 mmol, 1.2 eq), $Pd(dppf)Cl_2$ (341 mg, 0.46 mmol, 0.10 eq) and Na_2CO_3 (985 mg, 9.3 mmol, 2.0 eq) in dioxane (21 mL) and H_2O (3.5 mL) was de-gassed and then heated to 100° C. for 3 h under N_2. TLC (100% EtOAc) showed the starting material was consumed completely. The reaction mixture was concentrated in vacuum to give a residue, which was pre-purified by silica gel column chromatography (PE:EtOAc=10:1→1:1) to afford pure 5-(5-(isopropylamino)pyridin-3-yl)-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole-3-carbaldehyde (CXXIV) as a red brown oil (1.8 g, 4.38 mmol, 94.3% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm −0.03 (s, 9H), 0.93 (t, J=8.4 Hz, 2H), 1.29 (d, J=6 Hz, 6H), 1.76 (brs, 1H), 3.62 (t, J=8.4 Hz, 2H), 3.71-3.82 (m, 1H), 5.86 (s, 2H), 7.10 (t, J=2 Hz, 1H), 7.73 (s, 1H), 8.01 (d, J=2.4 Hz, 1H), 8.22 (s, 1H), 8.49 (s, 1H), 10.29 (s, 1H); ESIMS found for $C_{22}H_{30}N_4O_2Si$ m/z 411.1 (M+H).

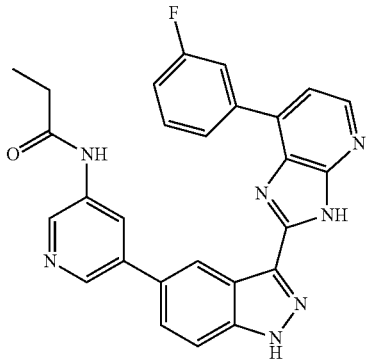
Step 2-3

[0922] A solution of 5-(5-(isopropylamino)pyridin-3-yl)-1-((2-(trimethylsilyl) ethoxy)methyl)-1H-indazole-3-carbaldehyde (CXXIV) (100.0 mg, 0.24 mmol, 1.0 eq), [3,4'-bipyridine]-2',3'-diamine (LXXXVII) (45 mg, 0.24 mmol, 1.0 eq) and Na_2S20_5 (53 mg, 0.29 mmol, 1.20 eq) in DMF (2 mL) was stirred at 120° C. for 20 h. LC/MS showed the starting material was consumed. Water (5 mL) was then added dropwise to the mixture and stirred at room temperature for 10 min, the mixture was filtered, then the filtrate was washed by H_2O (2 mL×3), dried over anhydrous $MgSO_4$, and evaporated under vacuum to give crude N-isopropyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1-((2-(trimethylsilyl) ethoxy)methyl)-1H-indazol-5-yl)pyridin-3-amine (CXXV). CXXV was dissolved in dry DCM (5 mL) before adding triethylsilane (92 μL, 0.57 mmol) and TFA (2.5 mL). The reaction was stirred at room temperature for 2 h under N_2. The solvent was evaporated under reduced pressure; the residue was taken up water (10 mL), and basified with 5N NH_4OH. The precipitates were filtered, washed by cold water and dried under vacuum at room

temperature. The crude product was suspended in DCM (10 mL), sonicated briefly and then heated to boiling for 5 min. The solution was cooled to room temperature and the solids were filtered, washed with DCM and dried under vacuum at room temperature to produce N-isopropyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-amine (90) as a white solid (43.9 mg, 0.10 mmol, 41.0%). ^{1}H NMR (DMSO-d_6, 400 MHz) 1.23 (d, J=6.27 Hz, 6H), 3.80-3.91 (m, 1H), 7.88 (d, J=5.27 Hz, 1H), 7.90 (s, 2H), 8.02 (brs, 1H), 8.10 (d, J=2.01 Hz, 1H), 8.26-8.35 (m, 1H), 8.50 (s, 1H), 8.56 (d, J=5.27 Hz, 1H), 8.86 (s, 1H), 9.03 (d, J=5.52 Hz, 1H), 9.44-9.55 (m, 1H), 9.93-10.00 (m, 1H), 14.32 (brs, 1H); ESIMS found for $C_{26}H_{22}N_8$ m/z 447.3 (M+1).

[0923] The following compounds were prepared in accordance with the procedure described in the above Example 1.

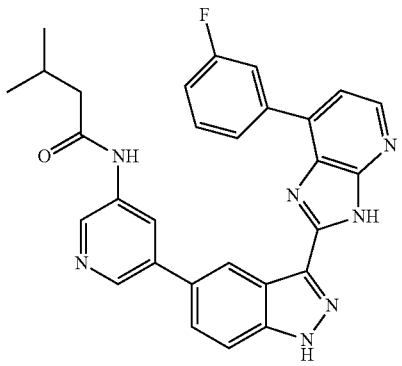
1



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide 1

[0924] White solid (38.5 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.14 (t, J=7.53 Hz, 3H), 2.41-2.47 (m, 2H), 7.33 (td, J=8.16, 2.26 Hz, 1H), 7.60-7.68 (m, 1H), 7.70 (d, J=5.27 Hz, 1H), 7.82-7.92 (m, 2H), 8.30-8.39 (m, 1H), 8.43 (d, J=5.52 Hz, 1H), 8.45-8.54 (m, 1H), 8.66 (brs, 1H), 8.82 (s, 1H), 8.91 (s, 1H), 8.94 (d, J=1.00 Hz, 1H), 10.64 (brs, 1H), 14.09 (brs, 1H); ESIMS found for $C_{27}H_{20}FN_7O$ m/z 478.2 (M+1).

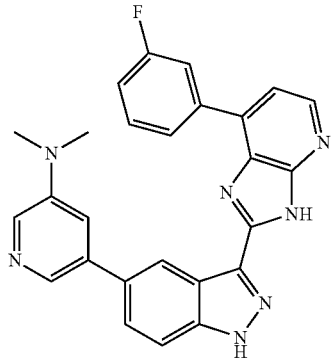
2



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide 2

[0925] White solid (18.8 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.98 (d, J=7 Hz, 6H), 2.12 (non, J=6.75 Hz, 1H), 2.28 (d, J=7 Hz, 2H), 7.30 (td, J=2 Hz, J=8 Hz, 1H), 7.63 (q, J=8 Hz, 1H), 7.70 (d, J=5 Hz, 1H), 7.81 (dd, J=1.5 Hz, J=8.5 Hz, 1H), 7.85 (d, J=8.5 Hz, 1H), 8.38 (d, J=8 Hz, 1H), 8.42 (d, J=5.5 Hz, 1H), 8.49 (s, 1H), 8.54 (d, J=11 Hz, 1H), 8.58 (d, J=2 Hz, 1H), 8.77 (d, J=2 Hz, 1H), 8.89 (s, 1H), 10.21 (s, 1H), 13.93 (s, 1H); ESIMS found for $C_{29}H_{24}FN_7O$ m/z 506.2 (M+1).

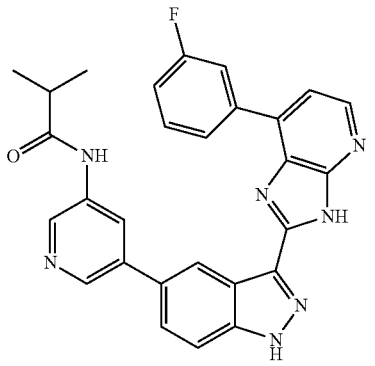
7



5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine 7

[0926] White solid (46.0 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.14 (s, 6H), 7.35 (td, J=8.34, 1.88 Hz, 1H), 7.62-7.72 (m, 2H), 7.84-7.90 (m, 2H), 7.92-7.98 (m, 1H), 8.23 (d, J=2.51 Hz, 1H), 8.30-8.38 (m, 1H), 8.43 (d, J=5.27 Hz, 1H), 8.47 (s, 1H), 8.48-8.56 (m, 1H), 8.91 (s, 1H), 13.99 (brs, 1H), 14.12 (s, 1H); ESIMS found for $C_{26}H_{20}FN_7$ m/z 450.3 (M+1).

9

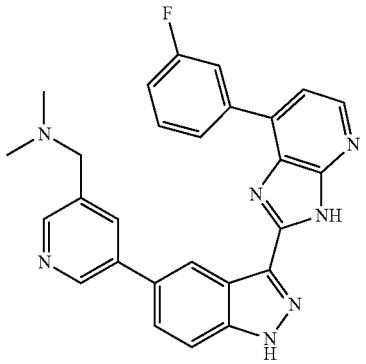


N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide 9

[0927] White solid (15.1 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.16 (d, J=7 Hz, 6H), 2.64-

2.72 (m, 1H), 7.30 (td, J=2.5 Hz, J=8 Hz, 1H), 7.63 (q, J=8 Hz, 1H), 7.70 (d, J=5 Hz, 1H), 7.82 (dd, J=1.5 Hz, J=9 Hz, 1H), 7.85 (d, J=9 Hz, 1H), 8.40 (d, J=8 Hz, 1H), 8.42 (d, J=5.5 Hz, 1H), 8.52 (t, J=2.5 Hz, 1H), 8.55 (d, J=10 Hz, 1H), 8.68 (d, J=2 Hz, 1H), 8.79 (d, J=2.5 Hz, 1H), 8.89 (s, 1H), 10.18 (s, 1H), 13.93 (s, 1H); ESIMS found for $C_{22}H_{22}FN_7O$ m/z 492.1 (M+1).

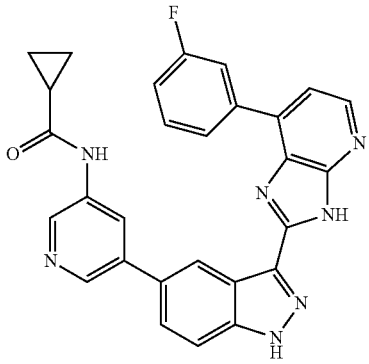
13



1-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 13

[0928] White solid (58.7 mg, 0.13 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.79 (d, J=4.27 Hz, 6H), 4.51 (d, J=4.77 Hz, 2H), 7.40 (td, J=8.53, 2.01 Hz, 1H), 7.64-7.70 (m, 1H), 7.71 (d, J=5.27 Hz, 1H), 7.88-7.94 (m, 1H), 8.00 (dd, J=8.78, 1.76 Hz, 1H), 8.28 (d, J=6.52 Hz, 1H), 8.46-8.52 (m, 1H), 8.49 (d, J=4.02 Hz, 1H), 8.75 (s, 1H), 8.92 (d, J=1.76 Hz, 1H), 8.96 (s, 1H), 9.22 (d, J=2.01 Hz, 1H), 11.34 (brs, 1H), 14.21 (brs, 1H); ESIMS found for $C_{27}H_{22}FN_7$ m/z 464.3 (M+1).

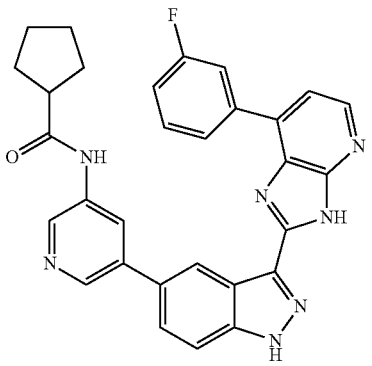
19



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide 19

[0929] White solid (15.3 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.85-1.00 (m, 4H), 1.88-1.98 (m, 1H), 7.29-7.39 (m, 1H), 7.61-7.70 (m, 1H), 7.70-7.76 (m, 1H), 7.85-7.95 (m, 2H), 8.25-8.36 (m, 1H), 8.37-8.54 (m, 2H), 8.77-8.85 (m, 1H), 8.93 (d, J=0.75 Hz, 1H), 8.94-9.03 (m, 1H), 9.05-9.16 (m, 1H), 11.27 (brs, 1H), 14.16 (brs, 1H); ESIMS found for $C_{28}H_{20}FN_7O$ m/z 490.2 (M+1).

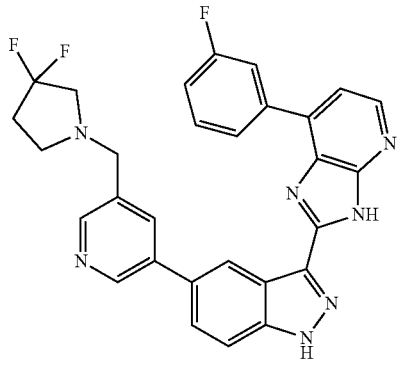
21



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide 21

[0930] White solid (12.2 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.55-1.65 (m, 2H), 1.65-1.74 (m, 2H), 1.75-1.85 (m, 2H), 1.89-2.00 (m, 2H), 2.93 (quin, J=7.92 Hz, 1H), 7.31 (td, J=8.60, 1.76 Hz, 1H), 7.62-7.70 (m, 1H), 7.72 (d, J=5.14 Hz, 1H), 7.85-7.96 (m, 2H), 8.25-8.34 (m, 1H), 8.39-8.55 (m, 2H), 8.85 (brs, 1H), 8.92 (s, 1H), 8.96 (brs, 1H), 9.15 (brs, 1H), 10.96 (brs, 1H), 14.19 (brs, 1H); ESIMS found for $C_{30}H_{24}FN_7O$ m/z 518.1 (M+1).

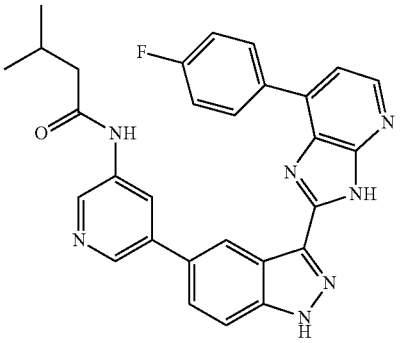
25



2-(5-(5-((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine 25

[0931] White solid (44.7 mg, 0.09 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.36-2.51 (m, 4H), 2.56-2.67 (m, 2H), 4.49-4.63 (m, 2H), 7.39 (td, J=8.60, 2.89 Hz, 1H), 7.63-7.74 (m, 2H), 7.90 (d, J=8.78 Hz, 1H), 7.96-8.02 (m, 1H), 8.31 (dt, J=7.09, 1.10 Hz, 1H), 8.46 (d, J=5.27 Hz, 1H), 8.49-8.60 (m, 1H), 8.67 (s, 1H), 8.88 (s, 1H), 8.97 (s, 1H), 9.18 (d, J=2.01 Hz, 1H), 14.12 (brs, 1H); ESIMS found for $C_{29}H_{22}F_3N_7$ m/z 526.3 (M+1).

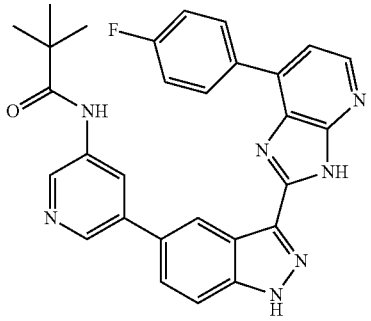
28



N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide 28

[0932] White solid (13.0 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.98 (d, J=6.53 Hz, 6H), 2.15 (non, J=6.76 Hz, 1H), 2.31 (d, J=7.03 Hz, 2H), 7.36-7.48 (m, 2H), 7.59-7.66 (m, 1H), 7.81-7.88 (m, 1H), 7.88-8.07 (m, 1H), 8.40 (t, J=5.04 Hz, 1H), 8.56-8.66 (m, 3H), 8.66-8.77 (m, 2H), 8.88 (d, J=11.8 Hz, 1H), 10.32 (s, 1H), 13.93 (brs, 2H); ESIMS found for $C_{29}H_{24}FN_7O$ m/z 506.1 (M+1).

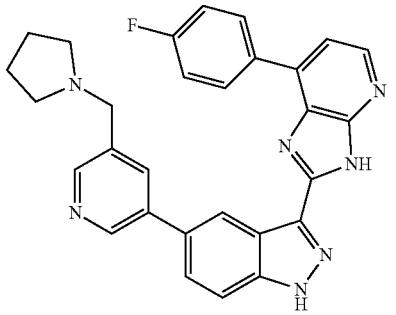
34



N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide 34

[0933] White solid (10.0 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm 1.30 (s, 9H), 5.94 (s, 1H), 7.41 (t, J=8.85 Hz, 2H), 7.62 (d, J=5.27 Hz, 1H), 7.94 (dd, J=8.85, 1.32 Hz, 1H), 8.04 (d, J=8.67 Hz, 1H), 8.37-8.46 (m, 1H), 8.63 (d, J=5.65 Hz, 2H), 8.70 (s, 1H), 8.72-8.79 (m, 1H), 8.85-8.93 (m, 1H), 8.98 (d, J=1.88 Hz, 1H), 9.74 (s, 1H), 13.98 (brs, 2H); ESIMS found for $C_{29}H_{24}FN_7O$ m/z 506.2 (M+1).

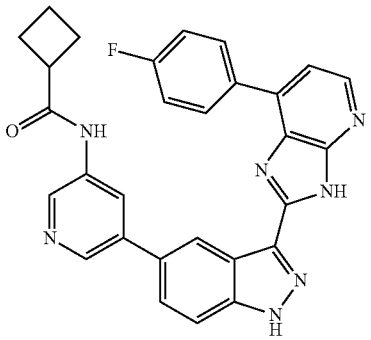
40



7-(4-Fluorophenyl)-2-(5-(5-(pyrrolidin-1-ylmethyl) pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b] pyridine 40

[0934] White solid (23.6 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.82-1.94 (m, 2H), 2.02-2.14 (m, 2H), 3.15-3.28 (m, 2H), 3.44-3.55 (m, 2H), 4.56 (d, J=5.52 Hz, 2H), 7.44 (t, J=8.76 Hz, 2H), 7.61 (d, J=5.31 Hz, 1H), 7.85-7.95 (m, 2H), 8.40 (d, J=1.00 Hz, 1H), 8.43 (d, J=5.02 Hz, 1H), 8.52-8.69 (m, 2H), 8.75-8.81 (m, 1H), 8.96 (s, 1H), 9.13-9.18 (m, 1H), 9.85-10.01 (m, 1H), 13.99 (brs, 1H); ESIMS found for $C_{29}H_{24}FN_7$ m/z 490.2 (M+1).

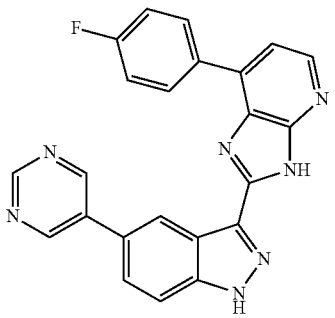
46



N-(5-(3-(7-(4-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide 46

[0935] White solid (12.0 mg, 0.02 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm δ 1.94-2.06 (m, 1H), 2.08-2.21 (m, 1H), 2.29-2.40 (m, 2H), 2.41-2.53 (m, 2H), 3.47 (quin, J=8.52 Hz, 1H), 7.48 (t, J=8.78 Hz, 2H), 7.82 (d, J=6.27 Hz, 1H), 7.96 (d, J=1.00 Hz, 2H), 8.11 (dd, J=8.03, 4.77 Hz, 2H), 8.63 (d, J=6.02 Hz, 1H), 8.98 (d, J=5.27 Hz, 2H), 9.02 (t, J=1.88 Hz, 1H), 9.32 (d, J=2.01 Hz, 1H); ESIMS found for $C_{29}H_{22}FN_7O$ m/z 504.1 (M+1).

52

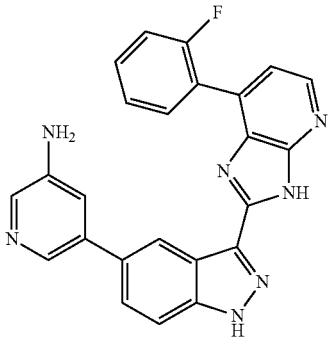


7-(4-Fluorophenyl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 52

[0936] White solid (167.2 mg, 0.41 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.41 (t, J=9.04 Hz, 2H), 7.61 (d, J=5.27 Hz, 1H), 7.87 (d, J=8.53 Hz, 1H), 7.97 (dd, J=8.56 Hz, J=1.52 Hz, 1H), 8.41 (d, J=5.27 Hz, 1H), 8.64 (dd, J=9.03, 5.52 Hz, 2H), 9.01 (s, 1H), 9.26 (s, 1H), 9.29 (s, 2H),

13.91 (brs, 1H), 13.96 (brs, 1H); ESIMS found for $C_{23}H_{14}FN_7$ m/z 408.0 (M+1).

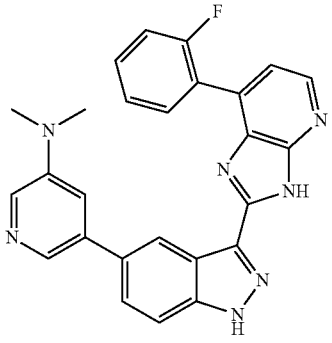
55



5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine 55

[0937] White solid (7.9 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.46-7.53 (m, 2H), 7.56 (d, J=5.27 Hz, 1H), 7.59-7.67 (m, 1H), 7.85 (dd, J=8.80 Hz, J=1.76 Hz, 1H), 7.91 (d, J=8.52 Hz, 1H), 7.97 (s, 1H), 8.00-8.07 (m, 1H), 8.09 (d, J=2.26 Hz, 1H), 8.39 (s, 1H), 8.56 (d, J=4.27 Hz, 1H), 8.79 (s, 1H), 14.36 (brs, 1H); ESIMS found for $C_{24}H_{16}FN_7$ m/z 422.1 (M+1).

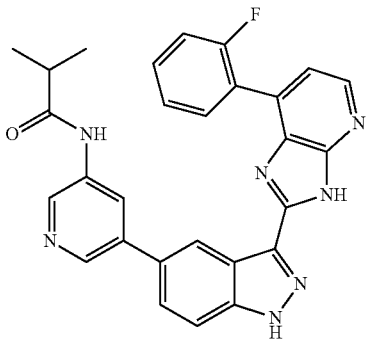
59



5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine 59

[0938] White solid (11.0 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.17 (s, 6H), 7.44-7.52 (m, 3H), 7.57-7.65 (m, 1H), 7.88 (d, J=8.66 Hz, 1H), 7.94 (brs, 1H), 7.98 (dd, J=8.72, 1.57 Hz, 1H), 8.07 (brs, 1H), 8.23 (d, J=2.51 Hz, 1H), 8.44 (s, 1H), 8.51 (d, J=4.89 Hz, 1H), 8.81 (s, 1H), 14.24 (brs, 1H); ESIMS found for $C_{26}H_{20}FN_7$ m/z 450.1 (M+1).

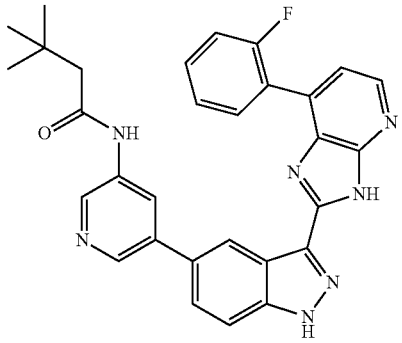
61



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide 61

[0939] White solid (18.9 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.18 (d, J=6.78 Hz, 5H), 2.66-2.77 (m, 1H), 7.38-7.50 (m, 3H), 7.51-7.60 (m, 1H), 7.77-7.87 (m, 2H), 8.34 (s, 1H), 8.40-8.47 (m, 1H), 8.47-8.54 (m, 1H), 8.63 (s, 1H), 8.78 (s, 2H), 10.27 (s, 1H); ESIMS found for $C_{28}H_{22}FN_7O$ m/z 492.2 (M+1).

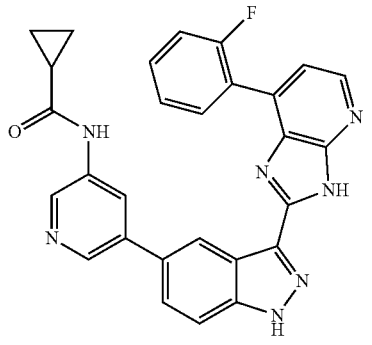
68



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide 68

[0940] White solid (24.0 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.07 (m, 9H), 2.29 (s, 2H), 7.32-7.50 (m, 3H), 7.51-7.60 (m, 1H), 7.74-7.87 (m, 2H), 8.25-8.36 (m, 1H), 8.38-8.52 (m, 2H), 8.59-8.67 (m, 1H), 8.73 (brs, 1H), 8.77 (s, 1H), 10.16-10.29 (m, 1H), 13.93 (brs, 2H); ESIMS found for $C_{30}H_{26}FN_7O$ m/z 520.3 (M+1).

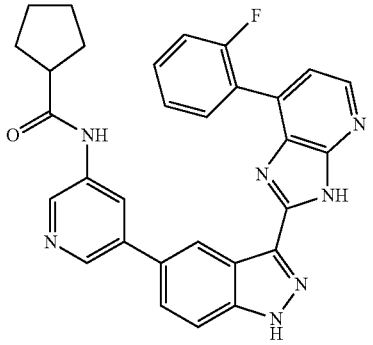
71



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide 71

[0941] White solid (14.9 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.88 (d, J=5.65 Hz, 4H), 1.87-1.97 (m, 1H), 7.36-7.50 (m, 3H), 7.55 (brs, 1H), 7.74-7.88 (m, 2H), 8.32 (brs, 1H), 8.40-8.51 (m, 2H), 8.62 (brs, 1H), 8.71-8.85 (m, 2H), 10.74 (brs, 1H), 13.88 (brs, 1H); ESIMS found for $C_{28}H_{20}FN_7O$ m/z 490.1 (M+1).

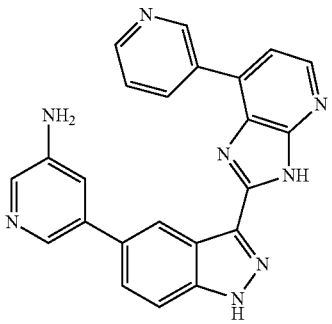
73



N-(5-(3-(7-(2-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide 73

[0942] White solid (12.0 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.53-1.64 (m, 2H), 1.65-1.74 (m, 2H), 1.74-1.85 (m, 2H), 1.87-1.98 (m, 2H), 2.88 (quin, J=7.8 Hz, 1H), 7.37-7.50 (m, 3H), 7.51-7.59 (m, 1H), 7.75-7.86 (m, 2H), 8.27-8.37 (m, 1H), 8.38-8.46 (m, 1H), 8.46-8.53 (m, 1H), 8.62 (brs, 1H), 8.70-8.76 (m, 1H), 8.78 (s, 1H), 10.25-10.34 (m, 1H), (13.93 (brs, 2H); ESIMS found for $C_{30}H_{24}FN_7O$ m/z 518.2 (M+1).

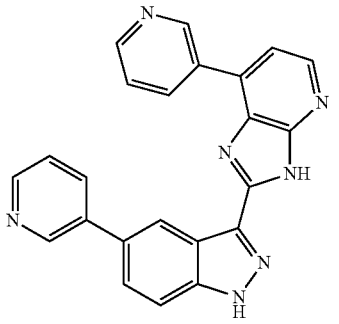
81



5-(3-(7-(Pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-amine 81

[0943] White solid (5.0 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.82 (d, J=5.02 Hz, 1H), 7.84-7.93 (m, 2H), 8.05-8.16 (m, 3H), 8.51 (s, 1H), 8.53 (d, J=5.14 Hz, 1H), 8.88 (s, 1H), 8.93 (d, J=4.39 Hz, 1H), 9.30 (brs, 1H), 9.86 (brs, 1H), 14.20 (brs, 1H); ESIMS found for $C_{23}H_{16}N_8$ m/z 405.0 (M+1).

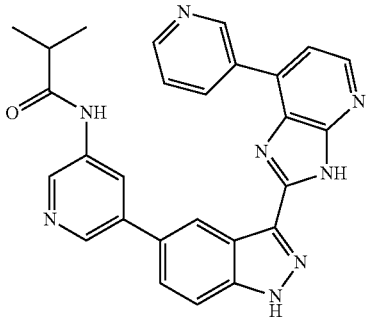
82



7-(Pyridin-3-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 82

[0944] White solid (18.9 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.88 (d, J=5.02 Hz, 1H), 7.92 (d, J=9.03 Hz, 1H), 8.03 (dd, J=8.78, 1.51 Hz, 1H), 8.23 (dd, J=8.16, 5.65 Hz, 1H), 8.29 (dd, J=7.91, 5.65 Hz, 1H), 8.55 (d, J=5.02 Hz, 1H), 8.94 (d, J=5.52 Hz, 1H), 8.99 (d, J=0.75 Hz, 1H), 9.00-9.07 (m, 2H), 9.44 (d, J=1.51 Hz, 1H), 9.46-9.53 (m, 1H), 10.02 (brs, 1H), 14.32 (brs, 1H); ESIMS found for $C_{23}H_{15}N_7$ m/z 390.0 (M+1).

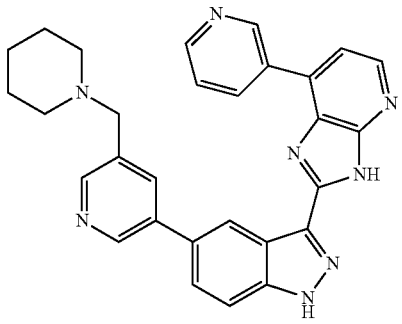
87



N-(5-(3-(7-(Pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide 87

[0945] White solid (84.4 mg, 0.18 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.18 (d, J=6.78 Hz, 6H), 2.65-2.74 (m, 1H), 7.59-7.67 (m, 1H), 7.73 (d, J=5.02 Hz, 1H), 7.79-7.88 (m, 2H), 8.45 (d, J=5.02 Hz, 1H), 8.53 (brs, 1H), 8.68 (brs, 2H), 8.79 (d, J=1.25 Hz, 1H), 8.86 (s, 1H), 8.97-9.03 (m, 1H), 9.59 (s, 1H), 10.25 (s, 1H), 13.97 (s, 1H), 13.98 (s, 1H); ESIMS found for $C_{27}H_{22}N_8O$ m/z 475.1 (M+1).

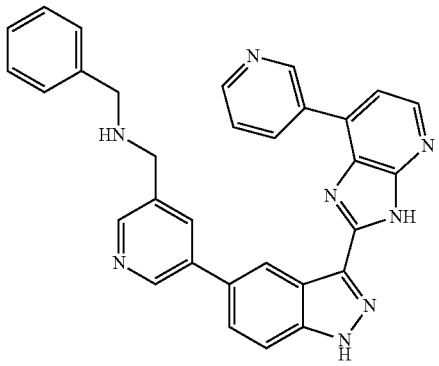
93



2-(5-(5-(Piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine 93

[0946] White solid (29.8 mg, 0.06 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.53-1.68 (m, 1H), 1.85-2.04 (m, 5H), 3.13-3.27 (m, 2H), 3.61-3.72 (m, 2H), 4.76 (s, 2H), 7.95 (d, J=8.78 Hz, 1H), 7.99 (d, J=5.77 Hz, 1H), 8.10 (d, J=8.78 Hz, 1H), 8.38-8.45 (m, 1H), 8.75 (d, J=5.77 Hz, 1H), 9.10-9.16 (m, 2H), 9.17 (s, 1H), 9.31 (d, J=8.28 Hz, 1H), 9.48 (s, 2H), 9.83 (s, 1H); ESIMS found for $C_{29}H_{26}N_8$ m/z 487.3 (M+1).

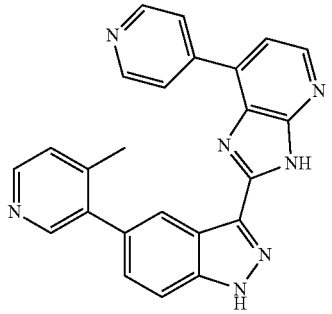
101



N-Benzyl-1-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine 101

[0947] White solid (35.2 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 4.31 (brs, 2H), 4.52 (brs, 2H), 7.38-7.49 (m, 2H), 7.61 (d, J=7.78 Hz, 2H), 7.81-7.87 (m, 1H), 7.92 (d, J=8.78 Hz, 1H), 8.01 (d, J=8.78 Hz, 1H), 8.07-8.17 (m, 1H), 8.54 (d, J=5.02 Hz, 1H), 8.84-9.01 (m, 3H), 9.22-9.39 (m, 2H), 9.90-10.12 (m, 3H), 14.21 (brs, 1H); ESIMS found for $C_{31}H_{24}N_8$ m/z 509.3 (M+1).

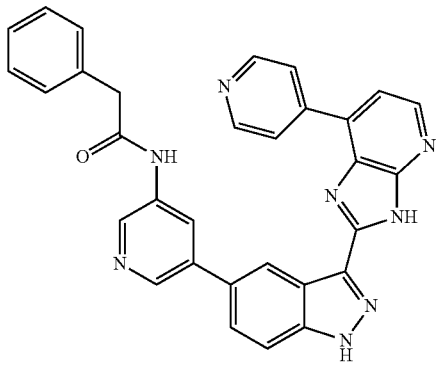
109



2-(5-(4-Methylpyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo [4,5-b]pyridine 109

[0948] White solid (40.9 mg, 0.10 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 2.70 (s, 3H), 7.66 (dd, J=8.66, 1.63 Hz, 1H), 7.89-7.97 (m, 2H), 8.14 (d, J=6.02 Hz, 1H), 8.68 (d, J=5.77 Hz, 1H), 8.71 (dd, J=1.51, 0.75 Hz, 1H), 8.80 (dd, J=6.02, 0.75 Hz, 1H), 8.90 (s, 1H), 8.95 (d, J=6.78 Hz, 2H), 9.10 (d, J=6.78 Hz, 2H); ESIMS found for $C_{24}H_{17}N_7$ m/z 404.2 (M+1).

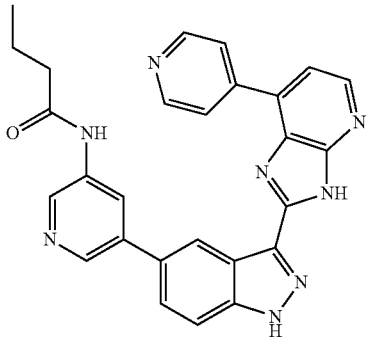
114



2-Phenyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide 114

[0949] White solid (4.7 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.87 (s, 2H), 7.22-7.29 (m, 1H), 7.30-7.37 (m, 2H), 7.40 (s, 1H), 7.42 (d, J=1.25 Hz, 1H), 7.87-7.96 (m, 3H), 8.57 (d, J=5.02 Hz, 1H), 8.85 (dd, J=3.26, 1.51 Hz, 1H), 8.91 (s, 1H), 8.94 (brs, 1H), 8.97-9.08 (m, 3H), 9.08-9.15 (m, 2H), 11.26 (brs, 1H), 14.20 (brs, 2H); ESIMS found for $C_{31}H_{22}N_8O$ m/z 523.2 (M+1).

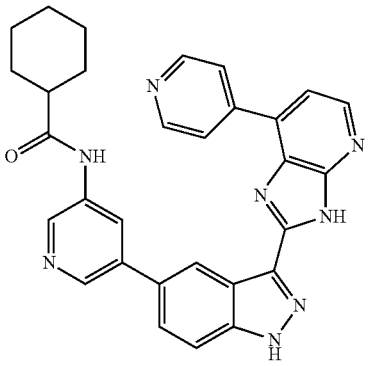
121



N-(5-(3-(7-(Pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide 121

[0950] White solid (10.7 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.96 (t, J=7.40 Hz, 3H), 1.68 (sxt, J=7.28 Hz, 2H), 2.51-2.58 (m, 2H), 7.92 (s, 2H), 7.94 (d, J=5.52 Hz, 1H), 8.58 (d, J=5.02 Hz, 1H), 8.89 (brs, 1H), 8.92 (s, 1H), 8.97 (s, 1H), 9.02 (d, J=1.00 Hz, 1H), 9.04-9.12 (m, 4H), 10.98 (brs, 1H), 14.22 (brs, 1H); ESIMS found for $C_{27}H_{22}N_8O$ m/z 475.2 (M+1).

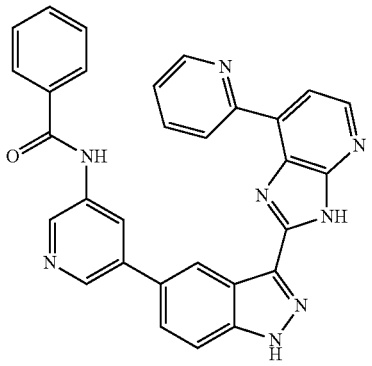
126



N-(5-(3-(7-(Pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide 126

[0951] White solid (30.0 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.14-1.39 (m, 4H), 1.39-1.54 (m, 2H), 1.64-1.72 (m, 1H), 1.75-1.84 (m, 2H), 1.89-1.98 (m, 2H), 7.87-7.98 (m, 3H), 8.59 (d, J=5.27 Hz, 1H), 8.93 (s, 2H), 9.01 (s, 1H), 9.09 (brs, 5H), 10.95 (brs, 1H), 14.24 (brs, 1H); ESIMS found for $C_{30}H_{26}N_8O$ m/z 515.2 (M+1).

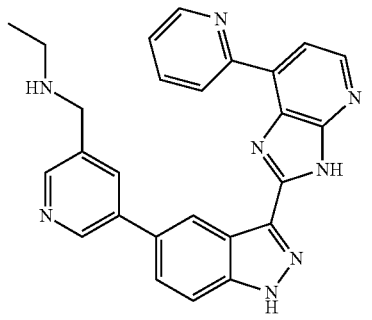
141



N-(5-(3-(7-(Pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide 141

[0953] White solid (18.0 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.36-7.44 (m, 1H), 7.59-7.68 (m, 2H), 7.68-7.75 (m, 1H), 7.91-8.00 (m, 2H), 8.10 (d, J=8.03 Hz, 3H), 8.14 (d, J=5.27 Hz, 1H), 8.54 (d, J=5.52 Hz, 1H), 8.86 (d, J=4.02 Hz, 1H), 8.97-9.04 (m, 3H), 9.23 (s, 2H), 11.04 (s, 1H), 14.17 (brs, 1H); ESIMS found for $C_{30}H_{20}N_8O$ m/z 509.2 (M+1).

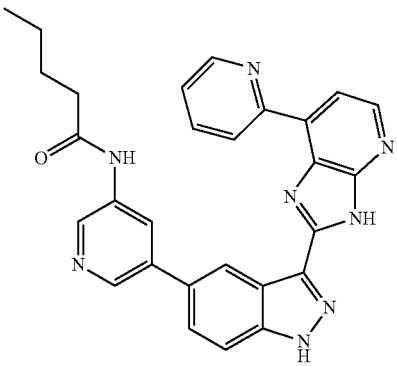
136



N-((5-(3-(7-(Pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine 136

[0952] White solid (20.7 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.28 (t, J=7.15 Hz, 3H), 3.00-3.12 (m, 2H), 4.36-4.44 (m, 2H), 7.64 (ddd, J=7.28 Hz, J=5.28 Hz, J=0.76 Hz, 1H), 7.94 (d, J=8.76 Hz, 1H), 8.03 (dd, J=8.56 Hz, J=1.76 Hz, 1H), 8.15 (d, J=5.27 Hz, 1H), 8.22 (dt, J=7.76 Hz, J=2.00 Hz, 1H), 8.57 (d, J=5.27 Hz, 1H), 8.86 (d, J=1.25 Hz, 1H), 8.91-8.96 (m, 2H), 9.00 (s, 1H), 9.10-9.22 (m, 1H), 9.28 (d, J=1.51 Hz, 1H), 9.54-9.65 (m, 2H), 14.27 (brs, 1H); ESIMS found for $C_{26}H_{22}N_8$ m/z 447.1 (M+1).

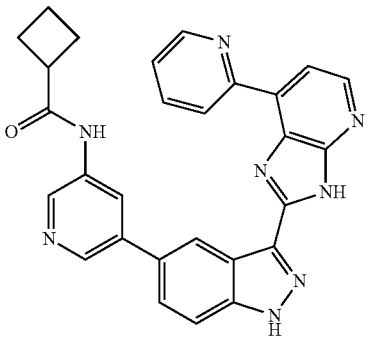
148



N-(5-(3-(7-(Pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide 148

[0954] White solid (38.7 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.93 (t, J=7.40 Hz, 3H), 1.39 (sxt, J=7.52 Hz, 2H), 1.65 (quin, J=7.52 Hz, 2H), 2.42-2.50 (m, 11H), 7.56 (dd, J=7.04 Hz, J=4.28 Hz, 1H), 7.86-7.96 (m, 2H), 8.09-8.19 (m, 2H), 8.54 (d, J=5.52 Hz, 1H), 8.79 (s, 1H), 8.89 (d, J=4.27 Hz, 1H), 8.93 (s, 2H), 9.02 (s, 1H), 9.15-9.31 (m, 1H), 10.81 (brs, 1H), 14.16 (brs, 1H); ESIMS found for $C_{28}H_{24}N_8O$ m/z 489.2 (M+1).

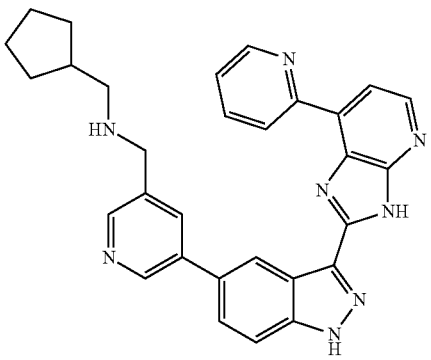
150



N-(5-(3-(7-(Pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)cyclobutanecarboxamide 150

[0955] White solid (48.0 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.79-1.92 (m, 1H), 1.93-2.06 (m, 1H), 2.13-2.23 (m, 2H), 2.24-2.36 (m, 2H), 7.49 (brs, 1H), 7.86 (s, 2H), 8.06 (t, J=7.28 Hz, 1H), 8.16 (brs, 1H), 8.48 (brs, 1H), 8.65-8.78 (m, 3H), 8.82 (brs, 1H), 8.90-8.98 (m, 1H), 9.49 (brs, 1H), 10.20 (s, 1H), 13.92 (brs, 1H); ESIMS found for $C_{28}H_{22}N_8O$ m/z 487.1 (M+1).

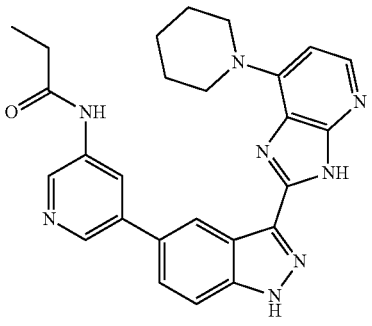
154



1-Cyclopentyl-N-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine 154

[0956] White solid (52.4 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.22-1.34 (m, 2H), 1.48-1.56 (m, 2H), 1.57-1.66 (m, 2H), 1.76-1.86 (m, 2H), 2.22-2.31 (m, 1H), 2.95-3.03 (m, 2H), 4.39-4.46 (m, 2H), 7.60-7.67 (m, 1H), 7.93-7.98 (m, 1H), 8.02-8.07 (m, 1H), 8.15 (d, J=5.27 Hz, 1H), 8.19-8.27 (m, 1H), 8.57 (d, J=5.02 Hz, 1H), 8.92 (brs, 2H), 8.97 (s, 1H), 9.01 (s, 1H), 9.30 (s, 1H), 9.49-9.59 (m, 2H), 14.28 (brs, 1H); ESIMS found for $C_{30}H_{28}N_8$ m/z 501.2 (M+1).

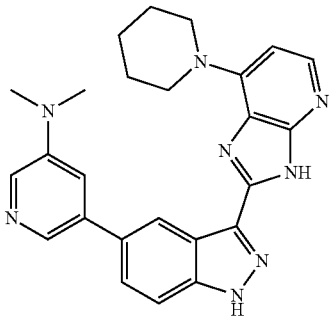
157



N-(5-(3-(7-(Piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide 157

[0957] White solid (23.6 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.13 (t, J=7.53 Hz, 3H), 1.59-1.77 (m, 6H), 2.41 (q, J=7.36 Hz, 2H), 3.96-4.06 (m, 4H), 7.74-7.83 (m, 2H), 7.93 (d, J=5.77 Hz, 1H), 8.23 (s, 1H), 8.56 (d, J=2.01 Hz, 1H), 8.63 (dd, J=7.78, 2.26 Hz, 2H), 8.78 (s, 1H), 10.25 (s, 1H), 13.70 (brs, 2H); ESIMS found for $C_{26}H_{26}N_8O$ m/z 467.3 (M+1).

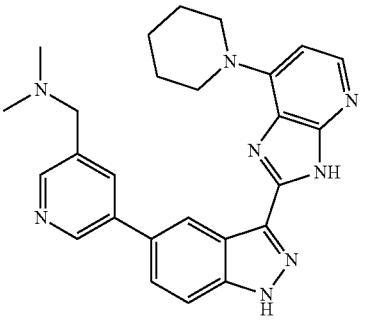
163



N,N-Dimethyl-5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine 163

[0958] White solid (16.3 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.75 (brs, 6H), 3.12 (s, 6H), 4.17-4.44 (m, 4H), 6.87-6.96 (m, 1H), 7.72 (brs, 1H), 7.86 (d, J=8.76 Hz, 1H), 7.94 (dd, J=8.53, 1.25 Hz, 1H), 7.96-8.03 (m, 1H), 8.21 (d, J=2.26 Hz, 1H), 8.36 (s, 1H), 8.66 (s, 1H), 14.05 (brs, 1H); ESIMS found for $C_{25}H_{26}N_8$ m/z 439.1 (M+1).

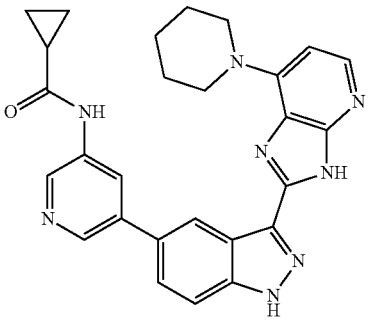
169



N,N-Dimethyl-1-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine 169

[0959] White solid (9.8 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.77 (brs, 6H), 2.78 (d, J=4.27 Hz, 6H), 4.45 (d, J=3.26 Hz, 2H), 6.97 (d, J=7.53 Hz, 1H), 7.90 (d, J=8.80 Hz, 1H), 7.97 (dd. J=9.04 Hz, J=0.76 Hz, 2H), 8.61 (brs, 1H), 8.69 (s, 1H), 8.80 (s, 1H), 9.06 (s, 1H), 11.26 (brs, 1H), 14.19 (brs, 1H), 14.87 (brs, 1H); ESIMS found for $C_{26}H_{28}N_8$ m/z 453.2 (M+1).

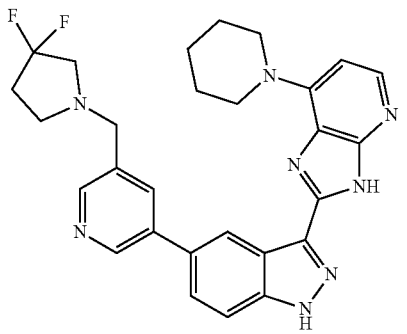
175



N-(5-(3-(7-(Piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide 175

[0960] White solid (13.7 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.86-0.96 (m, 4H), 1.75 (brs, 6H), 1.93-2.02 (m, 1H), 6.95 (d, J=7.28 Hz, 1H), 7.89 (s, 2H), 7.92-8.02 (m, 1H), 8.64 (s, 1H), 8.83 (brs, 1H), 8.87-8.98 (m, 2H), 11.40 (brs, 1H), 14.21 (brs, 1H), 14.84 (brs, 1H); ESIMS found for $C_{27}H_{26}N_8O$ m/z 479.2 (M+1).

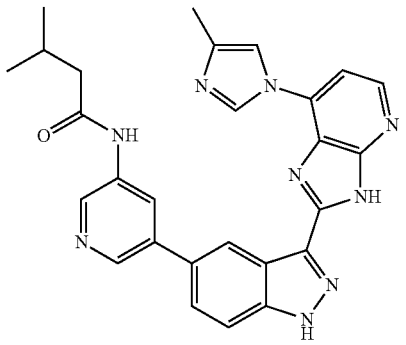
181



2-(5-(5-((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine 181

[0961] White solid (42.4 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.77 (brs, 6H), 2.56-2.66 (m, 2H), 3.46-3.62 (m, 2H), 4.48-4.61 (m, 2H), 6.97 (d, J=7.53 Hz, 1H), 7.88-7.93 (m, 1H), 7.94-8.02 (m, 1H), 7.98 (dd, J=8.66, 1.63 Hz, 1H), 8.66 (brs, 1H), 8.69 (s, 1H), 8.84 (s, 1H), 9.06 (d, J=1.76 Hz, 1H), 14.19 (brs, 1H), 14.85 (brs, 1H); ESIMS found for $C_{28}H_{28}F_2N_8$ m/z 515.2 (M+1).

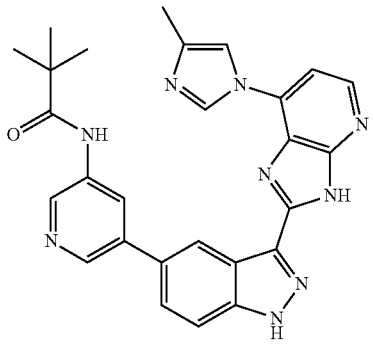
184



3-Methyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide 184

[0962] White solid (14.5 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.968 (d, J=6.80 Hz, 6H), 2.12 (non, J=6.80 Hz, 1H), 2.24 (s, 3H), 2.29 (d, J=7.2 Hz, 2H), 7.64 (d, J=5.2 Hz, 1H), 7.79-7.90 (m, 2H), 8.30 (s, 1H), 8.39 (d, J=5.2 Hz, 1H), 8.49 (s, 1H), 8.69 (d, J=2.0 Hz, 1H), 8.82 (s, 1H), 8.84 (d, J=2.0 Hz, 1H), 9.00 (s, 1H), 10.41 (s, 1H), 14.12 (brs, 2H); ESIMS found for $C_{27}H_{25}N_9O$ m/z 492.2 (M+1).

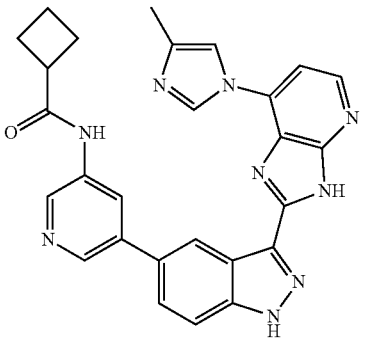
190



N-(5-(3-(7-(4-Methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide 190

[0963] White solid (41.1 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.28 (s, 9H), 2.23 (s, 3H), 7.62 (d, J=5.40 Hz, 1H), 7.78-7.89 (m, 2H), 8.26 (s, 1H), 8.38 (d, J=5.40 Hz, 1H), 8.50 (t, J=2.13 Hz, 1H), 8.69 (d, J=1.88 Hz, 1H), 8.83 (s, 1H), 8.93 (d, J=2.26 Hz, 1H), 9.01 (s, 1H), 9.56 (s, 1H), 13.99 (brs, 2H); ESIMS found for $C_{27}H_{25}N_9O$ m/z 492.2 (M+1).

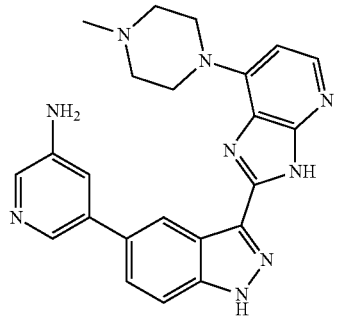
202



N-(5-(3-(7-(4-Methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide 202

[0964] White solid (66.3 mg, 0.14 mmol). ^{1}H NMR ($DMSO-d_6$, 400 MHz) δ ppm 1.75-1.90 (m, 1H), 1.92-2.04 (m, 1H), 2.10-2.36 (m, 4H), 2.22 (s, 3H), 3.23-3.32 (m, 1H), 7.62 (d, J=5.14 Hz, 1H), 7.77-7.91 (m, 2H), 8.29 (brs, 1H), 8.38 (d, J=5.14 Hz, 1H), 8.49 (brs, 1H), 8.68 (s, 1H), 8.82 (d, J=2.89 Hz, 2H), 8.98 (brs, 1H), 10.14 (s, 1H), 13.99 (brs, 2H); ESIMS found for $C_{27}H_{23}N_9O$ m/z 490.2 (M+1).

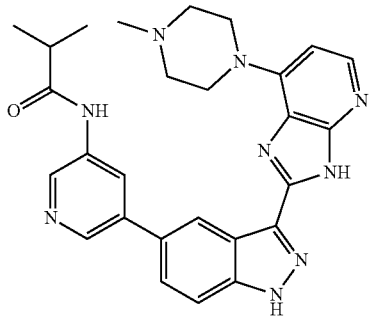
211



5-(3-(7-(4-Methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine 211

[0965] White solid (7.7 mg, 0.02 mmol). ^{1}H NMR ($DMSO-d_6$, 400 MHz) δ ppm 2.91 (brs, 3H), 3.69-3.78 (m, 4H), 3.80-3.89 (m, 4H), 7.00-7.07 (m, 1H), 7.85 (dd, J=8.52 Hz, J=1.52 Hz, 1H), 7.91 (d, J=8.76 Hz, 1H), 7.98 (s, 1H), 8.07 (d, J=2.26 Hz, 1H), 8.13-8.21 (m, 1H), 8.43 (brs, 1H), 8.64 (s, 1H), 11.42 (brs, 1H), 14.30 (brs, 1H); ESIMS found for $C_{23}H_{23}N_9$ m/z 426.1 (M+1).

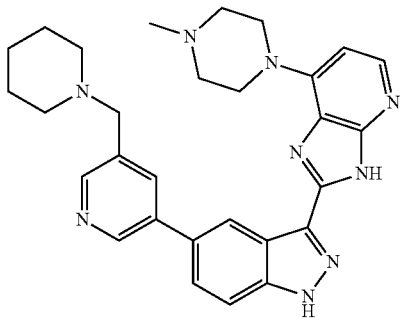
217



N-(5-(3-(7-(4-Methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl) isobutyramide 217

[0966] White solid (20.3 mg, 0.04 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.30 (d, J=6.78 Hz, 5H), 2.82 (spt, J=7.28 Hz, 2H), 3.04 (s, 3H), 3.23-3.35 (m, 2H), 3.43-3.57 (m, 2H), 3.80-4.04 (m, 4H), 7.12 (d, J=7.28 Hz, 1H), 7.92 (d, J=1.00 Hz, 2H), 8.09-8.18 (m, 1H), 8.76-8.83 (m, 1H), 8.98 (d, J=1.25 Hz, 1H), 9.03 (t, J=1.88 Hz, 1H), 9.28 (d, J=1.76 Hz, 1H); ESIMS found for $C_{27}H_{29}N_9O$ m/z 496.3 (M+1).

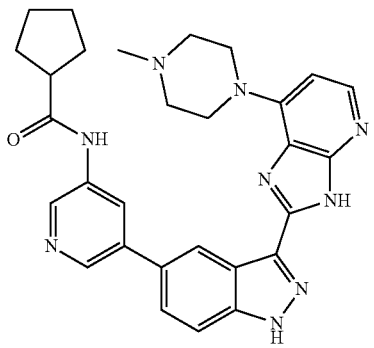
223



7-(4-Methylpiperazin-1-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 223

[0967] White solid (17.3 mg, 0.03 mmol). ^{1}H NMR ($DMSO-d_6$, 400 MHz) δ ppm 1.34-1.47 (m, 2H), 1.65-1.76 (m, 2H), 1.77-1.88 (m, 4H), 2.82-2.89 (m, 3H), 2.91-3.03 (m, 2H), 3.63-3.73 (m, 4H), 3.82-3.95 (m, 2H), 4.47 (d, J=5.02 Hz, 2H), 7.01-7.11 (m, 1H), 7.90 (d, J=8.78 Hz, 1H), 8.01 (d, J=8.53 Hz, 1H), 8.11-8.22 (m, 1H), 8.68-8.78 (m, 2H), 8.83 (s, 1H), 9.13 (brs, 1H), 11.16 (brs, 1H), 11.54 (brs, 1H), 14.23 (brs, 1H); ESIMS found for $C_{29}H_{33}N_9$ m/z 508.2 (M+1).

229

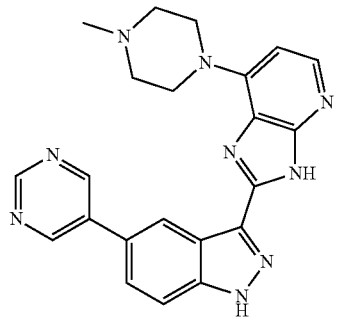


N-(5-(3-(7-(4-Methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide 229

[0968] White solid (32.7 mg, 0.06 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.65-1.76 (m, 2H), 1.76-1.86 (m, 2H), 1.87-1.98 (m, 2H), 1.99-2.11 (m, 2H), 3.02 (quin,

J=8.04 Hz, 4H), 3.04 (s, 3H), 3.24-3.33 (m, 2H), 3.44-3.57 (m, 2H), 3.79-4.04 (m, 4H), 7.09-7.15 (m, 1H), 7.91 (d, J=1.00 Hz, 2H), 8.09-8.19 (m, 1H), 8.76-8.83 (m, 1H), 8.97 (d, J=1.26 Hz, 1H), 9.00 (t, J=1.88 Hz, 1H), 9.30 (d, J=1.76 Hz, 1H); ESIMS found for $C_{29}H_{31}N_9O$ m/z 522.3 (M+1).

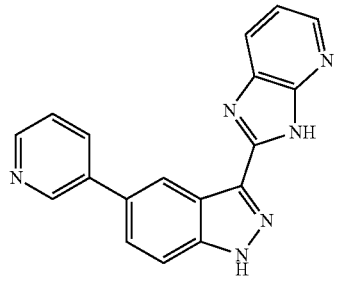
234



7-(4-Methylpiperazin-1-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 234

[0969] White solid (54.6 mg, 0.13 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.85 (brs, 3H), 3.26-3.41 (m, 4H), 3.76-3.91 (m, 4H), 7.03-7.12 (m, 1H), 7.88-7.94 (m, 1H), 7.94-8.00 (m, 1H), 8.13-8.26 (m, 1H), 8.67 (brs, 1H), 9.25 (d, J=3.01 Hz, 3H), 11.34 (brs, 1H), 14.25 (brs, 1H); ESIMS found for $C_{22}H_{21}N_9$ m/z 412.1 (M+1).

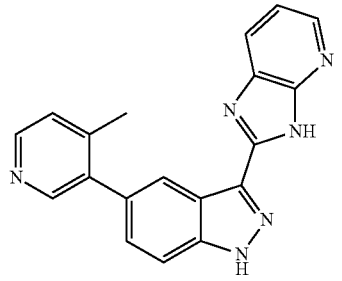
238



2-(5-(Pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 238

[0970] White solid (66.2 mg, 0.21 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.46-7.52 (m, 1H), 7.90-8.02 (m, 3H), 8.27 (d, J=8.28 Hz, 1H), 8.53 (d, J=5.27 Hz, 1H), 8.65-8.73 (m, 1H), 8.83 (d, J=0.75 Hz, 2H), 9.24 (d, J=1.51 Hz, 1H); ESIMS found for $C_{18}H_{12}N_6$ m/z 313.1 (M+1).

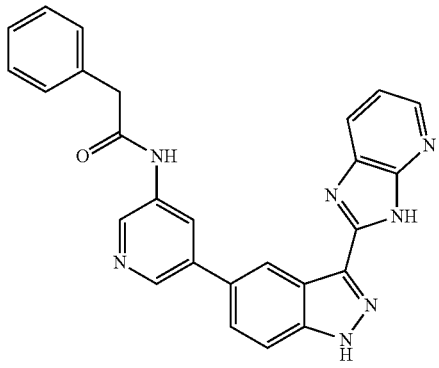
239



2-(5-(4-Methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 239

[0971] Light brown solid (21.1 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 300 MHz) δ ppm 2.31 (s, 3H), 7.24 (dd, J=8.01, 4.80 Hz, 1H) 7.39 (d, J=5.09 Hz, 1H) 7.52 (dd, J=8.57, 1.41 Hz, 1H) 7.78 (d, J=8.67 Hz, 1H) 8.35 (d, J=3.96 Hz, 1H) 8.48 (t, J=4.33 Hz, 3H); ESIMS found for $C_{19}H_{14}N_6$ m/z 327.6 (M+1).

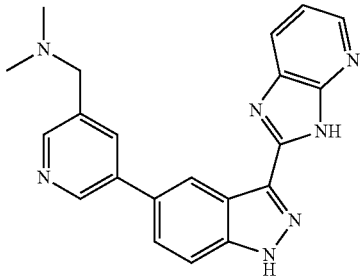
244



N-(5-(3-(3H-Imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide 244

[0972] White solid (28.4 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.79 (s, 2H), 7.28 (tt, J=7.04 Hz, J=1.76 Hz, 1H), 7.32-7.42 (m, 4H), 7.47-7.55 (m, 1H), 7.87 (dd, J=8.76 Hz, J=1.48 Hz, 1H), 7.91 (d, J=9.00 Hz, 1H), 8.29 (d, J=8.78 Hz, 1H), 8.53 (d, J=5.27 Hz, 1H), 8.62 (s, 1H), 8.75 (s, 1H), 8.83 (s, 1H), 9.01 (s, 1H), 11.05 (brs, 1H), 14.29 (brs, 1H); ESIMS found for $C_{26}H_{19}N_7O$ m/z 446.2 (M+1).

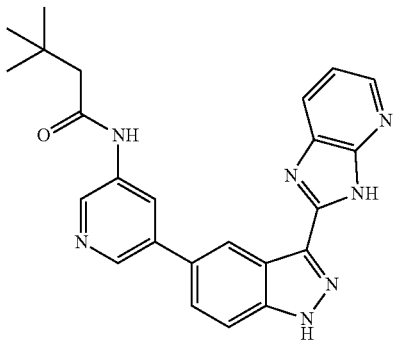
247



1-(5-(3-(3H-Imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 247

[0973] Beige solid (11.1 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.23 (s, 6H), 3.56 (s, 2H), 7.27 (dd, J=5 Hz, J=7.5 Hz, 1H), 7.78-7.96 (m, 3H), 8.04 (s, 1H), 8.39 (brs, 1H), 8.51 (s, 1H), 8.75 (s, 1H), 8.86 (s, 1H), 13.69 (brs, 1H), 13.89 (brs, 1H); ESIMS found for $C_{21}H_{19}N_7$ m/z 369.7 (M+1).

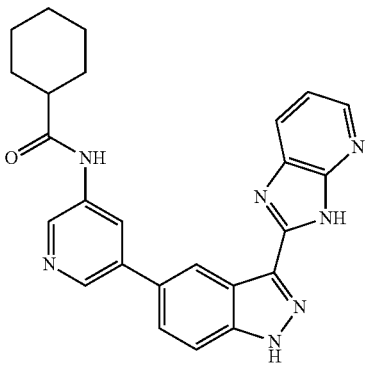
250



N-(5-(3-(3H-Imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide 250

[0974] White solid (47.7 mg, 0.11 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.06 (s, 9H), 2.38 (s, 2H), 7.70 (dd, J=8.03, 5.77 Hz, 1H), 7.91 (dd, J=8.80 Hz, J=1.76 Hz, 1H), 7.98 (d, J=9.28 Hz, 1H), 8.52 (dd, J=8.03, 1.00 Hz, 1H), 8.64 (dd, J=5.65, 1.13 Hz, 1H), 8.76 (d, J=0.75 Hz, 1H), 8.89 (t, J=2.01 Hz, 1H), 9.00 (d, J=1.76 Hz, 1H), 9.28 (d, J=2.01 Hz, 1H), 11.37 (s, 1H), 14.68 (brs, 1H); ESIMS found for $C_{24}H_{23}N_7O$ m/z 426.3 (M+1).

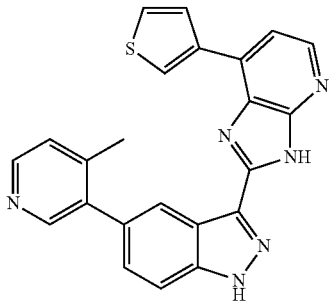
256



N-(5-(3-(3H-Imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl) cyclohexanecarboxamide 256

[0975] White solid (63.1 mg, 0.14 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.15-1.39 (m, 4H), 1.40-1.53 (m, 2H), 1.64-1.72 (m, 1H), 1.76-1.84 (m, 2H), 1.86-1.94 (m, 2H), 7.43-7.52 (m, 1H), 7.88 (dd, J=8.80 Hz, J=1.52 Hz, 1H), 7.92 (d, J=8.28 Hz, 1H), 8.23-8.28 (m, 1H), 8.52 (d, J=5.52 Hz, 1H), 8.64 (s, 1H), 8.77 (s, 1H), 8.83 (d, J=1.51 Hz, 1H), 9.03 (d, J=1.25 Hz, 1H), 10.62 (brs, 1H); ESIMS found for $C_{25}H_{23}N_7O$ m/z 438.2 (M+1).

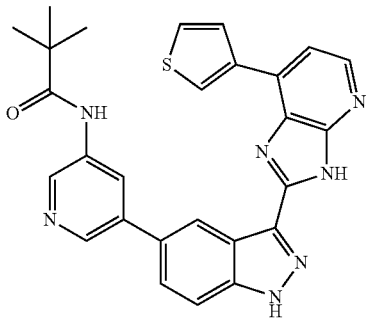
265



2-(5-(4-Methylpyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine 265

[0976] White solid (65.9 mg, 0.16 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.65 (s, 3H), 7.67-7.73 (m, 2H), 7.77 (dd, J=4.89, 2.89 Hz, 1H), 7.90 (d, J=8.78 Hz, 1H), 8.13 (d, J=6.02 Hz, 1H), 8.18 (d, J=4.52 Hz, 1H), 8.40 (d, J=5.02 Hz, 1H), 8.69 (s, 1H), 8.83-8.89 (m, 2H), 9.02 (s, 1H), 14.23 (brs, 1H); ESIMS found for $C_{23}H_{16}N_6S$ m/z 409.1 (M+1).

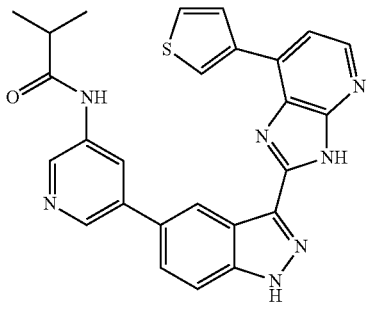
268



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)pivalamide 268

[0977] White solid (80.1 mg, 0.16 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.30 (s, 9H), 7.66 (d, J=5.27 Hz, 1H), 7.74 (dd, J=5.02, 3.01 Hz, 1H), 7.82-7.89 (m, 2H), 8.25 (d, J=5.15 Hz, 1H), 8.35 (d, J=5.14 Hz, 1H), 8.60 (s, 1H), 8.70 (d, J=1.88 Hz, 1H), 8.88-8.96 (m, 3H), 9.60 (s, 1H), 13.89 (brs, 2H); ESIMS found for $C_{27}H_{23}N_7OS$ m/z 494.1 (M+1).

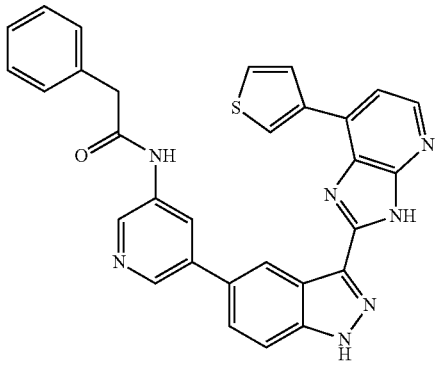
269



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)isobutyramide 269

[0978] White solid (66.8 mg, 0.14 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.18 (d, J=6.78 Hz, 6H), 2.70 (spt, J=6.88 Hz, 1H), 7.66 (d, J=5.02 Hz, 1H), 7.75 (dd, J=4.89, 2.89 Hz, 1H), 7.81-7.89 (m, 2H), 8.26 (d, J=4.02 Hz, 1H), 8.35 (d, J=5.02 Hz, 1H), 8.62 (brs, 1H), 8.69 (d, J=1.38 Hz, 1H), 8.76 (s, 1H), 8.87-8.94 (m, 2H), 10.25 (s, 1H), 13.77 (brs, 2H); ESIMS found for $C_{26}H_{21}N_7OS$ m/z 480.1 (M+1).

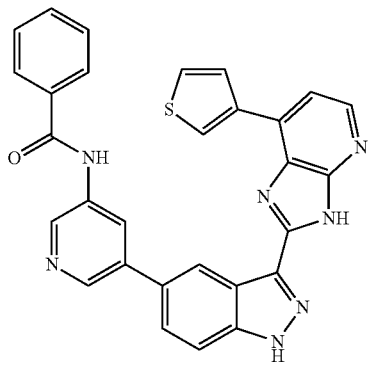
270



2-Phenyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide 270

[0979] White solid (11.1 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ pp 3.85 (s, 2H), 7.25-7.31 (m, 1H), 7.36 (t, J=7.40 Hz, 2H), 7.40-7.45 (m, 2H), 7.69-7.75 (m, 2H), 7.86-7.94 (m, 2H), 8.21 (d, J=3.89 Hz, 1H), 8.40 (d, J=5.40 Hz, 1H), 8.87 (d, J=1.63 Hz, 1H), 8.90 (s, 1H), 8.96 (d, J=4.89 Hz, 2H), 9.09 (d, J=1.13 Hz, 1H), 11.46 (s, 1H), 14.19 (brs, 1H); ESIMS found for $C_{30}H_{21}N_7OS$ m/z 528.1 (M+1).

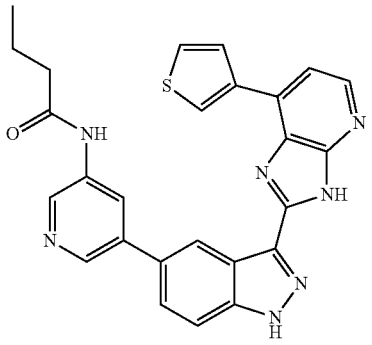
271



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide 271

[0980] White solid (59.8 mg, 0.12 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 7.59-7.65 (m, 2H), 7.67-7.78 (m, 3H), 7.92-8.01 (m, 2H), 8.14 (d, J=1.26 Hz, 1H), 8.16 (s, 1H), 8.19 (d, J=5.27 Hz, 1H), 8.41 (d, J=5.27 Hz, 1H), 8.94 (d, J=1.51 Hz, 1H), 8.99 (s, 1H), 9.08 (d, J=1.51 Hz, 1H), 9.23 (s, 1H), 9.35 (d, J=1.76 Hz, 1H), 11.30 (s, 1H), 14.23 (brs, 1H); ESIMS found for $C_{29}H_{19}N_7OS$ m/z 514.1 (M+1).

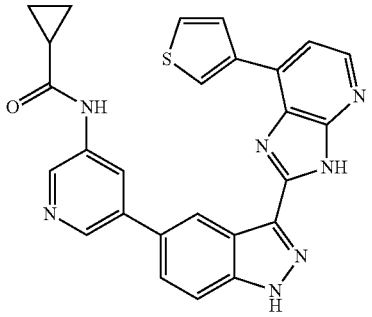
277



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide 277

[0981] White solid (7.6 mg, 0.02 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 1.07 (t, J=7.40 Hz, 3H), 1.82 (q, J=7.28 Hz, 2H), 2.54 (t, J=7.40 Hz, 3H), 7.81 (dd, J=5.14, 2.89 Hz, 1H), 7.92 (d, J=6.28 Hz, 1H), 7.93-7.98 (m, 3H), 8.52-8.57 (m, 1H), 8.54-8.54 (m, 1H), 8.61-8.68 (m, 1H), 8.95 (d, J=3.26 Hz, 2H), 9.00 (s, 1H), 9.24 (d, J=1.76 Hz, 1H); ESIMS found for $C_{26}H_{21}N_7OS$ m/z 480.1 (M+1).

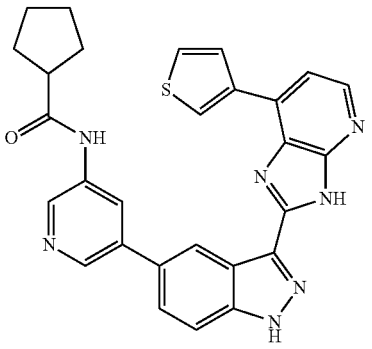
279



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)cyclopropanecarboxamide 279

[0982] White solid (25.2 mg, 0.05 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.90-0.98 (m, 4H), 1.89-1.98 (m, 1H), 7.71 (d, J=5.40 Hz, 1H), 7.78 (dd, J=4.89, 3.14 Hz, 1H), 7.87-7.94 (m, 2H), 8.21 (d, J=4.52 Hz, 1H), 8.40 (d, J=4.89 Hz, 1H), 8.86 (brs, 1H), 8.90 (d, J=2.51 Hz, 1H), 8.93 (s, 1H), 8.95 (brs, 1H), 9.02 (brs, 1H), 11.24 (brs, 1H), 14.12 (brs, 1H); ESIMS found for $C_{26}H_{19}N_7OS$ m/z 478.1 (M+1).

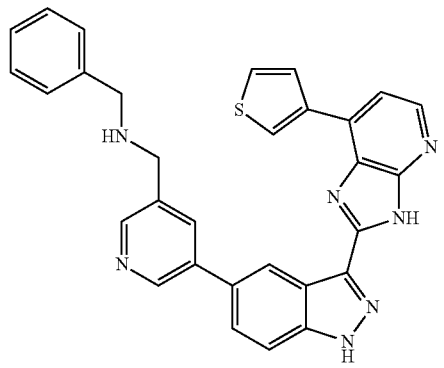
281



N-(5-(3-(7-(Thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)cyclopentanecarboxamide 281

[0983] White solid (18.0 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.53-1.64 (m, 2H), 1.65-1.75 (m, 2H), 1.75-1.88 (m, 2H), 1.90-2.01 (m, 2H), 2.99 (quin, J=7.91 Hz, 1H), 7.73 (d, J=5.40 Hz, 1H), 7.82 (dd, J=4.83, 2.95 Hz, 1H), 7.88-7.98 (m, 2H), 8.20 (d, J=4.52 Hz, 1H), 8.42 (d, J=5.14 Hz, 1H), 8.89 (brs, 1H), 8.92 (s, 1H), 9.00 (s, 1H), 9.03 (brs, 1H), 9.18 (s, 1H), 11.29 (brs, 1H), 14.28 (brs, 1H); ESIMS found for $C_{22}H_{23}N_7OS$ m/z 506.1 (M+1).

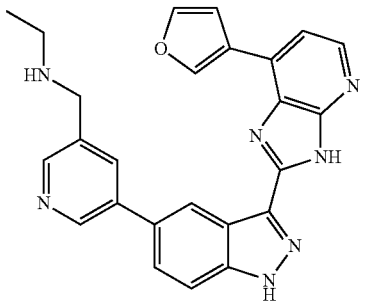
283



N-Benzyl-1-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl) methanamine 283

[0984] White solid (29.6 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 4.26-4.33 (m, 2H), 4.47 (d, J=5.02 Hz, 2H), 7.38-7.48 (m, 3H), 7.62 (dd, J=7.65, 1.63 Hz, 2H), 7.73 (d, J=5.52 Hz, 1H), 7.81 (dd, J=5.14, 2.89 Hz, 1H), 7.90-7.95 (m, 1H), 8.02 (dd, J=8.66, 1.63 Hz, 1H), 8.19-8.25 (m, 1H), 8.42 (d, J=5.02 Hz, 1H), 8.91-9.01 (m, 4H), 9.28 (d, J=0.75 Hz, 1H), 10.13 (brs, 2H), 14.24 (brs, 1H); ESIMS found for $C_{30}H_{23}N_7S$ m/z 514.2 (M+1).

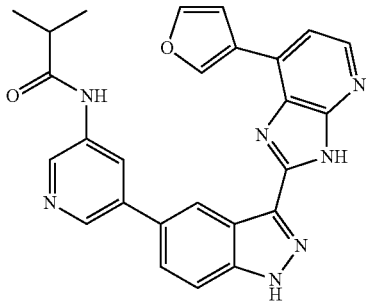
292



N-((5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine 292

[0985] White solid (16.7 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.29 (t, J=7.28 Hz, 3H), 3.08 (quin, J=6.28 Hz, 2H), 4.38 (t, J=5.27 Hz, 2H), 7.47 (d, J=1.00 Hz, 1H), 7.63 (d, J=4.52 Hz, 1H), 7.87-8.03 (m, 3H), 8.39 (d, J=4.52 Hz, 1H), 8.77 (d, J=1.25 Hz, 1H), 8.88 (s, 1H), 8.96 (s, 1H), 9.04 (s, 1H), 9.23 (s, 1H), 9.41-9.53 (m, 2H), 14.15 (brs, 1H); ESIMS found for $C_{25}H_{21}N_7O$ m/z 436.1 (M+1).

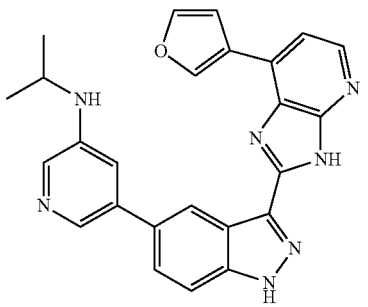
295



N-(5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)isobutyramide 295

[0986] White solid (34.7 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.19 (d, J=6.78 Hz, 6H), 2.77 (spt, J=6.87 Hz, 1H), 7.47 (d, J=1.25 Hz, 1H), 7.66 (d, J=5.27 Hz, 1H), 7.88-7.97 (m, 3H), 8.41 (d, J=5.27 Hz, 1H), 8.90 (s, 1H), 8.99 (s, 2H), 9.03 (s, 1H), 9.17 (s, 1H), 11.14 (brs, 1H), 14.26 (brs, 1H); ESIMS found for $C_{26}H_{21}N_7O_2$ m/z 464.1 (M+1).

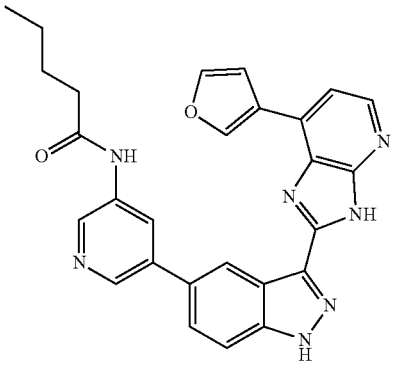
298



5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine 298

[0987] White solid (41.2 mg, 0.10 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.25 (d, J=6.27 Hz, 6H), 3.85-3.95 (m, 1H), 7.48 (d, J=1.25 Hz, 1H), 7.67 (d, J=5.27 Hz, 1H), 7.90 (s, 2H), 7.96 (t, J=1.63 Hz, 1H), 7.98 (s, 1H), 8.11 (d, J=2.01 Hz, 1H), 8.42 (d, J=4.77 Hz, 1H), 8.44 (s, 1H), 8.87 (s, 1H), 9.02 (s, 1H), 14.28 (brs, 1H); ESIMS found for $C_{25}H_{21}N_7O$ m/z 436.2 (M+1).

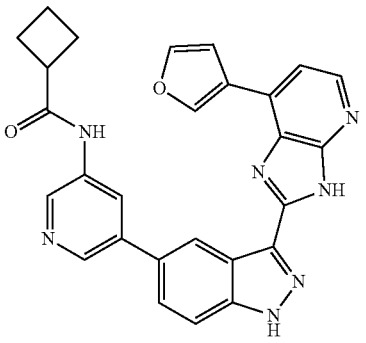
304



N-(5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)pentanamide 304

[0988] White solid (10.6 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.93 (t, J=7.28 Hz, 3H), 1.38 (dq, J=14.84, 7.27 Hz, 3H), 1.65 (quin, J=7.47 Hz, 2H), 7.49 (d, J=1.00 Hz, 1H), 7.66 (d, J=4.52 Hz, 1H), 7.87-7.97 (m, 3H), 8.41 (d, J=5.02 Hz, 1H), 8.90 (s, 1H), 8.91 (brs, 1H), 8.99 (s, 1H), 9.03 (s, 1H), 9.13 (s, 1H), 11.11 (brs, 1H), 14.24 (brs, 1H); ESIMS found for $C_{27}H_{23}N_7O_2$ m/z 478.2 (M+1).

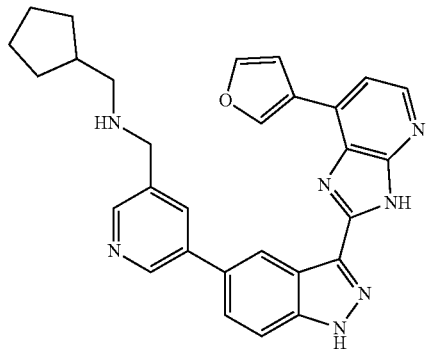
306



N-(5-(3-(7-(Furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)cyclobutanecarboxamide 306

[0989] White solid (11.0 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.79-1.91 (m, 1H), 1.92-2.07 (m, 1H), 2.15-2.26 (m, 2H), 2.26-2.37 (m, 2H), 3.42 (quin, J=8.25 Hz, 1H), 7.48 (d, J=1.13 Hz, 1H), 7.68 (d, J=4.77 Hz, 1H), 7.87-7.97 (m, 3H), 8.42 (d, J=5.02 Hz, 1H), 8.88 (s, 1H), 8.99 (s, 1H), 9.03 (s, 2H), 9.18 (brs, 1H), 11.14 (brs, 1H), 14.34 (brs, 1H); ESIMS found for $C_{27}H_{21}N_7O_2$ m/z 476.1 (M+1).

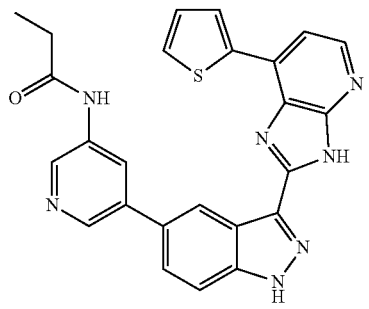
310



1-Cyclopentyl-N-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl) methyl)methanamine 310

[0990] White solid (69.3 mg, 0.14 mmol). ^{1}H NMR (CD_3OD 400 MHz) δ ppm 1.33-1.45 (m, 2H), 1.61-1.81 (m, 4H), 1.93-2.04 (m, 2H), 2.33-2.44 (m, 1H), 3.25 (d, J=7.28 Hz, 2H), 4.63 (brs, 2H), 7.26-7.32 (m, 1H), 7.82-7.96 (m, 3H), 8.00-8.07 (m, 1H), 8.47-8.54 (m, 1H), 8.79-8.85 (m, 1H), 8.97-9.04 (m, 1H), 9.07 (brs, 1H), 9.21-9.27 (m, 1H), 9.34 (s, 1H); ESIMS found for $C_{29}H_{27}N_7O$ m/z 490.1 (M+1).

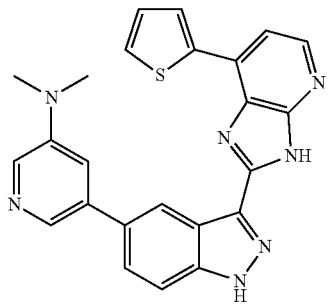
313



N-(5-(3-(7-(Thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)propionamide 313

[0991] White solid (6.5 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.16 (t, J=7.40 Hz, 3H), 3.36-3.50 (m, 2H), 7.34 (t, J=4.14 Hz, 1H), 7.69 (d, J=4.77 Hz, 1H), 7.87-7.96 (m, 3H), 8.36 (d, J=2.76 Hz, 2H), 8.97 (brs, 1H), 8.99 (brs, 1H), 9.09 (s, 1H), 9.12 (brs, 1H), 11.17 (s, 1H), 14.19 (brs, 1H); ESIMS found for $C_{25}H_{19}N_7OS$ m/z 466.1 (M+1).

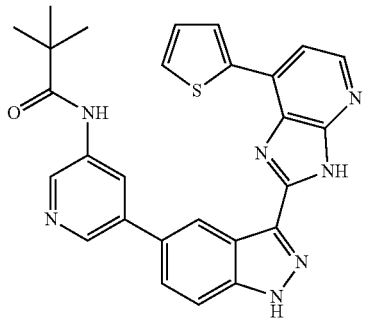
319



N,N-Dimethyl-5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine 319

[0992] White solid (15.0 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 3.21 (s, 6H), 7.32-7.38 (m, 1H), 7.69 (d, J=5.27 Hz, 1H), 7.90 (d, J=8.78 Hz, 1H), 7.94-8.01 (m, 1H), 8.04 (dd, J=8.28 Hz, J=0.76 Hz, 2H), 8.27 (d, J=2.76 Hz, 1H), 8.32-8.38 (m, 2H), 8.51 (s, 1H), 9.12 (s, 1H), 14.14 (brs, 1H); ESIMS found for $C_{24}H_{19}N_7S$ m/z 438.3 (M+1).

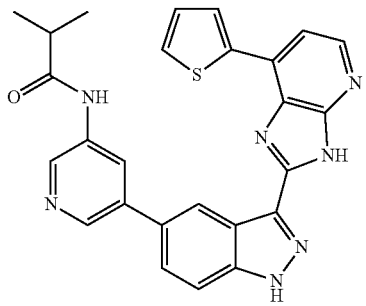
320



N-(5-(3-(7-(Thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)pivalamide 320

[0993] White solid (30.8 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.32 (s, 9H), 7.33 (dd, J=4.89, 3.76 Hz, 1H), 7.69 (d, J=5.27 Hz, 1H), 7.89-7.96 (m, 3H), 8.35 (d, J=5.40 Hz, 1H), 8.38 (d, J=3.01 Hz, 1H), 9.01 (d, J=1.38 Hz, 1H), 9.10 (s, 1H), 9.24 (s, 1H), 9.36 (d, J=1.51 Hz, 1H), 10.56 (s, 1H), 14.24 (brs, 1H); ESIMS found for $C_{27}H_{23}N_7OS$ m/z 494. (M+1).

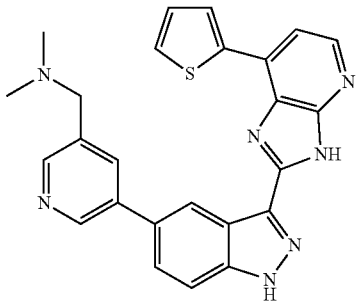
321



N-(5-(3-(7-(Thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)isobutyramide 321

[0994] White solid (18.3 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.20 (d, J=6.78 Hz, 6H), 2.79 (spt, J=6.40 Hz, 1H), 7.31-7.36 (m, 1H), 7.66-7.71 (m, 1H), 7.88-7.96 (m, 3H), 8.35 (d, J=5.40 Hz, 1H), 8.37 (d, J=3.01 Hz, 1H), 8.98 (s, 1H), 9.00-9.07 (m, 1H), 9.08 (s, 1H), 9.14-9.22 (m, 1H), 11.15 (brs, 1H), 14.21 (brs, 1H); ESIMS found for $C_{26}H_{21}N_7OS$ m/z 480.1 (M+1).

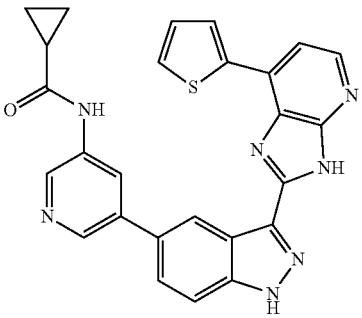
325



N,N-Dimethyl-1-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine 325

[0995] White solid (16.5 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.81 (d, J=4.27 Hz, 6H), 4.57 (d, J=3.76 Hz, 2H), 7.33-7.39 (m, 1H), 7.71 (d, J=5.27 Hz, 1H), 7.93 (d, J=8.78 Hz, 1H), 7.99 (d, J=4.77 Hz, 1H), 8.03-8.10 (m, 1H), 8.36 (d, J=5.52 Hz, 1H), 8.39 (dd, J=3.76 Hz, J=0.76 Hz, 1H), 8.97-9.09 (m, 2H), 9.12 (s, 1H), 9.31 (brs, 1H), 11.51 (brs, 1H), 14.24 (brs, 1H); ESIMS found for $C_{25}H_{21}N_7S$ m/z 452.2 (M+1).

331

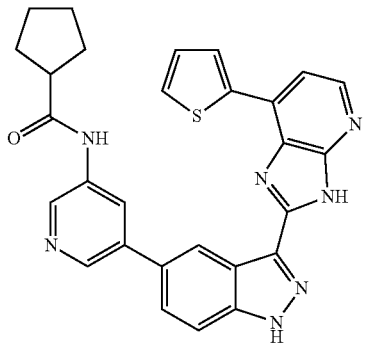


N-(5-(3-(7-(Thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)cyclopropanecarboxamide 331

[0996] White solid (32.6 mg, 0.07 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.79-0.95 (m, 4H), 1.88-2.03 (m, 1H), 7.26-7.32 (m, 1H), 7.64 (d, J=5.02 Hz, 1H), 7.75 (d, J=5.02 Hz, 1H), 7.84 (s, 2H), 8.32 (d, J=5.27 Hz, 1H), 8.34 (d, J=3.01 Hz, 1H), 8.62-8.65 (m, 1H), 8.70 (s, 1H), 8.75 (d,

J=1.51 Hz, 1H), 9.04 (s, 1H), 10.81 (s, 1H), 13.86 (brs, 1H), 14.03 (brs, 1H); ESIMS found for $C_{26}H_{19}N_7OS$ m/z 478.1 (M+1).

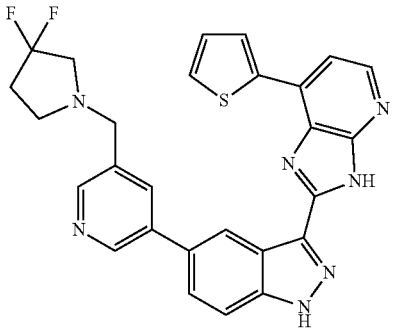
333



N-(5-(3-(7-(Thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl) pyridin-3-yl)cyclopentanecarboxamide 333

[0997] White solid (31.0 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.56-1.66 (m, 2H), 1.66-1.75 (m, 2H), 1.76-1.86 (m, 2H), 1.90-2.00 (m, 2H), 2.98 (quin, J=7.87 Hz, 1H), 7.31-7.37 (m, 1H), 7.68 (d, J=5.40 Hz, 1H), 7.87-7.96 (m, 3H), 8.35 (d, J=5.40 Hz, 1H), 8.37 (d, J=3.64 Hz, 1H), 8.98 (s, 1H), 9.04 (brs, 1H), 9.08 (s, 1H), 9.18 (s, 1H), 11.26 (brs, 1H), 14.21 (brs, 1H); ESIMS found for $C_{28}H_{23}N_7OS$ m/z 506.1 (M+1).

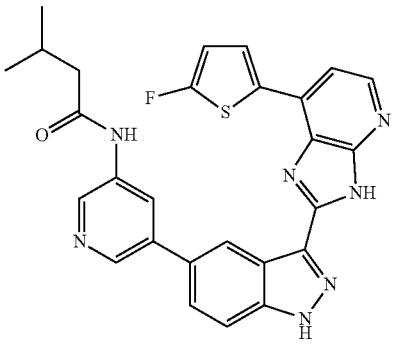
337



2-(5-(5-((3,3-Difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine 337

[0998] White solid (11.3 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.56-2.68 (m, 2H), 4.58-4.71 (m, 2H), 7.35 (d, J=4.27 Hz, 1H), 7.70 (dd, J=4.27, 3.01 Hz, 1H), 7.89-7.99 (m, 2H), 7.99-8.08 (m, 1H), 8.36 (d, J=5.02 Hz, 1H), 8.39 (d, J=3.26 Hz, 1H), 8.89-8.97 (m, 1H), 8.97-9.05 (m, 1H), 9.14 (s, 1H), 9.24-9.32 (m, 1H), 14.15 (brs, 1H); ESIMS found for $C_{27}H_{21}F_2N_7S$ m/z 514.2 (M+1).

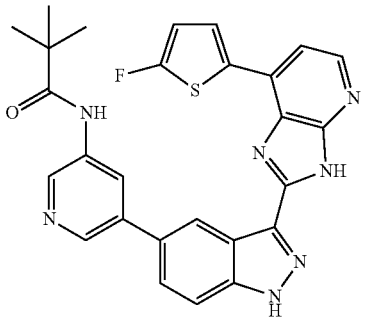
340



N-(5-(3-(7-(5-Fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide 340

[0999] White solid (6.9 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.97 (d, J=6.65 Hz, 6H), 2.10-2.16 (m, 1H), 2.30 (d, J=7.03 Hz, 2H), 6.91-6.95 (m, 1H), 7.69 (d, J=4.77 Hz, 1H), 7.88 (s, 2H), 7.95-8.01 (m, 1H), 8.32 (d, J=5.27 Hz, 1H), 8.73 (s, 1H), 8.82 (s, 1H), 8.91 (s, 1H), 9.05 (s, 1H), 10.53 (brs, 1H), 14.01 (s, 1H); ESIMS found for $C_{27}H_{22}FN_7OS$ m/z 512.2 (M+1).

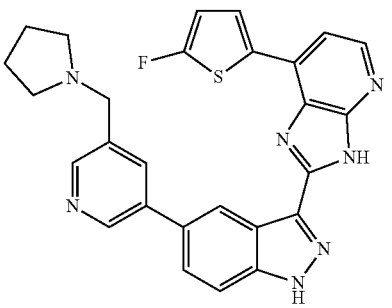
346



N-(5-(3-(7-(5-Fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide 346

[1000] White solid (12.8 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.29 (s, 9H), 6.94 (dd, J=4.08, 1.57 Hz, 1H), 7.67 (d, J=5.40 Hz, 1H), 7.87-7.97 (m, 2H), 8.02 (t, J=3.95 Hz, 1H), 8.31 (d, J=5.40 Hz, 1H), 9.02 (s, 2H), 9.32 (s, 1H), 9.39 (d, J=1.51 Hz, 1H), 10.59 (s, 1H), 14.30 (brs, 1H); ESIMS found for $C_{27}H_{22}FN_7OS$ m/z 512.2 (M+1).

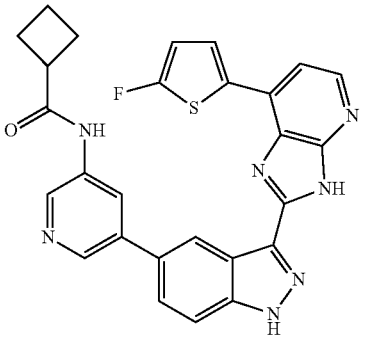
352



7-(5-Fluorothiophen-2-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 352

[1001] White solid (58.6 mg, 0.12 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.86-1.96 (m, 2H), 2.00-2.10 (m, 2H), 3.11-3.21 (m, 2H), 3.40-3.49 (m, 2H), 4.54 (d, J=5.40 Hz, 2H), 6.94-6.98 (m, 1H), 7.71 (d, J=5.27 Hz, 1H), 7.89 (d, J=8.53 Hz, 1H), 7.97-8.03 (m, 2H), 8.33 (d, J=5.40 Hz, 1H), 8.68 (s, 1H), 8.89 (s, 1H), 9.08 (s, 1H), 9.18 (s, 1H), 11.20 (s, 1H), 14.08 (brs, 1H); ESIMS found for $C_{27}H_{22}FN_7S$ m/z 496.1 (M+1).

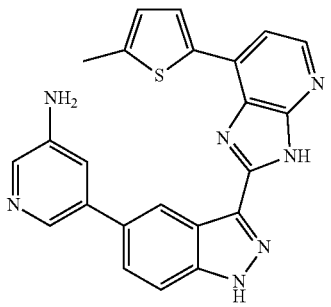
358



N-(5-(3-(7-(5-Fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide 358

[1002] White solid (6.7 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.78-1.90 (m, 1H), 1.94-2.06 (m, 1H), 2.13-2.35 (m, 4H), 3.33-3.44 (m, 1H), 6.95 (d, J=2.26 Hz, 1H), 7.69 (d, J=5.27 Hz, 1H), 7.88-7.97 (m, 2H), 8.01 (t, J=3.64 Hz, 1H), 8.33 (d, J=5.27 Hz, 1H), 8.99 (s, 1H), 9.05 (brs, 1H), 9.07 (s, 1H), 9.15 (s, 1H), 10.97 (s, 1H), 14.19 (brs, 1H); ESIMS found for $C_{27}H_{20}FN_7OS$ m/z 510.1 (M+1).

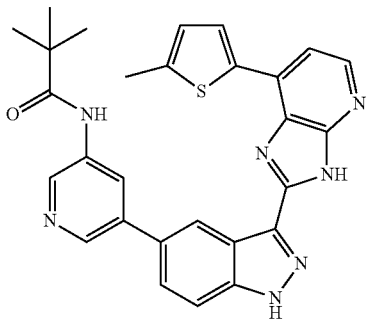
367



5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine 367

[1003] White solid (11.6 mg, 0.03 mmol). ^{1}H NMR (CD_3OD, 400 MHz) δ ppm 2.66 (s, 3H), 2.68 (s, 2H), 7.14 (dd. J=4.04 Hz, J=1.04 Hz, 1H), 7.82 (d, J=6.27 Hz, 1H), 7.85 (dd, J=8.76 Hz, J=1.48 Hz, 1H), 7.88 (d, J=8.76 Hz, 1H), 8.04-8.08 (m, 2H), 8.16 (d, J=3.51 Hz, 1H), 8.34 (s, 1H), 8.38 (d, J=6.52 Hz, 1H), 8.91 (s, 1H); ESIMS found for $C_{23}H_{17}N_7S$ m/z 424.0 (M+1).

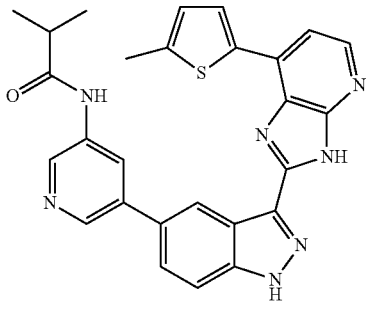
372



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide 372

[1004] White solid (56.6 mg, 0.11 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.30 (s, 9H), 2.52 (s, 3H), 7.01 (d, J=3.01 Hz, 1H), 7.58 (d, J=5.27 Hz, 1H), 7.87-7.95 (m, 2H), 8.22 (d, J=3.64 Hz, 1H), 8.31 (d, J=5.40 Hz, 1H), 9.00 (d, J=1.51 Hz, 1H), 9.05 (s, 1H), 9.09 (s, 1H), 9.31 (d, J=1.63 Hz, 1H), 10.31 (s, 1H), 14.15 (brs, 1H); ESIMS found for $C_{28}H_{25}N_7OS$ m/z 508.1 (M+1).

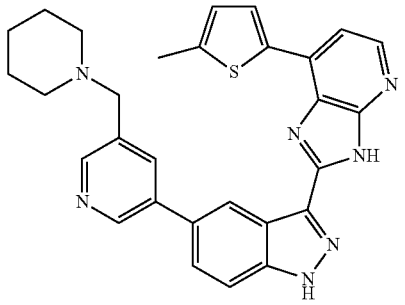
373



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide 373

[1005] White solid (10.3 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.17 (d, J=7.03 Hz, 6H), 2.54 (s, 3H), 2.69-2.77 (m, 1H), 7.01 (dd, J=3.64, 1.13 Hz, 1H), 7.60 (d, J=5.27 Hz, 1H), 7.84-7.93 (m, 2H), 8.16 (d, J=3.76 Hz, 1H), 8.30 (d, J=5.27 Hz, 1H), 8.76 (s, 1H), 8.92 (d, J=1.76 Hz, 1H), 9.08 (d, J=1.76 Hz, 1H), 9.11 (s, 1H), 10.77 (brs, 1H), 14.07 (brs, 1H); ESIMS found for $C_{27}H_{23}N_7OS$ m/z 494.2 (M+1).

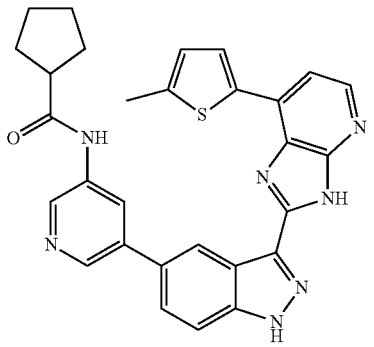
379



7-(5-Methylthiophen-2-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 379

[1006] White solid (18.9 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.29-1.44 (m, 2H), 1.44-1.64 (m, 4H), 2.30-2.49 (m, 4H), 2.61 (s, 3H), 3.54-3.69 (m, 2H), 6.99 (dd, J=3.51, 1.00 Hz, 1H), 7.59 (d, J=5.27 Hz, 1H), 7.82-7.87 (m, 1H), 7.88-7.95 (m, 1H), 8.02-8.16 (m, 2H), 8.29 (d, J=5.27 Hz, 1H), 8.52-8.63 (m, 1H), 9.00-9.11 (m, 1H), 9.16-9.22 (m, 1H), 13.83 (brs, 1H), 14.01 (s, 1H); ESIMS found for $C_{29}H_{27}N_7S$ m/z 506.3 (M+1).

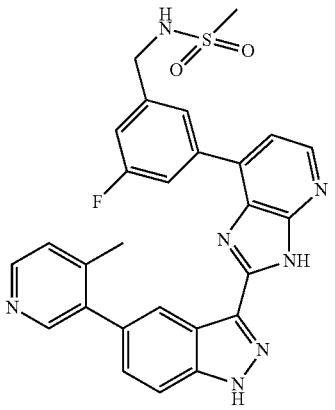
385



N-(5-(3-(7-(5-Methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide 385

[1007] White solid (21.9 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.55-1.65 (m, 2H), 1.65-1.74 (m, 2H), 1.74-1.84 (m, 2H), 1.87-1.99 (m, 2H), 2.53 (s, 3H), 2.86-2.98 (m, 1H), 7.01 (dd, J=3.64, 0.88 Hz, 1H), 7.60 (d, J=5.27 Hz, 1H), 7.84-7.95 (m, 2H), 8.17 (d, J=3.51 Hz, 1H), 8.31 (d, J=5.27 Hz, 1H), 8.82 (s, 1H), 8.95 (d, J=1.51 Hz, 1H), 9.10 (s, 1H), 9.13 (d, J=1.76 Hz, 1H), 10.94 (brs, 1H), 14.11 (brs, 1H); ESIMS found for $C_{29}H_{25}N_7OS$ m/z 520.1 (M+1).

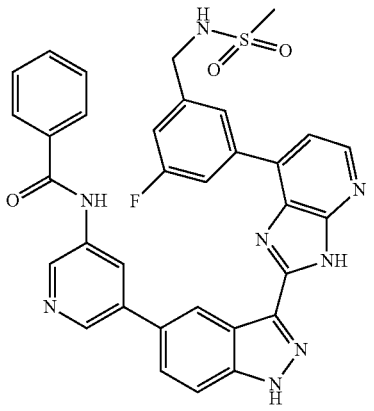
421



N-(3-fluoro-5-(2-(5-(4-Methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo [4,5-b]pyridin-7-yl)benzyl) methanesulfonamide 421

[1008] White solid (12.5 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.60 (s, 3H), 2.88 (s, 3H), 4.23 (d, J=6.02 Hz, 2H), 7.31 (d, J=9.04 Hz, 1H), 7.64-7.69 (m, 2H), 7.74 (t, J=6.02 Hz, 1H), 7.90 (d, J=9.03 Hz, 1H), 8.12 (d, J=6.02 Hz, 2H), 8.29-8.38 (m, 1H), 8.46 (d, J=5.02 Hz, 1H), 8.66 (s, 1H), 8.86 (d, J=6.27 Hz, 1H), 8.99 (s, 1H), 14.22 (brs, 1H); ESIMS found for $C_{27}H_{22}FN_7O_2S$ m/z 528.3 (M+1).

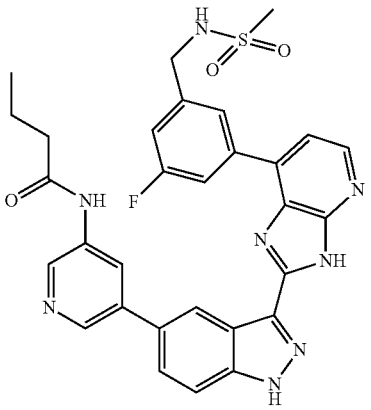
427



N-(5-(3-(7-(3-Fluoro-5-(methylsulfonamidomethyl) phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide 427

[1009] White solid (23.1 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.90 (s, 3H), 4.28 (d, J=6.27 Hz, 2H), 7.14 (dd, J=7.15, 1.63 Hz, 1H), 7.57-7.64 (m, 2H), 7.65-7.70 (m, 2H), 7.73 (t, J=6.53 Hz, 1H), 7.90 (d, J=1.00 Hz, 2H), 8.02-8.07 (m, 2H), 8.13-8.20 (m, 1H), 8.46 (d, J=5.02 Hz, 1H), 8.52-8.64 (m, 1H), 8.71 (brs, 1H), 8.85 (d, J=1.76 Hz, 1H), 8.95 (s, 1H), 9.13 (d, J=2.01 Hz, 1H), 10.72 (s, 1H), 14.03 (s, 1H); ESIMS found for $C_{33}H_{25}FN_8O_3S$ m/z 633.1 (M+1).

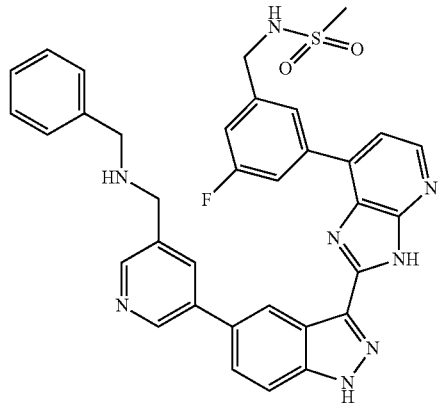
433



N-(5-(3-(7-(3-Fluoro-5-(methylsulfonamidomethyl) phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide 433

[1010] White solid (6.4 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.97 (t, J=7.40 Hz, 3H), 1.67 (sxt, J=7.28 Hz, 3H), 2.43 (t, J=7.28 Hz, 2H), 2.89 (s, 3H), 4.30 (d, J=6.02 Hz, 2H), 7.28-7.37 (m, 1H), 7.70 (d, J=5.27 Hz, 1H), 7.71-7.79 (m, 2H), 7.87 (dd, J=8.76 Hz, J=1.76 Hz, 1H), 7.92 (d, J=8.28 Hz, 1H), 8.11-8.22 (m, 1H), 8.48 (d, J=5.27 Hz, 1H), 8.70 (s, 1H), 8.90 (s, 1H), 8.93 (d, J=1.51 Hz, 1H), 9.10 (d, J=1.76 Hz, 1H), 10.79 (brs, 1H), 14.15 (brs, 1H); ESIMS found for $C_{30}H_{27}FN_8O_3S$ m/z 599.2 (M+1).

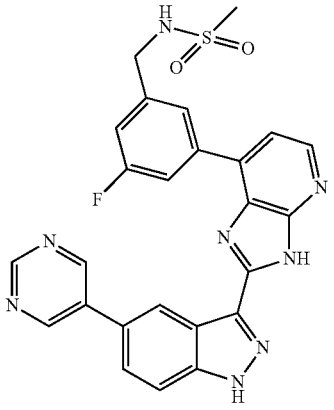
439



N-(3-(2-(5-(5-((Benzylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide 439

[1011] White solid (50.1 mg, 0.08 mmol). ^{1}H NMR (CD_3MSO-d_6, 400 MHz) δ ppm 3.01 (s, 3H), 4.46 (s, 2H), 4.48 (s, 2H), 4.69 (s, J=97.44-7.543 (Hz, 4H), 7.65 (dd, J=7.53, 2.01 Hz, 2H), 7.73-7.79 (Hz, 1H), 7.87 (d, J=6.27 Hz, 1H), 7.95 (dd, J=8.80 Hz, J=0.72 Hz, 1H), 8.03 (dd, J=8.8 Hz, J=1.76 Hz, 1H), 8.66 (d, J=6.27 Hz, 1H), 9.04 (d, J=1.51 Hz, 1H), 9.07 (d, J=0.75 Hz, 1H), 9.19 (s, 1H), 9.35 (d, J=1.76 Hz, 1H); ESIMS found for $C_{34}H_{29}FN_8O_2S$ m/z 633.3 (M+1).

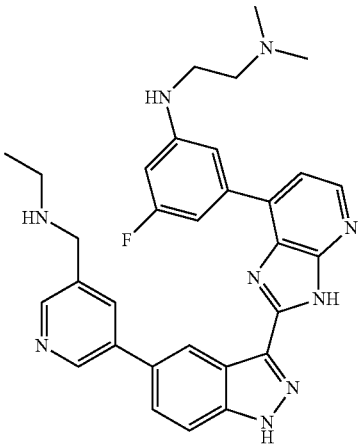
442



N-(3-Fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methane-sulfonamide 442

[1012] White solid (17.3 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.94 (s, 3H), 4.34 (d, J=6.40 Hz, 2H), 7.35 (d, J=9.54 Hz, 1H), 7.68 (d, J=5.27 Hz, 1H), 7.76 (t, J=6.34 Hz, 1H), 7.88 (d, J=8.56 Hz, 1H), 7.96 (dd, J=8.64 Hz, J=1.60 Hz, 1H), 8.21 (s, 1H), 8.44 (d, J=5.14 Hz, 1H), 8.57 (d, J=10.29 Hz, 1H), 8.95 (d, J=0.63 Hz, 1H), 9.24 (s, 1H), 9.26 (s, 2H), 13.98 (brs, 1H), 14.00 (s, 1H); ESIMS found for $C_{25}H_{19}FN_8O_2S$ m/z 515.0 (M+1).

448

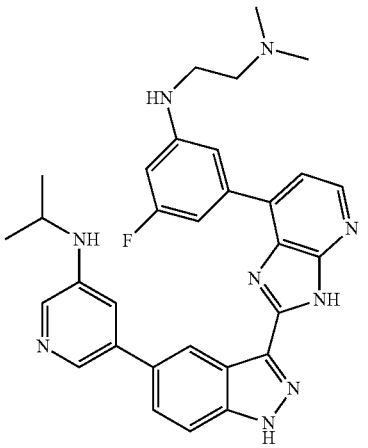


N^1-(3-(2-(5-(5-((Ethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine 448

[1013] White solid (13.9 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.29 (t, J=7.28 Hz, 3H), 2.81 (s, 3H), 2.82 (s, 3H), 3.00-3.11 (m, 3H), 3.23-3.31 (m, 2H),

3.57 (t, J=6.40 Hz, 2H), 4.39 (t, J=5.52 Hz, 4H), 6.68 (d, J=11.80 Hz, 1H), 7.33 (d, J=1.25 Hz, 1H), 7.44-7.55 (m, 1H), 7.65 (d, J=5.52 Hz, 1H), 7.94 (d, J=8.80 Hz, 1H), 8.02 (dd, J=8.80 Hz, J=1.52 Hz, 1H), 8.50 (d, J=5.02 Hz, 1H), 8.88 (s, 1H), 8.93 (s, 1H), 8.99 (s, 1H), 9.26 (d, J=2.01 Hz, 1H), 9.80 (brs, 2H); ESIMS found for $C_{31}H_{32}FN_9$ m/z 550.2 (M+1).

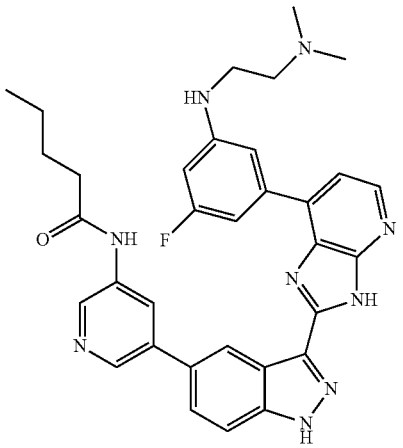
454



N^1-(3-Fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl) phenyl)-N^2,N^2-dimethylethane-1,2-diamine 454

[1014] White solid (21.9 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.21 (d, J=6.27 Hz, 6H), 2.80 (s, 3H), 2.81 (s, 3H), 3.19-3.26 (m, 2H), 3.50-3.57 (m, 2H), 3.79-3.89 (m, 1H), 6.60 (d, J=11.04 Hz, 1H), 7.04-7.16 (m, 1H), 7.26-7.35 (m, 1H), 7.59 (d, J=5.77 Hz, 1H), 7.82-7.92 (m, 3H), 8.09 (d, J=2.26 Hz, 1H), 8.38 (s, 1H), 8.42 (d, J=5.77 Hz, 1H), 8.83 (s, 1H), 10.34 (brs, 2H), 14.13 (brs, 2H); ESIMS found for $C_{31}H_{32}FN_9$ m/z 550.3 (M+1).

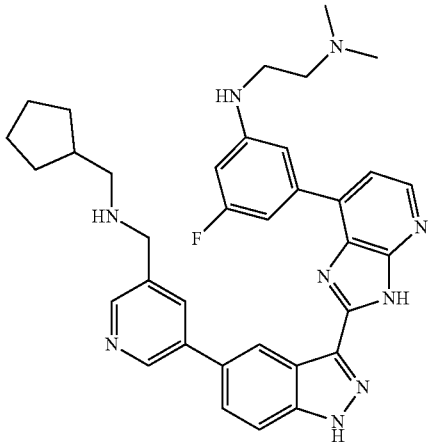
460



N-(5-(3-(7-(3-((2-(Dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide 460

[1015] White solid (51.5 mg, 0.09 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 0.93 (t, J=7.40 Hz, 3H), 1.37 (sxt, J=7.28 Hz, 2H), 1.63 (quin, J=7.28 Hz, 2H), 2.44 (t, J=7.53 Hz, 2H), 2.82 (brs, 3H), 2.83 (brs, 3H), 3.21-3.30 (m, 2H), 3.50-3.57 (m, 2H), 6.61 (d, J=11.80 Hz, 1H), 7.34-7.44 (m, 1H), 7.60 (d, J=5.27 Hz, 1H), 7.84 (dd, J=9.00 Hz, J=1.28 Hz, 1H), 7.92 (d, J=8.56 Hz, 1H), 8.42-8.48 (m, 1H), 8.60 (d, J=1.25 Hz, 1H), 8.88 (s, 2H), 9.00-9.05 (m, 1H), 10.09 (brs, 1H), 10.69 (brs, 1H), 14.11 (brs, 1H); ESIMS found for $C_{33}H_{34}FN_9O$ m/z 592.4 (M+1).

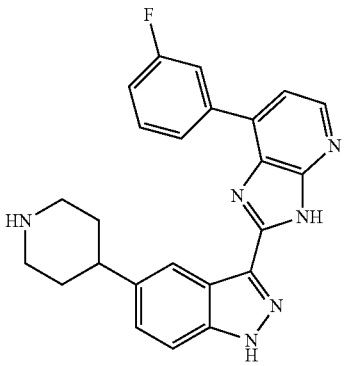
466



N^1-(3-(2-(5-(5-(((Cyclopentylmethyl)amino)methyl) pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b] pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethyl-ethane-1,2-diamine 466

[1016] White solid (54.9 mg, 0.09 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 1.20-1.32 (m, 2H), 1.45-1.65 (m, 4H), 1.74-1.85 (m, 2H), 2.19-2.31 (m, 1H), 2.82 (brs, 3H), 2.83 (brs, 3H), 2.90-2.99 (m, 2H), 3.23-3.32 (m, 2H), 3.33-3.44 (m, 2H), 4.32 (brs, 2H), 6.64 (d, J=11.04 Hz, 1H), 7.39-7.47 (m, 1H), 7.58 (d, J=5.02 Hz, 1H), 7.64-7.74 (m, 1H), 7.86-7.98 (m, 2H), 8.42 (d, J=5.52 Hz, 1H), 8.57 (brs, 1H), 8.83 (s, 1H), 8.93 (s, 1H), 9.14 (s, 1H), 9.33-9.45 (m, 2H), 10.41 (brs, 1H), 14.09 (brs, 1H); ESIMS found for $C_{35}H_{38}FN_9$ m/z 604.4 (M+1).

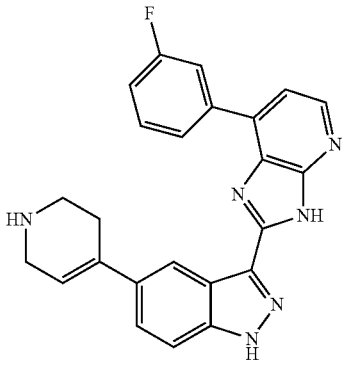
1873



7-(3-Fluorophenyl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1873

[1017] Gray solid (5.0 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.59-1.70 (m, 2H), 1.90 (br d, J=10.70 Hz, 2H), 2.62-2.72 (m, 2H), 2.78 (br t, J=11.66 Hz, 1H), 3.11 (br d, J=11.80 Hz, 2H), 7.35-7.44 (m, 2H), 7.58-7.70 (m, 4H), 8.31 (br s, 1H), 8.39 (d, J=4.94 Hz, 1H), 8.50 (s, 1H), 8.64 (br s, 1H), 13.62 (brs, 1H); ESIMS found for $C_{24}H_{21}FN_6$ m/z 413.2 (M+1).

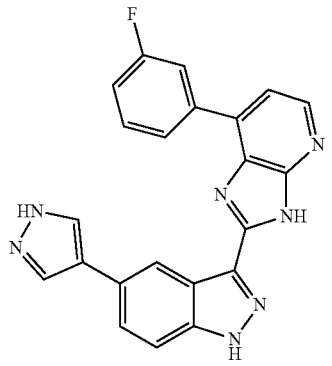
1874



7-(3-Fluorophenyl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1874

[1018] Brown solid (17.0 mg, 0.04 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.71 (br s, 2H), 3.22 (br t, J=5.63 Hz, 1H), 3.63 (br s, 2H), 6.37 (br s, 1H), 7.35-7.43 (m, 1H), 7.61-7.68 (m, 2H), 7.68-7.76 (m, 2H), 8.28 (br s, 1H), 8.41 (d, J=5.21 Hz, 1H), 8.64-8.76 (m, 2H), 13.78 (brs, 1H); ESIMS found for $C_{24}H_{19}FN_6$ m/z 411.2 (M+1).

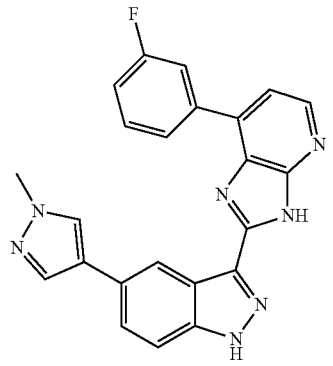
1875



2-(5-(1H-Pyrazol-4-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine 1875

[1019] Pink solid (4.7 mg, 0.01 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.38-7.44 (m, 1H), 7.64-7.72 (m, 3H), 7.79 (br d, J=7.68 Hz, 1H), 7.98 (br s, 1H), 8.19 (br s, 1H), 8.29 (br d, J=7.68 Hz, 1H), 8.41 (br d, J=4.94 Hz, 1H), 8.72-8.81 (m, 2H), 13.03 (br s, 1H), 13.75 (br s, 1H), 13.81 (br s, 1H); ESIMS found for $C_{22}H_{14}FN_7$ m/z 396.2 (M+1).

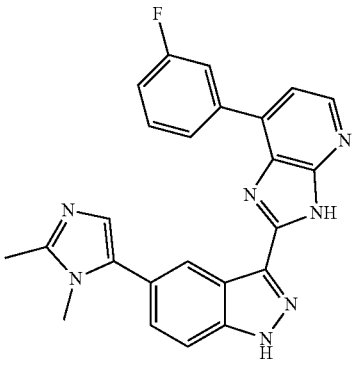
1876



7-(3-Fluorophenyl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1876

[1020] Yellow solid (10.0 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 3.93 (s, 3H), 7.38-7.45 (m, 1H), 7.65-7.76 (m, 4H), 7.90 (s, 1H), 8.14 (s, 1H), 8.26 (br d, J=7.14 Hz, 1H), 8.41 (d, J=5.21 Hz, 1H), 8.76 (br s, 2H), 13.77 (br s, 2H); ESIMS found for $C_{23}H_{16}FN_7$ m/z 410.1 (M+1).

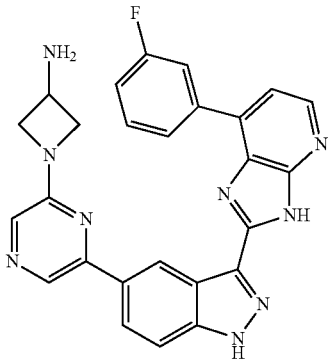
1877



2-(5-(1,2-Dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine 1877

[1021] Brown solid (9.3 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.41 (s, 3H), 3.64 (s, 3H), 6.97 (s, 1H), 7.37 (br s, 1H), 7.56-7.68 (m, 3H), 7.77 (br d, J=8.51 Hz, 1H), 8.25 (br d, J=7.14 Hz, 1H), 8.41 (br d, J=4.94 Hz, 1H), 8.52 (br d, J=10.70 Hz, 1H), 8.61 (s, 1H), 13.88 (br s, 2H); ESIMS found for $C_{24}H_{18}FN_7$ m/z 424.1 (M+1).

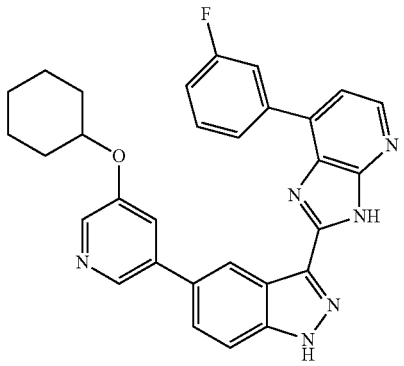
1878



1-(6-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine 1878

[1022] Yellow solid (2.1 mg, 0.004 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 3.71 (dd, J=8.23, 5.76 Hz, 2H), 3.86-3.94 (m, 1H), 4.28 (t, J=7.68 Hz, 2H), 7.35-7.42 (m, 1H), 7.60-7.69 (m, 2H), 7.78 (d, J=8.78 Hz, 1H), 7.84 (s, 1H), 8.20 (br d, J=8.78 Hz, 1H), 8.34 (br s, 1H), 8.40 (br d, J=4.94 Hz, 1H), 8.50 (s, 2H), 9.22 (s, 1H), 13.83 (br s, 2H); ESIMS found for $C_{26}H_{20}FN_9$ m/z 478.2 (M+H).

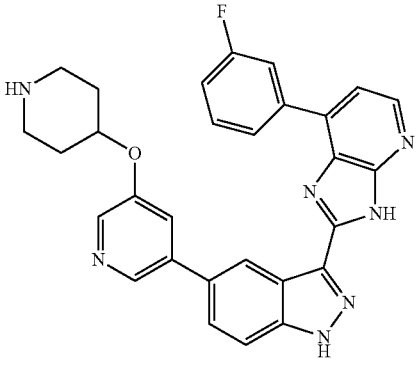
1879



2-(5-(5-(Cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine 1879

[1023] Brown solid (35 mg, 0.062 mmol, 73.5% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.26-1.34 (m, 1H), 1.40 (dtd, J=13.21, 10.14, 10.14, 3.29 Hz, 2H), 1.47-1.58 (m, 3H), 1.68-1.78 (m, 2H), 1.95-2.04 (m, 2H), 4.57-4.66 (m, 1H), 7.34 (td, J=8.37, 2.47 Hz, 1 H), 7.63 (td, J=8.03, 6.45 Hz, 1H), 7.68-7.73 (m, 2H), 7.82 (d, J=8.51 Hz, 1H), 7.90 (dd, J=8.64, 1.78 Hz, 1H), 8.33 (d, J=2.74 Hz, 1H), 8.39 (d, J=7.96 Hz, 1H), 8.42 (d, J=5.21 Hz, 1H), 8.54 (dt, J=10.98, 2.06 Hz, 1H), 8.59 (d, J=1.92 Hz, 1H), 8.91 (s, 1H), 13.91 (s, 1H), 13.93 (s, 1H); ESIMS found for $C_{30}H_{25}FN_6O$ m/z 505.2 (M+1).

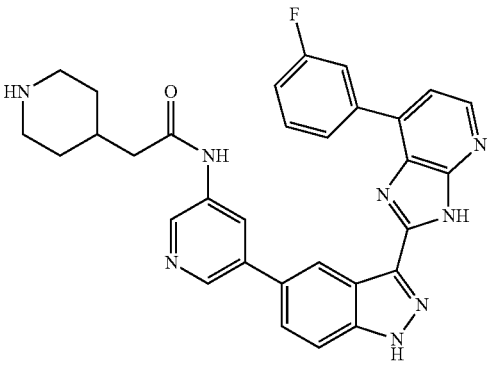
1880



7-(3-Fluorophenyl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1880

[1024] Brown solid (14 mg, 0.026 mmol, 74.4% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.86-1.97 (m, 2H), 2.17 (ddd, J=10.15, 7.00, 3.43 Hz, 2H), 3.11 (ddd, J=12.69, 8.71, 3.57 Hz, 2H), 3.26-3.32 (m, 2H), 4.91 (tt, J=7.41, 3.43 Hz, 1H), 7.38 (td, J=8.58, 2.33 Hz, 1H), 7.64 (td, J=7.96, 6.31 Hz, 1H), 7.69 (br d, J=3.84 Hz, 1H), 7.78-7.86 (m, 2H), 7.90 (dd, J=8.78, 1.65 Hz, 1H), 8.38 (br d, J=3.84 Hz, 1H), 8.40-8.46 (m, 2H), 8.58 (br d, J=9.33 Hz, 1H), 8.65 (d, J=1.65 Hz, 1H), 8.93 (s, 1H), 13.94 (brs, 1H); ESIMS found for $C_{29}H_{24}FN_7O$ m/z 506.2 (M+1).

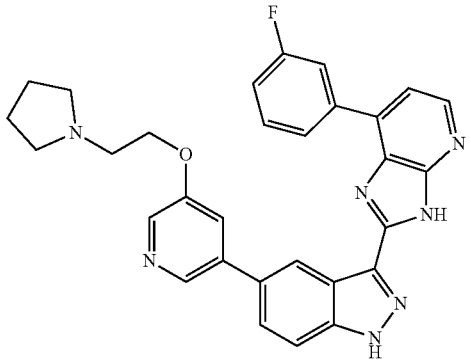
1881



N-(5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide 1881

[1025] Orange solid (9.1 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.09-1.20 (m, 2H) 1.64 (br d, J=11.53 Hz, 2H) 1.84-1.93 (m, 1H) 2.30 (br d, J=6.86 Hz, 2H) 2.43-2.49 (m, 2H) 2.93 (br d, J=12.08 Hz, 2H) 7.30 (td, J=8.44, 2.06 Hz, 1H) 7.58-7.65 (m, 1H) 7.67 (d, J=4.94 Hz, 1H) 7.77-7.87 (m, 2H) 8.35 (br d, J=7.41 Hz, 1H) 8.41 (d, J=4.94 Hz, 1H) 8.47-8.55 (m, 2H) 8.68 (d, J=1.65 Hz, 1H) 8.77 (d, J=1.92 Hz, 1H) 8.89 (s, 1H) 10.23 (s, 1H); ESIMS found for $C_{31}H_{27}FN_8O$ m/z 547.3 (M+1).

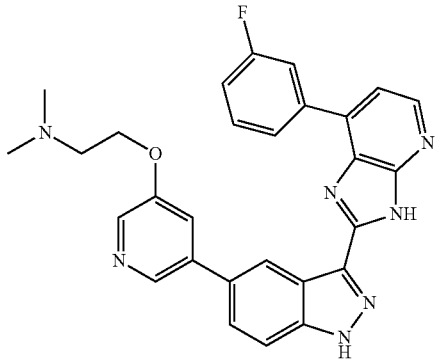
1882



7-(3-Fluorophenyl)-2-(5-(5-(2-(pyrrolidin-1-yl) ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo [4,5-b]pyridine 1882

[1026] Brown solid (15 mg, 0.027 mmol, 46.4% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 1.68 (dt, J=6.72, 3.22 Hz, 4H), 2.52-2.57 (m, 4H), 2.86 (t, J=5.76 Hz, 2H), 4.27 (t, J=5.90 Hz, 2H), 7.35 (td, J=8.44, 2.33 Hz, 1H), 7.60-7.66 (m, 1H), 7.68 (br d, J=4.39 Hz, 1H), 7.73 (t, J=2.20 Hz, 1H), 7.81 (d, J=8.51 Hz, 1H), 7.91 (dd, J=8.64, 1.51 Hz, 1H), 8.34 (d, J=2.47 Hz, 1H), 8.37 (br d, J=8.51 Hz, 1H), 8.42 (d, J=4.94 Hz, 1H), 8.55 (br d, J=11.25 Hz, 1H), 8.61 (d, J=1.37 Hz, 1H), 8.92 (s, 1H), 13.91 (br s, 2H); ESIMS found for $C_{30}H_{26}FN_7O$ m/z 520.3 (M+1).

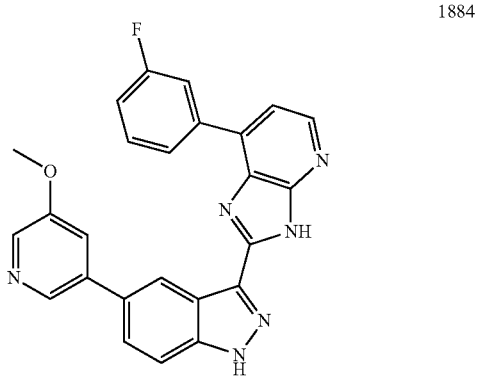
1883



2-((5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b] pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N, N-dimethylethanamine 1883

[1027] Yellow solid (3.5 mg, 0.008 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.24 (s, 6H) 2.70 (t, J=5.76 Hz, 2H) 4.25 (t, J=5.76 Hz, 2H) 7.35 (td, J=8.37, 2.20 Hz, 1H) 7.63 (td, J=8.03, 6.45 Hz, 1H) 7.67 (br s, 1H) 7.71-7.74 (m, 1H) 7.81 (d, J=8.51 Hz, 1H) 7.91 (dd, J=8.78, 1.65 Hz, 1H) 8.34 (d, J=2.74 Hz, 1H) 8.36 (br s, 1H) 8.41 (d, J=4.94 Hz, 1H) 8.54 (br d, J=7.41 Hz, 1H) 8.61 (d, J=1.92 Hz, 1H) 8.93 (s, 1H) 13.87 (br s, 1H); ESIMS found for $C_{28}H_{24}FN_7O$ m/z 494.3 (M+1).

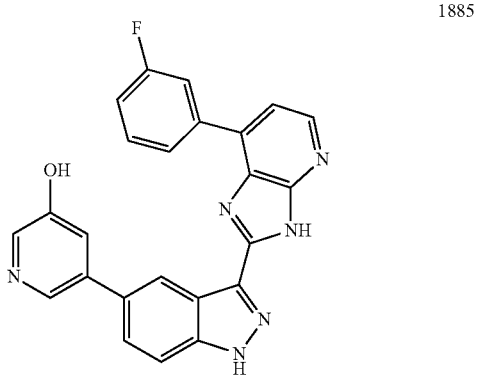
1884



7-(3-Fluorophenyl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1884

[1028] Yellow solid (12.3 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 3.95 (s, 3H) 7.37 (td, J=8.51, 1.92 Hz, 1H) 7.60-7.65 (m, 1H) 7.68 (br d, J=4.94 Hz, 1H) 7.70-7.73 (m, 1H) 7.80-7.85 (m, 1H) 7.91 (dd, J=8.78, 1.65 Hz, 1H) 8.32-8.37 (m, 2H) 8.42 (d, J=4.94 Hz, 1H) 8.55 (br d, J=10.70 Hz, 1H) 8.62 (d, J=1.37 Hz, 1H) 8.92 (s, 1H) 13.91 (s, 2H); ESIMS found for $C_{25}H_{17}FN_6O$ m/z 437.2 (M+1).

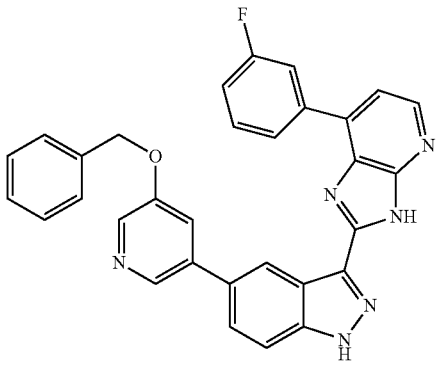
1885



5-(3-(7-(3-Fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol 1885

[1029] Yellow solid (3.6 mg, 0.009 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.32-7.40 (m, 1H) 7.50 (br s, 1H) 7.59-7.72 (m, 2H) 7.81 (s, 2H) 8.19 (br s, 1H) 8.41 (br d, J=4.39 Hz, 2H) 8.49 (br s, 2H) 8.89 (br s, 1H) 10.10 (s, 1H) 13.88 (br s, 2H); ESIMS found for $C_{24}H_{15}FN_6O$ m/z 423.1 (M+1).

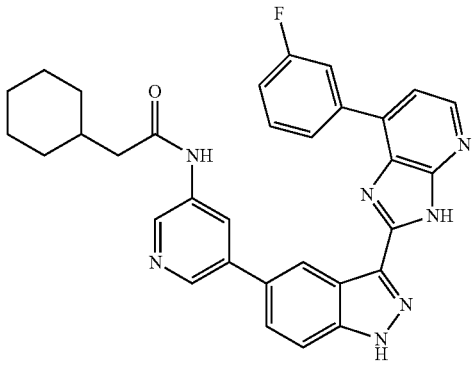
1886



2-(5-(5-(Benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine 1886

[1030] Light brown solid (33 mg, 0.061 mmol, 20.25% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 5.31 (s, 2H), 7.21 (br t, J=7.41 Hz, 1H), 7.36-7.41 (m, 1H), 7.42-7.48 (m, 2H), 7.54 (d, J=7.14 Hz, 2H), 7.62 (td, J=7.96, 6.31 Hz, 1H), 7.69 (br d, J=4.39 Hz, 1H), 7.80-7.86 (m, 2H), 7.92 (dd, J=8.64, 1.51 Hz, 1H), 8.38 (br d, J=7.68 Hz, 1H), 8.41-8.45 (m, 2H), 8.54 (br d, J=11.25 Hz, 1H), 8.66 (d, J=1.37 Hz, 1H), 8.96 (s, 1H), 13.93 (br s, 2H); ESIMS found for $C_{31}H_{21}FN_6O$ m/z 513.2 (M+1).

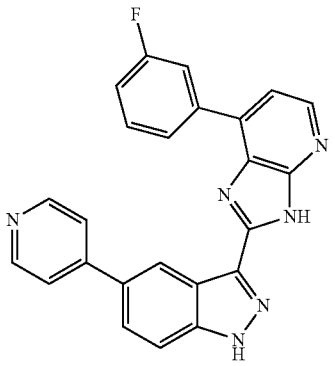
1887



2-Cyclohexyl-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide 1887

[1031] Cream colored solid (14 mg, 0.024 mmol, 27.9% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.95-1.06 (m, 2H), 1.10-1.30 (m, 3H), 1.62 (brd, J=11.53 Hz, 1H), 1.67 (brd, J=13.17 Hz, 2H), 1.74 (brd, J=11.53 Hz, 2H), 1.81 (ddd, J=10.91, 7.34, 3.43 Hz, 1H), 2.28 (d, J=7.14 Hz, 2H), 7.26-7.34 (m, 1H), 7.58-7.66 (m, 1H), 7.70 (brd, J=5.21 Hz, 1H), 7.78-7.88 (m, 2H), 8.38 (brd, J=7.68 Hz, 1H), 8.42 (d, J=4.94 Hz, 1H), 8.50 (brs, 1H), 8.54 (brd, J=10.70 Hz, 1H), 8.67 (d, J=2.20 Hz, 1H), 8.76 (brd, J=1.65 Hz, 1H), 8.89 (s, 1H), 10.22 (s, 1H), 13.94 (brs, 2H); ESIMS found for $C_{32}H_{28}FN_7O$ m/z 546.3 (M+1).

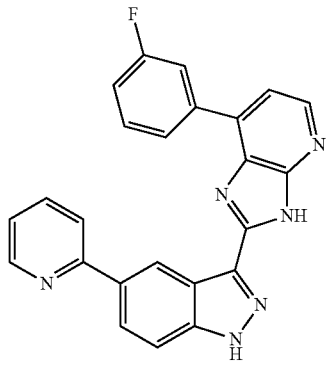
1888



7-(3-Fluorophenyl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1888

[1032] Cream colored solid (70.0 mg, 0.16 mmol). ESIMS found for $C_{24}H_{15}FN_6$ m/z 407.2 (M+1).

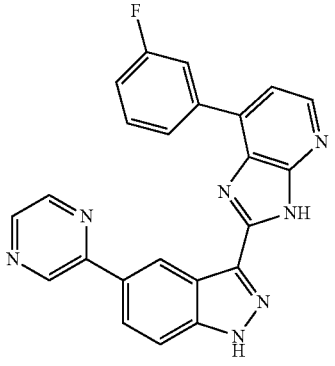
1889



7-(3-Fluorophenyl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1889

[1033] Cream colored solid (10 mg, 0.023 mmol, 26.6% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 7.40 (br dd, J=7.00, 4.53 Hz, 2H), 7.63-7.73 (m, 2H), 7.79 (d, J=8.51 Hz, 1H), 7.94 (td, J=7.75, 1.78 Hz, 1H), 8.08 (d, J=7.96 Hz, 1H), 8.26-8.32 (m, 1H), 8.34 (br d, J=7.96 Hz, 1H), 8.42 (br d, J=4.94 Hz, 1H), 8.70 (br d, J=10.70 Hz, 1H), 8.74 (br d, J=4.12 Hz, 1H), 9.40 (s, 1H), 13.90 (br s, 2H); ESIMS found for $C_{24}H_{15}FN_6$ m/z 407.1 (M+1).

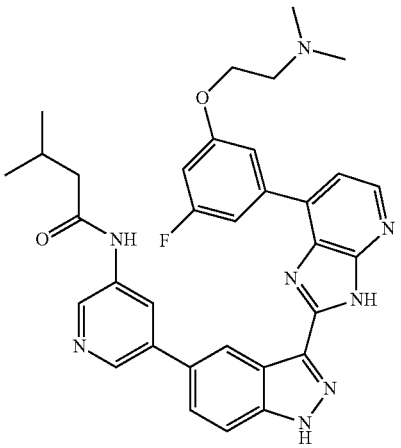
1890



7-(3-Fluorophenyl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine 1890

[1034] Brick red colored solid (5 mg, 0.012 mmol, 4.59% yield). ^{1}H NMR (DMSO-do, 500 MHz) δ ppm 7.36-7.45 (m, 1H), 7.63-7.75 (m, 2H), 7.84 (d, J=8.78 Hz, 1H), 8.31 (dd, J=8.78, 1.65 Hz, 1H), 8.37 (br d, J=6.86 Hz, 1H), 8.43 (d, J=4.94 Hz, 1H), 8.61-8.69 (m, 2H), 8.75-8.81 (m, 1H), 9.35 (d, J=1.37 Hz, 1H), 9.46 (s, 1H); ESIMS found for $C_{23}H_{14}FN_7$ m/z 408.1 (M+1).

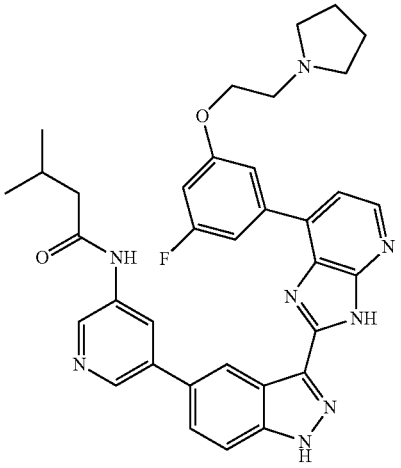
2198



N-(5-(3-(7-(3-(2-(Dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide 2198

[1035] Brown solid (13.7 mg, 0.023 mmol, 17.4% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.96 (d, J=6.59 Hz, 6H), 2.04-2.17 (m, 7H), 2.26 (d, J=7.14 Hz, 2H), 2.42 (t, J=5.63 Hz, 2H), 4.09 (t, J=5.76 Hz, 2H), 6.92 (br d, J=10.43 Hz, 1H), 7.70 (d, J=4.94 Hz, 1H), 7.75-7.80 (m, 1H), 7.83-7.88 (m, 1H), 7.98-8.05 (m, 2H), 8.36-8.44 (m, 2H), 8.64 (d, J=1.92 Hz, 1H), 8.81 (d, J=2.20 Hz, 1H), 8.83 (s, 1H), 10.20 (s, 1H), 13.94 (br s, 2H); ESIMS found for $C_{33}H_{33}FN_8O_2$ m/z 593.3 (M+1).

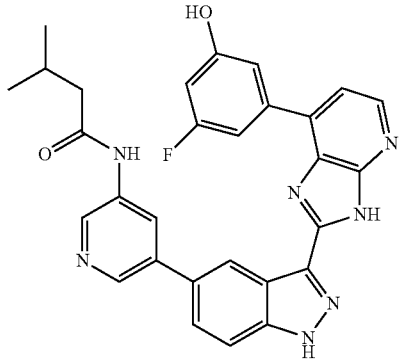
2242



N-(5-(3-(7-(3-Fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide 2242

[1036] Orange solid (9.3 mg, 0.015 mmol, 23.48% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.96 (d, J=6.59 Hz, 6H), 1.62 (br s, 4H), 2.10 (tt, J=13.45, 6.72 Hz, 1H), 2.26 (d, J=7.14 Hz, 2H), 2.44 (br s, 4H), 2.63 (br s, 1H), 4.13 (br s, 2H), 6.93 (br d, J=10.70 Hz, 1H), 7.70 (d, J=5.21 Hz, 1H), 7.76-7.81 (m, 1H), 7.82-7.87 (m, 1H), 8.01 (br d, J=9.88 Hz, 1H), 8.04 (s, 1H), 8.37-8.44 (m, 2H), 8.64 (d, J=1.92 Hz, 1H), 8.81 (d, J=1.92 Hz, 1H), 8.83 (s, 1H), 10.20 (s, 1H), 13.92 (br s, 1H), 13.94 (br s, 1H); ESIMS found for $C_{35}H_{35}FN_8O_2$ m/z 619.3 (M+1).

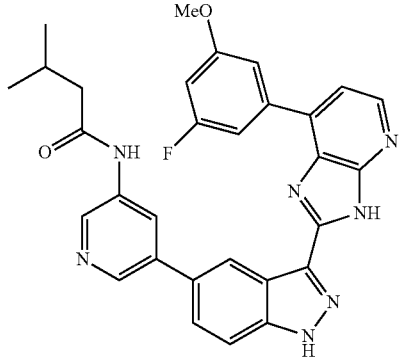
2286



N-(5-(3-(7-(3-Fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide 2286

[1037] Yellow solid (8.8 mg, 0.017 mmol, 18.25% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.97 (d, J=6.59 Hz, 6H), 2.12 (dquin, J=13.55, 6.84, 6.84, 6.84, 6.84 Hz, 1H), 2.27 (d, J=7.14 Hz, 2H), 6.68 (dt, J=10.57, 1.99 Hz, 1H), 7.57 (d, J=5.21 Hz, 1H), 7.71 (s, 1H), 7.76-7.88 (m, 2H), 7.99 (br d, J=10.43 Hz, 1H), 8.36-8.42 (m, 2H), 8.70 (d, J=1.92 Hz, 1H), 8.81 (d, J=1.92 Hz, 1H), 8.88 (s, 1H), 10.10 (s, 1H), 10.15 (s, 1H), 13.88 (s, 1H), 13.93 (s, 1H); ESIMS found for $C_{29}H_{24}FN_7O_2$ m/z 522.3 (M+1).

2330

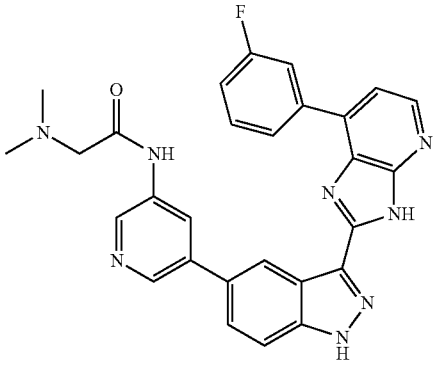


N-(5-(3-(7-(3-Fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide 2330

[1038] Yellow solid (2.5 mg, 4.67 μmol, 3.62% yield). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 0.96 (d, J=6.59 Hz, 6H), 2.06-2.17 (m, 1H), 2.27 (d, J=7.14 Hz, 2H), 3.81 (s, 3H), 6.92 (br d, J=10.70 Hz, 1H), 7.65 (br s, 1H), 7.73-7.78 (m,

1H), 7.81-7.86 (m, 1H), 7.99 (br s, 1H), 8.13 (br s, 1H), 8.38 (br d, J=4.94 Hz, 1H), 8.40 (s, 1H), 8.66 (d, J=1.92 Hz, 1H), 8.81 (d, J=2.20 Hz, 1H), 8.86 (s, 1H), 10.21 (s, 1H), 13.87 (brs, 1H); ESIMS found for $C_{30}H_{26}FN_7O_2$ m/z 536.2 (M+1).

2373



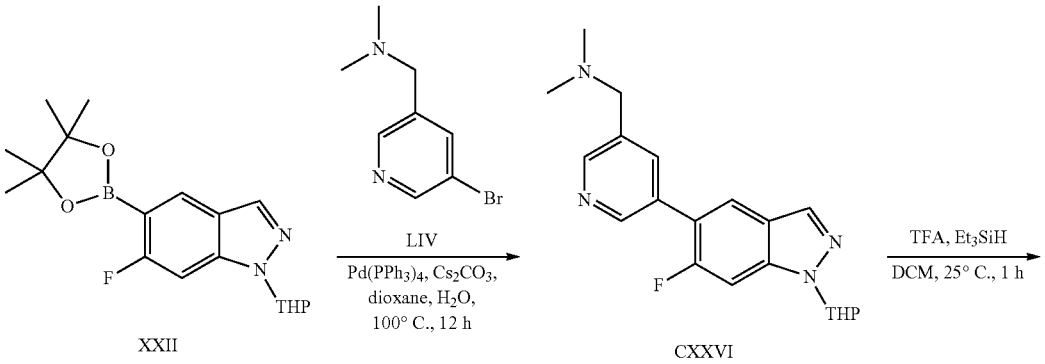
2-(Dimethylamino)-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide 2373

[1039] Yellow solid (4.4 mg, 0.009 mmol). ^{1}H NMR (DMSO-d_6, 500 MHz) δ ppm 2.33 (s, 6H) 3.16 (s, 2H) 7.32 (td, J=8.44, 2.33 Hz, 1H) 7.59-7.65 (m, 1H) 7.67 (br s, 1H) 7.79-7.87 (m, 2H) 8.37 (br s, 1H) 8.41 (br d, J=4.94 Hz, 1H) 8.54 (t, J=2.20 Hz, 1H) 8.55-8.59 (m, 1H) 8.70 (d, J=2.20 Hz, 1H) 8.90 (d, J=1.92 Hz, 2H) 10.08 (s, 1H) 13.91 (br s, 1H); ESIMS found for $C_{28}H_{23}FN_8O$ m/z 507.2 (M+1).

Example 2

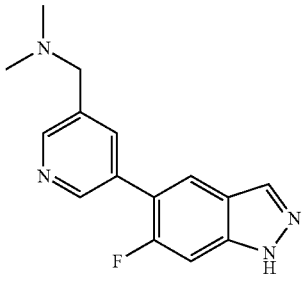
[1040] Preparation of intermediate 5-(5-((dimethylamino) methyl)pyridin-3-yl)-6-fluoro-1H-indazole-3-carbaldehyde (CXXX) is depicted below in Scheme 26.

Scheme 26



XXII

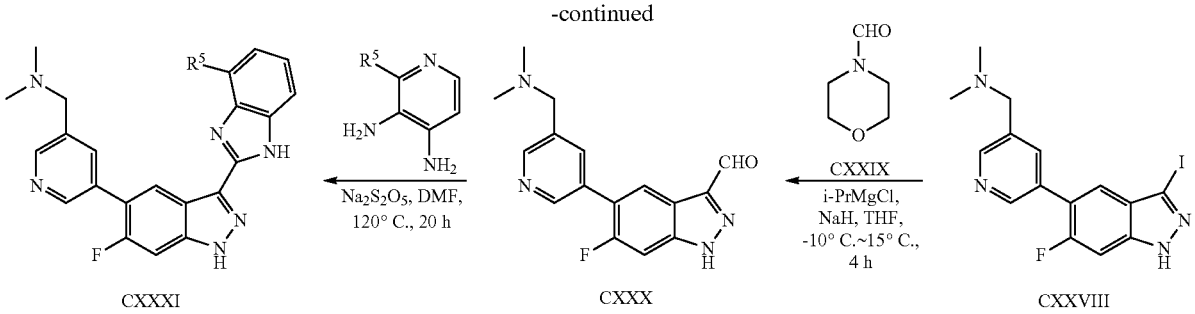
CXXVI



CXXVII

KOH, I_2
DMF, 25° C.
12 h

-continued



Step 1

[1041] A solution of 6-fluoro-1-(tetrahydro-2H-pyran-2-yl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indazole (XXII) (19.5 g, 56.3 mmol, 1.0 eq) in DME (215 mL) was added 1-(5-bromopyridin-3-yl)-N,N-dimethylmethanamine (LIV) (11.5 g, 53.5 mmol, 1.0 eq), $Pd(PPh_3)_4$ (1.95 g, 1.69 mmol, 0.03 eq), aq. Na_2CO_3 (2 M, 56 mL, 2.00 eq). The mixture was stirred at 100° C. for 12 h under N_2. TLC (DCM:MeOH=10:1, Rf=0.9) showed (XXII) was consumed completely. The solvent was concentrated under reduce pressure. The residue was dissolved in water (500 ml) and the aqueous phase was extracted with EtOAc (200 ml). The organic layer was washed with brine (100 mL), dried over anhydrous Na_2SO_4 and filtered. The filtrate was concentrated to give crude product which was purified by silica gel column (DCM:MeOH=30:1) to give 1-(5-(6-fluoro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N, N-dimethylmethanamine (CXXVI) as a brown oil (18 g, 50.8 mmol, 94.9% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 1.85-1.74 (m, 3H), 2.32-2.15 (m, 2H), 2.32 (s, 6H), 2.60-2.51 (m, 1H), 3.55 (s, 2H), 3.81-3.76 (m, 1H), 4.06 (d, J=11.8 Hz, 1H), 5.71 (d, J=8.8 Hz, 1H), 7.42 (d, J=11.8 Hz, 1H), 7.80 (s, 1H), 7.89 (s, 1H), 8.07 (s, 1H), 8.54 (s, 1H), 8.71 (s, 1H); ESIMS found $C_{20}H_{23}FN_4O$ m/z 355.1 (M+1).

Step 2

[1042] To a solution of 1-(5-(6-fluoro-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine (CXXVI) (18 g, 50.8 mmol, 1.0 eq) in DCM (50 mL) was added Et_3SiH (13.2 g, 113 mmol, 2.5 eq) and TFA (51 g, 454 mmol, 10 eq). The mixture was stirred at 25° C. for 12 h. LC/MS showed (CXXVI) was consumed. The reaction mixture was concentrated in vacuo. The residue was diluted with TBME (200 mL). The mixture was stirred for 0.5 h at −65° C., 1 h at 25° C. The precipitate was filtered and the solid was concentrated in vacuo. The residue was dissolve in MeOH (200 mL), weakly basic resin was added. The mixture was stirred for 0.5 h, pH=7. The solid was filtered and dried in vacuo to give 1-(5-(6-fluoro-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine (CXXVII) as white solid (12.0 g, 44.4 mmol, 88.3% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 2.96 (s, 6H), 4.52 (s, 2H), 7.42 (d, J=11.2 Hz, 1H), 8.02 (d, J=7.2 Hz, 1H), 8.16 (s, 1H), 8.27 (s, 1H), 8.73 (s, 1H), 8.89 (s, 1H); ESIMS found $C_{15}H_{15}FN_4$ m/z 271.1 (M+1).

Step 3

[1043] To a solution of 1-(5-(6-fluoro-1H-indazol-5-yl) pyridin-3-yl)-N,N-dimethylmethanamine (CXXVII) (12.0 g, 44.4 mmol, 1.0 eq) in DMF (70 mL) was added KOH (7.4 g, 133.2 mmol, 3.0 eq) and I_2 (16.9 g, 66.6 mmol, 1.5 eq) at 25° C. The reaction mixture was stirred at 25° C. for 1 h. LC/MS showed (CXXVII) was consumed. The reaction mixture was quenched with 10% aqueous Na_2SO_3 (100 mL) and diluted with water (300 mL) and EtOAc (200 mL). The precipitated solid was filtered, dried to afford product. The solution was separated, and the organic layer was washed with water (100 mL) and sat NaCl (100 mL), then dried over anhydrous Na_2SO_4 and concentrated to afford 1-(5-(6-fluoro-3-iodo-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine (CXXVIII) as a yellow solid (10.0 g, 25.2 mmol, 56.8% yield). ^1H NMR ($CDCl_3$, 400 MHz) δ ppm 2.31 (s, 6H), 4.02 (d, J=7.2 Hz, 2H), 7.59-7.55 (m, 2H), 7.92 (s, 1H), 8.53 (s, 1H), 8.69 (s, 1H), 13.71 (br, 1H); ESIMS found $C_{15}H_{14}FIN_4$ m/z 397.1 (M+1).

Step 4

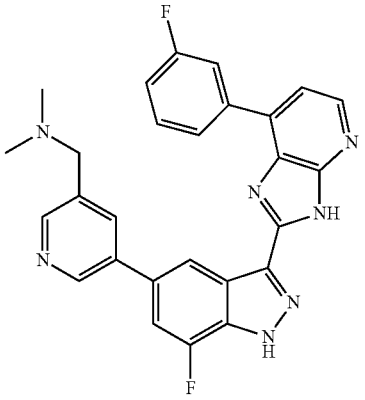
[1044] To a solution of 1-(5-(6-fluoro-3-iodo-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine (CXXVIII) (1.50 g, 3.79 mmol, 1.00 eq) in THF (20 mL) was added NaH (181 mg, 4.55 mmol, 1.20 eq) portion-wise at 0° C. The reaction mixture was stirred at 20° C. for 10 min then cooled to −10° C. and i-PrMgCl (2 M, 11.37 mL, 6.00 eq) was added. The reaction mixture was stirred at −10° C. for 1 h then morpholine-4-carbaldehyde (CXXIX) (3.49 g, 30.32 mmol, 8.00 eq) was slowly added. The mixture was stirred at −10° C. for 20 min then at 20° C. for 3 h. TLC (DCM:MeOH=5/1, R_f=0.55) show the reaction is complete. The reaction mixture was quenched with water (3 mL). The mixture was acidified with HCl (1N, 20 mL) to pH=7 and then concentrated to give crude product, which was further purified by silica gel on column chromatography (DCM/MeOH=50:1→3:1) to give 5-(5-((dimethylamino)methyl) pyridin-3-yl)-6-fluoro-1H-indazole-3-carbaldehyde (CXXXX) (2.9 g, 50% TLC purity) as yellow solid. The crude product was used for step 5 without further purification. ESIMS found $C_{16}H_{15}FN_4O$ m/z 299.1 (M+1).

Step 5

[1045] Preparation of the following compounds were performed following the procedure listed in Scheme 25, Step 2.

[1046] The following compounds were prepared in accordance with the procedure described in the above Example 2.

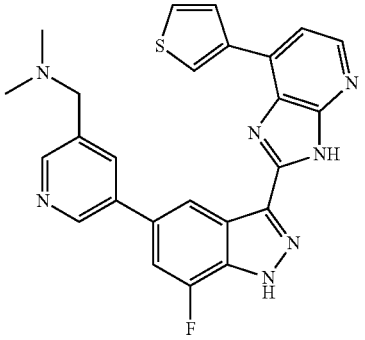
481



1-(5-(7-fluoro-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 481

[1047] White solid (10.1 mg, 0.02 mmol). ESIMS found for $C_{27}H_{21}F_2N_7$ m/z 482.2 (M+1).

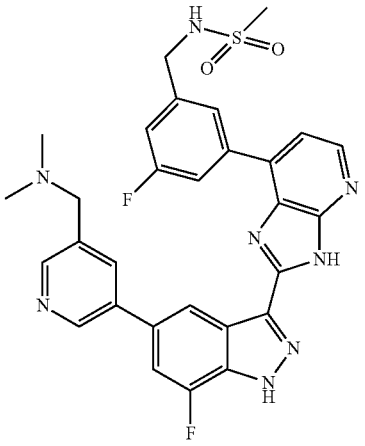
741



1-(5-(7-Fluoro-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 741

[1048] White solid (29.6 mg, 0.06 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.81 (br s, 6H), 4.60 (br s, 2H), 7.78 (br s, 3H), 8.10 (br s, 1H), 8.44 (br s, 1H), 8.73 (br d, J=7.03 Hz, 1H), 8.88 (br d, J=5.27 Hz, 2H), 9.14 (br s, 1H), 9.19 (br s, 1H), 11.78 (br s, 1H), 14.55 (br s, 1H); ESIMS found for $C_{25}H_{20}FN_7S$ m/z 470.1 (M+1).

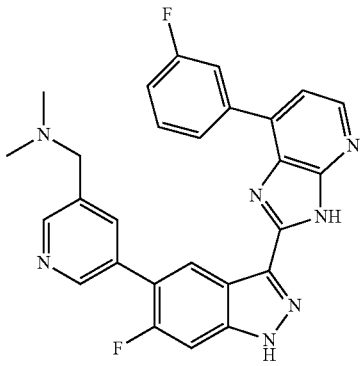
897



N-(3-(2-(5-(5-((Dimethylamino)methyl)pyridin-3-yl)-7-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide 897

[1049] White solid (49.7 mg, 0.08 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.79 (br s, 6H), 2.92 (s, 3H), 4.30 (br s, 2H), 4.60 (br s, 2H), 7.38 (br d, J=9.54 Hz, 1H), 7.72 (d, J=5.52 Hz, 1H), 7.78 (d, J=10.79 Hz, 1H), 7.84 (br s, 1H), 8.00 (br s, 1H), 8.07 (br d, J=8.03 Hz, 1H), 8.54 (br d, J=5.27 Hz, 1H), 8.70 (d, J=7.28 Hz, 1H), 8.85 (s, 1H), 9.14 (br s, 1H), 9.19 (br s, 1H), 11.64 (br s, 1H), 14.61 (br s, 1H); ESIMS found for $C_{29}H_{26}F_2N_8O_2S$ m/z 589.2 (M+1).

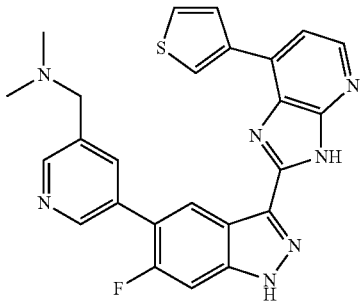
949



1-(5-(6-Fluoro-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 949

[1050] White solid (11.9 mg, 0.02 mmol). ESIMS found for $C_{27}H_{21}F_2N_7$ m/z 482.1 (M+1).

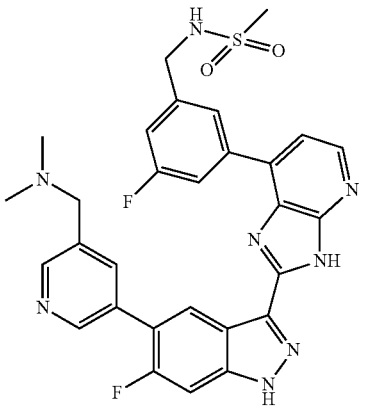
1209



1-(5-(6-Fluoro-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 1209

[1051] White solid (3.6 mg, 0.008 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.81 (br s, 6H), 4.49 (br s, 2H), 7.91 (d, J=7.03 Hz, 1H), 7.97 (br d, J=12.05 Hz, 1H), 8.04 (d, J=7.03 Hz, 1H), 8.45 (d, J=5.52 Hz, 1H), 8.59 (d, J=5.27 Hz, 1H), 8.77 (br s, 1H), 8.86 (br d, J=6.78 Hz, 2H), 9.12 (br s, 1H), 9.32 (s, 1H), 11.41 (br s, 1H), 14.83 (s, 1H); ESIMS found for $C_{25}H_{20}FN_7S$ m/z 470.1 (M+1).

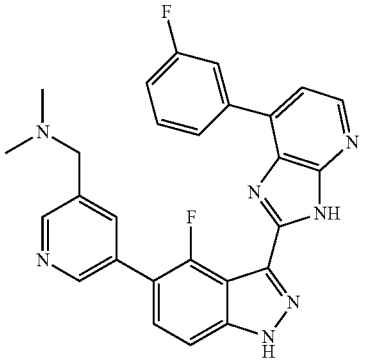
1365



N-(3-(2-(5-(5-((Dimethylamino)methyl)pyridin-3-yl)-6-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide 1365

[1052] White solid (10.2 mg, 0.02 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.80 (br d, J=2.51 Hz, 6H), 2.92 (s, 3H), 4.33 (br s, 2H), 4.57 (br s, 2H), 7.38 (br d, J=9.54 Hz, 1H), 7.71 (d, J=5.52 Hz, 1H), 7.83 (br s, 1H), 7.99 (br d, J=12.05 Hz, 1H), 8.06 (br s, 1H), 8.25 (br d, J=7.53 Hz, 1H), 8.53 (br d, J=5.52 Hz, 1H), 8.73 (s, 1H), 9.01 (br s, 1H), 9.04 (br s, 1H), 9.31 (s, 1H), 11.69 (br s, 1H), 14.84 (br s, 1H); ESIMS found for $C_{29}H_{26}F_2N_8O_2S$ m/z 589.3 (M+1).

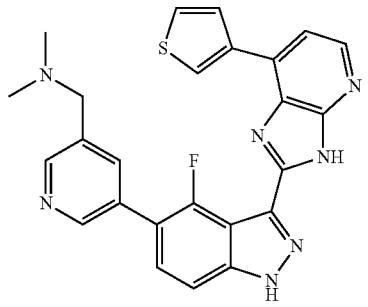
1417



1-(5-(4-Fluoro-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 1417

[1053] White solid (11.1 mg, 0.2 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.79 (br s, 6H), 4.55 (br s, 2H), 7.32-7.41 (m, 1H), 7.59-7.68 (m, 1H), 7.71-7.78 (m, 2H), 7.84-7.92 (m, 1H), 8.14 (br d, J=7.03 Hz, 1H), 8.33 (br d, J=8.53 Hz, 1H), 8.52 (br d, J=5.02 Hz, 1H), 8.84 (br s, 1H), 9.03 (br s, 1H), 9.16 (br s, 1H), 11.76 (br s, 1H), 14.76 (br s, 1H); ESIMS found for $C_{27}H_{21}F_2N_7$ m/z 482.1 (M+1).

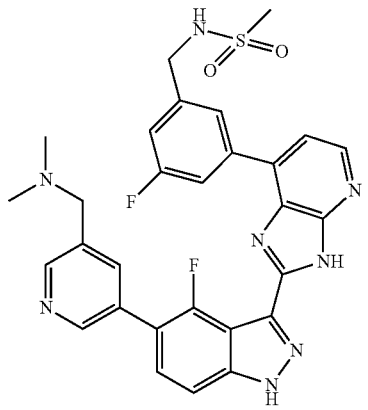
1677



1-(5-(4-Fluoro-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine 1677

[1054] White solid (14.4 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.80 (br s, 6H), 4.58 (br s, 2H), 7.74 (br d, J=8.78 Hz, 1H), 7.78-7.85 (m, 3H), 7.86-7.92 (m, 2H), 8.17 (br d, J=4.77 Hz, 1H), 8.47 (br d, J=5.27 Hz, 1H), 8.92 (br s, 1H), 8.94 (br s, 1H), 9.06 (s, 1H), 9.19 (s, 1H), 11.83 (br s, 1H), 14.83 (br s, 1H); ESIMS found for $C_{25}H_{20}FN_7S$ m/z 470.0 (M+1).

1833



N-(3-(2-(5-(5-((Dimethylamino)methyl)pyridin-3-yl)-4-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide 1833

[1055] White solid (14.9 mg, 0.03 mmol). ^{1}H NMR (DMSO-d_6, 400 MHz) δ ppm 2.77 (br d, J=3.31 Hz, 6H), 2.91 (s, 3H), 4.31 (d, J=2.84 Hz, 2H), 4.49 (br d, J=3.31 Hz, 2H), 7.34 (br d, J=8.82 Hz, 1H), 7.68-7.79 (m, 3H), 7.81-7.88 (m, 1H), 8.22 (br s, 1H), 8.36 (d, J=7.72 Hz, 1H), 8.50 (br d, J=4.85 Hz, 1H), 8.65 (br s, 1H), 8.92 (s, 1H), 9.11 (br s, 1H), 11.42 (br s, 1H), 14.55 (br s, 1H); ESIMS found for $C_{29}H_{26}F_2N_8O_2S$ m/z 589.1 (M+1).

Example 3

[1056] The screening assay for Wnt activity is described as follows. Reporter cell lines can be generated by stably transducing cancer cell lines (e.g., colon cancer) or primary

cells (e.g., IEC-6 intestinal cells) with a lentiviral construct that includes a Wnt-responsive promoter driving expression of the firefly luciferase gene.

[1057] SW480 colon carcinoma cells were transduced with a lentiviral vector expressing luciferase with a human Sp5 promoter consisting of a sequence of eight TCF/LEF binding sites. SW480 cells stably expressing the Sp5-Luc reporter gene and a hygromycin resistance gene were selected by treatment with 150 μg/ml of hygromycin for 7 days. These stably transduced SW480 cells were expanded in cell culture and used for all further screening activities. For Sp5-Luc reporter gene assays, the cells were plated at 10,000 cells/well in 96-well plates with growth medium containing 10% fetal calf serum and incubated overnight at 37° C. and 5% CO_2. Each compound was dissolved in DMSO as a 10 mM stock in standard j-vials and used to prepare compound source plates in dose-response format with 3-fold serial dilutions and a 10 mM top concentration. Compound transfer from serially diluted source plates to assay plates containing the cells was accomplished using a pintool (Multimek 96, Beckman equipped with V&P Scientific FP1S50H pins) based liquid handling protocol. This protocol used a slotted pin to transfer 50 nl of compound from a source plate well to an assay plate well containing 50 μl of cells in growth medium. The 1000-fold dilution resulted in a final DMSO concentration of 0.1% on the cells in each well. Control wells received 50 nl of DMSO treatment for normalization and calculating IC_{50} values. The treated cells were incubated at 37° C. and 5% CO_2 for an additional forty-two hours. Following incubation, the growth medium was removed and 50 μl of BrightGlo luminescence reagent (Promega) was added to each well of the 96-well assay plates. The plates were placed on an orbital shaker for 5 min and then luminescence was quantified on the Victor3 (Perkin Elmer) plate reader. Readings were normalized to DMSO only treated cells, and normalized activities were utilized for IC_{50} calculations using the dose-response log (inhibitor) vs. response-variable slope (four parameters) nonlinear regression feature available in GraphPad Prism 5.0 or 6.0. Table 2 shows the measured activity for selected compounds of Formula I as described herein.

TABLE 2

Compound	IC_{50} (μM)
1	<0.001
2	0.002
7	<0.001
9	0.003
13	0.116
19	0.001
21	0.0091
25	<0.001
28	0.004
34	0.019
40	4.025
46	0.002
52	0.0256
55	0.0018
59	0.0319
61	0.006
68	0.052
71	0.0111
73	0.013
81	0.0058
82	0.0035
87	0.0068

TABLE 2-continued

Compound	IC_{50} (μM)
90	0.012
93	>10
101	>10
109	0.0137
114	0.054
121	0.035
126	0.0307
136	1.546
141	0.0137
148	0.0081
150	0.015
154	1.462
157	0.015
163	0.122
169	1.448
175	0.0993
181	2.580
184	0.0023
190	0.0074
202	0.0047
211	0.0663
217	0.1734
223	3.072
229	0.2842
234	0.7948
238	0.0288
239	4.100
244	0.3518
247	0.077
250	0.124
256	0.0663
265	0.0094
268	0.0065
269	0.0051
270	0.0163
271	0.0084
277	0.001
279	0.0052
281	0.0098
283	0.1366
292	0.04767
295	0.0051
298	0.005
304	0.006
306	0.0067
310	1.274
313	0.002
319	0.0628
320	0.0088
321	0.0411
325	0.932
331	0.0347
333	0.0063
337	0.015
340	0.0049
346	0.0004
352	0.0132
358	0.0069
367	0.0043
372	0.0006
373	0.0064
379	0.076
385	0.0192
421	0.0061
427	0.0192
433	0.003
439	0.3537
442	0.0058
448	0.203
454	0.0517
460	0.0116
466	0.4419
481	0.155
741	0.9355
897	0.074

TABLE 2-continued

Compound	IC_{50} (μM)
949	>10
1209	>10
1365	0.804
1417	0.923
1677	0.673
1833	0.773
1873	3.271
1874	>1.0
1875	0.005
1876	0.061
1877	>10
1878	0.215
1879	>10
1880	1.194
1881	0.065
1882	4.135
1883	0.753
1884	>10
1885	0.011
1886	>10
1887	>10
1888	>10
1889	>1.0
1890	0.039
2198	0.180
2242	0.440
2286	0.055
2330	0.020
2373	0.091

Example 4

[1058] The above synthesized compounds were screened using primary human mesenchymal stem cells (hMSCs) to determine their ability to induce chondrogenesis (process by which cartilage is developed).

[1059] Human Mesenchymal Stem Cell Culture:

[1060] Primary human mesenchymal stem cells (hMSCs) were purchased from Lonza (Walkersville, Md.) and expanded in Mesenchymal Stem Cell Growth Media (Lonza). Cells between passage 3 and 6 were used for the experiments.

[1061] Compound Screening:

[1062] Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:3, 6-point dose-response curves from 2700 nM to 10 nM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, Calif.) into 96-well clear bottom assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.03%. hMSCs were plated at 20,000 cells/well in 250 μL/well Incomplete Chondrogenic Induction Medium (Lonza; DMEM, dexamethasone, ascorbate, insulin-transferrin-selenium [ITS supplement], gentamycin-amphotericin [GA-1000], sodium pyruvate, proline and L-glutamine). TGF-β3 (10 ng/mL) was used as a positive control for differentiation while negative control wells were treated with 75 nL DMSO for normalization and calculating EC_{50} values. Cells were incubated at 37° C. and 5% CO_2 for 6 days. To image chondrogenic nodules, the cells were fixed using 4% formaldehyde (Electron Microscopy Sciences), and stained with 2 μg/mL Rhodamine B (Sigma-Aldrich) and 20 μM Nile Red (Sigma-Aldrich) [Johnson K., et. al, A Stem Cell-Based Approach to Cartilage Repair, *Science*, (2012), 336(6082), 717-721]. The nodules imaged (4 images per well at 4× magnification) by excitation at 531 nm and emission at 625 nm and quantified using the CellInsight CX5 (Thermo Scientific). Number of nodules in each well was normalized to the average of 3 DMSO treated wells on the same plate using Excel (Microsoft Inc.). The normalized averages (fold change over DMSO) of 3 replicate wells for each compound concentration were calculated. Due to solubility limitations of some of the compounds, curve fitting was incomplete leading to inaccurate EC_{50} determinations.

[1063] Using TGF-β3 as a positive control, the concentration of test compounds required to induce equivalent levels of chondrogenesis is reported. In addition, the maximum activity of each compound and the respective dose that each compound reached maximum chondrogenesis activity is reported. Table 3 shows the activity of selected compounds as provided herein.

TABLE 3

Compound	Conc (nM) of Max. activity	Max. Activity as % TGF-β3 activity	Conc (nM) of 100% TGF-β3 activity
2	30	N/A	61.0
7	100	30	83.7
25	30	10	85.8
55	30	30	112.8
82	10	10	68.7
109	30	10	149.7
148	100	30	89.3
184	300	N/A	60.1
277	30	30	72.6
298	30	30	84.2
346	300	30	120.1
373	30	30	70.3
433	2700	2700	117.4
460	30	N/A	29.6
1875	2700	2700	174.4
1885	100	N/A	52.2

Example 5

[1064] The above synthesized compounds were screened using primary human fibroblasts (derived from IPF patients) treated with TGF-β1 to determine their ability to inhibit the fibrotic process.

[1065] Human Fibroblast Cell Culture:

[1066] Primary human fibroblasts derived from IPF patients (LL29 cells) [[1]Xiaoqiu Liu, et. al., "Fibrotic Lung Fibroblasts Show Blunted Inhibition by cAMP Due to Deficient cAMP Response Element-Binding Protein Phosphorylation", *Journal of Pharmacology and Experimental Therapeutics* (2005), 315(2), 678-687; [2]Watts, K. L., et. al., "RhoA signaling modulates cyclin D1 expression in human lung fibroblasts; implications for idiopathic pulmonary fibrosis", *Respiratory Research* (2006), 7(1), 88] were obtained from American Type Culture Collection (ATCC) and expanded in F12 medium supplemented with 15% Fetal Bovine Serum and Penicillin/Streptomycin.

[1067] Compound Screening:

[1068] Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:2, 11-point dose-response curves from 10 M to 1.87 nM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, Calif.) into 384-well clear bottom assay plates (Greiner Bio-One) with appropriate DMSO backfill for a final DMSO concentration of 0.1%.

LL29 cells were plated at 1,500 cells/well in 80 μl/well F12 medium supplemented with 1% Fetal Bovine Serum. One hour after addition of the cells, TGF-β1 (Peprotech; 20 ng/mL) was added to the plates to induce fibrosis (ref. 1 and 2 above). Wells treated with TGF-β1 and containing DMSO were used as controls. Cells were incubated at 37° C. and 5% CO_2 for 4 days. Following incubation for 4 days, SYTOX green nucleic acid stain (Life Technologies [Thermo Fisher Scientific]) was added to the wells at a final concentration of 1 uM and incubated at room temperature for 30 min. Cells were then fixed using 4% formaldehyde (Electron Microscopy Sciences), washed 3 times with PBS followed by blocking and permeabilization using 3% Bovine Serum Albumin (BSA; Sigma) and 0.3% Triton X-100 (Sigma) in PBS. Cells were then stained with antibody specific to α-smooth muscle actin (αSMA; Abcam) (ref. 1 and 2 above) in 3% Bovine Serum Albumin (BSA; Sigma) and 0.3% Triton X-100 (Sigma) in PBS, and incubated overnight at 4° C. Cells were then washed 3 times with PBS, followed by incubation with Alexa Flor-647 conjugated secondary antibody (Life Technologies [Thermo Fisher Scientific]) and DAPI at room temperature for 1 hour. Cells were then washed 3 times with PBS and plates were sealed for imaging. αSMA staining was imaged by excitation at 630 nm and emission at 665 nm and quantified using the Compartmental Analysis program on the CellInsight CX5 (Thermo Scientific). Dead or apoptotic cells were excluded from analysis based on positive SYTOX green staining. % of total cells positive for αSMA were counted in each well and normalized to the average of 11 wells treated with TGF-β1 on the same plate using Dotmatics' Studies Software. The normalized averages (fold change over untreated) of 3 replicate wells for each compound concentration were used to create dose-responses curves and EC_{50} values were calculated using non-linear regression curve fit in the Dotmatics' Studies Software. The EC_{50} values are reported.

[1069] Table 4 shows the activity of selected compounds as provided herein.

TABLE 4

Compound	Inhibition of fibrosis EC_{50} (nM)
1	0.015
2	0.041
7	0.066
9	9.990
13	1.147
19	0.043
21	0.027
25	0.099
34	0.334
40	0.009
46	0.080
52	1.246
55	0.017
59	0.009
61	0.009
71	9.990
73	0.379
81	0.009
82	0.303
90	0.078
93	0.016
101	0.235
109	0.781
136	1.772

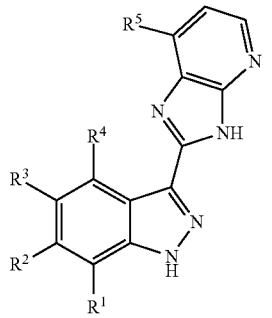
TABLE 4-continued

Compound	Inhibition of fibrosis EC_{50} (nM)
141	9.990
148	0.085
150	0.133
154	9.990
157	0.605
163	0.009
169	0.396
175	9.990
181	0.009
184	0.142
190	0.009
202	0.018
217	2.826
223	0.009
229	1.075
234	0.434
238	0.013
239	0.171
247	0.184
250	2.596
256	0.401
265	0.131
269	9.990
270	0.010
271	0.068
277	0.016
279	0.306
281	0.359
283	0.605
292	0.009
295	0.405
298	0.102
304	0.079
306	0.527
310	9.990
313	0.027
320	0.016
325	0.040
331	0.155
333	0.009
337	1.312
346	0.009
352	0.125
367	0.314
372	0.009
373	0.045
379	0.405
385	0.084
421	0.045
433	>10
439	0.009
448	0.701
454	0.019
460	0.111
466	1.110
1873	0.037
1874	0.317
1875	0.009
1876	9.990
1877	9.990
1878	9.990
1879	9.990
1880	0.417
1881	0.071
1883	0.095
1884	9.990
1885	0.009
1887	9.990
1888	9.990
1889	0.018
1890	0.167
2373	0.233

This listing of claims replaces all prior versions and listings of claims in the application:

1. (canceled)

2. A method of treating a bone or cartilage disease selected from the group consisting of osteoarthritis, bone spur (osteophytes), craniosynostosis, fibrodysplasia ossificans progressive, fibrous dysplasia, giant cell tumor of bone, hip labral tear, meniscal tears, bone/osteoporotic fractures, articular cartilage (chondral) defects, degenerative disc disease, osteochondritis dissecans, osteochondroma, osteopetrosis, relapsing polychondritis, and Salter-Harris fractures in a subject, the method comprising administering to the subject a therapeutically effective amount of a compound of Formula I, or a pharmaceutically acceptable salt thereof:



I

wherein:

R^1, R^2, and R^4 are independently selected from the group consisting of H and halide;

R^3 is selected from the group consisting of -heteroaryl$(R^6)_q$ and -heterocyclyl$(R^7)_h$;

R^5 is selected from the group consisting of H, -heteroaryl$(R^8)_q$, -heterocyclyl$(R^9)_h$, and -aryl$(R^{10})_k$;

each R^6 is one substituent attached to the heteroaryl and is independently selected from the group consisting of halide, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl$(R^{11})_h$, —(C_{1-4} alkylene)$_p$carbocyclyl$(R^{12})_j$, —(C_{1-4} alkylene)$_p$aryl$(R^{13})_k$, —$NHC(=O)R^{14}$, —$NR^{15}R^{16}$, —(C_{1-6} alkylene)$NR^{17}R^{18}$, and —OR^{24};

each R^7 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^8 is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-6} alkyl), halide, —CF_3, —OCH_3, —CN, and —$C(=O)R^{19}$;

each R^9 is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-6} alkyl), halide, —CF_3, —CN, and —OCH_3;

each R^{10} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-6} alkyl), halide, —CF_3, —CN, —OCH_3, —(C_{1-6} alkylene)$_p$$NHSO_2R^{19}$, —$NR^5$($C_{1-6}$ alkylene)$NR^{15}R^{16}$, —(C_{1-6} alkylene)$_p$$NR^{15}R^{16}$, and —$OR^{27}$;

each R^{11} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of amino, —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{12} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{13} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{14} is independently selected from the group consisting of —(C_{1-9} alkyl), -heteroaryl$(R^{20})_q$, -aryl$(R^{21})_k$, —CH_2aryl$(R^{21})_k$, -carbocyclyl$(R^{22})_j$, —CH_2carbocyclyl$(R^{22})_j$, —(C_{1-4} alkylene)$_p$$NR^{25}R^{26}$, -heterocyclyl$(R^{23})_h$, and —$CH_2$heterocyclyl$(R^{23})_h$;

each R^{15} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

each R^{16} is independently selected from the group consisting of H, —(C_{1-6} alkyl), —CH_2aryl$(R^{21})_k$, and —CH_2carbocyclyl$(R^{22})_j$;

each R^{17} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

each R^{18} is independently selected from the group consisting of H, —(C_{1-6} alkyl), —CH_2aryl$(R^{21})_k$, and —CH_2carbocyclyl$(R^{22})_j$;

each R^{19} is a —(C_{1-6} alkyl);

each R^{20} is one substituent attached to the heteroaryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{21} is one substituent attached to the aryl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{22} is one substituent attached to the carbocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

each R^{23} is one substituent attached to the heterocyclyl and is independently selected from the group consisting of —(C_{1-4} alkyl), halide, —CF_3, and —CN;

R^{24} is selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl$(R^{23})_h$, —(C_{1-4} alkylene)$_p$carbocyclyl(R^{22}), —(C_{1-4} alkylene)$_p$aryl$(R^{21})_k$, and —(C_{1-6} alkylene)$_p$$NR^{25}R^{26}$;

each R^{25} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

each R^{26} is independently selected from the group consisting of H and —(C_{1-6} alkyl);

R^{27} is selected from the group consisting of H, —(C_{1-6} alkyl), —(C_{1-4} alkylene)$_p$heterocyclyl$(R^{23})_h$, and —(C_{1-6} alkylene)$_p$$NR^{25}R^{26}$;

each p is independently 0 or 1;

each q is independently 0 to 4;

each h is independently 0 to 10;

each k is independently 0 to 5; and

each j is independently 0 to 12.

3. The method of claim **2**, wherein R^3 is -heteroaryl$(R^6)_q$.

4. The method of claim **3**, wherein R^3 is selected from the group consisting of -pyridinyl$(R^6)_q$, -pyrimidinyl$(R^6)_q$, -pyrazolyl$(R^6)_q$, and -imidazolyl$(R^6)_q$.

5. The method of claim **4**, wherein R^6 is selected from the group consisting of —(C_{1-3} alkyl), —CH_2heterocyclyl$(R^{11})_h$, —$NHC(=O)R^4$, —$NR^{15}R^{16}$, —$CH_2NR^{17}R^{18}$, and —OR^{24}.

6. The method of claim **2**, wherein R^5 is -aryl$(R^{10})_k$.

7. The method of claim **6**, wherein R^5 is -phenyl$(R^{10})_k$.

8. The method of claim **7**, wherein each R^{10} is independently selected from the group consisting of halide and is —$CH_2NHSO_2R^9$.

9. The method of claim **2**, wherein R^5 is -heteroaryl$(R^8)_q$.

10. The method of claim **9**, wherein R^5 is selected from the group consisting of -pyridinyl$(R^8)_q$, -imidazolyl$(R^8)_q$, -furanyl$(R^8)_q$, and -thiophenyl$(R^8)_q$.

11. The method of claim **10**, wherein q is 1 and R^8 is selected from the group consisting of halide, —(C_{1-3} alkyl), and —C(═O)R^{19}.

12. The method of claim **2**, wherein R^5 is -heterocyclyl $(R^9)_h$.

13. The method of claim **12**, wherein R^5 is selected from the group consisting of -piperidinyl$(R^9)_h$, -morpholinyl$(R^9)_h$, and -piperazinyl$(R^9)_h$.

14. The method of claim **13**, wherein h is 1 or 2 and each R^9 is independently selected from the group consisting of a halide and —(C_{1-3} alkyl).

15. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [1];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [2];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [3];

7-(3-fluorophenyl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [4];

7-(3-fluorophenyl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [5];

N-((5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [6];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [7];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [8];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [9];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [10];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [11];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [12];

1-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [13];

7-(3-fluorophenyl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [14];

7-(3-fluorophenyl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [15];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [16];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [17];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [18];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [19];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [20];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [21];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [22];

N-benzyl-1-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [23];

1-cyclopentyl-N-((5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [24];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine [25];

7-(3-fluorophenyl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [26];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [27];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [28];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [29];

7-(4-fluorophenyl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [30];

7-(4-fluorophenyl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [31];

N-((5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [32];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [33];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [34];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [35];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [36];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [37];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [38];

1-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [39];

7-(4-fluorophenyl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [40];

7-(4-fluorophenyl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [41];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [42];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [43];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [44];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [45];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [46];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [47];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [48];

N-benzyl-1-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [49];

1-cyclopentyl-N-((5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [50];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridine [51];

7-(4-fluorophenyl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [52];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [53];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [54];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [55];

7-(2-fluorophenyl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [56];

7-(2-fluorophenyl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [57];

N-((5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [58];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [59];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [60];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [61];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [62];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [63];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [64];

1-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [65];

7-(2-fluorophenyl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [66];

7-(2-fluorophenyl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [67];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [68];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [69];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [70];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [71];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [72];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [73];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [74];

N-benzyl-1-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [75];

1-cyclopentyl-N-((5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [76];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridine [77];

7-(2-fluorophenyl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [78];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [79];

3-methyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [80];

5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [81];

7-(pyridin-3-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [82];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [83];

N-((5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [84];

N,N-dimethyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [85];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [86];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [87];

2-phenyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [88];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [89];

N-isopropyl-5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [90];

N,N-dimethyl-1-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [91];

7-(pyridin-3-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [92];

2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [93];

3,3-dimethyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [94];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [95];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [96];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [97];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [98];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [99]; and

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [100]; or a pharmaceutically acceptable salt thereof.

16. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

N-benzyl-1-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [101];

1-cyclopentyl-N-((5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [102];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [103];

7-(pyridin-3-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [104];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [105];

3-methyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [106];

5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [107];

2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [108];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [109];

N-((5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [110];

N,N-dimethyl-5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [111];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [112];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [113];

2-phenyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [114];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [115];

N-isopropyl-5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [116];

N,N-dimethyl-1-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [117];

7-(pyridin-4-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [118];

2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [119];

3,3-dimethyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [120];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [121];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [122];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [123];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [124];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [125];

N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [126];

N-benzyl-1-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [127];

1-cyclopentyl-N-((5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [128];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [129];

7-(pyridin-4-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [130];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [131];

3-methyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [132];

5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [133];

7-(pyridin-2-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [134];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [135];

N-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [136];

N,N-dimethyl-5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [137];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [138];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [139];

2-phenyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [140];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [141];

N-isopropyl-5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [142];

N,N-dimethyl-1-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [143];

7-(pyridin-2-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [144];

2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [145];

3,3-dimethyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [146];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [147];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [148];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [149];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [150];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [151];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [152];

N-benzyl-1-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [153];

1-cyclopentyl-N-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [154];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [155];

7-(pyridin-2-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [156];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [157];

3-methyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [158];

5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [159];

7-(piperidin-1-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [160];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [161];

N-((5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [162];

N,N-dimethyl-5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [163];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [164];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [165];

2-phenyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [166];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [167]

N-isopropyl-5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [168];

N,N-dimethyl-1-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [169];

7-(piperidin-1-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [170];

7-(piperidin-1-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [171];

3,3-dimethyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [172];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [173];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [174];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [175];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [176];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [177];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [178];

N-benzyl-1-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [179];

1-cyclopentyl-N-((5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [180];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [181];

7-(piperidin-1-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [182];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [183];

3-methyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [184];

5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [185];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [186];

7-(4-methyl-1H-imidazol-1-yl)-2-(S -(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [187];

N-((5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [189];

N,N-dimethyl-5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [190];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [191];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [192];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [193];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [194];

N-isopropyl-5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [195];

N,N-dimethyl-1-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [196];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [196];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [197];

3,3-dimethyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [198];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [199]; and

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [200]; or a pharmaceutically acceptable salt thereof.

17. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [201];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [202];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [203];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [204];

N-benzyl-1-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [205];

1-cyclopentyl-N-((5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [206];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridine [207];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [208];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [209];

3-methyl-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [210];

5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [211];

7-(4-methylpiperazin-1-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [212];

7-(4-methylpiperazin-1-yl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [213];

N-((5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [214];

N,N-dimethyl-5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [215];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [216];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [217];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [218];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [219];

N-isopropyl-5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [220];

N,N-dimethyl-1-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [221];

7-(4-methylpiperazin-1-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [222];

7-(4-methylpiperazin-1-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [223];

3,3-dimethyl-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [224];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [225];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [226];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [227];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [228];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [229];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [230];

N-benzyl-1-(5-(3-(7-(4-methylpiperazin-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [231];

1-cyclopentyl-N-((5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [232];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [233];

7-(4-methylpiperazin-1-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [234];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [235];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [236];

5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [237];

2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [238];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [239];

N-((5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [240];

5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [241];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [242];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [243];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [244];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [245];

5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [246];

1-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [247];

2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [248];

2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [249];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [250];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [251];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [252];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [253];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [254];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [255];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [256];

1-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N-benzylmethanamine [257];

1-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N-(cyclopentylmethyl)methanamine [258]

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [259];

2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [260];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [261];

3-methyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [262];

5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [263];

2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [264];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [265];

N-((5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [266];

N,N-dimethyl-5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [267];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [268];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [269];

2-phenyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [270];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [271];

N-isopropyl-5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [272];

N,N-dimethyl-1-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [273];

2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [274];

2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [275];

3,3-dimethyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [276];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [277];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [278];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [279];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [280];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [281];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [282];

N-benzyl-1-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [283];

1-cyclopentyl-N-((5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [284];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [285];

2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [286];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [287];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [288];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [289];

7-(furan-3-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [290];

7-(furan-3-yl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [291];

N-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [292];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [293];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [294];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [295];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [296];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [297];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [298];

1-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [299]; and

7-(furan-3-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [300]; or a pharmaceutically acceptable salt thereof.

18. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

7-(furan-3-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [301];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [302];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [303];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [304];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [305];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [306];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [307];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [308];

N-benzyl-1-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [309];

1-cyclopentyl-N-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [310];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(furan-3-yl)-3H-imidazo[4,5-b]pyridine [311];

7-(furan-3-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [312];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [313];

3-methyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [314];

5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [315];

2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [316];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [317];

N-((5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [318];

N,N-dimethyl-5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [319];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [320];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [321];

2-phenyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [322];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [323];

N-isopropyl-5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [324];

N,N-dimethyl-1-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [325];

2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [326];

2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [327];

3,3-dimethyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [328];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [329];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [330];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [331];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [332];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [333];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [334];

N-benzyl-1-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [335];

1-cyclopentyl-N-((5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [336];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [337];

2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [338];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [339];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [340];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [341];

7-(5-fluorothiophen-2-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [342];

7-(5-fluorothiophen-2-yl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [343];

N-((5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [344];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [345];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [346];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [347];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [348];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [349];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [350];

1-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [351];

7-(5-fluorothiophen-2-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [352];

7-(5-fluorothiophen-2-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [353];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [354];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [355];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [356];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [357];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [358];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [359];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [360];

N-benzyl-1-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [361];

1-cyclopentyl-N-((5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [362];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridine [363];

7-(5-fluorothiophen-2-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [364];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [365];

3-methyl-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [366];

5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [367];

7-(5-methylthiophen-2-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [368];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [369];

N-((5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [370];

N,N-dimethyl-5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [371];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [372];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [373];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [374];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [375];

N-isopropyl-5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [376];

N,N-dimethyl-1-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [377];

7-(5-methylthiophen-2-yl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [378];

7-(5-methylthiophen-2-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [379];

3,3-dimethyl-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [380];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [381];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [382];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [383];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [384];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [385];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [386];

N-benzyl-1-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [387];

1-cyclopentyl-N-((5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [388];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [389];

7-(5-methylthiophen-2-yl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [390];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [391];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [392];

1-(5-(2-(5-(5-aminopyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [393];

1-(5-(2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [394];

1-(5-(2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [395];

1-(5-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [396];

1-(5-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [397];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [398];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [399]; and

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [400]; or a pharmaceutically acceptable salt thereof.

19. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [401];

1-(5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [402];

1-(5-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [403];

1-(5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [404];

1-(5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [405];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [406];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [407];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [408];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [409];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [410];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [411];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [412];

1-(5-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [413];

1-(5-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [414];

1-(5-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [415];

1-(5-(2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethanone [416];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [417];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [418];

N-(3-(2-(5-(5-aminopyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [419];

N-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [420];

N-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [421];

N-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [422];

N-(3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [423];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [424];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [425];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [426];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [427];

N-(3-fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methane sulfonamide [428];

N-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methane sulfonamide [429];

N-(3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methane sulfonamide [430];

N-(3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methane sulfonamide [431];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [432];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [433];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [434];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [435];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [436];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [437];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [438];

N-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methane sulfonamide [439];

N-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [440];

N-(3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [441];

N-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methane sulfonamide [442];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [443];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [444];

N^1-(3-(2-(5-(5-aminopyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [445];

N^1-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [446];

N^1-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [447];

N^1-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [448];

N^1-(3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [449];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [450];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [451];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [452];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [453];

N^1-(3-fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [454];

N^1-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [455];

N^1-(3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [456];

N^1-(3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [457];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [458];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [459];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [460];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [461];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [462];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [463];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [464];

N^1-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [465];

N^1-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [466];

N^1-(3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [467];

N^1-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [468];

1-(5-(7-fluoro-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [481];

1-(5-(7-fluoro-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [741];

N-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-7-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [897];

1-(5-(6-fluoro-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [949];

1-(5-(6-fluoro-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [1209];

N-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-6-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1365];

1-(5-(4-fluoro-3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [1417];

1-(5-(4-fluoro-3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [1677];

N-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-4-fluoro-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [1833];

7-(3-fluorophenyl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1873];

7-(3-fluorophenyl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1874];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1875];

7-(3-fluorophenyl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1876];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1877];

1-(6-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [1878];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1879];

7-(3-fluorophenyl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1880];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1881];

7-(3-fluorophenyl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1882];

2-((5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1883];

7-(3-fluorophenyl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1884];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1885];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1886];

2-cyclohexyl-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1887];

7-(3-fluorophenyl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1888];

7-(3-fluorophenyl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1889];

7-(3-fluorophenyl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1890];

7-(4-fluorophenyl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1891];

7-(4-fluorophenyl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1892];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1893];

7-(4-fluorophenyl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1894];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1895];

1-(6-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [1896];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1897];

7-(4-fluorophenyl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1898];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1899]; and

7-(4-fluorophenyl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1900]; or a pharmaceutically acceptable salt thereof.

20. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

2-((5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1901];

7-(4-fluorophenyl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1902];

5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1903];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1904];

2-cyclohexyl-N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1905];

7-(4-fluorophenyl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1906];

7-(4-fluorophenyl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1907];

7-(4-fluorophenyl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1908];

7-(2-fluorophenyl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1909];

7-(2-fluorophenyl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1910];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1911];

7-(2-fluorophenyl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1912];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1913];

1-(6-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [1914];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1915];

7-(2-fluorophenyl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1916];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1917];

7-(2-fluorophenyl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1918];

2-((5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [1919];

7-(2-fluorophenyl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1920];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1921];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1922];

2-cyclohexyl-N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1923];

7-(2-fluorophenyl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1924];

7-(2-fluorophenyl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1925];

7-(2-fluorophenyl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1926];

2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1927];

7-(pyridin-3-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1928];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1929];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1930];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1931];

1-(6-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [1932];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1933];

2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1934];

2-(piperidin-4-yl)-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1935];

7-(pyridin-3-yl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1936];

N,N-dimethyl-2-((5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1937];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1938];

5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1939];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1940];

2-cyclohexyl-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1941];

7-(pyridin-3-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1942];

2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1943];

2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridine [1944];

2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1945];

7-(pyridin-4-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1946];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1947];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1948];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1949];

1-(6-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [1950];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1951];

2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1952];

2-(piperidin-4-yl)-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1953];

7-(pyridin-4-yl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1954];

N,N-dimethyl-2-((5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1955];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1956];

5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1957];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1958];

2-cyclohexyl-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1959];

7-(pyridin-4-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1960];

2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1961];

2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [1962];

2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1963];

7-(pyridin-2-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1964];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1965];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1966];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1967];

1-(6-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [1968];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1969];

2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1970];

2-(piperidin-4-yl)-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1971];

7-(pyridin-2-yl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1972];

N,N-dimethyl-2-((5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1973];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1974];

5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1975];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1976];

2-cyclohexyl-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1977];

7-(pyridin-2-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1978];

7-(pyridin-2-yl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1979];

2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridine [1980];

7-(piperidin-1-yl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1981];

7-(piperidin-1-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1982];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [1983];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [1984];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [1985];

1-(6-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [1986];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [1987];

7-(piperidin-1-yl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1988];

N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [1989];

7-(piperidin-1-yl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1990];

N,N-dimethyl-2-((5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [1991];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [1992];

5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1993];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [1994];

2-cyclohexyl-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [1995];

7-(piperidin-1-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1996];

7-(piperidin-1-yl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1997];

7-(piperidin-1-yl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1998];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [1999]; and

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2000]; or a pharmaceutically acceptable salt thereof.

21. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridine [2001];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2002];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridine [2003];

1-(6-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2004];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridine [2005];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2006];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2007];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2008];

N,N-dimethyl-2-((5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [2009];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(4-methyl-1H-indazol-3-yl)-7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridine [2010];

5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2011];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridine [2012];

2-cyclohexyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2013];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2014];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2015];

7-(4-methyl-1H-imidazol-1-yl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2016];

7-(4-methylpiperazin-1-yl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2017];

7-(4-methylpiperazin-1-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2018];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2019];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2020];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2021];

1-(6-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2022];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2023];

7-(4-methylpiperazin-1-yl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2024];

N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2025];

7-(4-methylpiperazin-1-yl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2026];

N,N-dimethyl-2-((5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [2027];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2028];

5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2029];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2030];

2-cyclohexyl-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2031];

7-(4-methylpiperazin-1-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2032];

7-(4-methylpiperazin-1-yl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2033];

7-(4-methylpiperazin-1-yl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2034];

2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2035];

2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2036];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2037];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2038];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2039];

1-(6-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2040];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2041];

2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2042];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2043];

2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2044];

2-((5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [2045];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2046];

5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2047];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2048];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-cyclohexylacetamide [2049];

2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2050];

2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2051];

2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2052];

2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2053];

2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2054];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2055];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2056];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2057];

1-(6-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2058];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2059];

2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2060];

2-(piperidin-4-yl)-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2061];

2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2062];

N,N-dimethyl-2-((5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [2063];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2064];

5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2065];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2066];

2-cyclohexyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2067];

2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2068];

2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2069];

2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [2070];

7-(furan-3-yl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2071];

7-(furan-3-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2072];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(furan-3-yl)-3H-imidazo[4,5-b]pyridine [2073];

7-(furan-3-yl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2074];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(furan-3-yl)-3H-imidazo[4,5-b]pyridine [2075];

1-(6-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2076];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(furan-3-yl)-3H-imidazo[4,5-b]pyridine [2077];

7-(furan-3-yl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2077];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2079];

7-(furan-3-yl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2080];

2-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [2081];

7-(furan-3-yl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2082];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2083];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(furan-3-yl)-3H-imidazo[4,5-b]pyridine [2084];

2-cyclohexyl-N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2085];

7-(furan-3-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2086];

7-(furan-3-yl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2087];

7-(furan-3-yl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2088];

2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2089];

2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2090];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2091];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2092];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2093];

1-(6-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2094];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2095];

2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2096];

2-(piperidin-4-yl)-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2097];

2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2098];

N,N-dimethyl-2-((5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [2099]; and

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2100]; or a pharmaceutically acceptable salt thereof.

22. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2101];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2102];

2-cyclohexyl-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2103];

2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2104];

2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2105];

2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2106];

7-(5-fluorothiophen-2-yl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2107];

7-(5-fluorothiophen-2-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2108];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2109];

7-(5-fluorothiophen-2-yl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2110];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2111];

1-(6-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2112];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2113];

7-(5-fluorothiophen-2-yl)-2-(5-(5-(piperidin-4-yloxy) pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b] pyridine [2114];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b] pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2115];

7-(5-fluorothiophen-2-yl)-2-(5-(5-(2-(pyrrolidin-1-yl) ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2116];

2-((5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b] pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [2117];

7-(5-fluorothiophen-2-yl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2118];

5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2119];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2120];

2-cyclohexyl-N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2121];

7-(5-fluorothiophen-2-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2122];

7-(5-fluorothiophen-2-yl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2123];

7-(5-fluorothiophen-2-yl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2124];

7-(5-methylthiophen-2-yl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2125];

7-(5-methylthiophen-2-yl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2126];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2127];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2128];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2129];

1-(6-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b] pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2130];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2131];

7-(5-methylthiophen-2-yl)-2-(5-(5-(piperidin-4-yloxy) pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b] pyridine [2132];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b] pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2133];

7-(5-methylthiophen-2-yl)-2-(5-(5-(2-(pyrrolidin-1-yl) ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2134];

N,N-dimethyl-2-((5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)ethan-1-amine [2135];

2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2136];

5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2137];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridine [2138];

2-cyclohexyl-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2139];

7-(5-methylthiophen-2-yl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2140];

7-(5-methylthiophen-2-yl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2141];

7-(5-methylthiophen-2-yl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2142];

1-(5-(2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo [4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2143];

1-(5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl) ethan-1-one [2144];

1-(5-(2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2145];

1-(5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2146];

1-(5-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl) ethan-1-one [2147];

1-(5-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2148];

1-(5-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl) ethan-1-one [2149];

1-(5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2150];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b] pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2151];

1-(5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2152];

1-(5-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2153];

1-(5-(2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2154];

1-(5-(2-(5-(5-hydroxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2155];

1-(5-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2156];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b] pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-cyclohexylacetamide [2157];

1-(5-(2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo [4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2158];

1-(5-(2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo [4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2159];

1-(5-(2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo [4,5-b]pyridin-7-yl)thiophen-2-yl)ethan-1-one [2160];

N-(3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2161];

N-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2162];

N-(3-(2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [2163];

N-(3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2164];

N-(3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [2165];

N-(3-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [2166];

N-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [2167];

N-(3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2168];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2169];

N-(3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2170];

N-(3-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [2171];

N-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2172];

N-(3-fluoro-5-(2-(5-(5-hydroxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2173];

N-(3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [2174];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2175];

N-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2176];

N-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2177];

N-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [2178];

N^1-(3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [2179];

N^1-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N_2-dimethylethane-1,2-diamine [2180];

N^1-(3-(2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [2181];

N^1-(3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [2182];

N^1-(3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [2183];

N^1-(3-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [2184];

N^1-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [2185];

N^1-(3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [2186];

N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2187];

N^1-(3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [2188];

N^1-(3-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [2189];

N_1-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2, N^2-dimethylethane-1,2-diamine [2190];

5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2191];

N^1-(3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenyl)-N^2,N^2-dimethylethane-1,2-diamine [2192];

2-cyclohexyl-N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2193];

N^1-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [2194];

N^1-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [2195];

N^1-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenyl)-N^2,N^2-dimethylethane-1,2-diamine [2196];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [2197];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [2198];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [2199]; and

2-(3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2200]; or a pharmaceutically acceptable salt thereof.

23. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

2-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2201];

2-(3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2202];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [2203];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [2204];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [2205];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [2206];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [2207];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [2208];

2-(3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2209];

2-(3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2210];

2-(3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2211];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [2212];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [2213];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [2214];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [2215];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [2216];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [2217];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [2218];

2-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2219];

2-(3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2220];

2-(3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2221];

2-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2222];

2-(3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2223];

2-(3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2224];

2-(3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2225];

2-(3-(2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2226];

2-(3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2227];

2-(3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2228];

1-(6-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2229];

2-(3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2230];

2-(3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2231];

N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2232];

2-(3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2233];

2-((5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [2234];

2-(3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2235];

5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2236];

2-(3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenoxy)-N,N-dimethylethan-1-amine [2237];

2-cyclohexyl-N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2238];

2-(3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2239];

2-(3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenoxy)-N,N-dimethylethan-1-amine [2240];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [2241];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [2242];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [2243];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2244];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2245];

N-((5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [2246];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [2247];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [2248];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [2249];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [2250];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [2251];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [2252];

1-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [2253];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2254];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2255];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [2256];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [2257];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [2258];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [2259];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [2260];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [2261];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [2262];

N-benzyl-1-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [2263];

1-cyclopentyl-N-((5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [2264];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridine [2265];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2266];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2267];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2268];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2269];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridine [2270];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2271];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridine [2272];

1-(6-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2273];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridine [2274];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2275];

N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2276];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2277];

2-((5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [2278];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2279];

5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2280];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridine [2281];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2282];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2283];

7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2284];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [2285];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [2286];

3-(2-(5-(5-aminopyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2287];

3-fluoro-5-(2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2288];

3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2289];

3-(2-(5-(5-((ethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2290];

3-(2-(5-(5-(dimethylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2291];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [2292];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [2293];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [2294];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [2295];

3-fluoro-5-(2-(5-(5-(isopropylamino)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2296];

3-(2-(5-(5-((dimethylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2297];

3-fluoro-5-(2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2298];

3-fluoro-5-(2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2299]; and

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [2300]; or a pharmaceutically acceptable salt thereof.

24. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [2301];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [2302];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [2303];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [2304];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [2305];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [2306];

3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2307];

3-(2-(5-(5-(((cyclopentylmethyl)amino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2308];

3-(2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2309];

3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2310];

3-fluoro-5-(2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2311];

3-fluoro-5-(2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2312];

3-fluoro-5-(2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [];

3-(2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2314];

3-fluoro-5-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2315];

3-(2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2316];

3-(2-(5-(6-(3-aminoazetidin-1-yl)pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2317];

3-(2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2318];

3-fluoro-5-(2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2319];

N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2320];

3-fluoro-5-(2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2321];

3-(2-(5-(5-(2-(dimethylamino)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2322];

3-fluoro-5-(2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2323];

5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2324];

3-(2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorophenol [2325];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2326];

3-fluoro-5-(2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2327];

3-fluoro-5-(2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)phenol [2328];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [2329];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [2330];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [2331];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2332];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2333];

N-((5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [2334];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [2335];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [2336];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [2337];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-phenylacetamide [2338];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [2339];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [2340];

1-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-N,N-dimethylmethanamine [2341];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2342];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2343];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3,3-dimethylbutanamide [2344];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [2345];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [2346];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [2347];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [2348];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [2349];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclohexanecarboxamide [2350];

N-benzyl-1-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methanamine [2351];

1-cyclopentyl-N-((5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)methanamine [2352];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridine [2353];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2354];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(pyridin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2355];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(piperidin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2356];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2357];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridine [2358];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2359];

2-(5-(1,2-dimethyl-1H-imidazol-5-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridine [2360];

1-(6-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyrazin-2-yl)azetidin-3-amine [2361];

2-(5-(5-(cyclohexyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridine [2362];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(5-(piperidin-4-yloxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2363];

N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(piperidin-4-yl)acetamide [2364];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(5-(2-(pyrrolidin-1-yl)ethoxy)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2365];

2-((5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)oxy)-N,N-dimethylethan-1-amine [2366];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(5-methoxypyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2367];

5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [2368];

2-(5-(5-(benzyloxy)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridine [2369];

2-cyclohexyl-N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2370];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(pyridin-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2371];

7-(3-fluoro-5-methoxyphenyl)-2-(5-(pyrazin-2-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2372];

2-(dimethylamino)-N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2373];

2-(dimethylamino)-N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2374];

2-(dimethylamino)-N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2375];

2-(dimethylamino)-N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2376];

2-(dimethylamino)-N-(5-(3-(7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2377];

2-(dimethylamino)-N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2378];

2-(dimethylamino)-N-(5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2379];

2-(dimethylamino)-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2380];

2-(dimethylamino)-N-(5-(3-(7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2381];

N-(5-(3-(3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(dimethylamino)acetamide [2382];

2-(dimethylamino)-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2383];

2-(dimethylamino)-N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2384];

2-(dimethylamino)-N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2385];

2-(dimethylamino)-N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2386];

2-(dimethylamino)-N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2387];

N-(5-(3-(7-(5-acetylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-2-(dimethylamino)acetamide [2388];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2389];

2-(dimethylamino)-N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2390];

2-(dimethylamino)-N-(5-(3-(7-(3-(2-(dimethylamino)ethoxy)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2391];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-(2-(pyrrolidin-1-yl)ethoxy)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2392];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-hydroxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2393];

2-(dimethylamino)-N-(5-(3-(7-(3-fluoro-5-methoxyphenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [2394];

4-(2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)morpholine [2395];

7-(4,4-difluoropiperidin-1-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b] pyridine [2396];

7-(1-methylpiperidin-4-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b] pyridine [2397];

4-(2-(5-(5-fluoropyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl) morpholine [2398];

2-(5-(5-fluoropyridin-3-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2399];

7-(4,4-difluoropiperidin-1-yl)-2-(5-(5-fluoropyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2400];

2-(5-(5-fluoropyridin-3-yl)-1H-indazol-3-yl)-7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-b]pyridine [2401];

2-(5-(5-fluoropyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [2402];

4-(2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)morpholine [2403];

7-(4,4-difluoropiperidin-1-yl)-2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [2404];

2-(5-(1-methyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-b]pyridine [2405];

4-(2-(5-(1-cyclopropyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)morpholine [2406];

2-(5-(1-cyclopropyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(4-methylpiperazin-1-yl)-3H-imidazo[4,5-b]pyridine [2407];

2-(5-(1-cyclopropyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(4,4-difluoropiperidin-1-yl)-3H-imidazo[4,5-b]pyridine [2408];

2-(5-(1-cyclopropyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-b]pyridine [2409];

2-(5-(1-cyclopropyl-1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [2410];

4-(2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)morpholine [2411];

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(4,4-difluoropiperidin-1-yl)-3H-imidazo[4,5-b]pyridine [2412]; and

2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(1-methylpiperidin-4-yl)-3H-imidazo[4,5-b]pyridine [2413]; or a pharmaceutically acceptable salt thereof.

25. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [1];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [2];

5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [7];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [9];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [19];

N-(5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [21];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine [25];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [28];

7-(4-fluorophenyl)-2-(5-(5-(pyrrolidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [40];

N-(5-(3-(7-(4-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [46];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [55];

5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N,N-dimethylpyridin-3-amine [59];

N-(5-(3-(7-(2-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [61];

5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [81];

7-(pyridin-3-yl)-2-(5-(pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [82];

N-(5-(3-(7-(pyridin-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [87];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(pyridin-4-yl)-3H-imidazo[4,5-b]pyridine [109];

N-(5-(3-(7-(pyridin-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [148];

N,N-dimethyl-5-(3-(7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [163];

2-(5-(5-((3,3-difluoropyrrolidin-1-yl)methyl)pyridin-3-yl)-1H-indazol-3-yl)-7-(piperidin-1-yl)-3H-imidazo[4,5-b]pyridine [181];

3-methyl-N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butanamide [184];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [190];

N-(5-(3-(7-(4-methyl-1H-imidazol-1-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [202];

7-(4-methylpiperazin-1-yl)-2-(5-(5-(piperidin-1-ylmethyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridine [223];

2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridine [265];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [268];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [269];

2-phenyl-N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)acetamide [270];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)benzamide [271];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [277];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopropanecarboxamide [279];

N-(5-(3-(7-(thiophen-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [281];

N-((5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)methyl)ethanamine [292];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [295];

5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)-N-isopropylpyridin-3-amine [298];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [304];

N-(5-(3-(7-(furan-3-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [306];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)propionamide [313];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [320];

N-(5-(3-(7-(thiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclopentanecarboxamide [333];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)-3-methylbutanamide [340];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [346];

N-(5-(3-(7-(5-fluorothiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)cyclobutanecarboxamide [358];

5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-amine [367];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pivalamide [372];

N-(5-(3-(7-(5-methylthiophen-2-yl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)isobutyramide [373];

N-(3-fluoro-5-(2-(5-(4-methylpyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [421];

N-(5-(3-(7-(3-fluoro-5-(methylsulfonamidomethyl)phenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)butyramide [433];

N-(3-(2-(5-(5-((benzylamino)methyl)pyridin-3-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)-5-fluorobenzyl)methanesulfonamide [439];

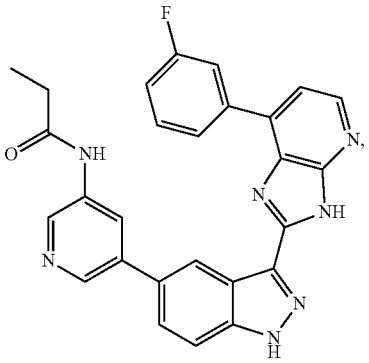
N-(3-fluoro-5-(2-(5-(pyrimidin-5-yl)-1H-indazol-3-yl)-3H-imidazo[4,5-b]pyridin-7-yl)benzyl)methanesulfonamide [442];

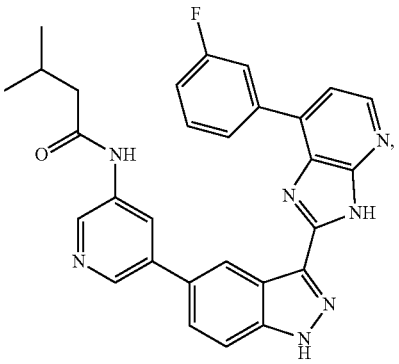
N-(5-(3-(7-(3-((2-(dimethylamino)ethyl)amino)-5-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-yl)pentanamide [460];

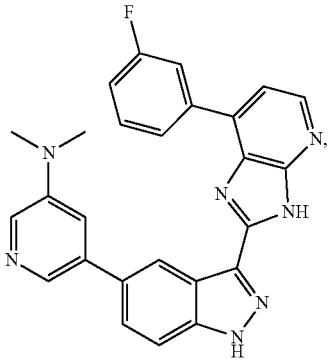
2-(5-(1H-pyrazol-4-yl)-1H-indazol-3-yl)-7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridine [1875]; and

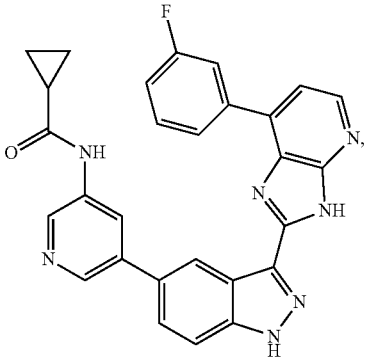
5-(3-(7-(3-fluorophenyl)-3H-imidazo[4,5-b]pyridin-2-yl)-1H-indazol-5-yl)pyridin-3-ol [1885]; or a pharmaceutically acceptable salt thereof.

26. The method of claim **2**, wherein the compound of Formula I is selected from the group consisting of:









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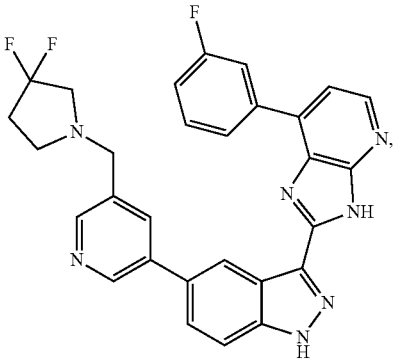

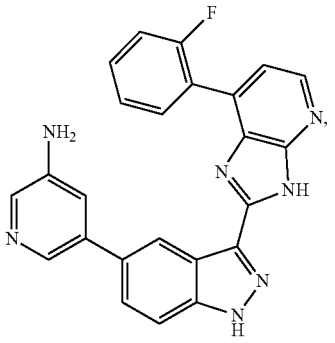

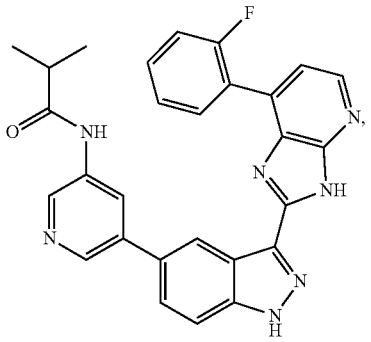

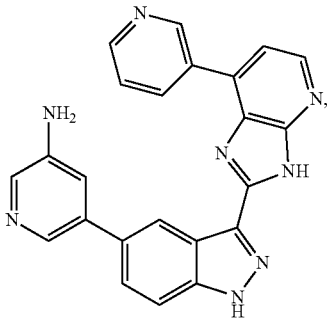

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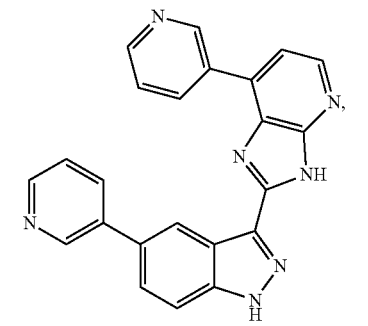

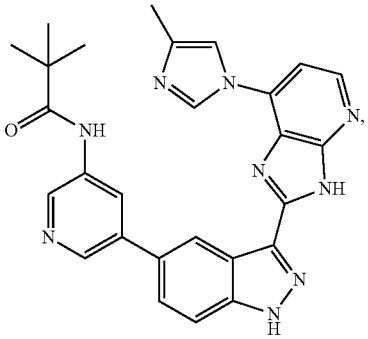

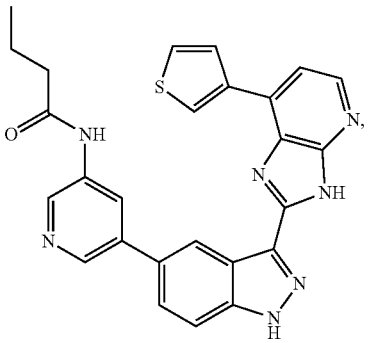

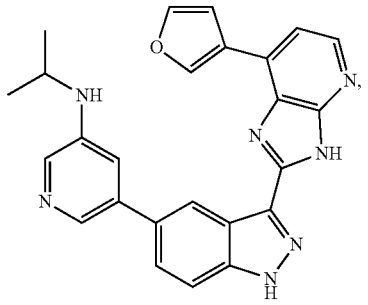

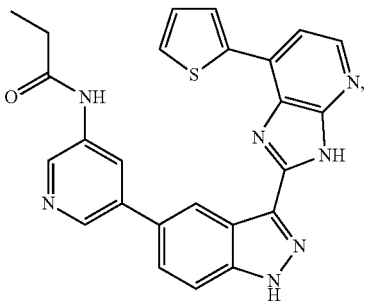

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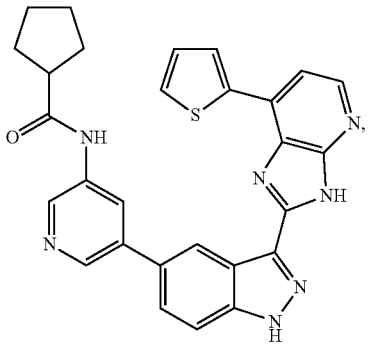

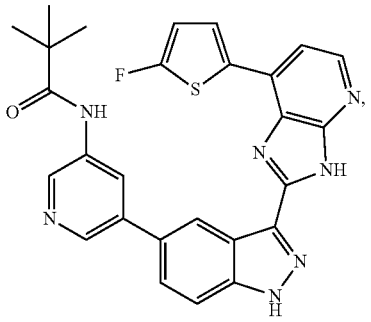

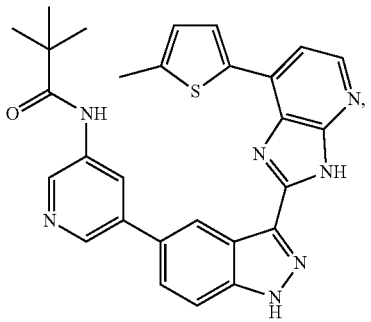

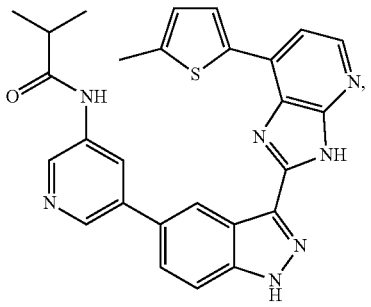

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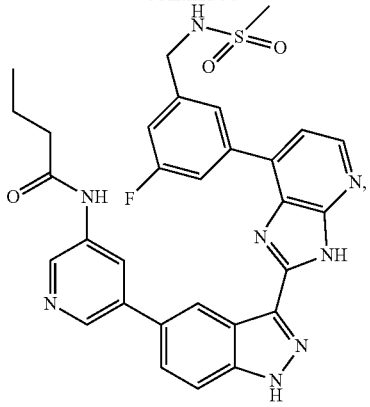

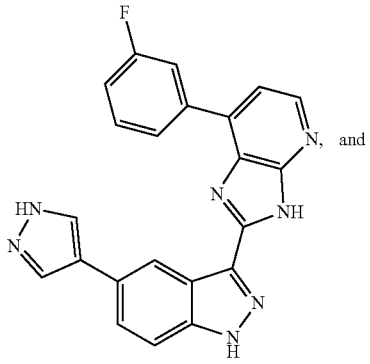

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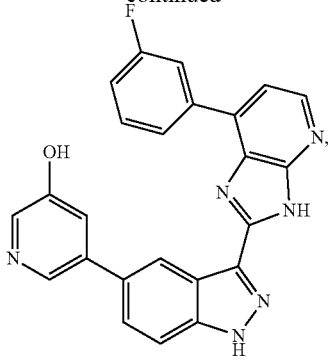

a pharmaceutically acceptable salt thereof.

27. The method of claim **2**, wherein the bone or cartilage disease is osteoarthritis.

28. The method of claim **2**, wherein the bone or cartilage disease is articular cartilage (chondral) defects.

29. The method of claim **2**, wherein the bone or cartilage disease is degenerative disc disease.

30. The method of claim **2**, wherein the bone or cartilage disease is relapsing polychondritis.

31. The method of claim **2**, wherein the bone or cartilage disease is osteochondritis dissecans.

32. The method of claim **2**, wherein the subject is a human.

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