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(54) **4-ALKOXYPYRROLO[2,1-F][1,2,4]TRIAZINES AND PREPARATION AND USES THEREOF**

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(57) **ABSTRACT**

4-Alkoxypyrrolo[2,1-f][1,2,4]triazine compounds for treating various diseases and pathologies are disclosed. More particularly, the present disclosure concerns the use of 4-alkoxypyrrolo[2,1-f][1,2,4]triazine compounds or analogs thereof, in the treatment of disorders characterized by overexpression of DYRK1A (e.g., cancer, Down syndrome, Alzheimer's disease, diabetes, viral infections, and osteoarthritis).

4-ALKOXYPYRROLO[2,1-F][1,2,4]TRIAZINES AND PREPARATION AND USES THEREOF

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Nos. 63/355,076, filed Jun. 23, 2022, 63/427,322, filed Nov. 22, 2022, and 63/458,808, filed Apr. 12, 2023, which are incorporated herein by reference in their entirety.

BACKGROUND

Technical Field

[0002] This disclosure relates to inhibitors of dual-specificity tyrosine phosphorylation-regulated 1A kinase, and compositions comprising the same. More particularly, it concerns the use of a 4-alkoxypyrrolo[2,1-f][1,2,4]triazine compounds or salts or analogs thereof, in the treatment of disorders characterized by the abnormal expression and/or activity of DYRK1A (e.g., cancer, Down syndrome, Alzheimer's disease, diabetes, viral infections, and osteoarthritis).

Background

[0003] Dual-specificity tyrosine phosphorylation-regulated kinases (DYRK1A, 1B, 2-4) comprise a family of protein kinases within the CMGC group of the eukaryotic kinome. These protein kinases are involved in multiple cellular functions, including intracellular signaling, mRNA splicing, chromatin transcription, DNA damage repair, cell survival, cell cycle control, differentiation, homocysteine/methionine/folate regulation, body temperature regulation, endocytosis, neuronal development, synaptic plasticity, etc. Abnormal expression and/or activity of some of these kinases, DYRK1A in particular, is seen in many human nervous system diseases, such as cognitive deficits associated with Down syndrome, Alzheimer's disease, and related diseases, tauopathies, dementia, Pick's disease, Parkinson's disease, and other neurodegenerative diseases, Phelan-McDermid syndrome, autism, and CDKL5 deficiency disorder. DYRKs are also involved in diabetes, abnormal folate/methionine metabolism, osteoarthritis, several solid cancers (glioblastoma, breast, and pancreatic cancers) and leukemias (acute lymphoblastic leukemia, acute megakaryoblastic leukemia), viral infections (influenza, HIV-1, HCMV, HCV, CMV, HPV), as well as infections caused by unicellular parasites (*Leishmania, Trypanosoma, Plasmodium*) (*International Journal of Molecular Sciences* (2021), 22(11), 6047). DYRK1A has also been identified as a critical stabilizer of EGFR (*Cell Death & Disease* (2019), 10, 282) which is a crucial factor contributing to the keratinization, cell hyperproliferation, abnormal differentiation and inflammatory infiltration during the progress of psoriasis.

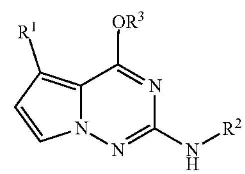
SUMMARY

[0004] The present disclosure provides methods and reagents, the method involving contacting a cell with an agent, such as a 4-alkoxypyrrolo[2,1-f][1,2,4]triazine compound, in a sufficient amount to antagonize DYRK1A activity, e.g., reduce the proliferation of head and neck squamous cell carcinoma, luminal/HER2 breast cancer, (Cell (2016), 164(1-2), 293-309) or pancreatic adenocarcinoma, as well as impair the self-renewal capacity of glioblastoma and compromise ovarian cancer spheroid cell viability (*Molecular Cancer Research* (2017), 15(4), 371-381).

[0005] The present disclosure also provides methods and reagents, the method involving contacting a cell with an agent, such as a 4-alkoxypyrrolo[2,1-f][1,2,4]triazine compound, in a sufficient amount to antagonize DYRK1A activity, e.g., i) to normalize prenatal and early postnatal brain development; ii) to improve cognitive function in youth and adulthood; and/or iii) to attenuate Alzheimer's-type neurodegeneration.

[0006] Some embodiments disclosed herein include DYRK1A inhibitors containing a 4-alkoxypyrrolo[2,1-f][1,2,4]triazine core. Other embodiments disclosed herein include pharmaceutical compositions and methods of treatment using these compounds.

[0007] One embodiment disclosed herein includes a compound having the structure of Formula I.



I

[0008] or a pharmaceutically acceptable salt thereof,

[0009] wherein,

[0010] R^1 is heteroaryl optionally substituted with 1-10 R^4;

[0011] R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^5, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^6, -heteroaryl optionally substituted with 1-10 R^7, and —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R^8, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0012] R^3 is selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0013] each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^9, —(C_{1-5} alkylene)CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{10}, -carbocyclyl optionally substituted with 1-12 R^{11}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^{20}, —(C_{1-5} alkylene)$_p$C(═O)N(R^{12})$_2$, and —C(═O)R^{13}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0014] each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0015] each R^6 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl),-heterocyclyl optionally substituted with 1-10 R^{16}, —(C_{1-5} alkylene)$_p$OR^{21},

—SO_2R^{23}, and —C(═O)R^{24}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0016] alternatively, two R^6 attached to the same carbon atom are taken together to form a carbonyl group;

[0017] each R^7 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —OMe;

[0018] each R^8 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —N(R^{14})$_2$, —(C_{1-5} alkylene)$_p$OR^{15}, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{16}, —C(═O)R^{22}, and —NHC(═O)R^{23}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0019] each R^9 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0020] each R^{10} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0021] each R^{11} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0022] each R^{12} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R^{17}, -heterocyclyl optionally substituted with 1-10 R^{18}, and -heteroaryl optionally substituted with 1-10 R^{19}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0023] each R^{13} is -heterocyclyl optionally substituted with 1-10 R^{18};

[0024] each R^{14} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0025] each R^{15} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —(C_{1-5} alkylene)$_p$OR^{21};

[0026] each R^{16} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0027] each R^{17} is independently selected from the group consisting of halide, —OMe, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0028] each R^{18} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0029] each R^{19} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0030] each R^{20} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-19} haloalkyl);

[0031] each R^{21} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0032] each R^{22} is independently selected from the group consisting of -heterocyclyl optionally substituted with 1-10 R^{18}, —N(R^{12})$_2$ and —OR^{21};

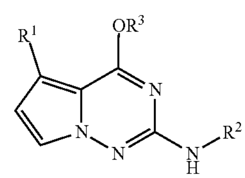
[0033] each R^{23} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0034] each R^{24} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —OR^{23}, and -carbocyclyl optionally substituted with 1-12 R^{25};

[0035] each R^{25} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl); and each p is independently 0 or 1;

[0036] wherein each H atom is optionally, independently replaced by ^{2}H (D) (deuterium).

[0037] In another embodiment disclosed herein, included is a compound having the structure of Formula I.



I

[0038] or a pharmaceutically acceptable salt thereof,

[0039] wherein,

[0040] R^1 is heteroaryl optionally substituted with 1-10 R^4;

[0041] R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR, —(C_{1-5}alkylene)pheterocyclyl optionally substituted with 1-10 R, —(C_{1-5} alkylene)$_p$aryl optionally substituted with 1-10 R^{26}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^7, and —(C_{1-5}alkylene)$_p$carbocyclyl optionally substituted with 1-12 R, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0042] R^3 is selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and heterocyclyl optionally substituted with 1-10 R^{18};

[0043] each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^9, —(C_{1-5} alkylene)$_p$CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{10}, -carbocyclyl optionally substituted with 1-12 R^{11}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^{20}, —(C_{1-5} alkylene)$_p$C(═O)N(R^{12})$_2$, and —C(═O)R^{13}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0044] each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0045] each R^6 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl),-heterocyclyl optionally substituted with 1-10 R^{16}, -carbocyclyl optionally substituted with 1-12 R^{17},—(C_{1-5} alkylene)$_p$OR^{21}, —SO$_2$R^{23}, and —C(═O)R^{24}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0046] alternatively, two R^6 attached to the same carbon atom are taken together to form a carbonyl group;

[0047] each R^7 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —OMe;

[0048] each R^8 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —N(R^{14})$_2$, —(C_{1-5} alkylene)$_p$OR^{15}, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{16}, —C(═O)R^{22}, and —NHC(═O)R^{23}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0049] each R^9 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0050] each R^{10} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0051] each R^{11} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0052] each R^{12} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^{21}, —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R^{17}, -heterocyclyl optionally substituted with 1-10 R^{18}, and -heteroaryl optionally substituted with 1-10 R^{19}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0053] each R^{13} is -heterocyclyl optionally substituted with 1-10 R^{18};

[0054] each R^{14} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0055] each R^{15} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —(C_{1-5} alkylene)$_p$OR^{21};

[0056] each R^{16} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0057] alternatively, two R^{16} attached to the same carbon atom are taken together to form a carbonyl group;

[0058] each R^{17} is independently selected from the group consisting of halide, —OMe, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0059] each R^{18} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0060] each R^{19} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0061] each R^{20} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0062] each R^{21} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0063] each R^{22} is independently selected from the group consisting of -heterocyclyl optionally substituted with 1-10 R^{18}, —N(R^{12})$_2$ and —OR^{21};

[0064] each R^{23} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —(C_{1-5} alkylene)$_p$OR^{21};

[0065] each R^{24} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —OR^{21}, and -carbocyclyl optionally substituted with 1-12 R^{25};

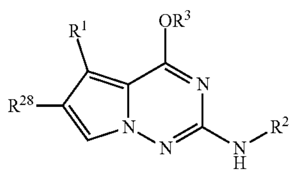
[0066] each R^{25} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0067] each R^{26} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl); and

[0068] each p is independently 0 or 1;

[0069] wherein each H atom is optionally, independently replaced by ^{2}H (D) (deuterium).

[0070] In another embodiment disclosed herein, included is a compound having the structure of Formula I:



I

[0071] or a pharmaceutically acceptable salt thereof,

[0072] wherein,

[0073] R^1 is heteroaryl optionally substituted with 1-10 R^4;

[0074] R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR, —(C_{1-5}alkylene)CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^6, —(C_{1-5} alkylene)$_p$aryl optionally substituted with 1-10 R^{26}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^7, and —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0075] R^3 is selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and heterocyclyl optionally substituted with 1-10 R^{18};

[0076] each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), unsubstituted —(C_{2-9} haloalkenyl), —(C_{1-5} alkylene)$_p$OR^9, —(C_{1-5} alkylene)$_p$CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{10}, -carbocyclyl optionally substituted with 1-12 R^{11}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^{20}, —(C_{1-5} alkylene)$_p$C(═O)N(R^{12})$_2$, and —C(═O)R^{13}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0077] each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0078] each R^6 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl),-heterocyclyl optionally substituted with 1-10 R^{16}, -carbocyclyl optionally substituted with 1-12 R^{17}, —(C_{1-5} alkylene)$_p$OR^{21}, —(C_{1-5} alkylene)CN, —SO$_2$R^{23}, and —C(═O)R^{24}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl); alternatively, two R^6 attached to the same carbon atom are taken together to form a carbonyl group;

[0079] each R^7 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —OMe;

[0080] each R^8 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —N(R^{14})$_2$, —(C_{1-5} alkylene)$_p$OR^{15}, —CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{16}, —C(═O)R^{22}, and —NR^{14}C(═O)R^{23}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0081] each R^9 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0082] each R^{10} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0083] each R^{11} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0084] each R^{12} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^{21}, —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R^{17}, -heterocyclyl optionally substituted with 1-10 R^{18}, and -heteroaryl optionally substituted with 1-10 R^{19}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0085] each R^{13} is -heterocyclyl optionally substituted with 1-10 R^{18};

[0086] each R^{14} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0087] each R^{15} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —(C_{1-5} alkylene)$_p$OR^{21};

[0088] each R^{16} is independently selected from the group consisting of halide, —CN, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and -carbocyclyl optionally substituted with 1-12 R^{27};

[0089] alternatively, two R^{16} attached to the same carbon atom are taken together to form a carbonyl group;

[0090] each R^{17} is independently selected from the group consisting of halide, —OMe, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0091] each R^{18} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0092] each R^{19} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0093] each R^{20} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0094] each R^{21} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0095] each R^{22} is independently selected from the group consisting of -heterocyclyl optionally substituted with 1-10 R^{18}, —$N(R^{12})_2$, and —OR^{21};

[0096] each R^{23} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$$OR^{21}$, and -carbocyclyl optionally substituted with 1-12 R^{25};

[0097] each R^{24} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —OR^{21}, and -carbocyclyl optionally substituted with 1-12 R^{25};

[0098] each R^{25} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —CN;

[0099] each R^{26} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0100] each R^{27} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

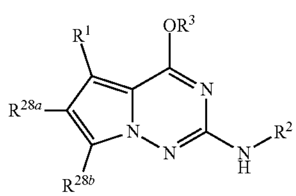
[0101] R^{28} is independently selected from the group consisting of H and halide; and

[0102] each p is independently 0 or 1;

[0103] wherein each H atom is optionally, independently replaced by ^2H (D) (deuterium).

[0104] In another embodiment disclosed herein, included is a compound having the structure of Formula I:

I



[0105] or a pharmaceutically acceptable salt thereof,

[0106] wherein,

[0107] R^1 is heteroaryl optionally substituted with 1-10 R^4;

[0108] R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR, —(C_{1-5}alkylene)CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^6, —(C_{1-5} alkylene)$_p$aryl optionally substituted with 1-10 R^{26}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^7, and —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0109] R^3 is selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and heterocyclyl optionally substituted with 1-10 R^{18};

[0110] each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), unsubstituted —(C_{2-9} haloalkenyl), —(C_{1-5} alkylene)$_p$$OR^9$, —($C_{1-5}$ alkylene)$_p$CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{10}, -carbocyclyl optionally substituted with 1-12 R^{11}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^{20}, —(C_{1-5} alkylene)$_p$C(═O)$N(R^{12})_2$, and —C(═O)R^{13}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0111] each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0112] each R^6 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl),-heterocyclyl optionally substituted with 1-10 R^{16}, -carbocyclyl optionally substituted with 1-12 R^{17}, —(C_{1-5} alkylene)$_p$$OR^{21}$, —($C_{1-5}$ alkylene)CN, —SO_2R^{23}, and —C(═O)R^{24}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl); alternatively, two R^6 attached to the same carbon atom are taken together to form a carbonyl group;

[0113] each R^7 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —OMe;

[0114] each R^8 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —$N(R^{14})_2$, —(C_{1-5} alkylene)$_p$$OR^{15}$, —CN, —($C_{1-5}$ alkylene)pheterocyclyl optionally substituted with 1-10 R^{16}, —C(═O)R^{22}, and —NR^4C(═O)R^{23}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0115] each R^9 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0116] each R^{10} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0117] each R^{11} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0118] each R^{12} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$$OR^{21}$, —($C_{1-5}$ alkylene)$_p$carbocyclyl optionally substituted with 1-12 R^{17}, -heterocyclyl optionally substituted with 1-10 R^{18}, and -heteroaryl optionally substituted with 1-10 R^{19}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

[0119] each R^{13} is -heterocyclyl optionally substituted with 1-10 R^{18};

[0120] each R^{14} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0121] each R^{15} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —(C_{1-5} alkylene)$_p$OR^{21};

[0122] each R^{16} is independently selected from the group consisting of halide, —CN, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and -carbocyclyl optionally substituted with 1-12 R^{27};

[0123] alternatively, two R^{16} attached to the same carbon atom are taken together to form a carbonyl group;

[0124] each R^{17} is independently selected from the group consisting of halide, —OMe, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0125] each R^{11} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0126] each R^{19} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0127] each R^{20} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0128] each R^{21} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0129] each R^{22} is independently selected from the group consisting of -heterocyclyl optionally substituted with 1-10 R^{18}, —N(R^{12})$_2$, and —OR^{21};

[0130] each R^{23} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^{21}, and -carbocyclyl optionally substituted with 1-12 R^{25};

[0131] each R^{24} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —OR^{21}, and -carbocyclyl optionally substituted with 1-12 R^{25};

[0132] each R^{25} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —CN;

[0133] each R^{26} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0134] each R^{27} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

[0135] R^{28a} is independently selected from the group consisting of H and halide;

[0136] R^{28b} is independently selected from the group consisting of H and D; and

[0137] each p is independently 0 or 1;

[0138] wherein each H atom is optionally, independently replaced by ^{2}H (D) (deuterium).

[0139] Some embodiments include stereoisomers and pharmaceutically acceptable salts of a compound of Formula I. Some embodiments include pharmaceutically acceptable salts of a compound of Formula I.

[0140] Some embodiments include pro-drugs of a compound of Formula I.

[0141] Some embodiments of the present disclosure include pharmaceutical compositions comprising a compound of Formula I and a pharmaceutically acceptable carrier, diluent, or excipient.

[0142] Other embodiments disclosed herein include methods of inhibiting DYRK1A by administering to a patient affected by a disorder or disease in which DYRK1A overexpression is implicated, such as Alzheimer's disease, amyotrophic lateral sclerosis, CDKL5 deficiency disorder, Down syndrome, frontotemporal dementia with parkinsonism-17 (FTDP-17), Lewy body dementia, Parkinson's disease, Pick's disease, and additional diseases with pronounced neurodegeneration such as autism, dementia, epilepsy, Huntington's disease, multiple sclerosis; diseases and disorders associated with acquired brain injury such as chronic traumatic encephalopathy, traumatic brain injury, tumor, and stroke.

[0143] Inhibitors of DYRK1A can also be used to treat tauopathies. Tauopathies are neurodegenerative disorders characterized by the deposition of abnormal tau protein in the brain. The spectrum of tau pathologies expands beyond the traditionally discussed disease forms like Pick's disease, progressive supranuclear palsy, corticobasal degeneration, and argyrophilic grain disease. Emerging entities and pathologies include globular glial tauopathies, primary age-related tauopathy, which includes neurofibrillary tangle dementia, chronic traumatic encephalopathy (CTE), frontotemporal lobar degeneration with tau inclusions (FTLD-tau), and aging-related tau astrogliopathy. Clinical symptoms include frontotemporal dementia, corticobasal syndrome, Richardson syndrome, parkinsonism, pure akinesia with gait freezing and, rarely, motor neuron symptoms or cerebellar ataxia (*Handbook of Clinical Neurology* (2018), 145, 355-368 and *Aging Cell* (2019), 18(5), e13000).

[0144] Inhibitors of DYRK1A can also be used to treat disorders associated with abnormal folate/methionine metabolism.

[0145] Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, diabetes, psoriasis, knee osteoarthritis, tendinopathy, human immunodeficiency virus type 1 (HIV-1), human cytomegalovirus (HCMV), hepatitis C virus (HCV), and herpes simplex virus 1 (HSV-1).

[0146] Some embodiments of the present disclosure include methods to prepare compounds of Formula I.

[0147] 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 disclosure, as claimed.

DETAILED DESCRIPTION

[0148] Provided herein are compositions and methods for inhibiting DYRK1A.

[0149] Some embodiments provided herein relate to a method for treating a disease including, but not limited to, neurological diseases or disorders, cancers, cognitive deficits, knee osteoarthritis, tendinopathy, viral infections, unicellular parasite infections, and motor deficits.

[0150] In some embodiments, non-limiting examples of a neurological disease or disorder which can be treated with the compounds and compositions provided herein include, but are not limited to, Alzheimer's disease, amyotrophic lateral sclerosis, Down syndrome, frontotemporal dementia with parkinsonism-17 (FTDP-17), Lewy body dementia, Parkinson's disease, Pick's disease tauopathies, and additional diseases with pronounced neurodegeneration such as autism, dementia, epilepsy, Huntington's disease, multiple sclerosis; diseases and disorders associated with acquired brain injury such as chronic traumatic encephalopathy, traumatic brain injury, tumor, and stroke.

[0151] In some embodiments, non-limiting examples of cancers which can be treated with the compounds and compositions provided herein include solid cancers (e.g., glioblastoma, ovarian, breast, and pancreatic cancers) and leukemias (e.g., acute lymphoblastic leukemia, acute megakaryoblastic leukemia, and chronic myeloid leukemia).

[0152] In some embodiments, pharmaceutical compositions are provided that are effective for treatment of a disease of an animal, e.g., a mammal, caused by DYRK1A overexpression. The composition includes a pharmaceutically acceptable carrier and a compound as described herein.

Definitions

[0153] 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.

[0154] 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, isobutyl, 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. 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).

[0155] As used herein, "alkenyl" means a straight or branched chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon double bond, such as ethenyl, 1-propenyl, 2-propenyl, 2-methyl-1-propenyl, 1-butenyl, 2-butenyl, and the like. In various embodiments, alkenyl groups can either be unsubstituted or substituted with one or more substituents. Typically, alkenyl groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[0156] As used herein, "alkynyl" means a straight or branched chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon triple bond, such as ethynyl, 1-propynyl, 1-butynyl, 2-butynyl, and the like. In various embodiments, alkynyl groups can either be unsubstituted or substituted with one or more substituents. Typically, alkynyl groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[0157] 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. 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).

[0158] As used herein, "alkenylene" means a bivalent branched or straight chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon double bond, such as ethenylene, 1-propenylene, 2-propenylene, 2-methyl-1-propenylene, 1-butenylene, 2-butenylene, and the like. In various embodiments, alkenylene groups can either be unsubstituted or substituted with one or more substituents. Typically, alkenylene groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[0159] As used herein, "alkynylene" means a bivalent branched or straight chain chemical group containing only carbon and hydrogen and containing at least one carbon-carbon triple bond, such as ethynylene, 1-propynylene, 1-butynylene, 2-butynylene, and the like. In various embodiments, alkynylene groups can either be unsubstituted or substituted with one or more substituents. Typically, alkynylene groups will comprise 2 to 9 carbon atoms (for example, 2 to 6 carbon atoms, 2 to 4 carbon atoms, or 2 carbon atoms).

[0160] As used herein, "alkoxy" means an alkyl-O— group in which the alkyl group is as described herein. Exemplary alkoxy groups include methoxy, ethoxy, n-propoxy, i-propoxy, n-butoxy, s-butoxy, t-butoxy, pentoxy, hexoxy and heptoxy, and also the linear or branched positional isomers thereof.

[0161] As used herein, "haloalkoxy" means a haloalkyl-O— group in which the haloalkyl group is as described herein. Exemplary haloalkoxy groups include fluoromethoxy, difluoromethoxy, trifluoromethoxy, and also the linear or branched positional isomers thereof.

[0162] 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 none of the rings in the ring system are 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.

[0163] 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.

[0164] As used herein, "arylalkylene" means an aryl-alkylene-group in which the aryl and alkylene moieties are as previously described. In some embodiments, arylalkylene groups contain a C_{1-4}alkylene moiety. Exemplary arylalkylene groups include benzyl and 2-phenethyl.

[0165] 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, tetrahydroquinoline, 2,3-dihydrobenzo[b][1,4]oxathiine, isoindoline, and others. In some embodiments, the heteroaryl is selected from thienyl, pyridinyl, furyl, pyrazolyl, imidazolyl, isoindolinyl, pyranyl, pyrazinyl, and pyrimidinyl.

[0166] 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.

[0167] 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 fluoroalkyl, wherein one or more of the hydrogen atoms have been substituted by fluoro. In some embodiments, haloalkyls are 1 to 3 carbons in length (e.g., 1 to 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.

[0168] 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 such as bicyclic and spirocyclic heterocyclyls. Heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, heterocycles have 3-11 members. In six membered monocyclic heterocycles, the heteroatom(s) are selected from one to three of O, N and S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, and 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. In some embodiments, the heterocyclyl is selected from azetidinyl, morpholinyl, piperazinyl, pyrrolidinyl, and tetrahydropyridinyl.

[0169] 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 3-7 members. In six membered monocyclic heterocycles, the heteroatom (s) are selected from one to three of O, N and S, and wherein when the heterocycle is five membered, it can have one or two heteroatoms selected from O, N, and S. Examples of monocyclic heterocyclyls 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.

[0170] As used herein, "bicyclic heterocyclyl" means a nonaromatic bicyclic ring system comprising at least one heteroatom in the ring system backbone. Bicyclic heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, bicyclic heterocycles have 4-11 members with the heteroatom(s) being selected from one to five of O, N and S. Examples of bicyclic heterocyclyls include 2-azabicyclo[1.1.0]butane, 2-azabicyclo[2.1.0]pentane, 2-azabicyclo[1.1.1]pentane, 3-azabicyclo[3.1.0]hexane, 5-azabicyclo[2.1.1]hexane, 3-azabicyclo[3.2.0]heptane, octahydrocyclopenta[c]pyrrole, 3-azabicyclo[4.1.0]heptane, 7-azabicyclo[2.2.1]heptane, 6-azabicyclo[3.1.1]heptane, 7-azabicyclo[4.2.0]octane, 2-azabicyclo[2.2.2]octane, and the like.

[0171] As used herein, "spirocyclic heterocyclyl" means a nonaromatic bicyclic ring system comprising at least one heteroatom in the ring system backbone and with the rings connected through just one atom. Spirocyclic heterocyclyls may be substituted or unsubstituted with one or more substituents. In some embodiments, spirocyclic heterocycles have 5-11 members with the heteroatom(s) being selected from one to five of O, N and S. Examples of spirocyclic heterocyclyls include 2-azaspiro[2.2]pentane, 4-azaspiro[2.5]octane, 1-azaspiro[3.5]nonane, 2-azaspiro[3.5]nonane, 7-azaspiro[3.5]nonane, 2-azaspiro[4.4]nonane, 6-azaspiro[2.6]nonane, 1,7-diazaspiro[4.5]decane, 2,5-diazaspiro[3.6]decane, and the like.

[0172] 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} alkoxy) 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 1-3 R'"; 5-10 membered heteroaryl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with 1-3 R'"; C_{3-7} carbocyclyl optionally substituted with 1-3 R'"; and 3-8 membered heterocyclyl having from 1-4 heteroatoms independently selected from N, O, and S and optionally substituted with 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).

[0173] 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.

[0174] The skilled artisan will recognize that some chemical structures described herein may be represented on paper by one or more other resonance forms; or may exist in one or more other tautomeric forms, even when kinetically, the artisan recognizes that such tautomeric forms represent 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 explicitly represented herein.

[0175] 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.

[0176] The present disclosure includes all pharmaceutically acceptable isotopically labeled compounds of Formula I wherein one or more atoms are replaced by atoms having the same atomic number, but an atomic mass or mass number different from the atomic mass or mass number which predominates in nature. Examples of isotopes suitable for inclusion in the compounds of the disclosure include, but are not limited to, isotopes of hydrogen, such as ^{2}H (deuterium) and ^{3}H (tritium), isotopes of carbon, such as ^{11}C, ^{13}C and ^{14}C, isotopes of chlorine, such as ^{36}Cl, isotopes of fluorine, such as ^{18}F, isotopes of iodine, such as ^{123}I and ^{125}I, isotopes of nitrogen, such as ^{13}N and ^{15}N, isotopes of oxygen, such as ^{15}O, ^{17}O and ^{18}O, isotopes of phosphorus, such as ^{32}P, and isotopes of sulfur, such as ^{35}S.

[0177] 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 of administration 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, 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 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.

[0178] 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.

[0179] 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.

[0180] The terms "pharmaceutically acceptable carrier," "pharmaceutically acceptable diluent," and "pharmaceutically acceptable excipient" include 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, NJ. 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.

[0181] 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.

[0182] "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.

[0183] A "therapeutically 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.

[0184] A therapeutic effect relieves, to some extent, one or more of the symptoms of the disease.

[0185] "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.

[0186] "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 overtime into the surrounding body tissue.

[0187] "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.

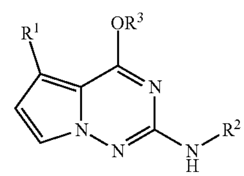
[0188] "Elutable drug" as used herein refers to any drug or combination of drugs having the ability to pass over time from the drug-eluting material in which it is incorporated into the surrounding areas of the body.

[0189] Compounds

[0190] The compounds and compositions described herein can be used to inhibit DYRK1A for treating a disorder or disease in which DYRK1A overexpression is implicated, such as in neurological diseases or disorders, cancers, cognitive deficits, knee osteoarthritis, tendinopathy, viral infections, unicellular parasite infections, and motor deficits.

[0191] Some embodiments of the present disclosure include compounds of Formula I:

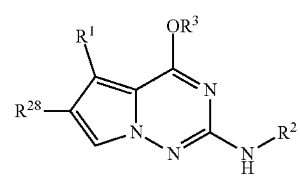
I



or salts, pharmaceutically acceptable salts, or prodrugs thereof.

[0192] Some embodiments of the present disclosure include compounds of Formula I:

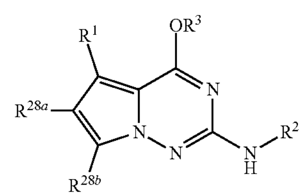
I



or salts, pharmaceutically acceptable salts, or prodrugs thereof.

[0193] Some embodiments of the present disclosure include compounds of Formula I:

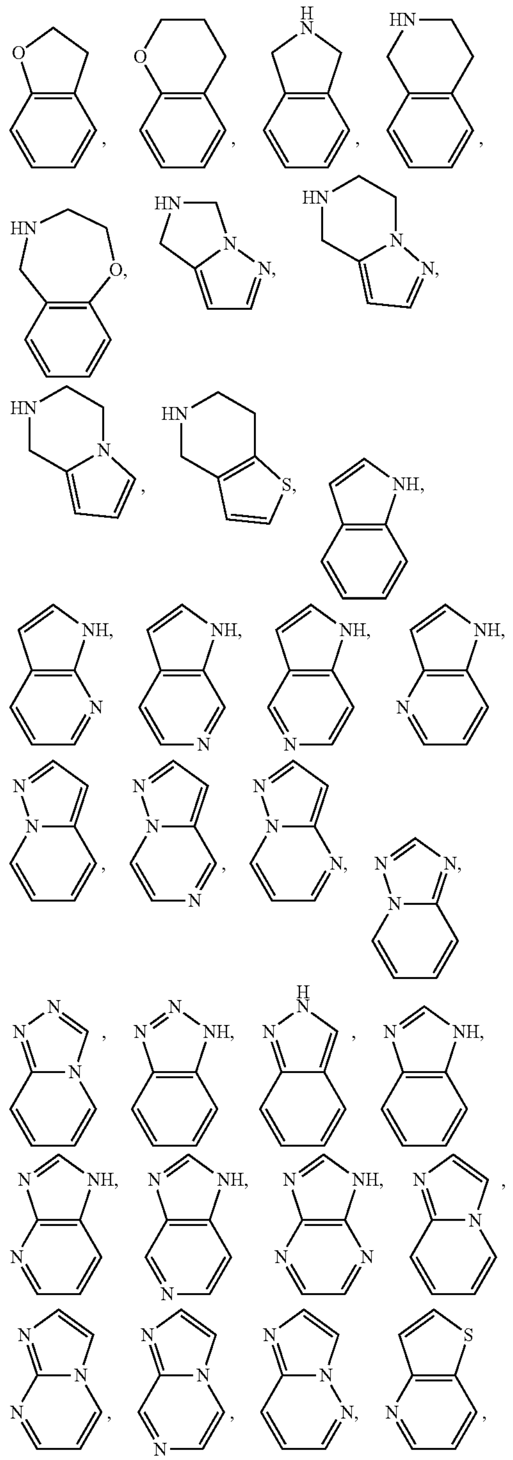
I



or salts, pharmaceutically acceptable salts, or prodrugs thereof.

[0194] In some embodiments of Formula I, R^1 is heteroaryl optionally substituted with 1-10 R^4. In some embodiments, R^1 is heteroaryl optionally substituted with 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, or 1 R^4.

[0195] In some embodiments of Formula I, R^1 is selected from the heteroaryl group consisting of:



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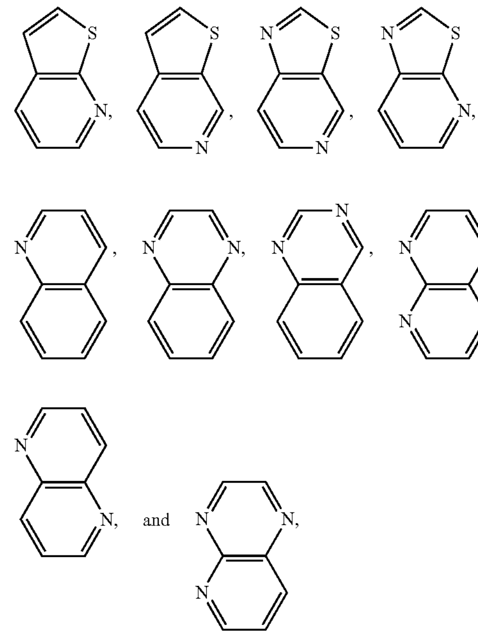
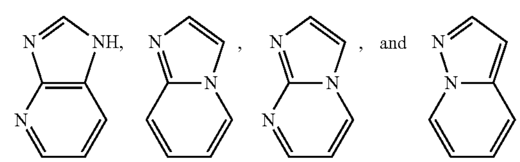


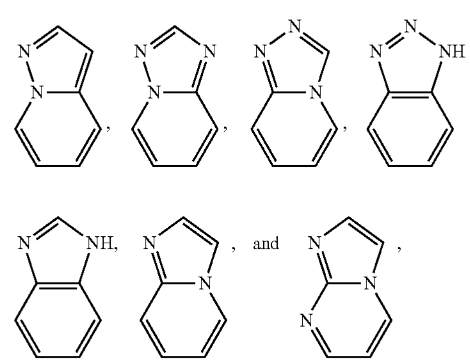
optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6,1-5,1-4, 1-3,1-2, 1) R^4.

[0196] In some embodiments of Formula I, R^1 is selected from the heteroaryl group consisting of:



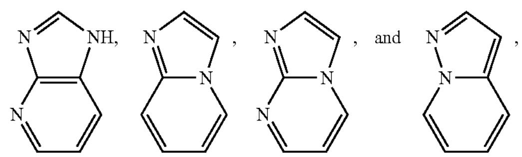
optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^4.

[0197] In some embodiments of Formula I, R^1 is selected from the heteroaryl group consisting of:



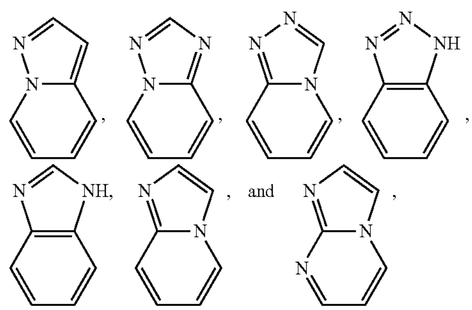
optionally substituted, 1 with 1-1-4, 1-3, 1-2, 1)) R^4.

[0198] In some embodiments of Formula I, R^1 is selected from the heteroaryl group consisting of:



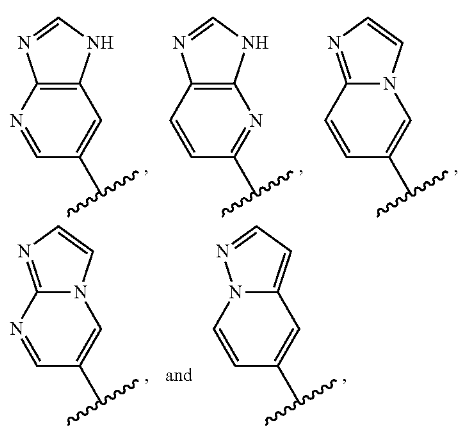
optionally substituted with 1-3 (e.g., 1-2, 1) R^4.

[0199] In some embodiments of Formula I, R^1 is selected from the heteroaryl group consisting of:



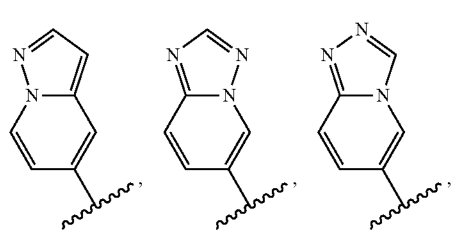
optionally substituted with 1-3 (e.g., 1-2, 1) R^4.

[0200] In some embodiments of Formula I, R^1 is selected from the group consisting of:



optionally substituted with 1-3 R^4.

[0201] In some embodiments of Formula I, R^1 is selected from the group consisting of:



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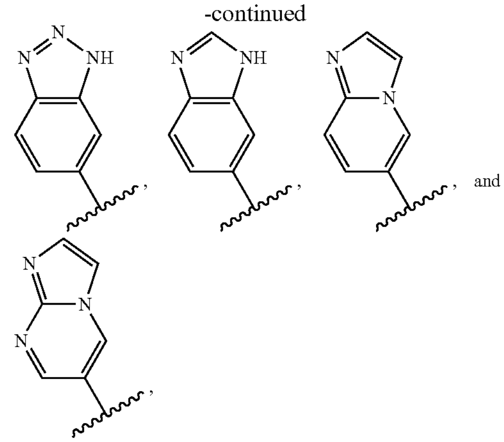
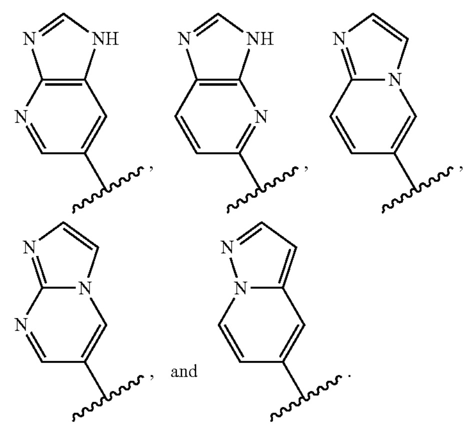


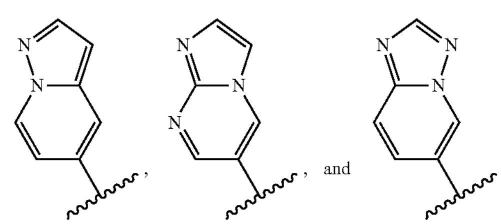
optionally substituted with 1-3 R^4.

[0202] In some embodiments of Formula I, R^1 is selected from the group consisting of:



unsubstituted

[0203] In some embodiments of Formula I, R^1 is selected from the group consisting of: unsubstituted



[0204] In some embodiments of Formula I, R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^6, -heteroaryl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^7, and —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1)R, wherein each

—(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) halide (e.g., F, Cl, Br, I) and/or 1-3 (e.g., 1-2, 1) unsubstituted —(C_{1-3} alkyl).

[0205] In some embodiments of Formula I, R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^6, —(C_{1-5} alkylene)$_p$aryl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{26}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^7, and —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1)R, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide (e.g., F, Cl, Br, I) and/or 1-3 (e.g., 1-2, 1) unsubstituted —(C_{1-3} alkyl).

[0206] In some embodiments of Formula I, R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^5, —(C_{1-5} alkylene)CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^6, —(C_{1-5} alkylene)$_p$aryl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{26}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^7, and —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1)R, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide (e.g., F, Cl, Br, I) and/or 1-3 unsubstituted —(C_{1-3} alkyl).

[0207] In some embodiments of Formula I, R^2 is selected from the group consisting of unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), —(C_{1-2} alkylene)$_p$OR, —(C_{1-2} alkylene)pheterocyclyl optionally substituted with 1-3 (e.g., 1-2, 1) R^6, and —(C_{1-2} alkylene)$_p$carbocyclyl optionally substituted with 1-3 (e.g., 1-2, 1)R, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-2 halide.

[0208] In some embodiments of Formula I, R^2 is selected from the group consisting of unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), -heterocyclyl optionally substituted with 1-4 R^6, —(C_{1-2} alkylene)$_p$aryl optionally substituted with 1-2 R^{26}, —(C_{1-2} alkylene)$_p$heteroaryl optionally substituted with 1-2 R^7, and —(C_{1-2} alkylene)$_p$carbocyclyl optionally substituted with 1-4 R^8, wherein each —(C_{1-2} alkylene) is, independently, optionally substituted with 1-2 halide.

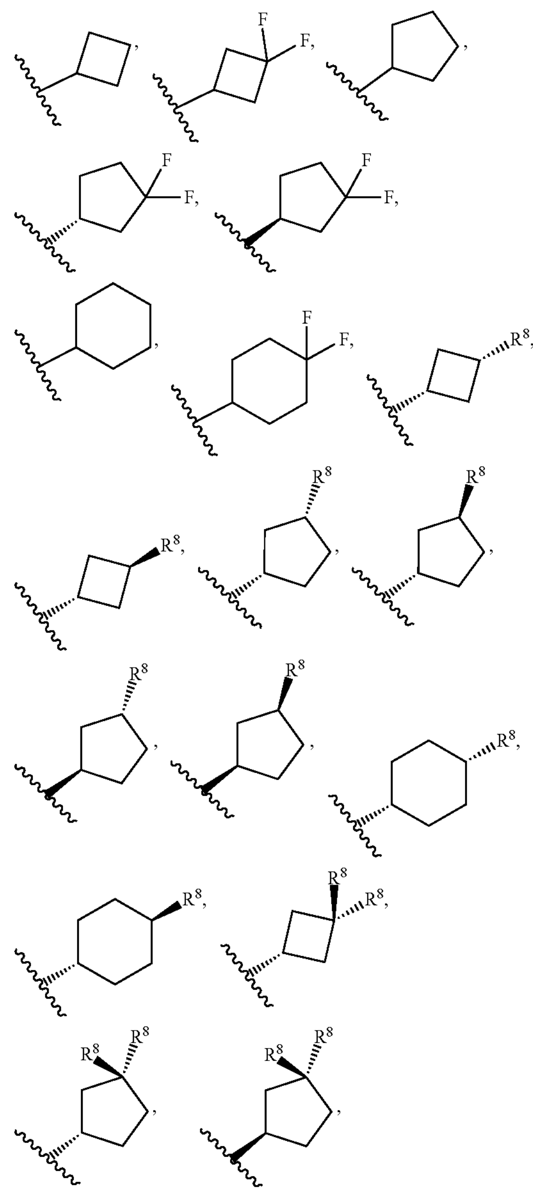
[0209] In some embodiments of Formula I, R^2 is —(C_{1-2} alkylene)$_p$carbocyclyl optionally substituted with 1-3 R, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-2 halide and wherein the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and spiro[3.3]heptanyl.

[0210] In some embodiments of Formula I, R^2 is —(C_{1-2} alkylene)$_p$carbocyclyl optionally substituted with 1-3 R, wherein the —(C_{1-2} alkylene) is optionally substituted with 1-2 halide (e.g., F, Cl) and wherein the carbocyclyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, bicyclo[3.1.0]hexane, bicyclo[2.2.1]heptane, and spiro[3.3]heptanyl.

[0211] In some embodiments of Formula I, R^2 is selected from the group consisting of unsubstituted —(C_{1-4} alkyl), unsubstituted —(C_{2-4} alkenyl), unsubstituted —(C_{2-4} alkynyl), unsubstituted —(C_{1-4} haloalkyl), —(C_{2-4} alkylene)OR, —(C_{2-4} alkylene)CN, —(C_{1-2} alkylene)pheterocyclyl optionally substituted with 1-3 R^6, —(C_{1-2} alkylene)$_p$aryl optionally substituted with 1-2 R^{26}, —(C_{1-2} alkylene)$_p$heteroaryl optionally substituted with 1-2 R^7, and —(C_{1-2} alkylene)$_p$carbocyclyl optionally substituted with 1-3 R, wherein each —(C_{1-2} alkylene) is, independently, optionally substituted with 1-2 halide (e.g., F, Cl).

[0212] In some embodiments of Formula I, R^2 is selected from the group consisting of unsubstituted —(C_{1-5} haloalkyl), —(C_{1-4} alkylene)OH, —(C_{1-4} alkylene)OMe, and —(C_1_4 alkylene)CN.

[0213] In some embodiments of Formula I, R^2 is selected from the group consisting PGP39,C_2 of:



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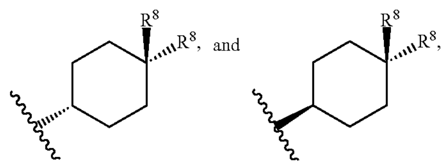
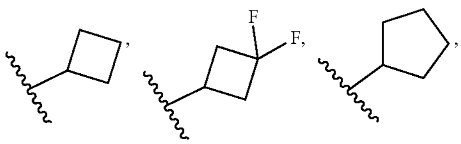
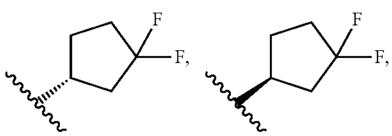
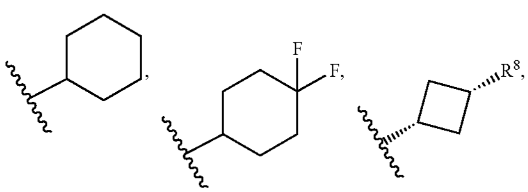


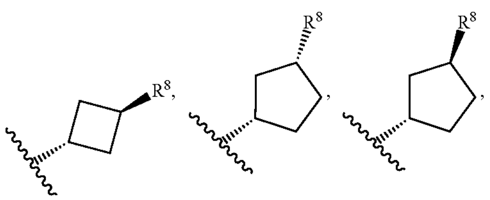
wherein each R^8 is independently selected from the group consisting of F, Me, —CH_2F, —CHF_2, —CF_3, —CH_2OH, —CH_2OMe, —OH, —OMe, -OEt, -OCD_3, —OCF_3, —OCH_2CH_2F, —OCH_2CHF_2, —OCH_2CF_3, —OCH_2CH_2OMe, —OCH_2CH_2OH, —NH_2, —NHMe, and —NMe_2.

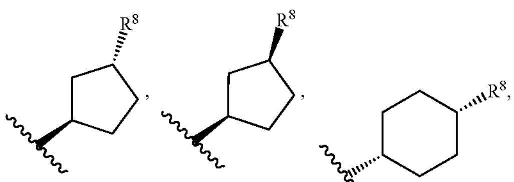
[0214] In some embodiments of Formula I, R^2 is selected from the group consisting of:

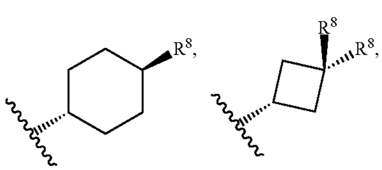












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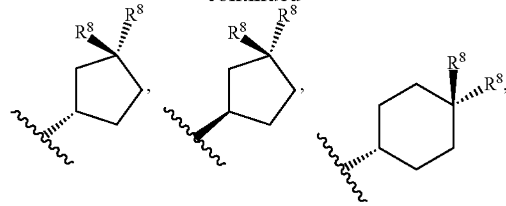
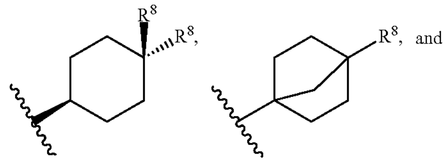
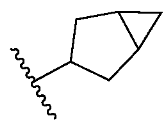
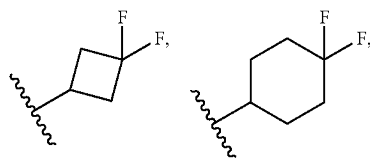


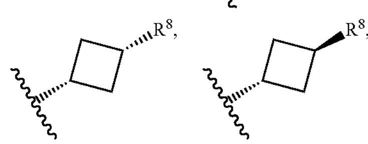


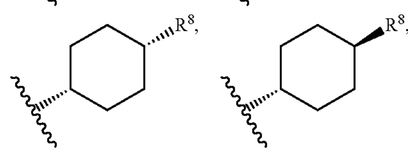


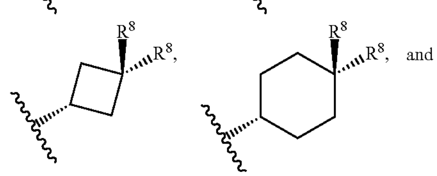
wherein each R^8 is independently selected from the group consisting of F, Me, —CH_2F, —CHF_2, —CF_3, —CH_2OH, —CH_2OMe, —OH, —OMe, —OEt, -OCD_3, —OCF_3, —OCH_2CH_2F, —OCH_2CHF_2, —OCH_2CF_3, —OCH_2CH_2OMe, —OCH_2CH_2OH, —CN, —NH_2, —NHMe, and —NMe_2.

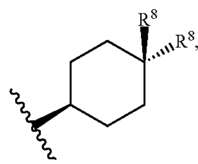
[0215] In some embodiments of Formula I, R^2 is selected from the group consisting of:







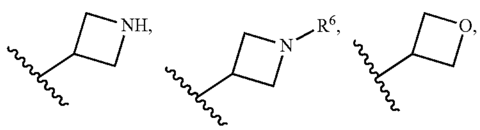
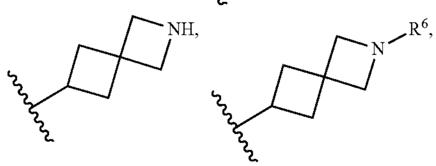
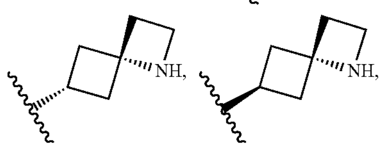
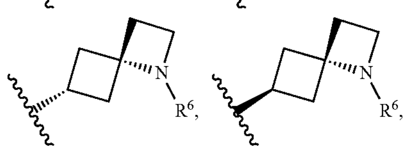
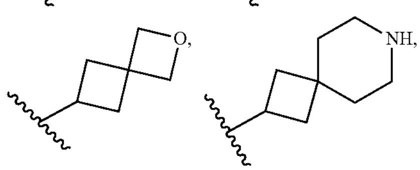
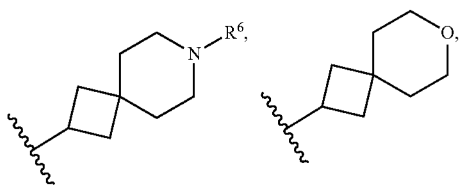
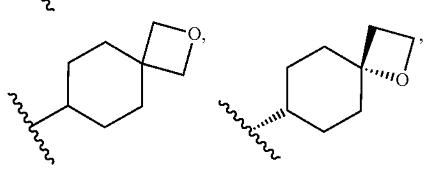
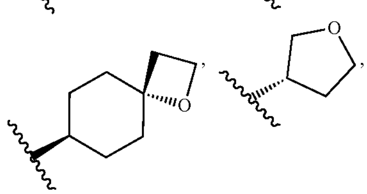
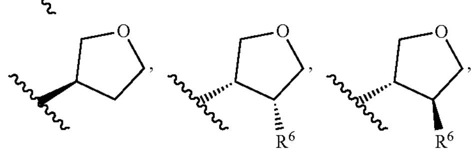




wherein each R^8 is independently selected from the group consisting of F, Me, —CHF_2, —CH_2OMe, —OH, —OMe, -OCD_3, —OCH_2CHF_2, and —OCH_2CH_2OMe.

[0216] In some embodiments of Formula I, R^2 is —(C_{1-2} alkylene)pheterocyclyl optionally substituted with 1-3 R^6, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-2 halide and wherein the heterocyclyl is selected from the group consisting of oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, azetidinyl, pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, oxaspiro[3.3]heptanyl, and oxaspiro[3.3]heptanyl.

[0217] In some embodiments of Formula I, R^2 is selected from the group consisting of:

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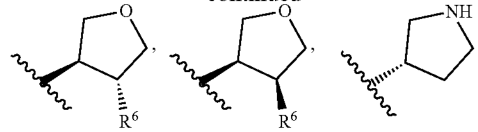
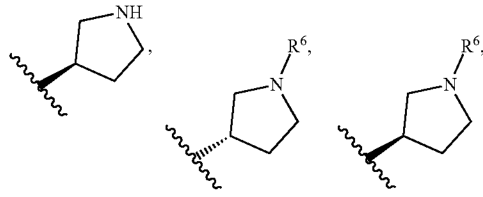
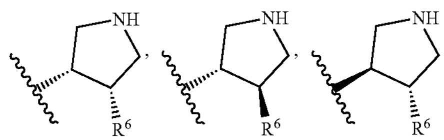
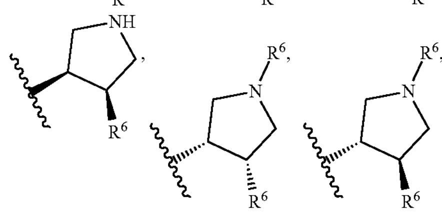
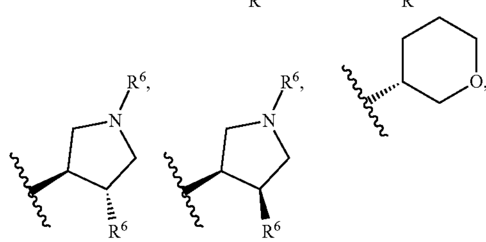
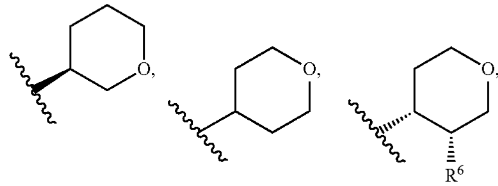
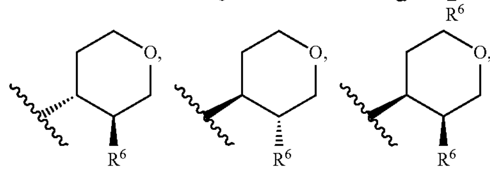
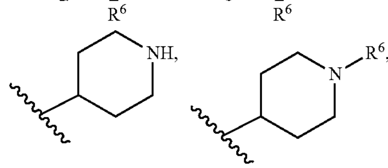
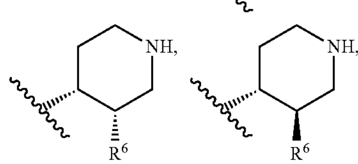
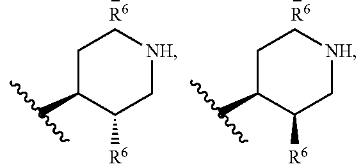

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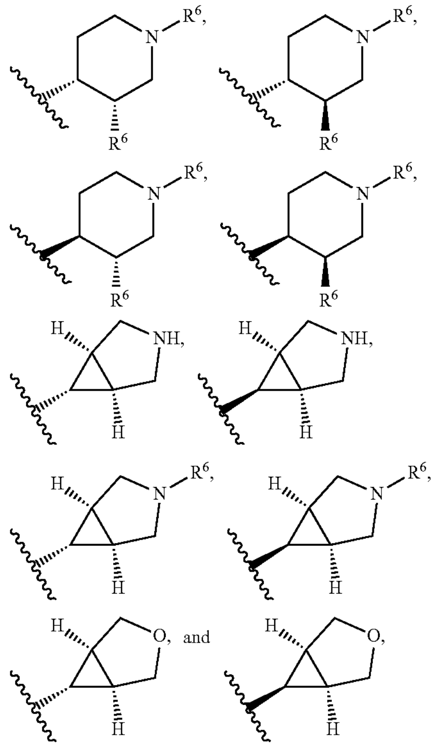
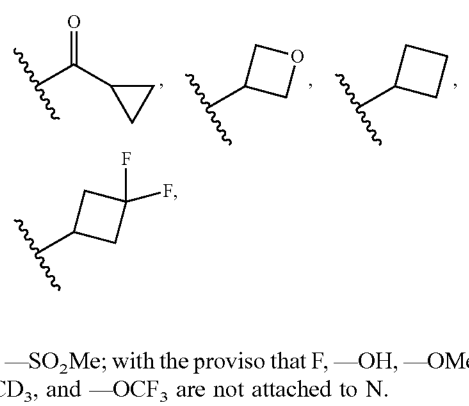
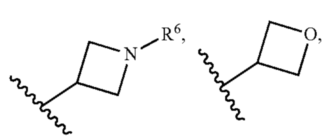


wherein each R^6 is independently selected from the group consisting of F, Me, Et, iPr, iBu, $—CH_2F$, $—CHF_2$, $—CF_3$, $—CH_2OH$, $—CH_2OMe$, —OH, —OMe, -OEt, $-OCD_3$, $—OCF_3$, $—CH_2CH_2F$, $—CH_2CHF_2$, $—CH_2CF_3$, $—CH_2CH_2CF_3$, $—CH_2CH_2OMe$, $—CH_2CH_2OH$, —C(═O)Me, —C(═O)Et, —C(═O)iPr,



and $—SO_2Me$; with the proviso that F, —OH, —OMe, -OEt, $-OCD_3$, and $—OCF_3$ are not attached to N.

[0218] In some embodiments of Formula I, R^2 is selected from the group consisting of:



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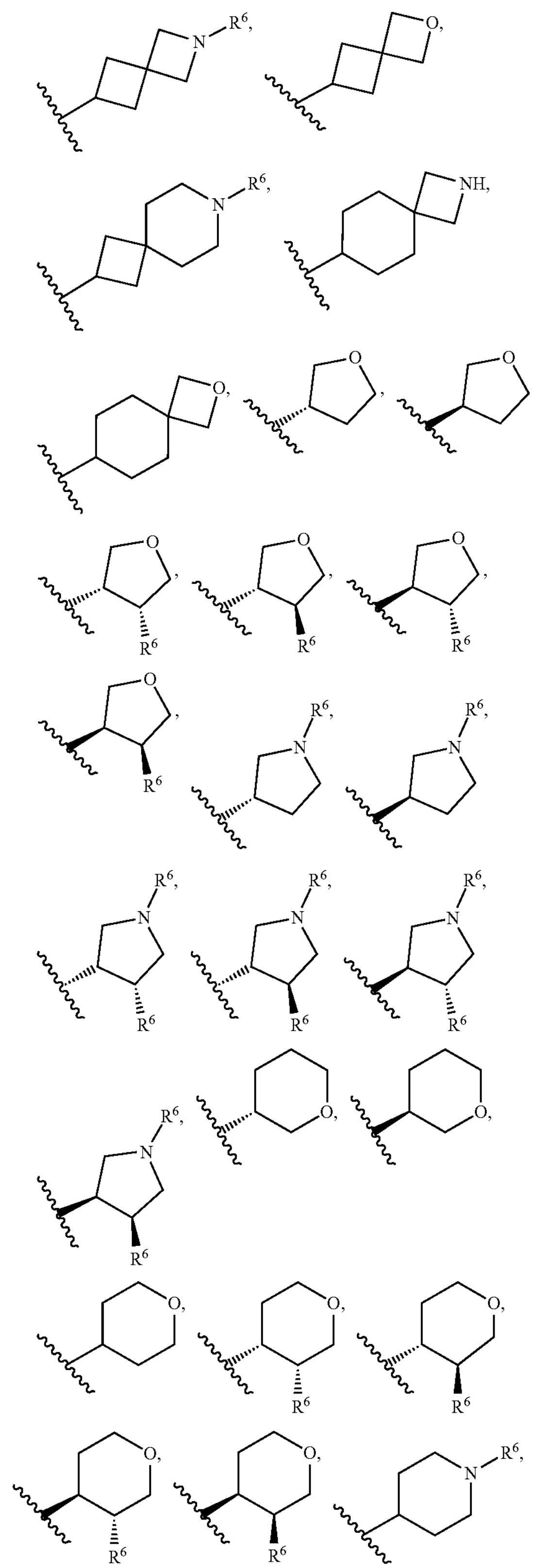

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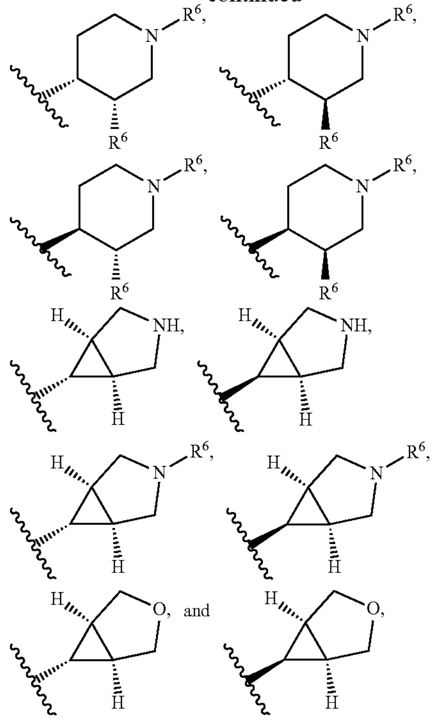

wherein each R^6 is independently selected from the group consisting of F, Me, iBu, —OH, —OMe, —CH_2CH_2F, —CH_2CHF_2, —CH_2CF_3, —$CH_2CH_2CF_3$, —CH_2CH_2OMe, —CH_2CH_2OH, —C(═O)Me, —C(═O)Et, and —C(═O)iPr; with the proviso that F, —OH, —OMe are not attached to N.

[0219] In some embodiments of Formula I, R^2 is -heteroaryl optionally substituted with 1-2 R^7, wherein the heteroaryl is pyrazolyl.

[0220] In some embodiments of Formula I, R^2 is —(C_{1-2} alkylene)heteroaryl optionally substituted with 1-2 R^7, wherein the heteroaryl is pyridine.

[0221] In some embodiments of Formula I, R^2 is —(C_{1-2} alkylene)aryl optionally substituted with 1-2 R^7, wherein the aryl is phenyl.

[0222] In some embodiments of Formula I, R^3 is selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0223] In some embodiments of Formula I, R^3 is selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and -heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{18}.

[0224] In some embodiments of Formula I, R^3 is selected from the group consisting of H, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{2-5} alkenyl), unsubstituted —(C_{2-5} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0225] In some embodiments of Formula I, R^3 is selected from the group consisting of unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), and -heterocyclyl optionally substituted with 1-2 R^{18}.

[0226] In some embodiments of Formula I, R^3 is selected from the group consisting of H, unsubstituted —(C_{1-3} alkyl), and unsubstituted —(C_{1-3} haloalkyl).

[0227] In some embodiments of Formula I, R^3 is unsubstituted —(C_{1-3} alkyl).

[0228] In some embodiments of Formula I, R^3 is Me.

[0229] In some embodiments of Formula I, R^3 is unsubstituted —(C_{1-3} haloalkyl).

[0230] In some embodiments of Formula I, R^3 is selected from the group consisting of —CH_2F, —CHF_2, —CF_3, —CH_2CH_2F, —CH_2CHF_2, and —CH_2CF_3.

[0231] In some embodiments of Formula I, R^3 is an unsubstituted -heterocyclyl.

[0232] In some embodiments of Formula I, R^3 is an unsubstituted -(3-4 membered heterocyclyl).

[0233] In some embodiments of Formula I, R^3 is an unsubstituted -(4 membered heterocyclyl).

[0234] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^9, —(C_{1-5}alkylene)CN, —(C_{1-5} alkylene)$_p$heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{10}, -carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{11}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{20}, —(C_{1-5} alkylene)$_p$C(═O)N(R^{12})$_2$, and —C(═O)R^{13}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) halide (e.g., F, Cl, Br, I) and/or 1-3 (e.g., 1-2, 1) unsubstituted —(C_{1-3} alkyl).

[0235] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{2-5} alkenyl), unsubstituted —(C_{2-5} alkynyl), unsubstituted —(C_{1-5} haloalkyl), —(C_{1-4} alkylene)$_p$OR^9, —(C_{1-2} alkylene)$_p$OR^9, —(C_{1-4} alkylene)CN, —(C_{1-2} alkylene)CN, —(C_{1-2} alkylene)$_p$heterocyclyl optionally substituted with 1-2 R^{10}, -carbocyclyl optionally substituted with 1-2 R^{11}, —(C_{1-2} alkylene)$_p$heteroaryl optionally substituted with 1-2 R^{20}, —(C_{1-2} alkylene)$_p$C(═O)N(R^{12})$_2$, and —C(═O)R^{13}, wherein each —(C_{1-2} alkylene) or —(C_{1-4} alkylene) is, independently, optionally substituted with 1-2 halide.

[0236] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), unsubstituted —(C_{2-9} haloalkenyl), —(C_{1-5} alkylene)$_p$OR^9, —(C_{1-5} alkylene)$_p$CN, —(C_{1-5} alkylene)$_p$heterocyclyl optionally substituted with 1-10 R^{10}, -carbocyclyl optionally substituted with 1-12 R^{11}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^{20}, —(C_{1-5} alkylene)$_p$C(═O)N(R^{12})$_2$, and —C(═O)R^{13}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl).

[0237] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of halide (e.g., F, Cl), unsubstituted —(C_{1-4} alkyl), unsubstituted —(C_{2-4} alkenyl), unsubstituted —(C_{2-4} alkynyl), unsubstituted —(C_{1-4} haloalkyl), unsubstituted —(C_{2-4} haloalkenyl), —(C_{1-4} alkylene)$_p$OR^9, —(C_{1-2} alkylene)OR^9, —(C_{1-4} alkylene)CN, —(C_{1-2} alkylene)CN, —(C_{1-2} alkylene)pheterocyclyl optionally substituted with 1-2 R^{10}, -carbocyclyl optionally substituted with 1-2 R^{11}, —(C_{1-2} alkylene)$_p$heteroaryl optionally substituted with 1-2 R^{20}, —(C_{1-2} alkylene)$_p$C(═O)N(R^{12})$_2$, and —C(═O)R^{13}, wherein each —(C_{1-2} alkylene) or —(C_{1-4} alkylene) is, independently, optionally substituted with 1-2 halide (e.g., F, Cl).

[0238] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of F, Cl, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), —(C_{1-4} alkylene)pOH, —(C_{1-2} alkylene)$_p$OMe, —(C_{1-4} alkylene)CN, —(C_{1-2} alkylene)CN, —(CH_2)pheterocyclyl optionally substituted with 1-2 R^{10}, -carbocyclyl optionally substituted with 1-2 R^{11}, —(CH_2)$_p$heteroaryl optionally substituted with 1-2 R^{20}, —(CH_2)C(═O)N(Me)$_2$, and —C(═O)R^{13}, wherein each —(C_{1-2} alkylene) or —(C_{1-4} alkylene) is, independently, optionally substituted with 1-2 halide.

[0239] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-4} alkyl), unsubstituted —(C_{1-4} haloalkyl), -heterocyclyl optionally substituted with 1-3 (e.g., 1-2, 1) R^{10}, and -carbocyclyl optionally substituted with 1-3 (e.g., 1-2, 1) R^{11}.

[0240] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-3} alkyl), unsubstituted —(C_{1-3} haloalkyl), —(C_{1-3} alkylene)$_p$OR^9, -heterocyclyl optionally substituted with 1-2 R^{10}, -carbocyclyl optionally substituted with 1-2 R^{11}, and —C(═O)R^{13}.

[0241] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-3} alkyl), unsubstituted —(C_{1-3} haloalkyl), —(C_{1-3} alkylene)OH, —(C_{1-3} alkylene)OMe, —CN, and —C(═O)N(R^{12})$_2$.

[0242] In some embodiments of Formula I, each R^4 is independently selected from the group consisting of chloro, methyl, ethyl, isopropyl, 2-fluoroethyl, 2,2-difluoroethyl, methoxy, methoxymethyl, tetrahydropyranyl, difluorocyclobutyl, and (pyrrolidin-1-yl)methanone.

[0243] In some embodiments of Formula I, each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0244] In some embodiments of Formula I, each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{2-5} alkenyl), unsubstituted —(C_{2-5} alkynyl), and unsubstituted —(C_{1-5} haloalkyl).

[0245] In some embodiments of Formula I, each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-3} alkyl), and unsubstituted —(C_{1-3} haloalkyl).

[0246] In some embodiments of Formula I, each R^6 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), -heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{16}, —(C_{1-5} alkylene)$_p$OR^{21}, —SO$_2$$R^{23}$, and —C(═O)$R^{24}$, wherein the —($C_{1-5}$ alkylene) is optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) halide (e.g., F, Cl, Br, I) and/or 1-3 (e.g., 1-2, 1) unsubstituted —(C_{1-3} alkyl).

[0247] In some embodiments of Formula I, each R^6 is independently selected from the group consisting of each R^6 is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), -heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{16}, -carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{17},—(C_{1-5} alkylene)$_p$OR^{21}, —SO$_2$$R^{23}$, and —C(═O)$R^{24}$, wherein the —($C_{1-5}$ alkylene) is optionally substituted with 1-5 halide (e.g., F, Cl, Br, I) and/or 1-3 (e.g., 1-2, 1) unsubstituted —(C_{1-3} alkyl).

[0248] In some embodiments of Formula I, each R^6 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), -heterocyclyl optionally substituted with 1-10 R^{16}, -carbocyclyl optionally substituted with 1-12 R^{17}, —(C_{1-5} alkylene)$_p$OR^{21}, —(C_1-s alkylene)CN, —SO$_2$$R^{23}$, and —C(═O)$R^{24}$, wherein the —($C_{1-5}$ alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl).

[0249] In some embodiments of Formula I, each R^6 is independently selected from the group consisting of F, Cl, unsubstituted —(C_{1-4} alkyl), unsubstituted —(C_{1-4} haloalkyl), -heterocyclyl optionally substituted with 1-2 R^{16}, —(C_{1-2} alkylene)$_p$OR^{21}, —(C_{1-2} alkylene)CN, —SO$_2$$R^{23}$, and —C(═O)$R^{24}$, wherein the —($C_{1-2}$ alkylene) is optionally substituted with 1-2 halide (e.g., F, Cl).

[0250] In some embodiments of Formula I, each R^6 is independently selected from the group consisting of F, Cl, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), -heterocyclyl optionally substituted with 1-2 R^{16}, —(C_{1-2} alkylene)$_p$OR^{21}, —SO$_2$$R^{23}$, and —C(═O)$R^{24}$, wherein the —($C_{1-2}$ alkylene) is optionally substituted with 1-2 halide.

[0251] In some embodiments of Formula I, each R^6 is independently selected from the group consisting of F, Cl, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), -heterocyclyl optionally substituted with 1-2 R^{16}, —OH, —OMe, —SO$_2$Me, and —C(═O)R^{24}.

[0252] In some embodiments of Formula I, each R^6 is independently selected from the group consisting of each R^6 is independently selected from the group consisting of F, Cl, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), -heterocyclyl optionally substituted with 1-2 R^{16}, -carbocyclyl optionally substituted with 1-4 R^{11}, and —C(═O)R^{24}.

[0253] In some embodiments of Formula I, two R^6 attached to the same carbon atom are taken together to form a carbonyl group.

[0254] In some embodiments of Formula I, each R^7 is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —OMe.

[0255] In some embodiments of Formula I, each R^7 is independently selected from the group consisting of F, Cl, Me, CF_3, and —OMe.

[0256] In some embodiments of Formula I, each R^8 is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —N(R^{14})$_2$, —(C_{1-5} alkylene)$_p$OR^{15}, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{16}, —C(═O)R^{22}, and —NHC(═O)R^{23}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) halide (e.g., F, Cl, Br, I) and/or 1-3 (e.g., 1-2, 1) unsubstituted —(C_{1-3} alkyl).

[0257] In some embodiments of Formula I, each R^8 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —N(R^{14})$_2$, —(C_{1-5} alkylene)$_p$OR^5, —CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{16}, —C(═O)R^{22}, and —NR^{14}C(═O)R^{23}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl).

[0258] In some embodiments of Formula I, each R^8 is independently selected from the group consisting of halide (e.g., F, Cl), unsubstituted —(C_{1-4} alkyl), unsubstituted —(C_{2-4} alkenyl), unsubstituted —(C_{2-4} alkynyl), unsubstituted —(C_{1-4} haloalkyl), —N(R^{14})$_2$, —(C_{1-2} alkylene)$_p$OR^5, —CN, —(C_{1-2} alkylene)pheterocyclyl optionally substituted with 1-2 R^{16}, —C(═O)R^{22}, and —NHC(═O)R^{23}, wherein each —(C_{1-2} alkylene) is, independently, optionally substituted with 1-2 halide (e.g., F, Cl).

[0259] In some embodiments of Formula I, each R^8 is independently selected from the group consisting of halide, unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{2-5} alkenyl), unsubstituted —(C_{2-5} alkynyl), unsubstituted —(C_{1-5} haloalkyl), —N(R^{14})$_2$, —(C_{1-2} alkylene)$_p$OR^5, —(C_{1-2} alkylene)$_p$heterocyclyl optionally substituted with 1-2 R^{16}, —C(═O)R^{22}, and —NHC(═O)R^{23}, wherein each —(C_{1-2} alkylene) is, independently, optionally substituted with 1-2 halide.

[0260] In some embodiments of Formula I, each R^9 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0261] In some embodiments of Formula I, each R^{10} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0262] In some embodiments of Formula I, each R^{11} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0263] In some embodiments of Formula I, each R^{12} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{17}, -heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{18}, and -heteroaryl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{19}, wherein —(C_{1-5} alkylene) is optionally substituted with 1-5 (e.g., 1-4, 1-3, 1-2, 1) halide (e.g., F, Cl, Br, I) and/or 1-3 (e.g., 1-2, 1) unsubstituted —(C_{1-3} alkyl).

[0264] In some embodiments of Formula I, each R^{13} is -heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{18}.

[0265] In some embodiments of Formula I, each R^{14} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0266] In some embodiments of Formula I, each R^{15} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —(C_{1-5} alkylene)$_p$OR^{21}.

[0267] In some embodiments of Formula I, each R^{16} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0268] In some embodiments of Formula I, each R^{16} is independently selected from the group consisting of halide, —CN, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and -carbocyclyl optionally substituted with 1-12 R^{27}.

[0269] In some embodiments of Formula I, two R^{16} attached to the same carbon atom are taken together to form a carbonyl group.

[0270] In some embodiments of Formula I, each R^{17} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), —OMe, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0271] In some embodiments of Formula I, each R^{18} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0272] In some embodiments of Formula I, each R^{19} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0273] In some embodiments of Formula I, each R^{20} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0274] In some embodiments of Formula I, each R^{21} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0275] In some embodiments of Formula I, each R^{22} is independently selected from the group consisting of-heterocyclyl optionally substituted with 1-10 (e.g., 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{18}, —N(R^{12})$_2$ and —OR^{21}.

[0276] In some embodiments of Formula I, each R^{23} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0277] In some embodiments of Formula I, each R^{23} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^{21}, and -carbocyclyl optionally substituted with 1-12 R^{25}.

[0278] In some embodiments of Formula I, each R^{24} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —OR^{23}, and -carbocyclyl optionally substituted with 1-12 (e.g., 1-11, 1-10, 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, 1-3, 1-2, 1) R^{25}.

[0279] In some embodiments of Formula I, each R^{25} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0280] In some embodiments of Formula I, each R^{26} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0281] In some embodiments of Formula I, each R^{27} is independently selected from the group consisting of halide (e.g., F, Cl, Br, I), unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl).

[0282] In some embodiments of Formula I, R^{28} is independently selected from the group consisting of H and halide (e.g., F, Cl, Br, I).

[0283] In some embodiments of Formula I, R^{28} is independently selected from the group consisting of H and halide (e.g., F, Cl).

[0284] In some embodiments of Formula I, R^{28} is independently selected from the group consisting of H and F.

[0285] In some embodiments of Formula I, R^{28a} is independently selected from the group consisting of H and halide (e.g., F, Cl, Br, I).

[0286] In some embodiments of Formula I, R^{28a} is independently selected from the group consisting of H and halide (e.g., F, Cl).

[0287] In some embodiments of Formula I, R^{28a} is independently selected from the group consisting of H and F.

[0288] In some embodiments of Formula I, R^{28b} is independently selected from the group consisting of H and D.

[0289] In some embodiments of Formula I, each p is independently 0 or 1.

[0290] In some embodiments of Formula I, each H atom is optionally, independently replaced by ^{2}H (D) (deuterium).

[0291] Illustrative compounds of Formula I are shown in Table 1.

TABLE 1

1

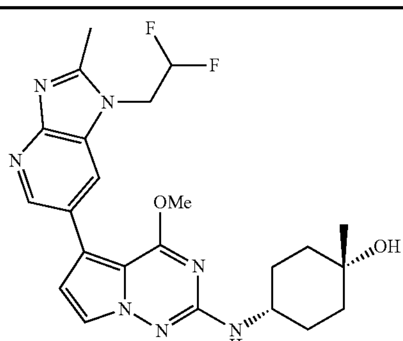

TABLE 1-continued

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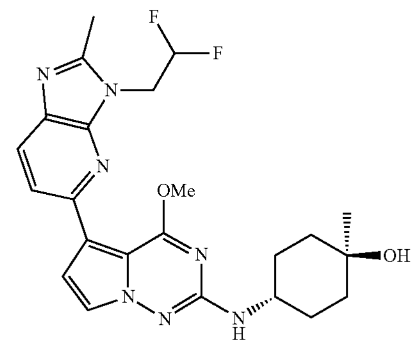

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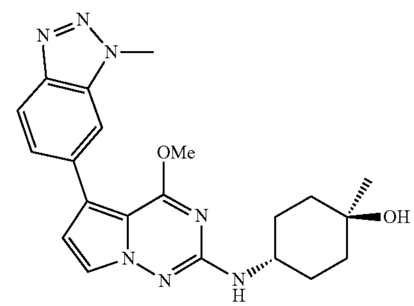

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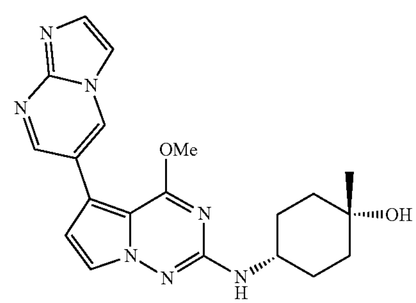

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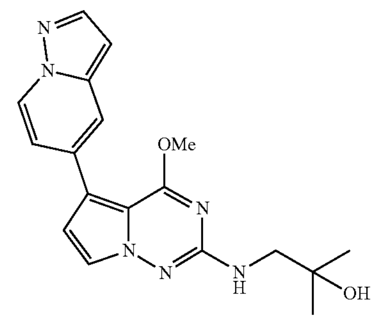

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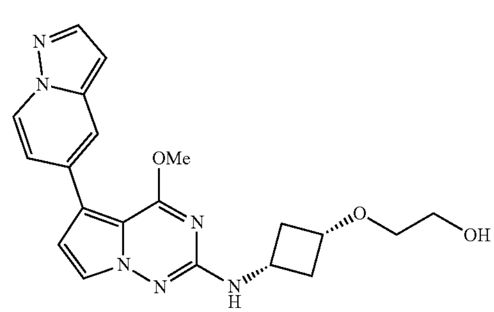

TABLE 1-continued

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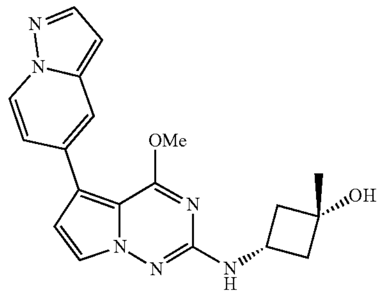

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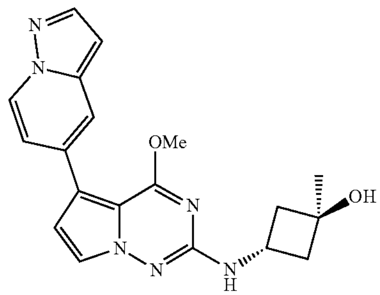

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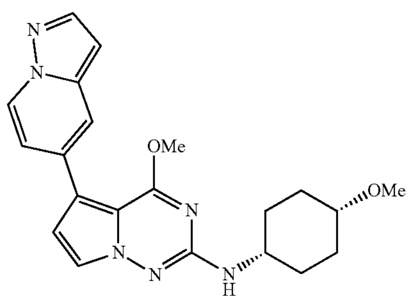

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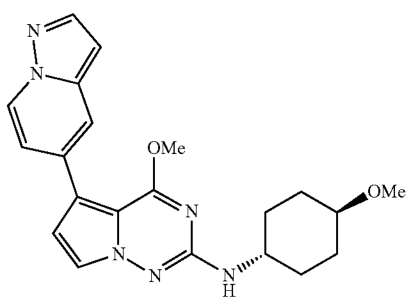

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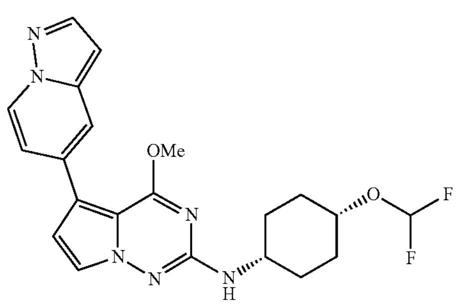

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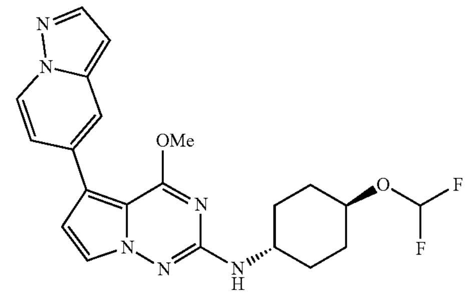

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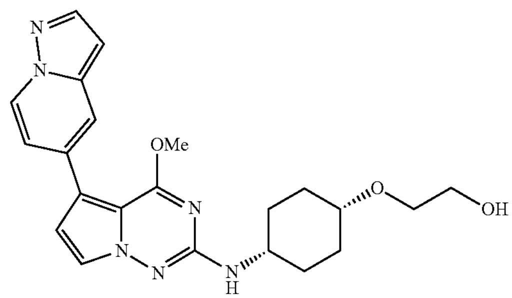

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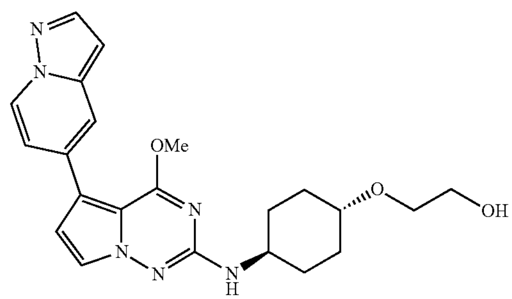

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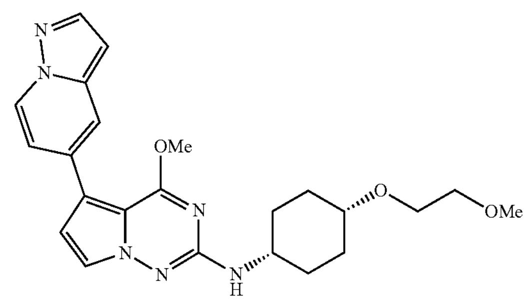

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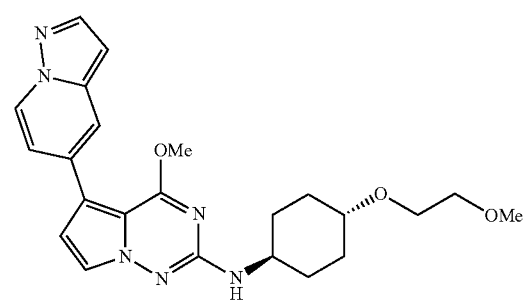

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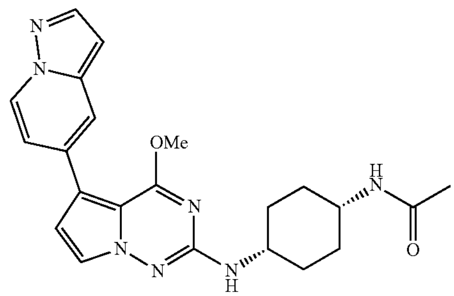

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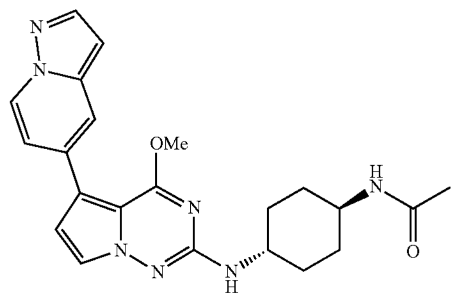

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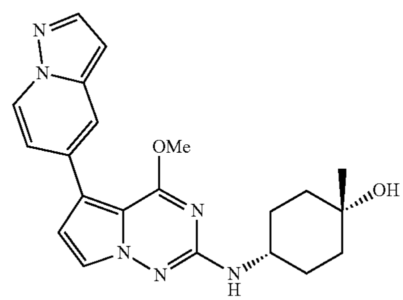

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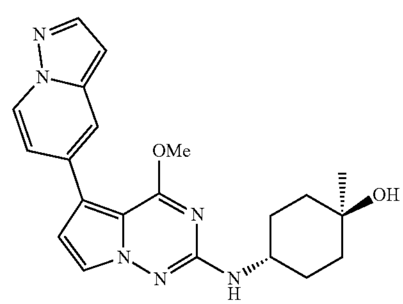

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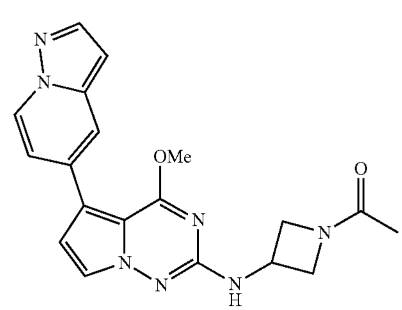

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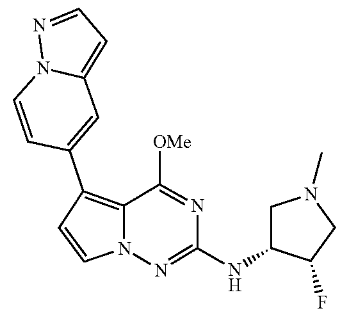

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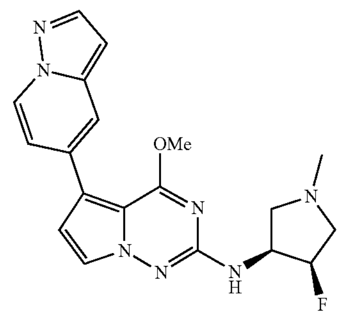

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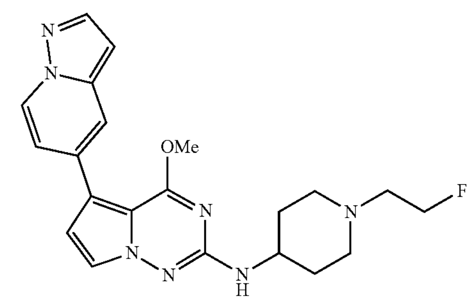

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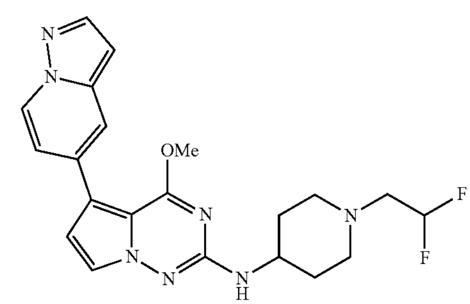

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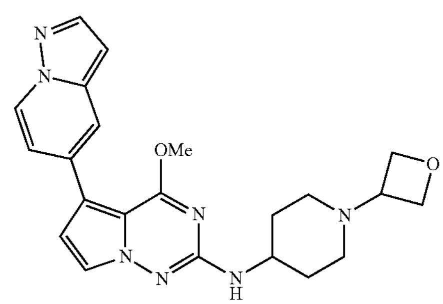

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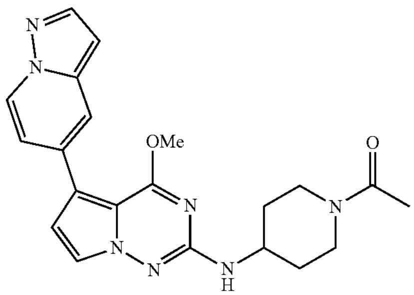
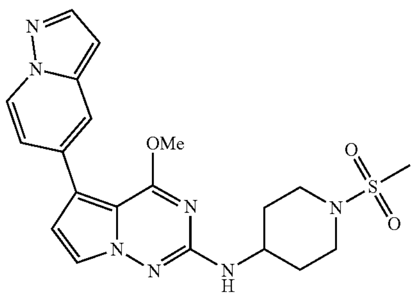
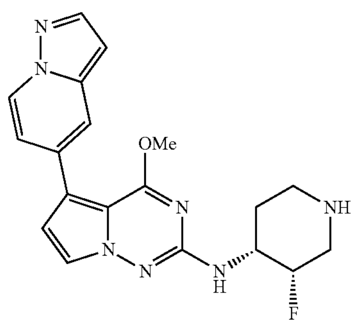
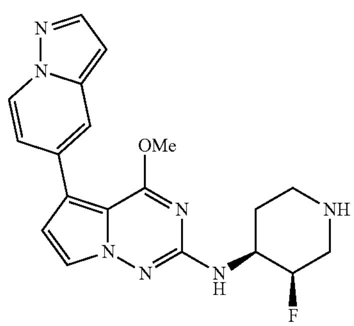
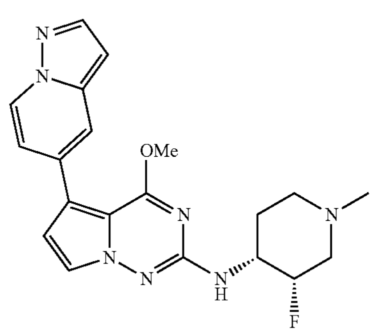
27 

28 

29 

30 

31 

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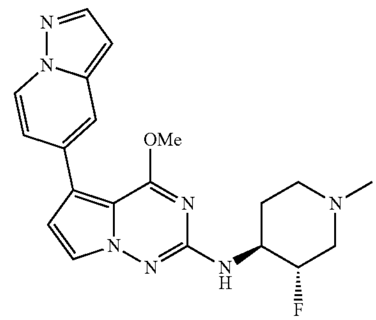
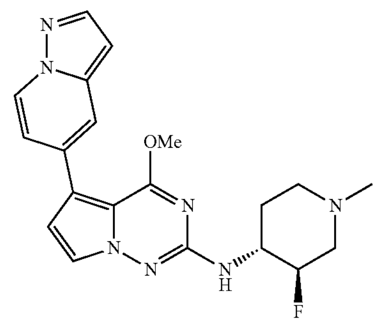
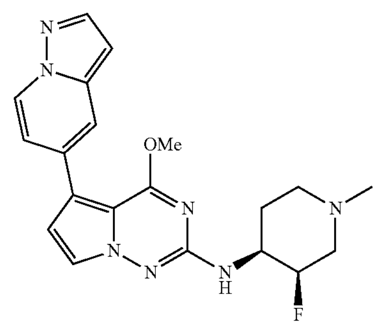
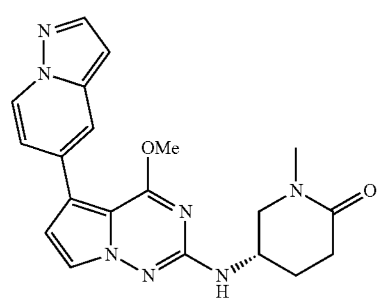
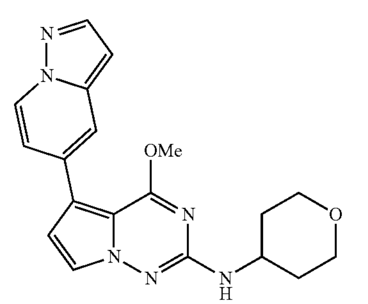
32 

33 

34 

35 

36 

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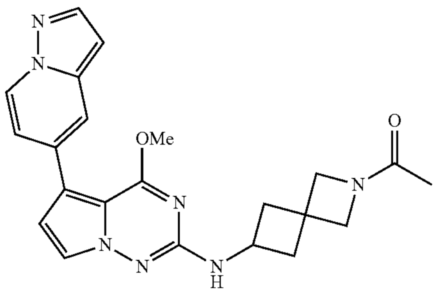

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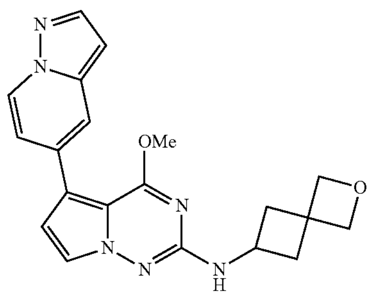

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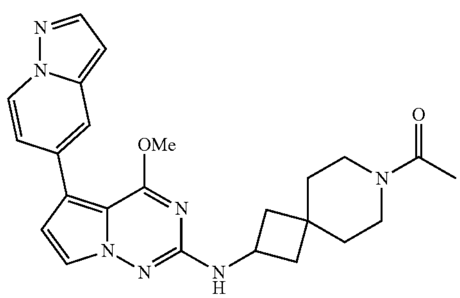

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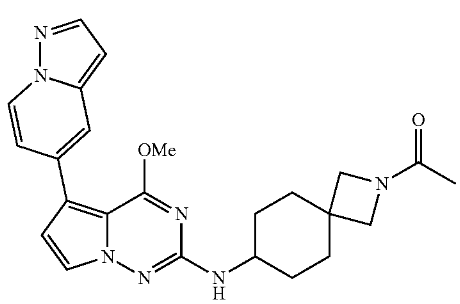

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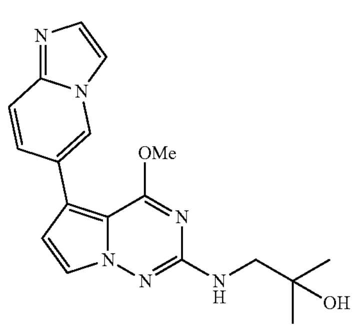

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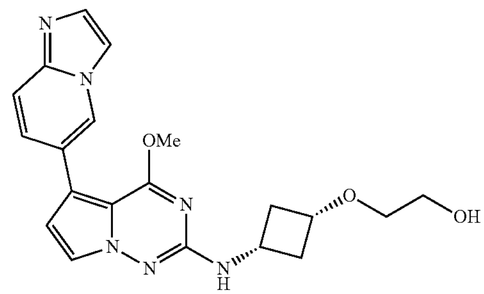

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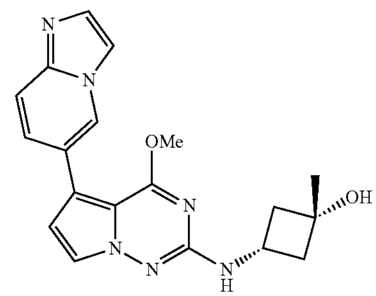

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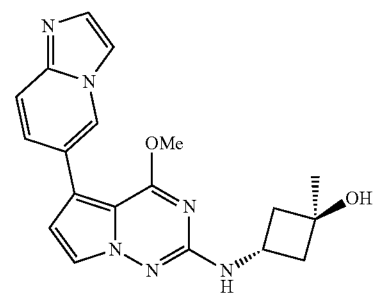

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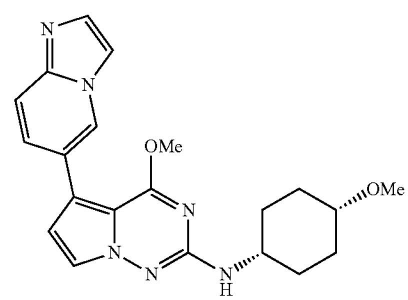

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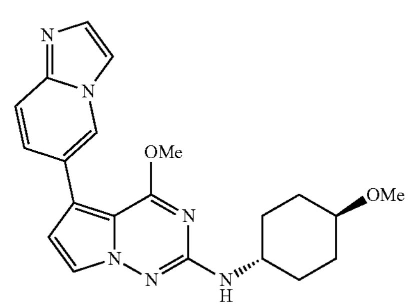

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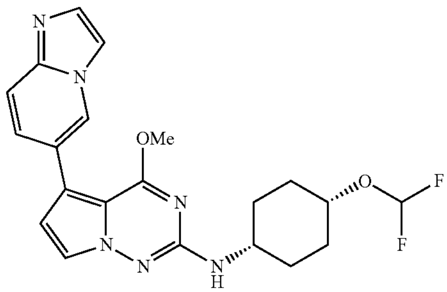

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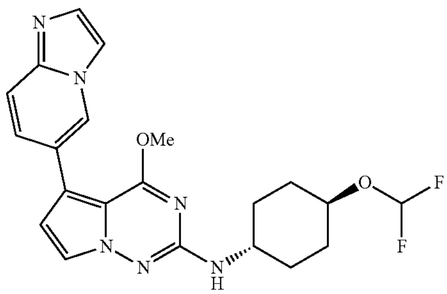

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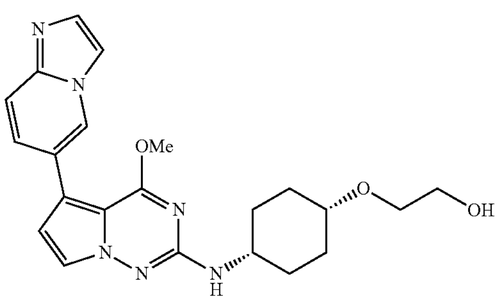

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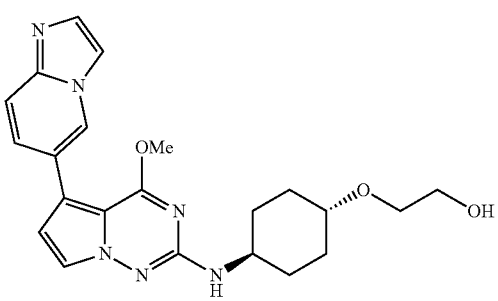

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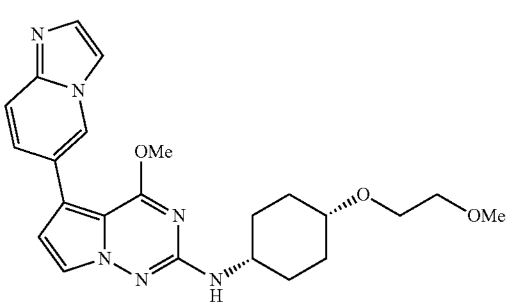

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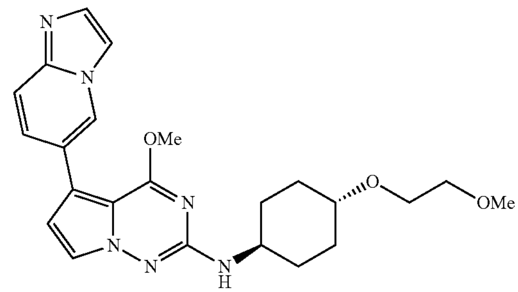

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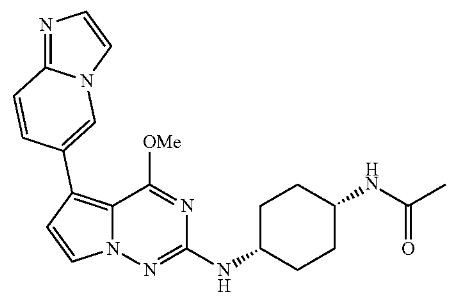

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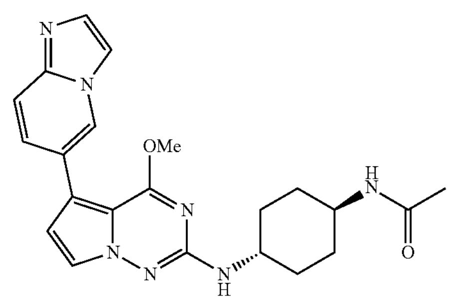

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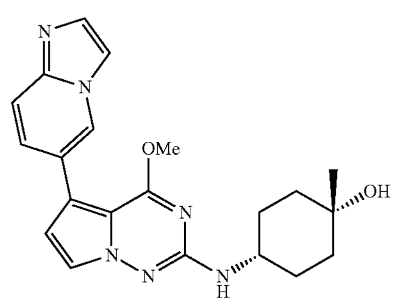

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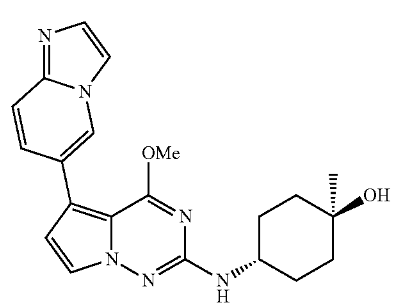

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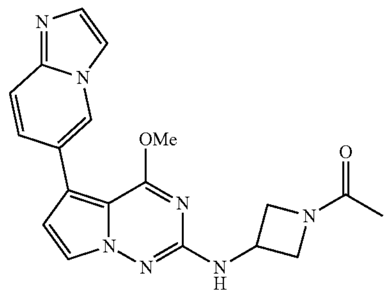

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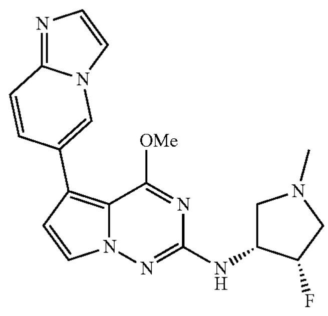

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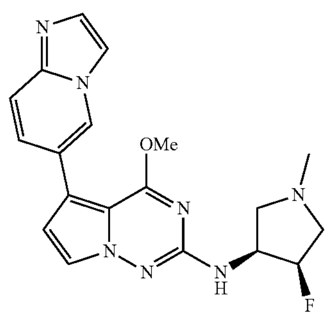

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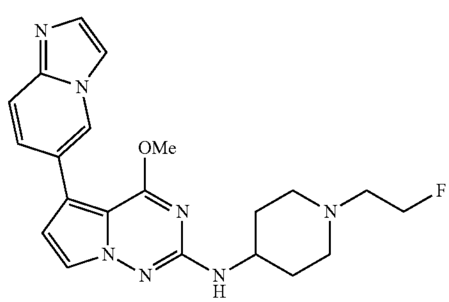

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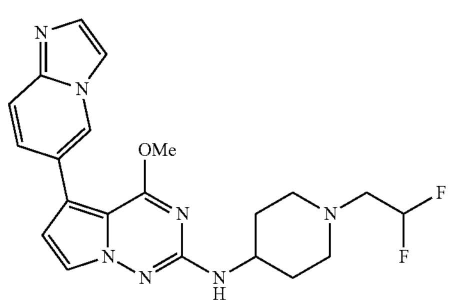

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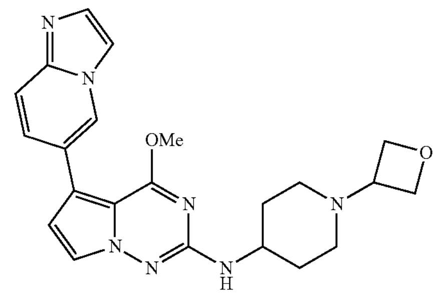

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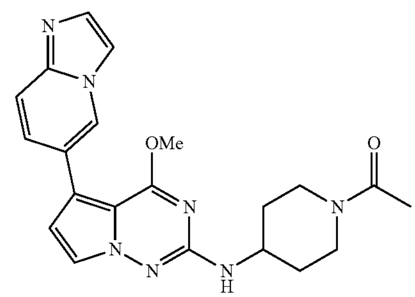

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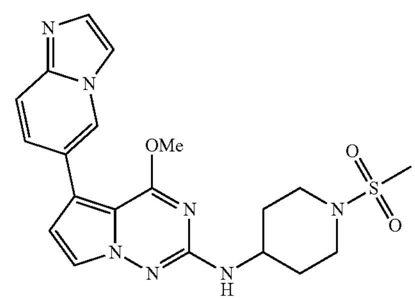

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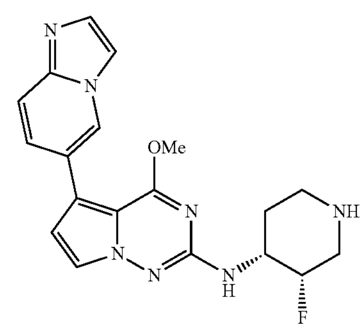

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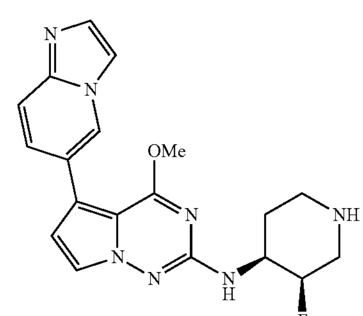

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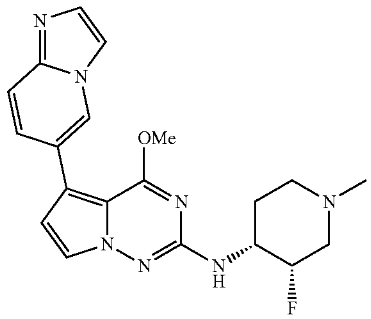

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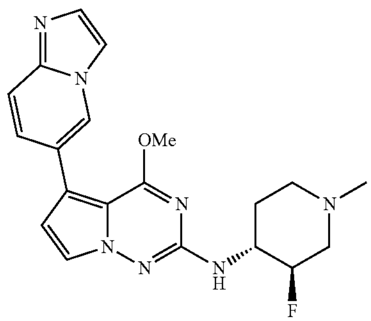

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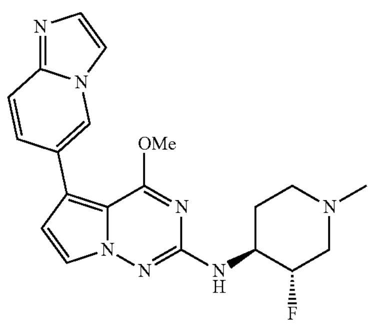

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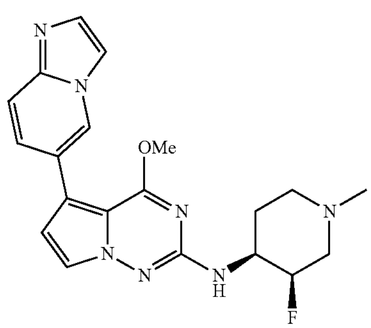

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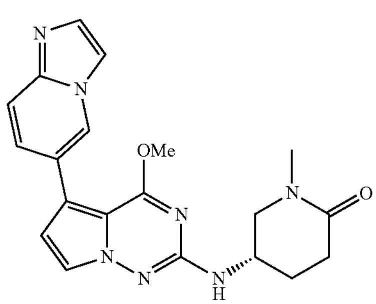

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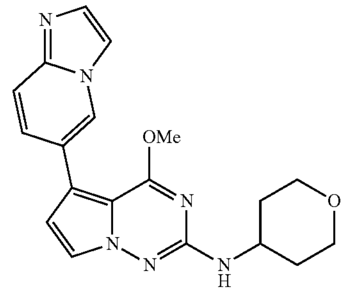

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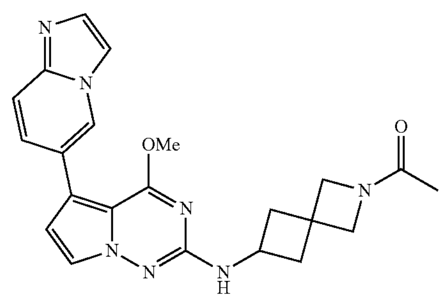

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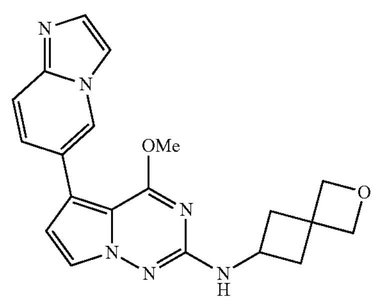

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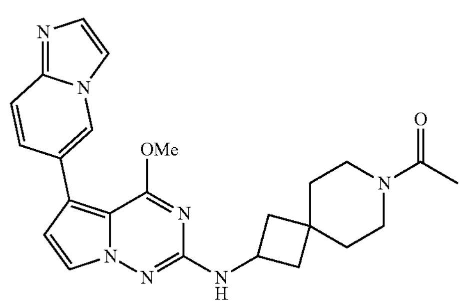

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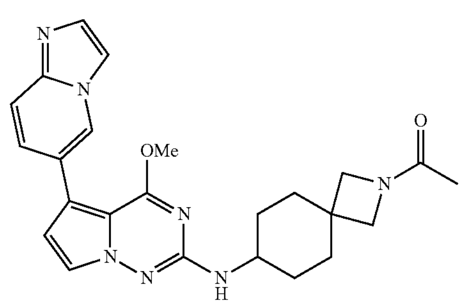

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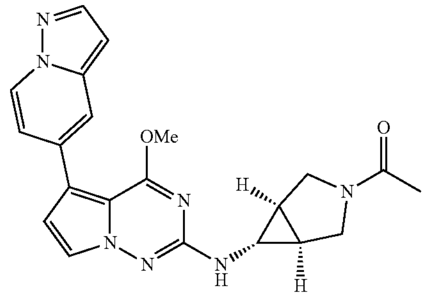

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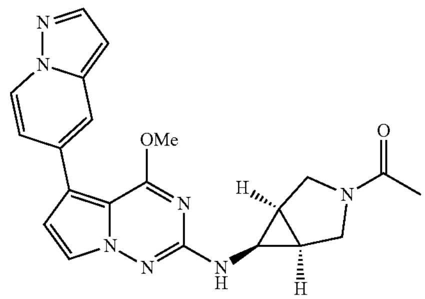

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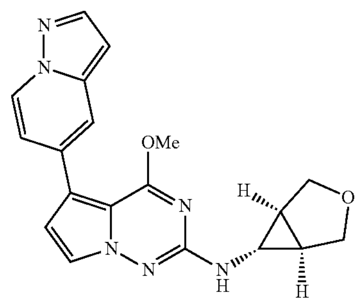

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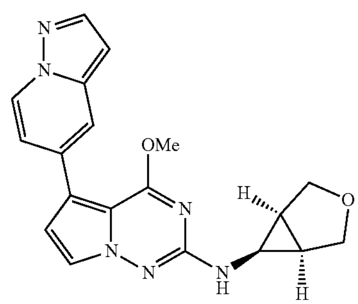

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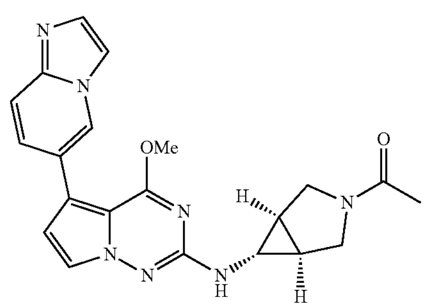

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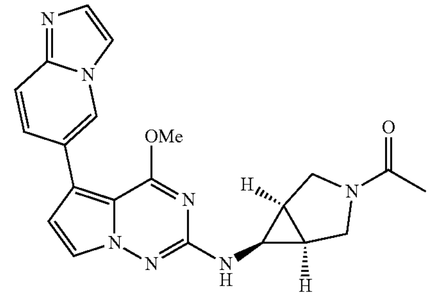

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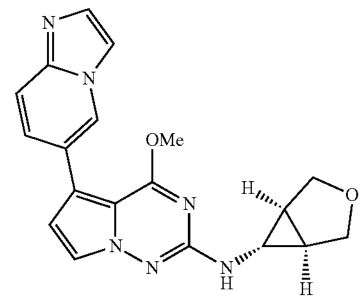

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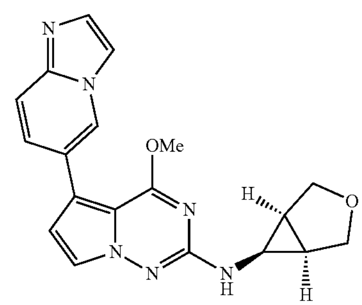

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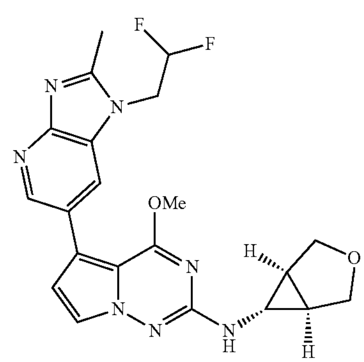

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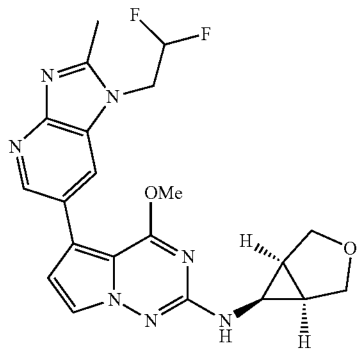

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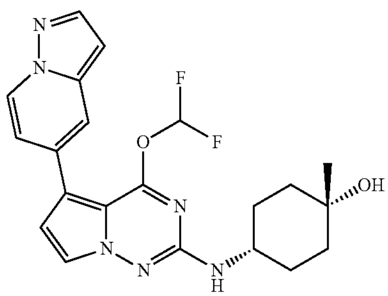

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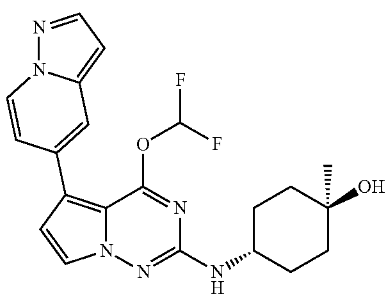

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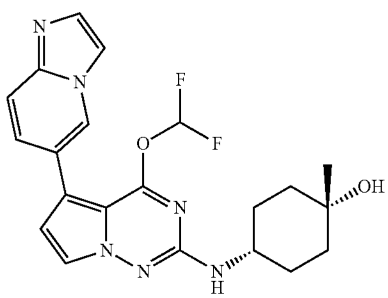

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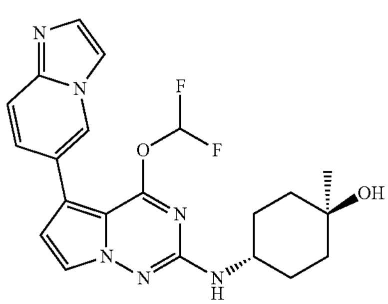

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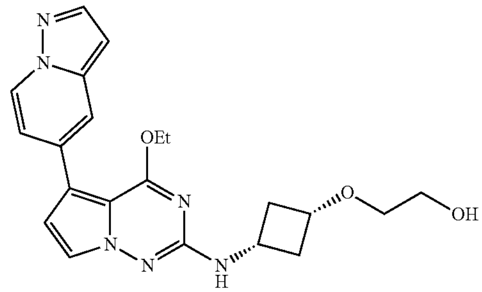

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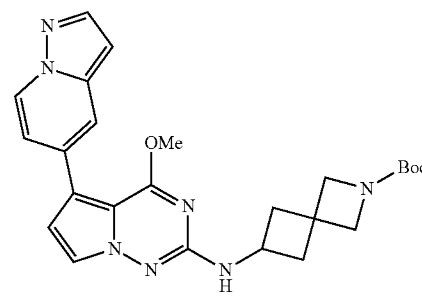

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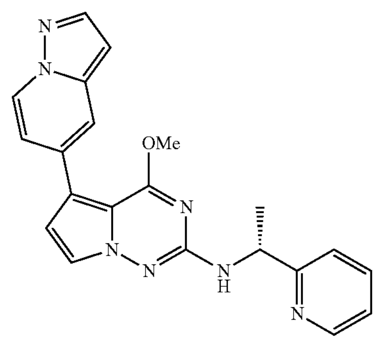

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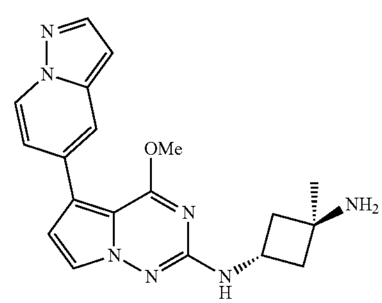

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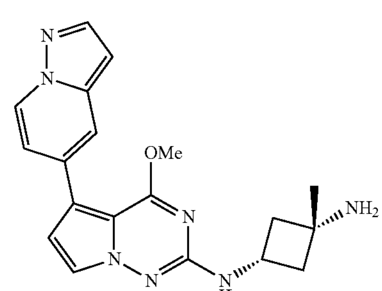

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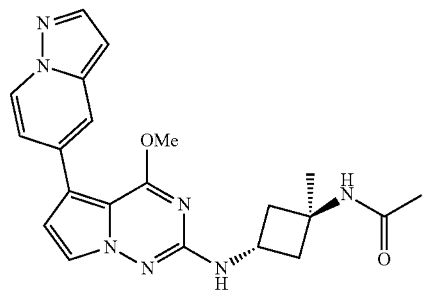

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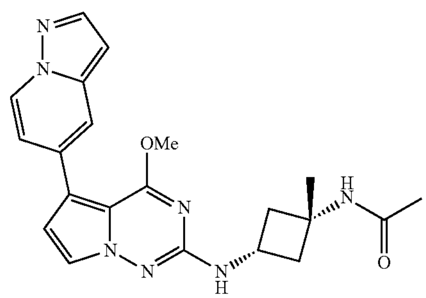

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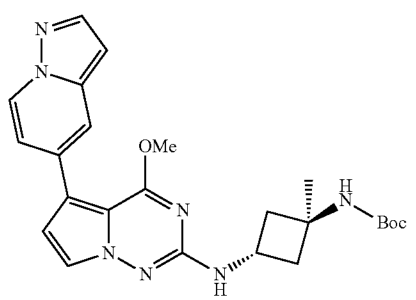

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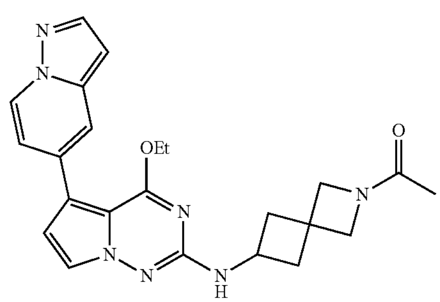

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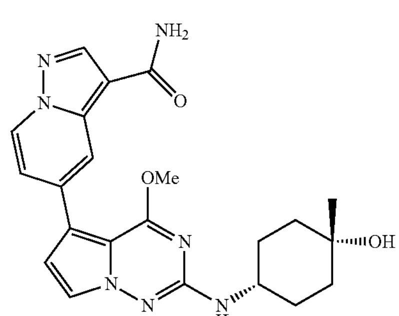

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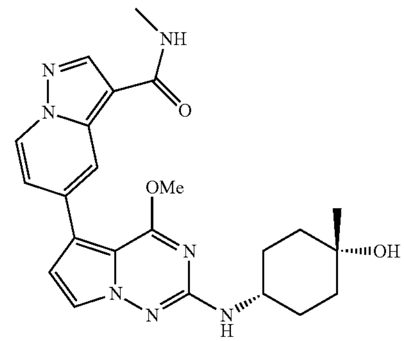

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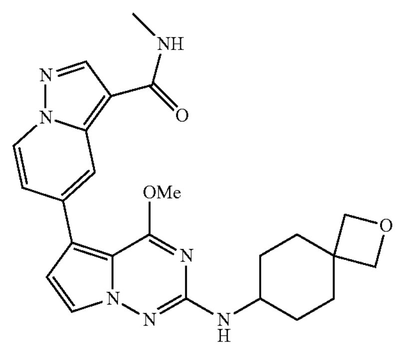

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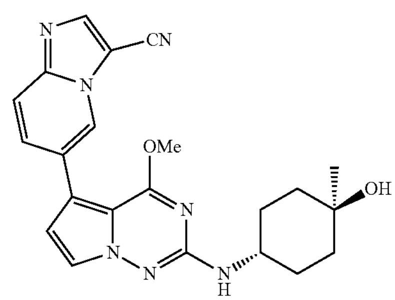

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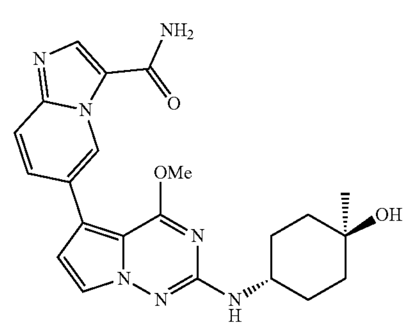

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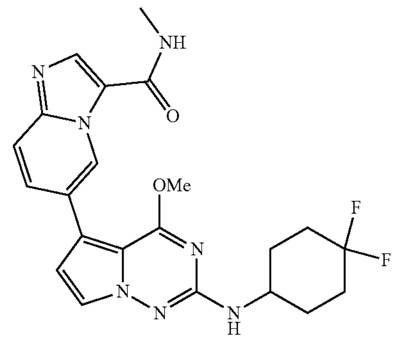

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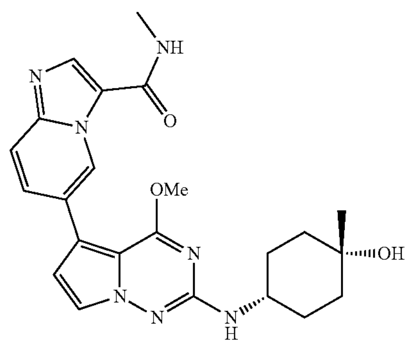

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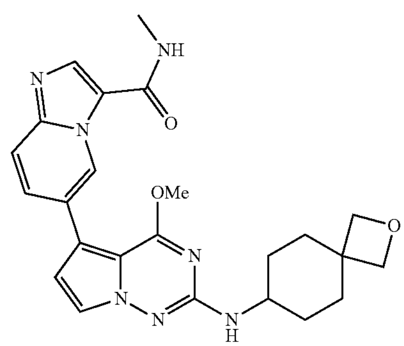

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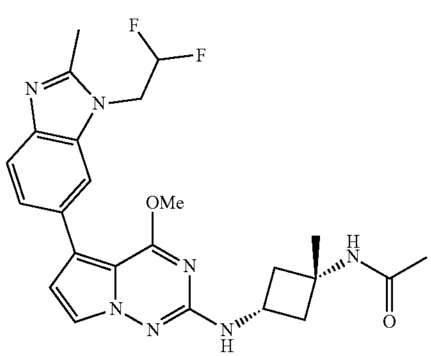

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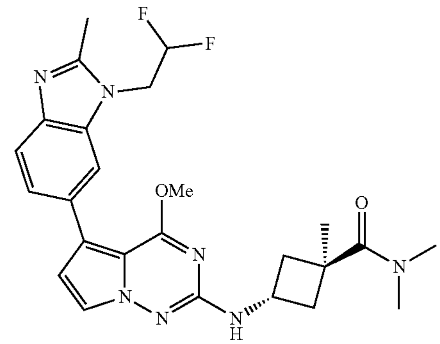

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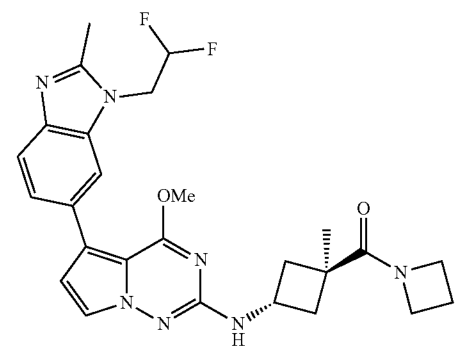

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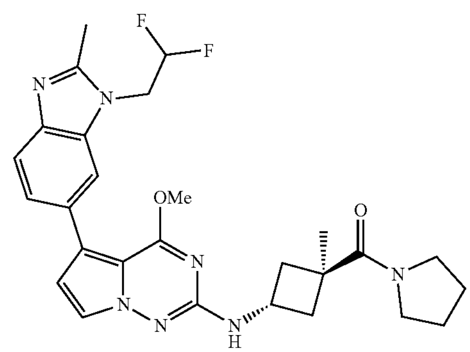

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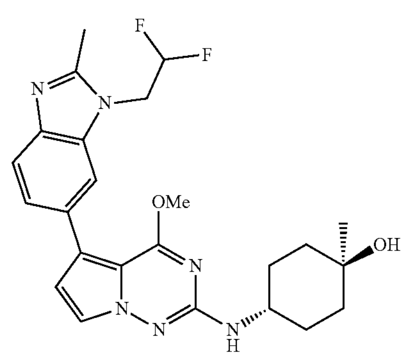

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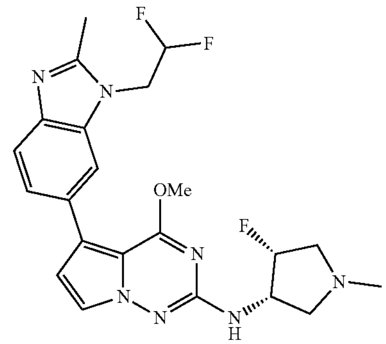

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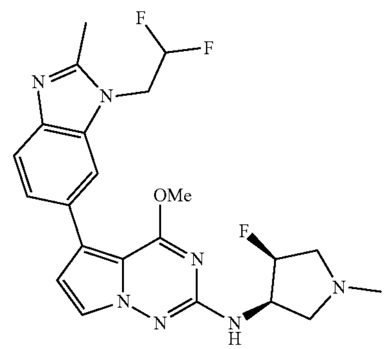

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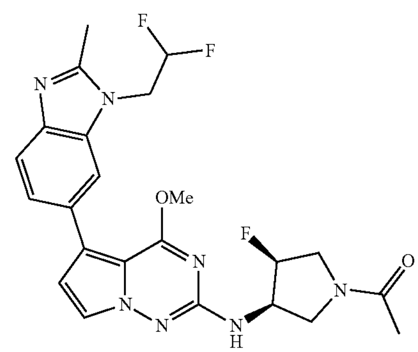

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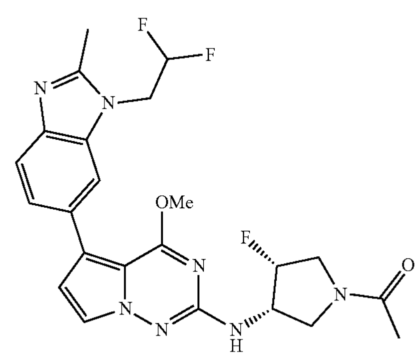

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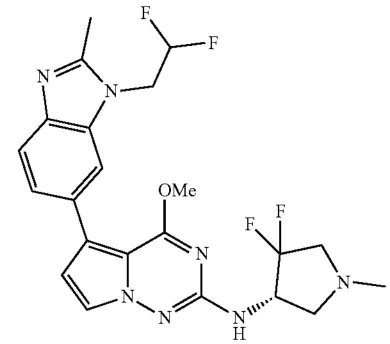

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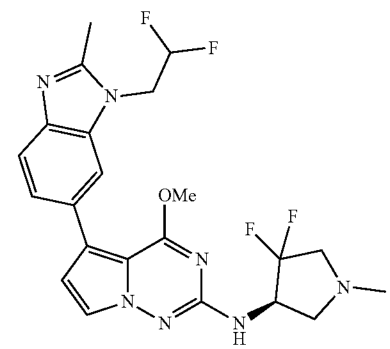

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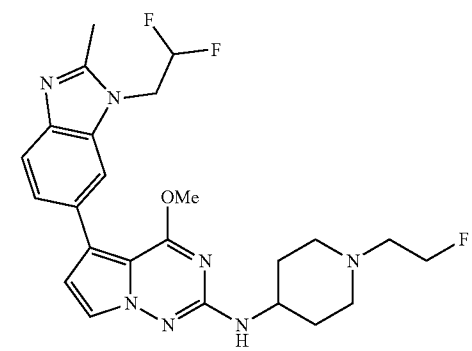

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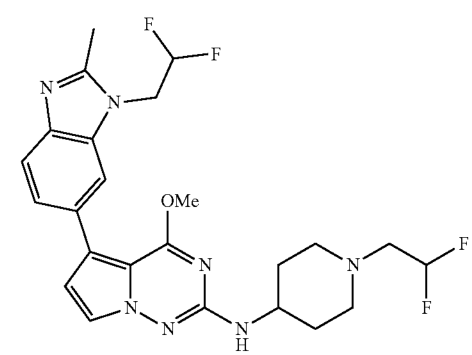

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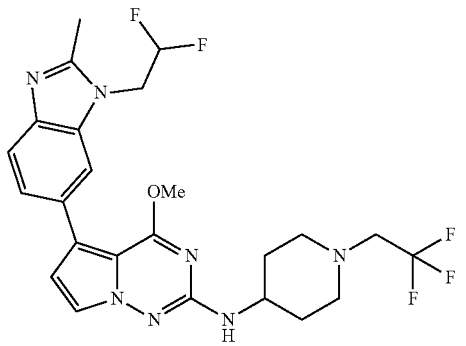

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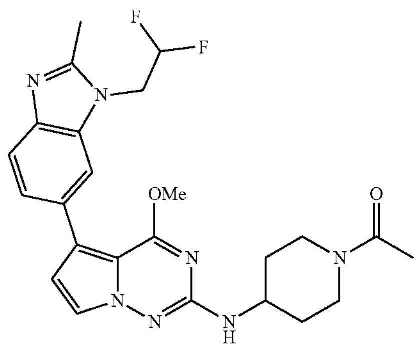

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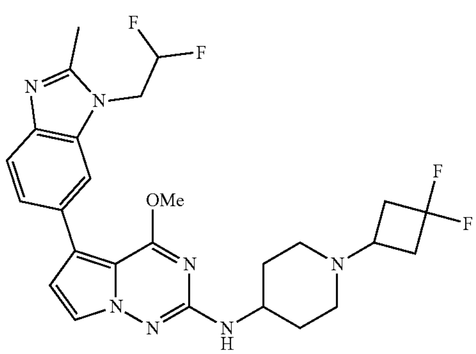

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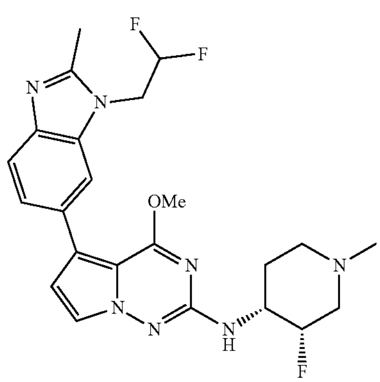

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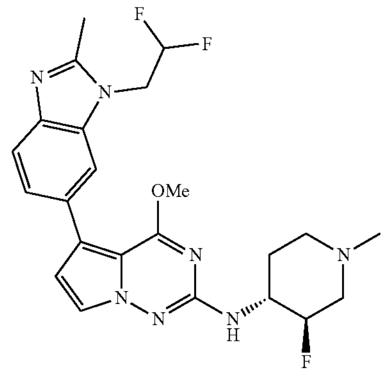

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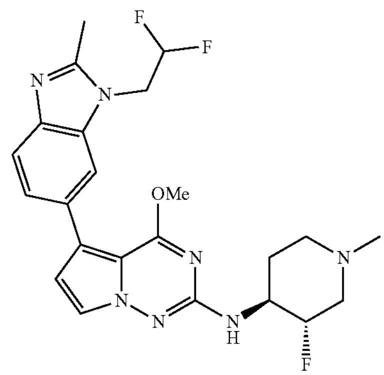

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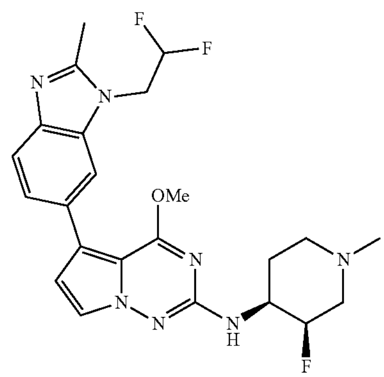

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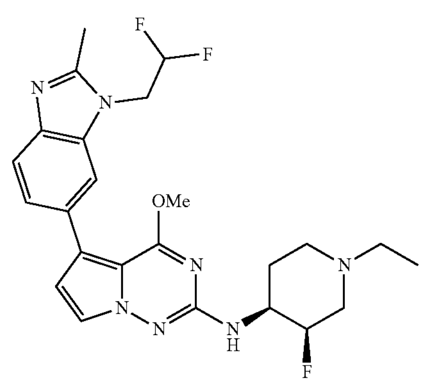

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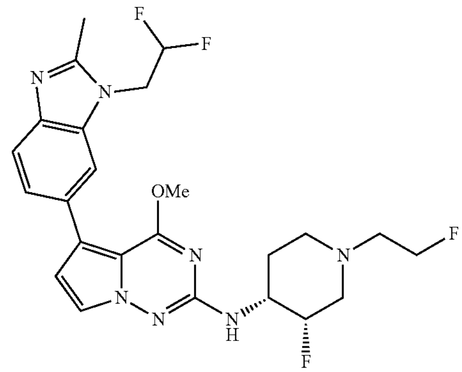

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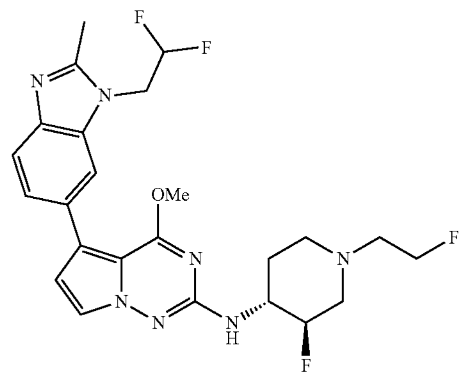

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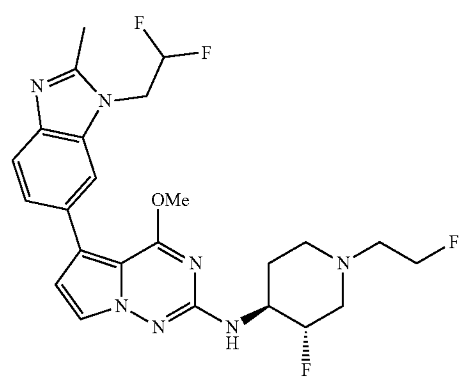

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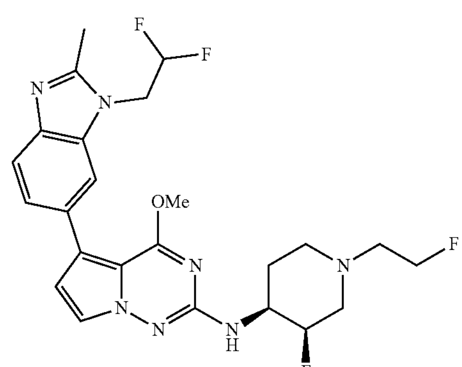

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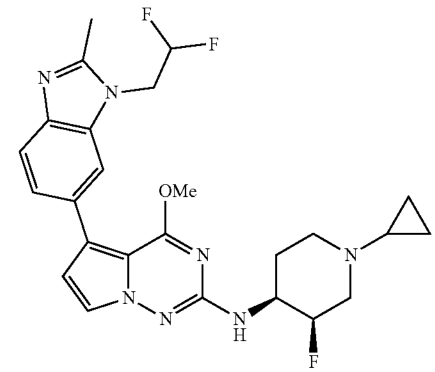

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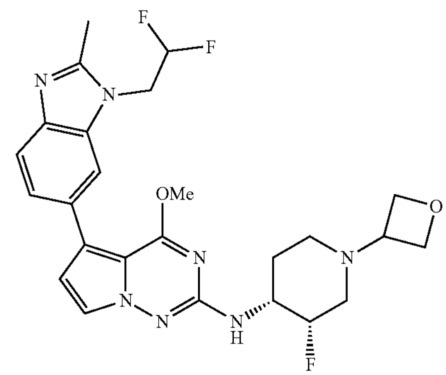

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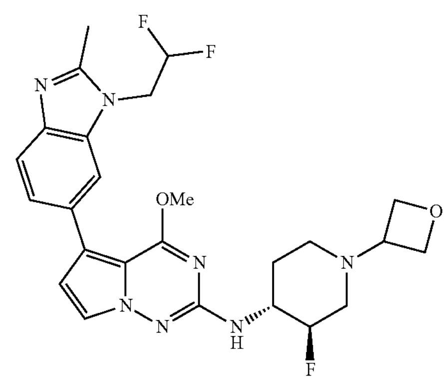

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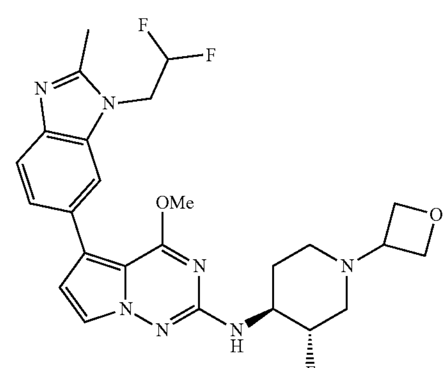

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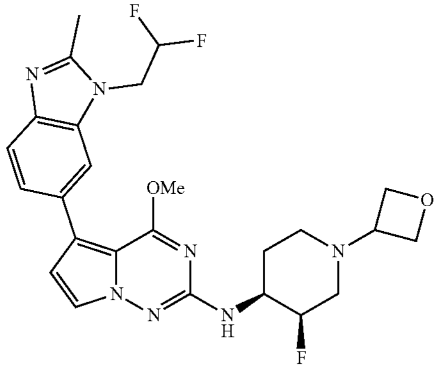

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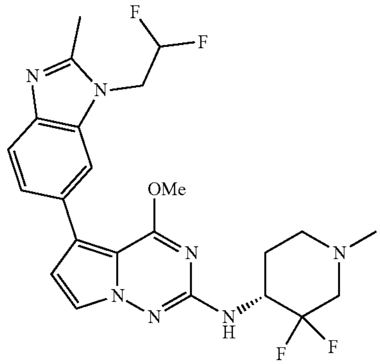

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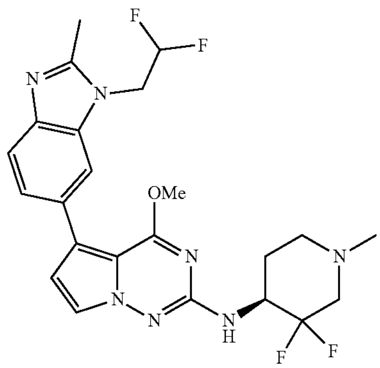

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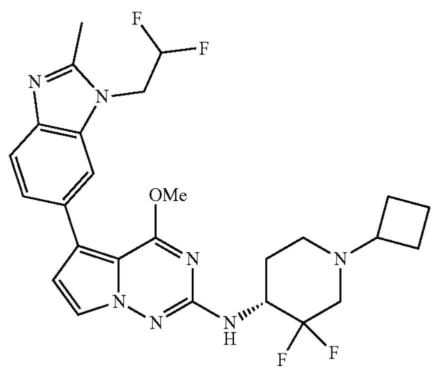

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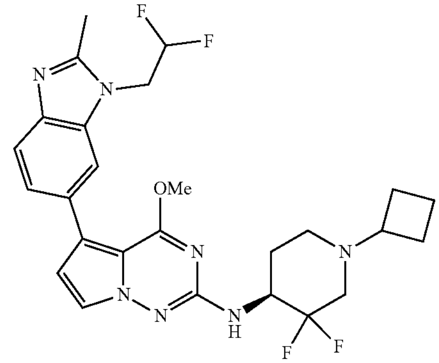

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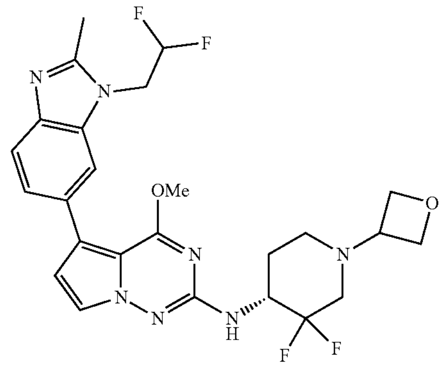

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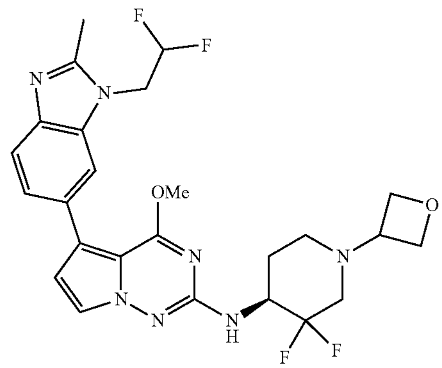

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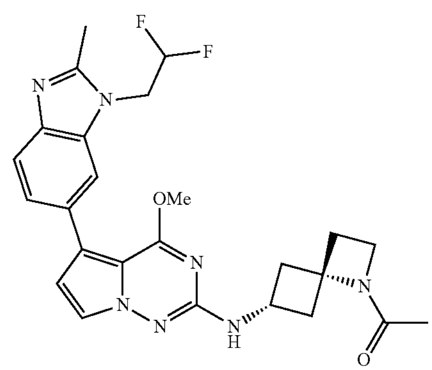

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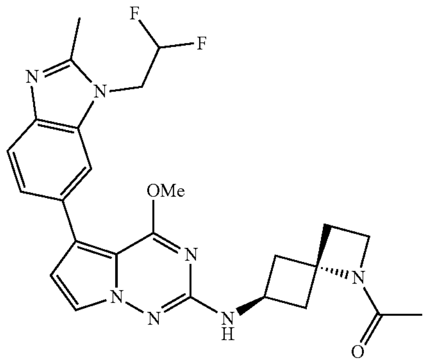

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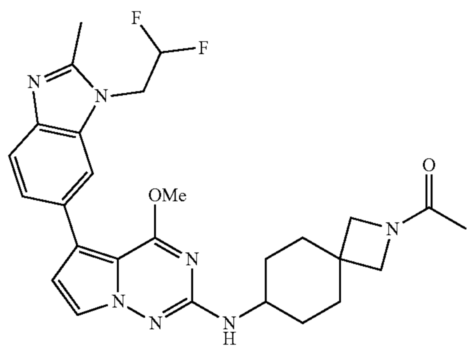

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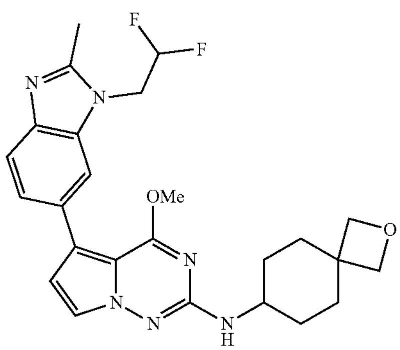

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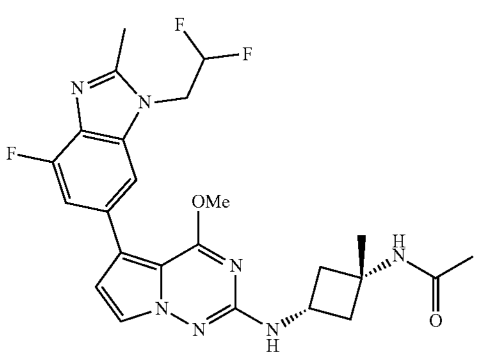

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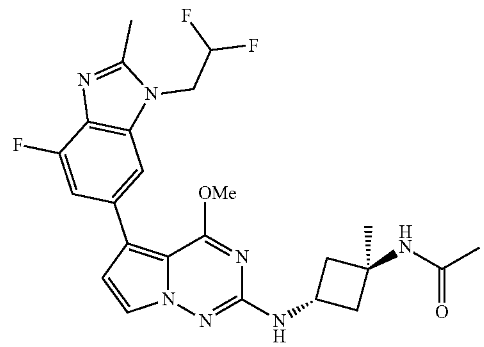

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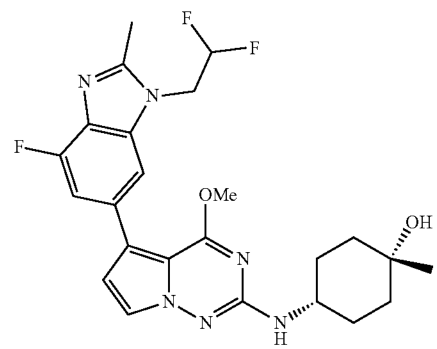

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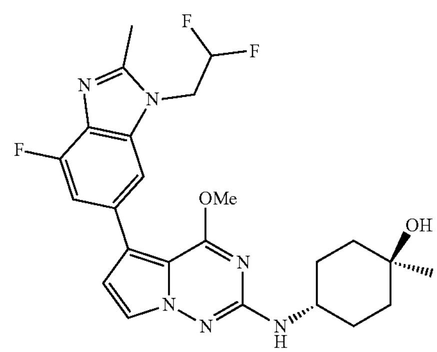

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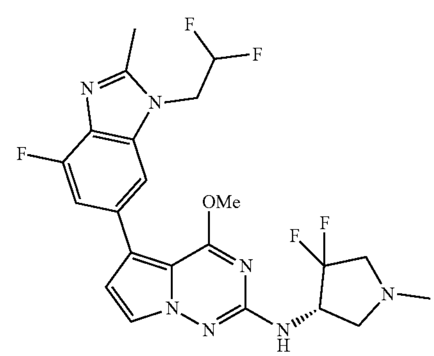

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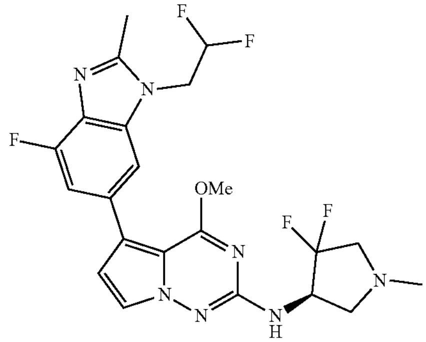
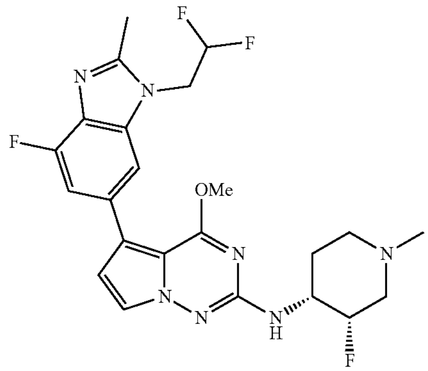
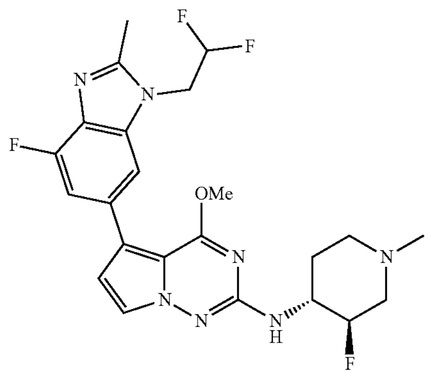
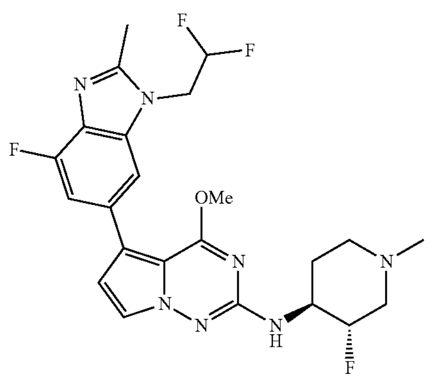
153	
154	
155	
156	

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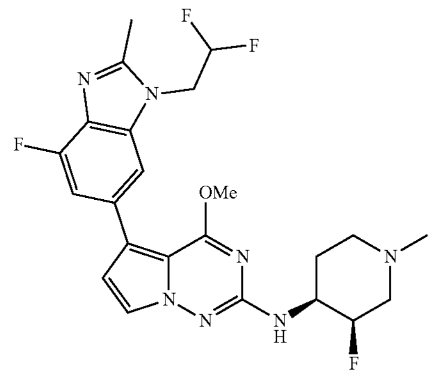
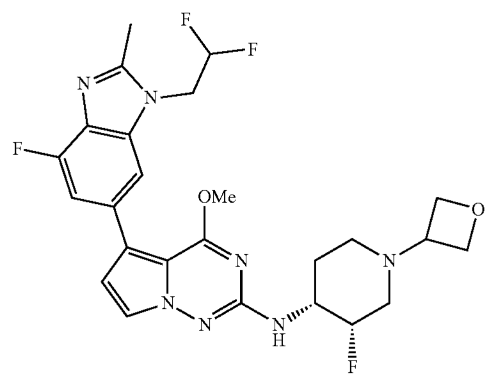
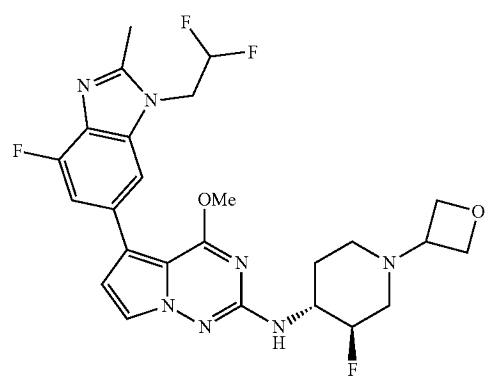
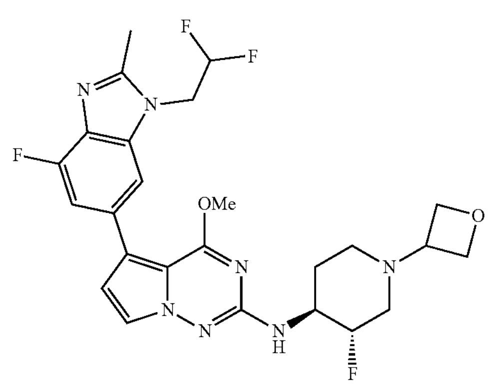
157	
158	
159	
160	

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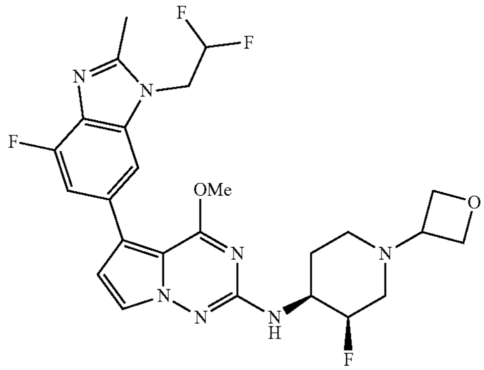
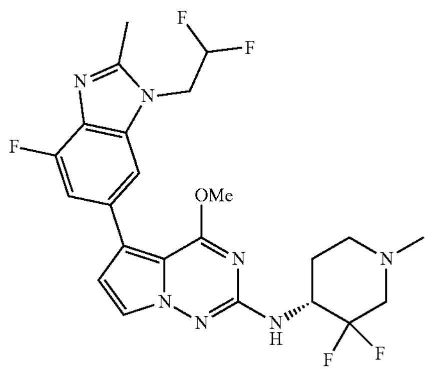
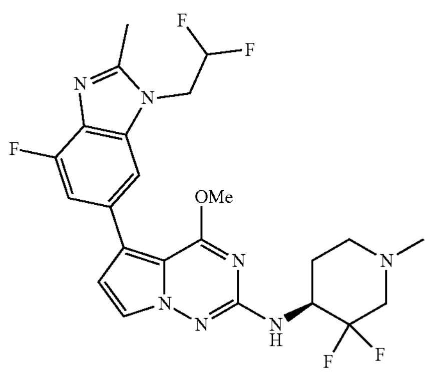
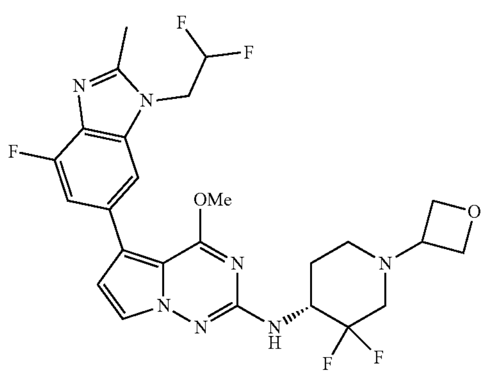
161	
162	
163	
164	

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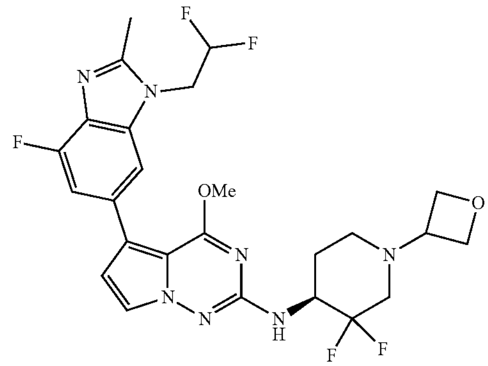
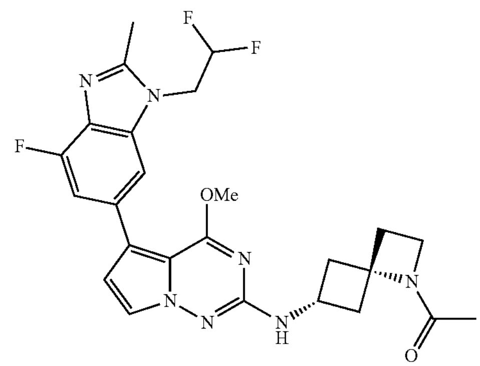
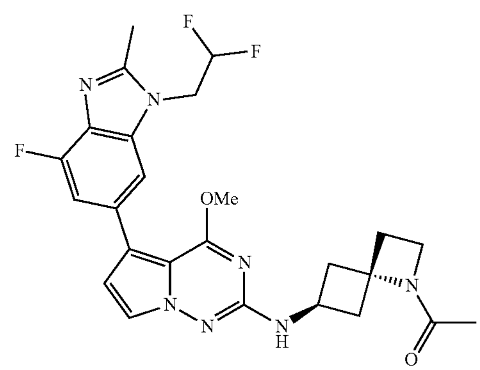
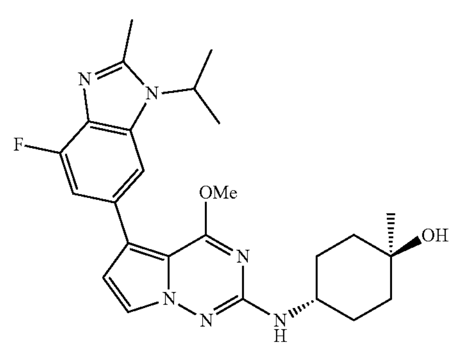
165	
166	
167	
168	

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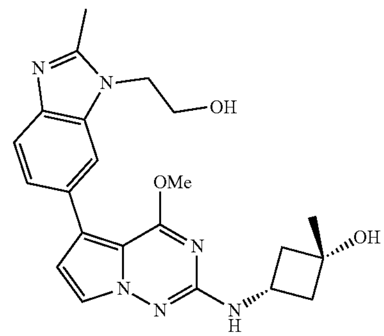

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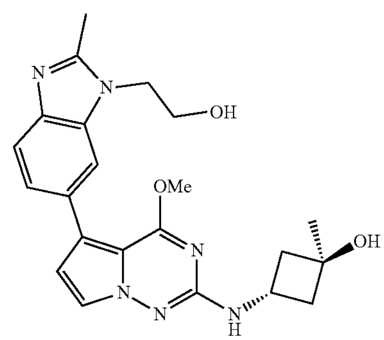

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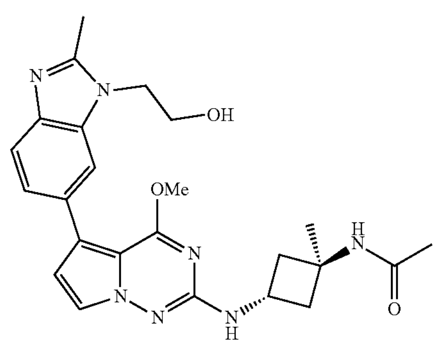

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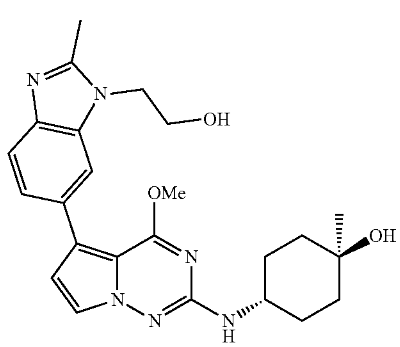

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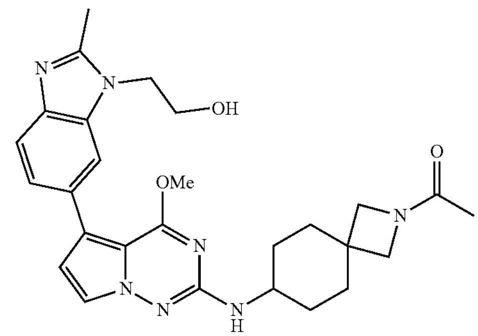

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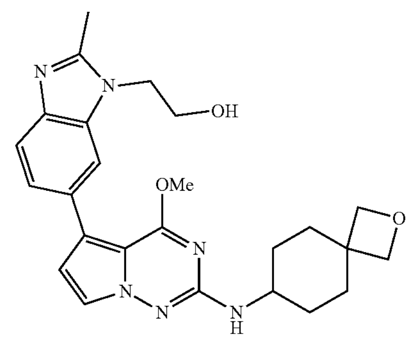

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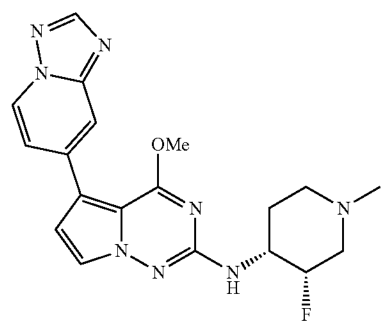

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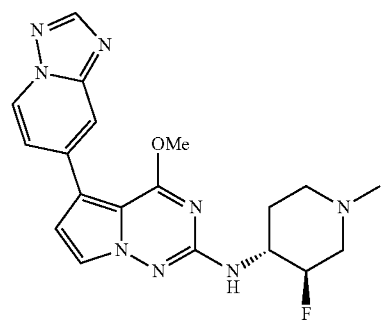

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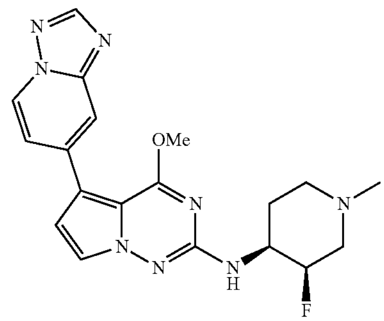

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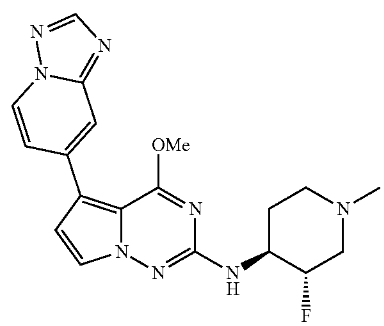

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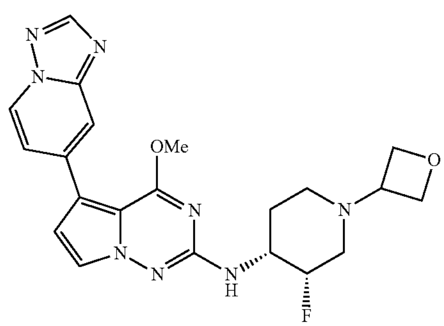

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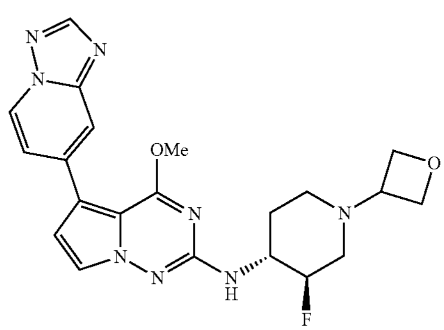

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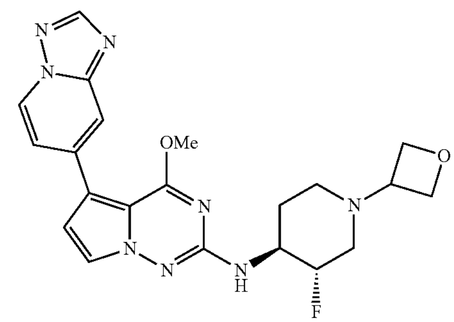

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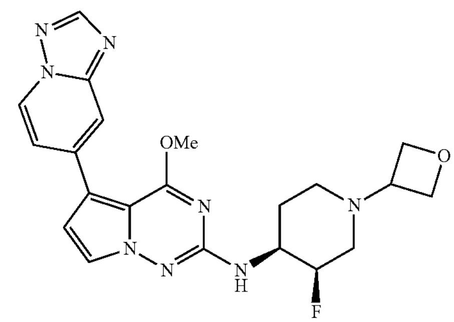

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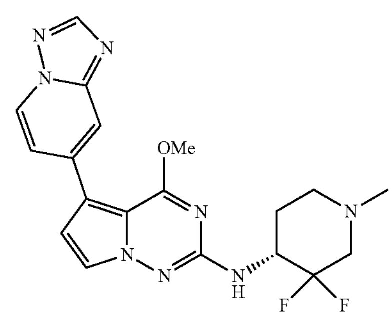

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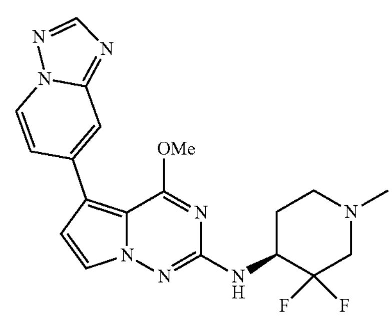

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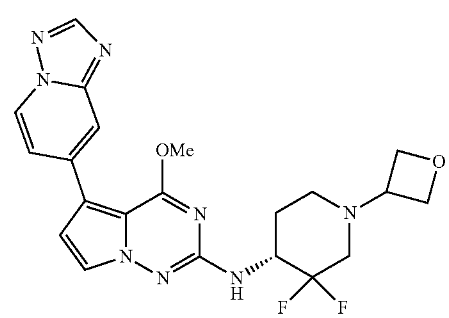

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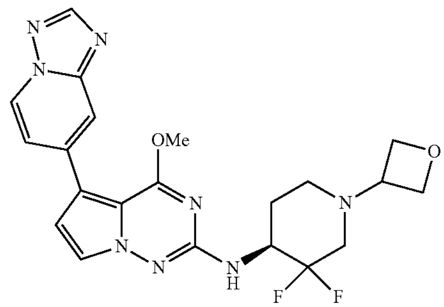

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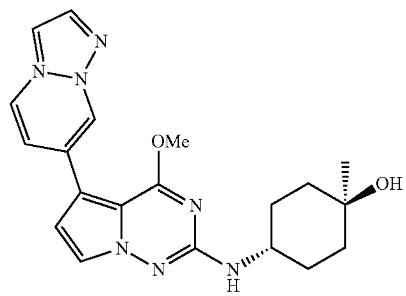

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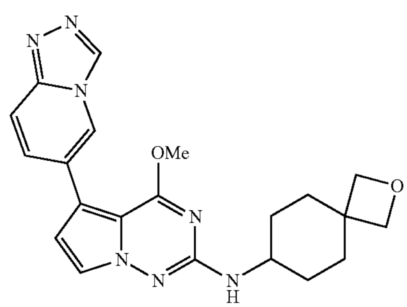

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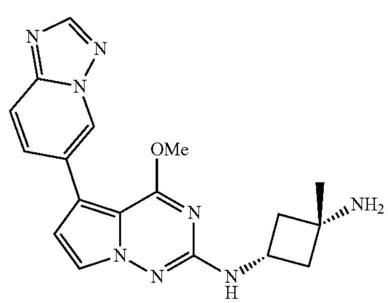

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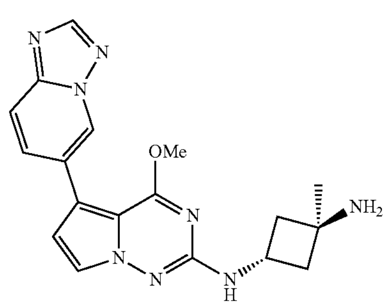

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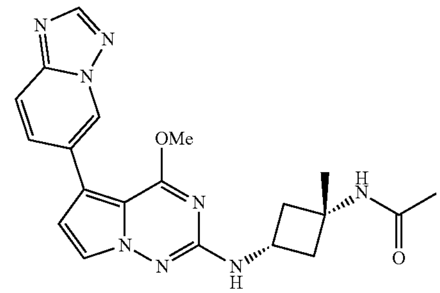

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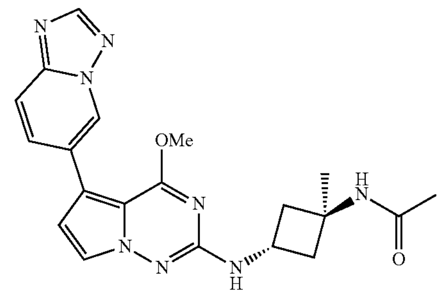

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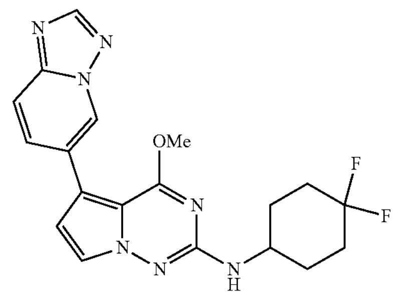

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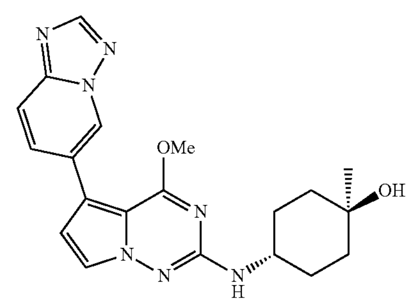

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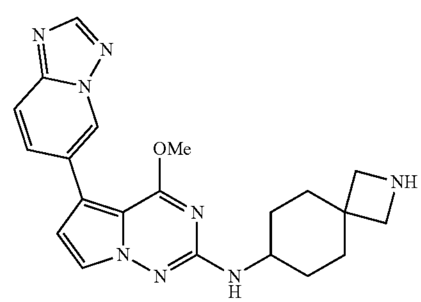

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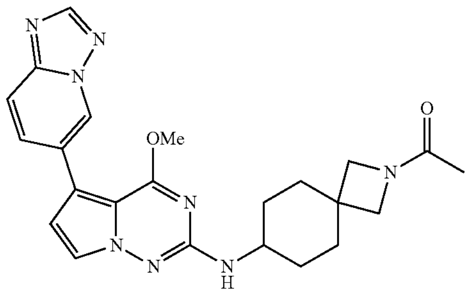

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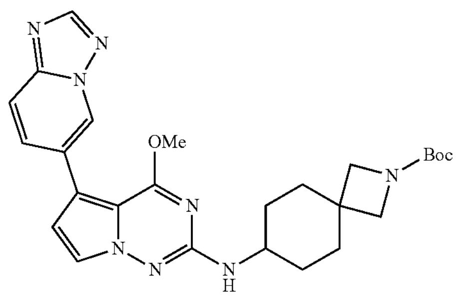

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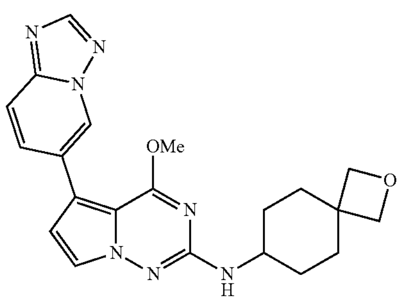

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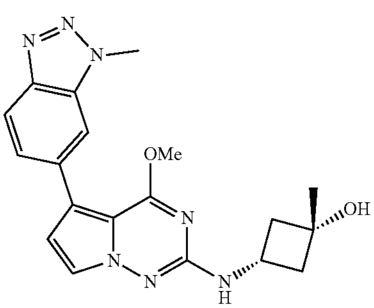

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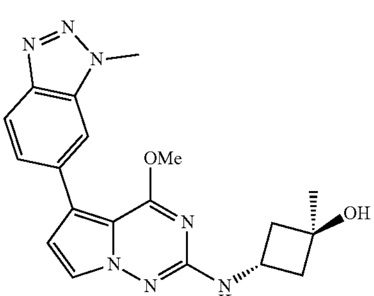

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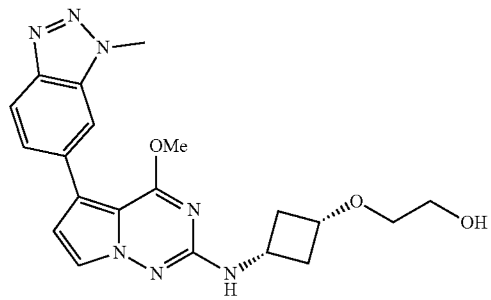

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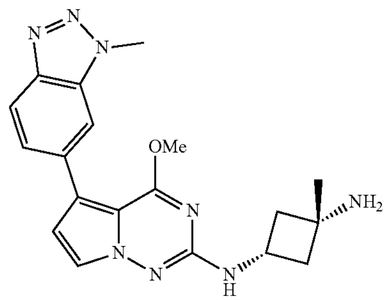

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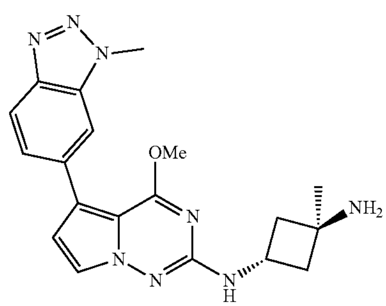

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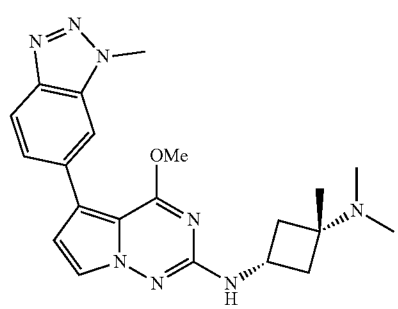

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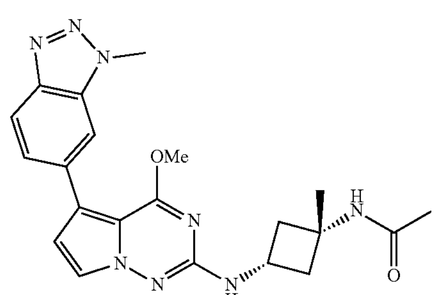

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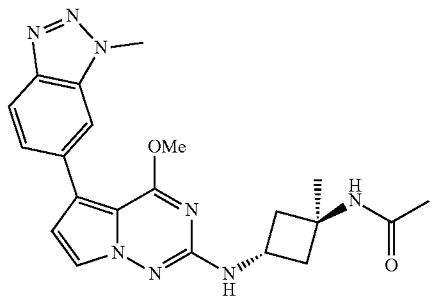

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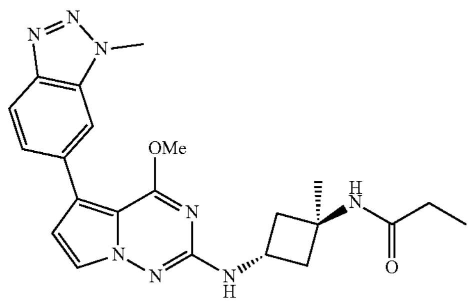

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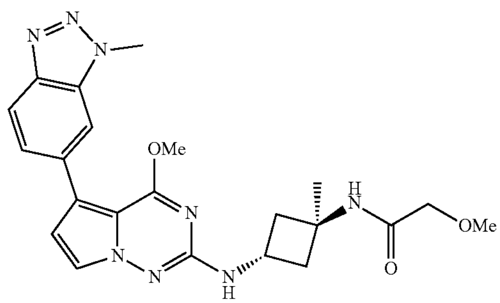

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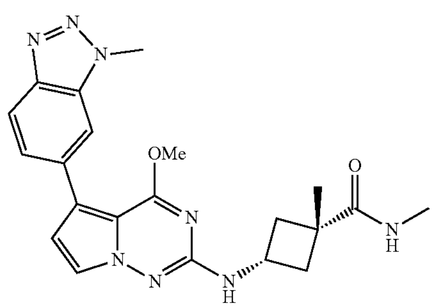

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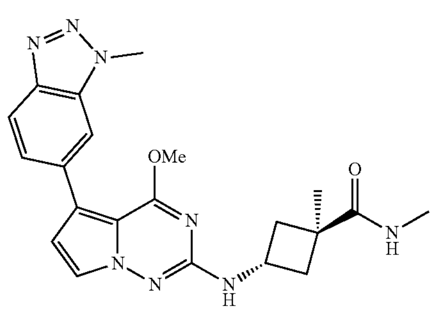

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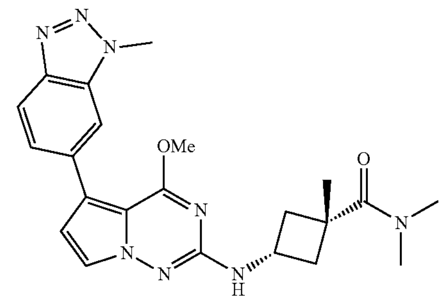

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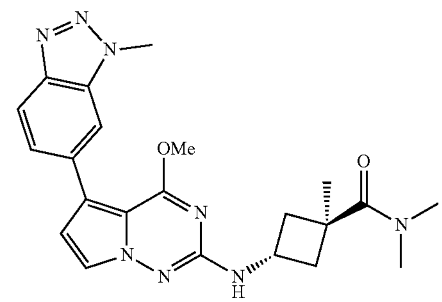

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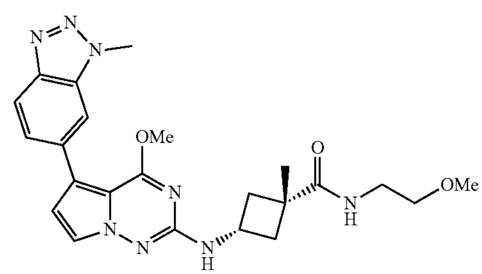

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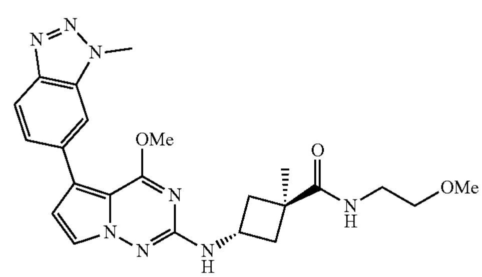

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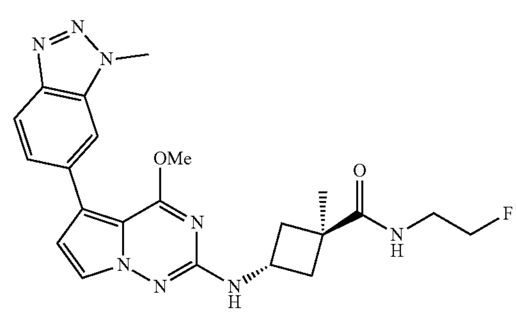

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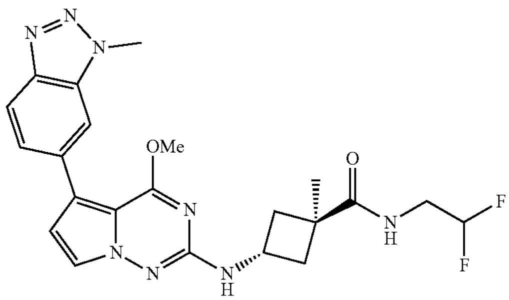

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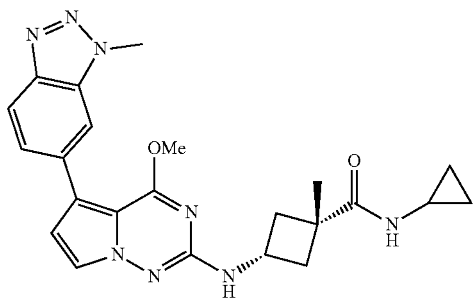

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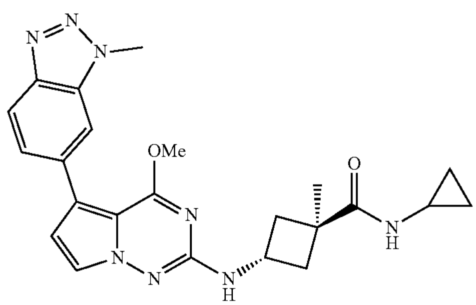

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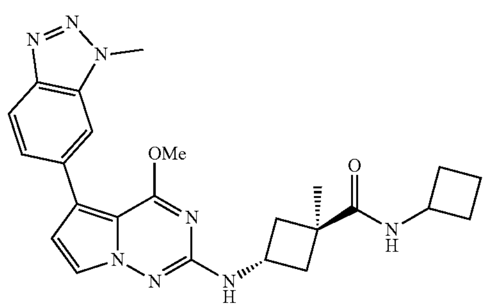

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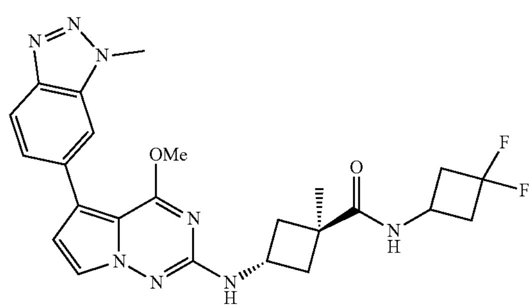

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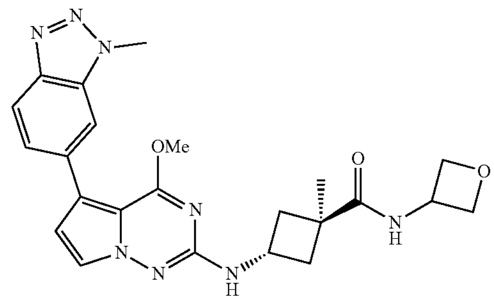

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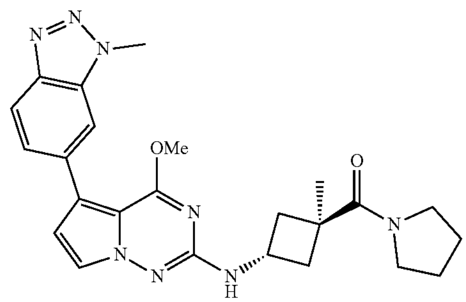

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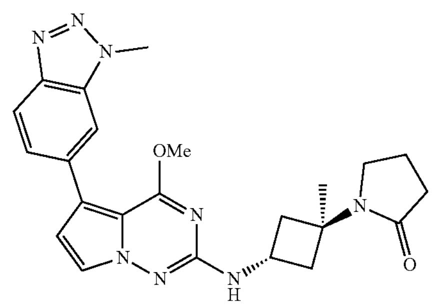

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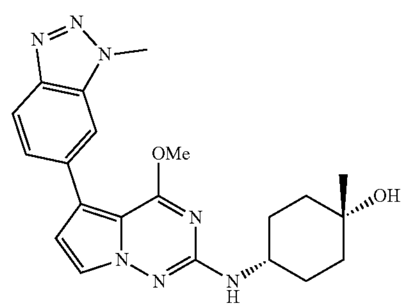

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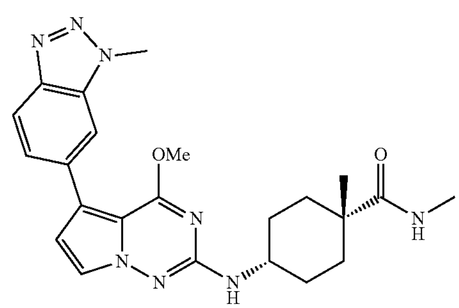

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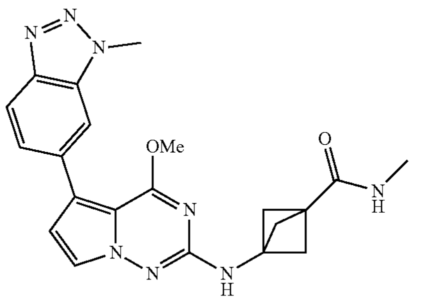

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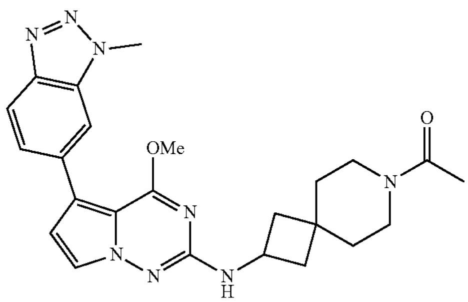

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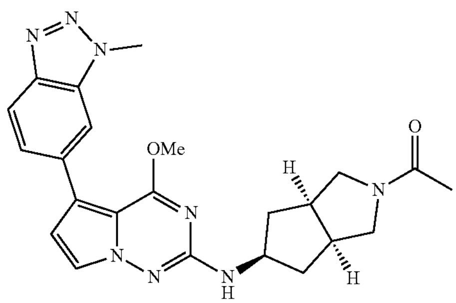

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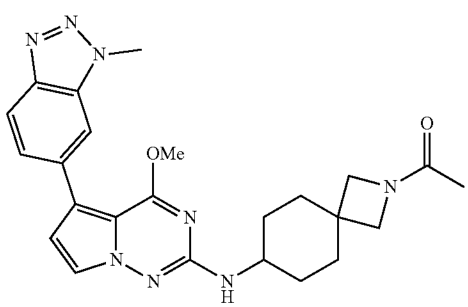

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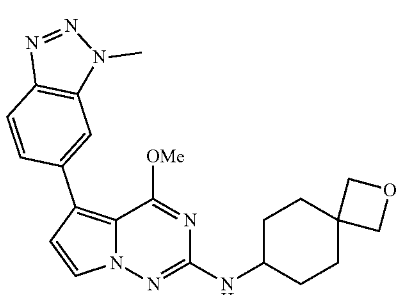

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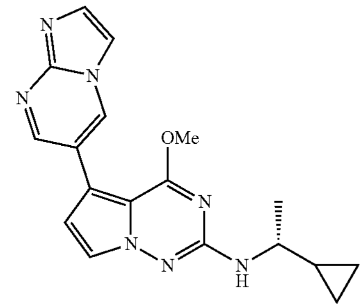

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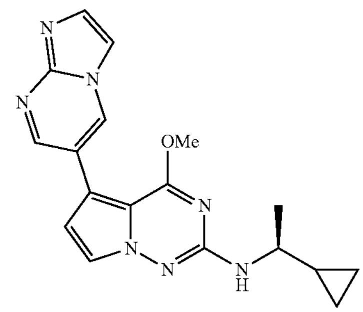

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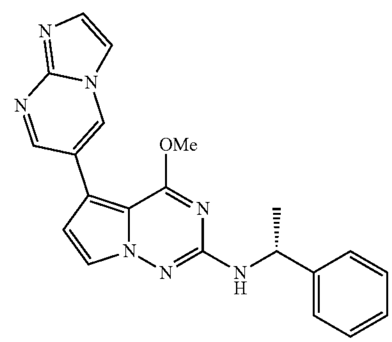

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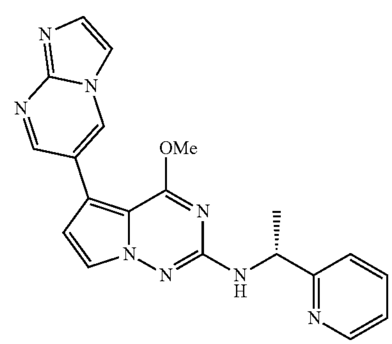

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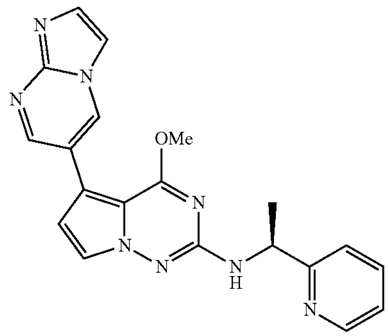

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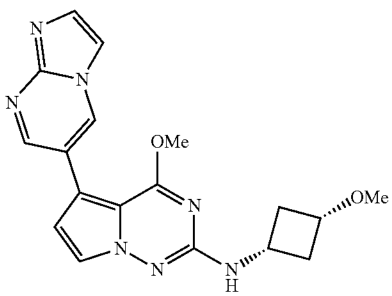

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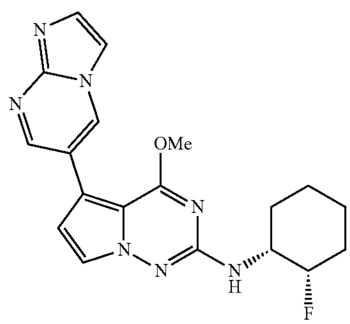

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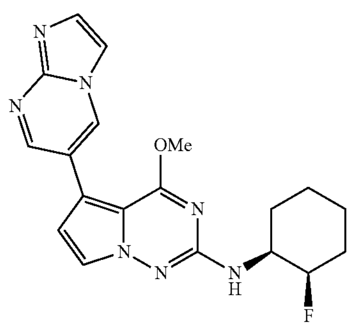

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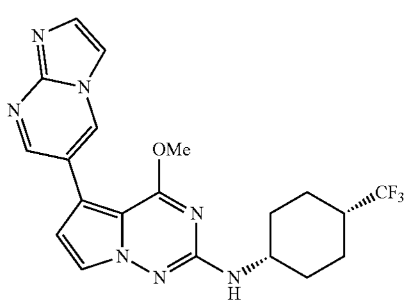

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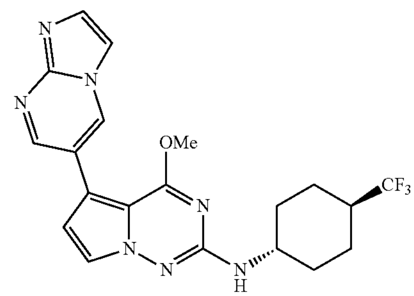

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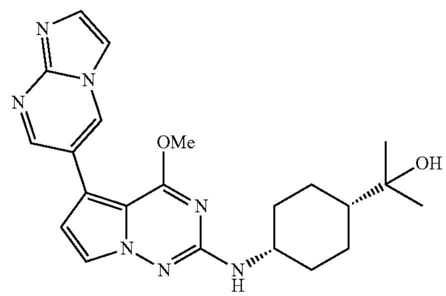

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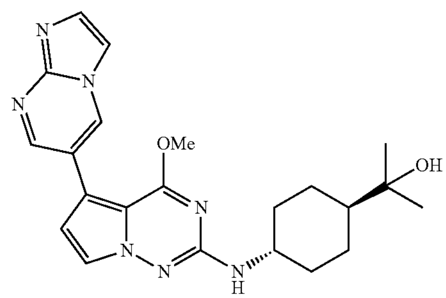

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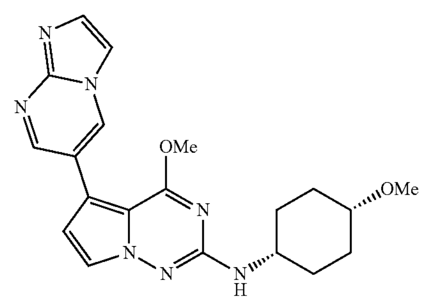

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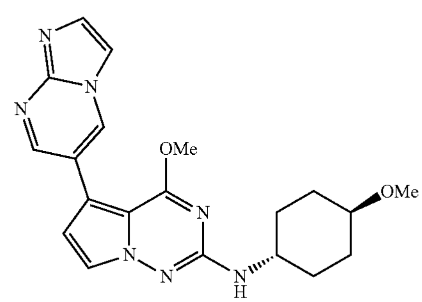

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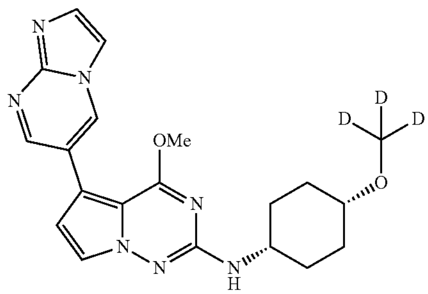

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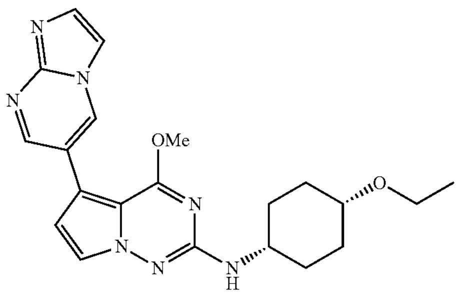

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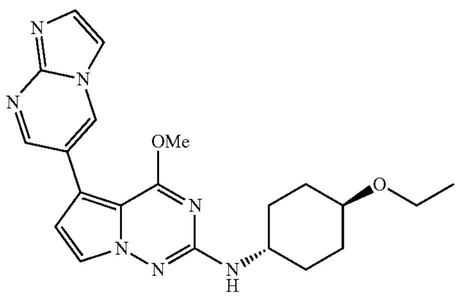

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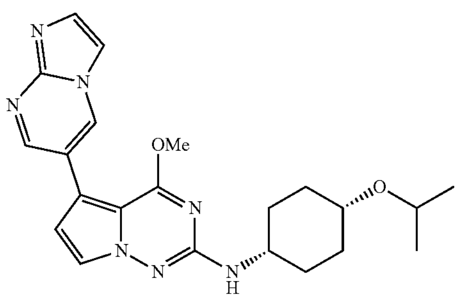

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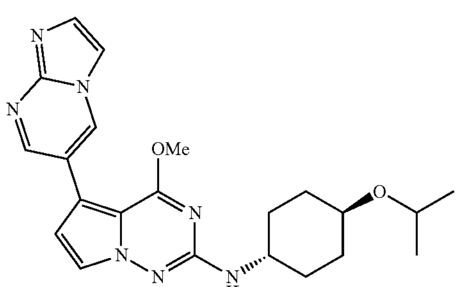

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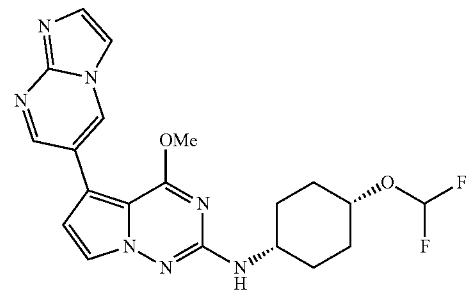

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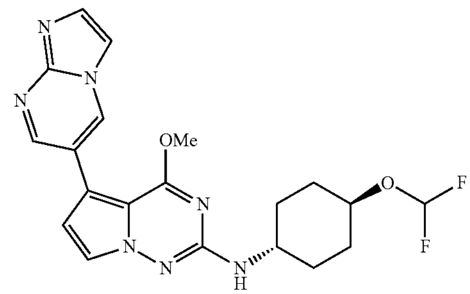

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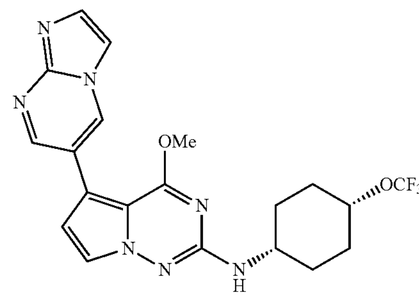

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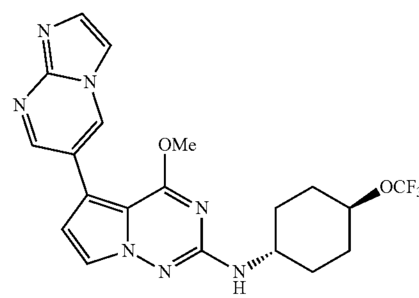

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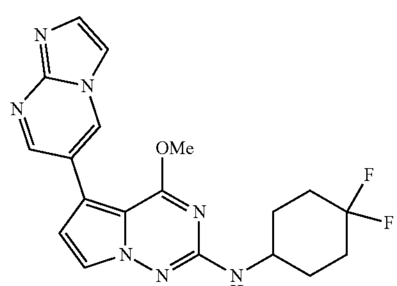

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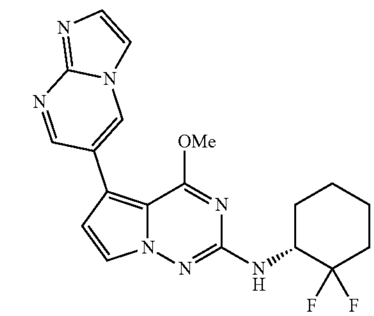

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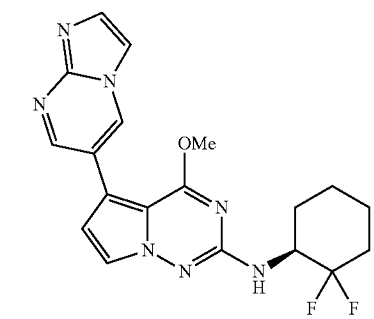

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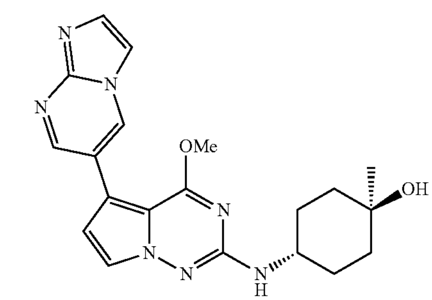

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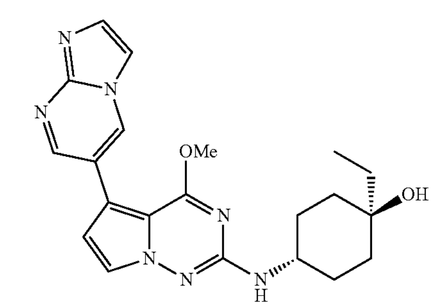

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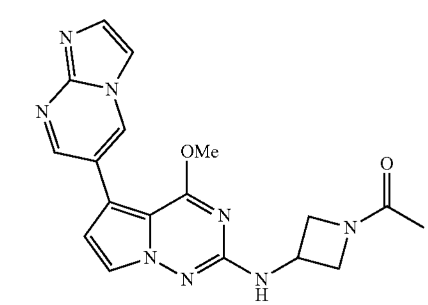

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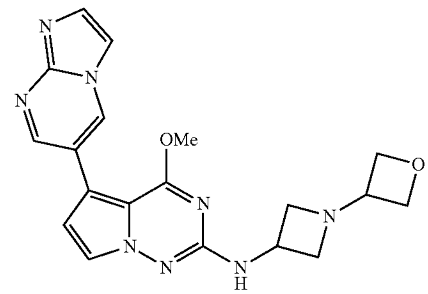

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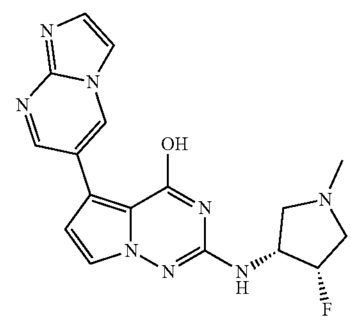

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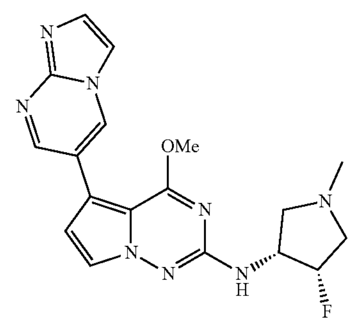

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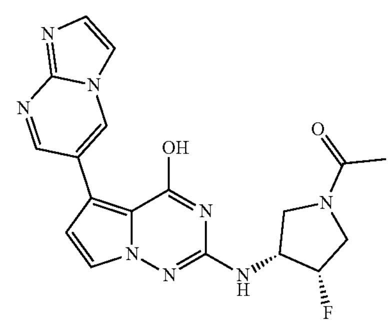

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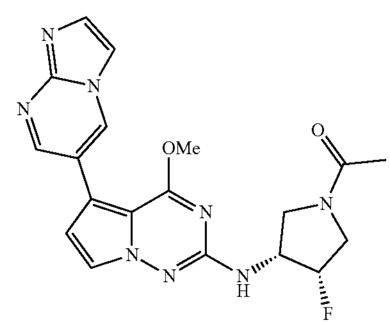

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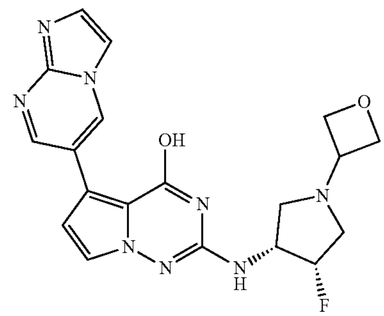

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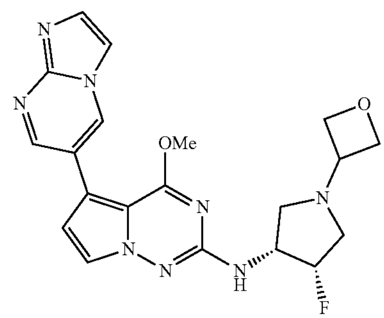

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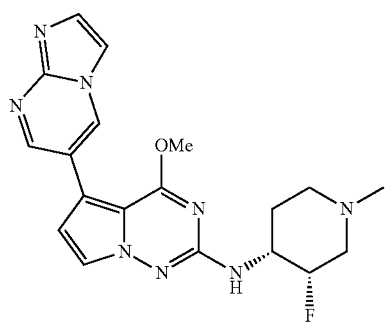

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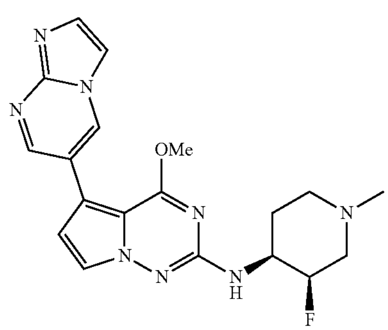

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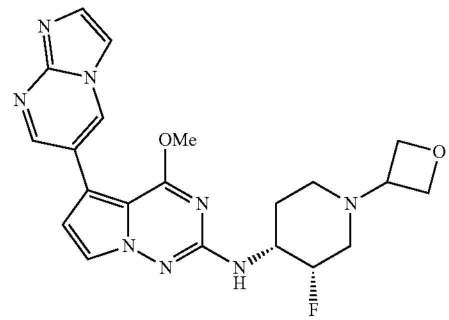

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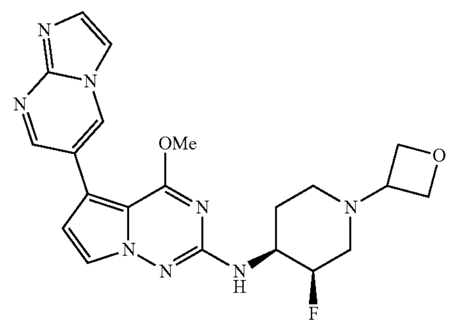

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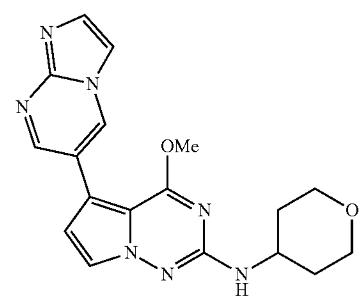

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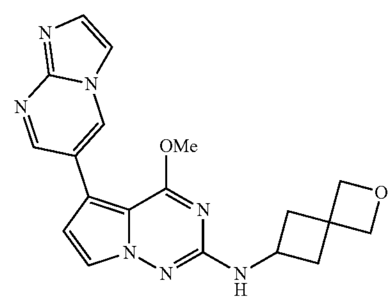

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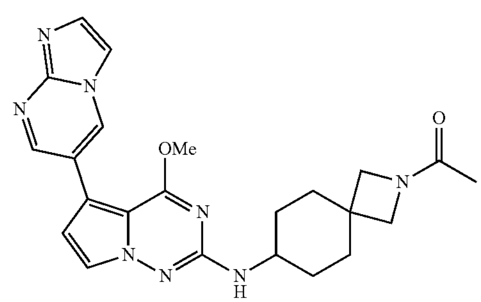

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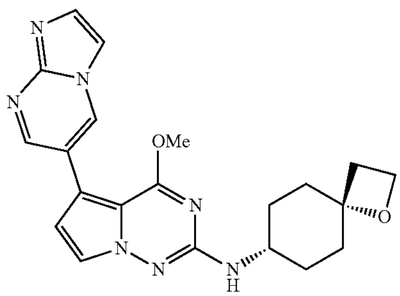

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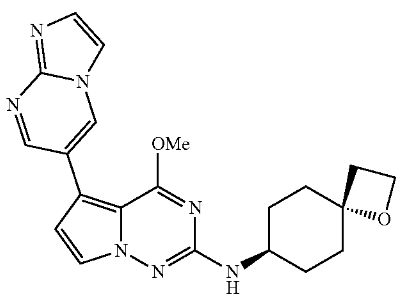

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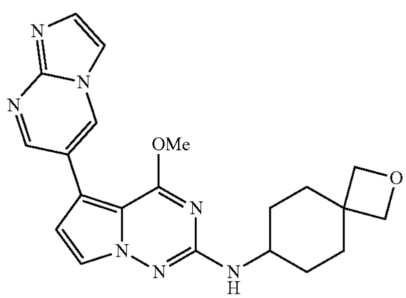

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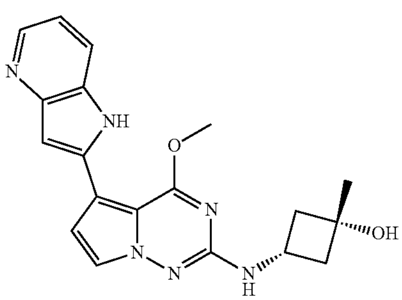

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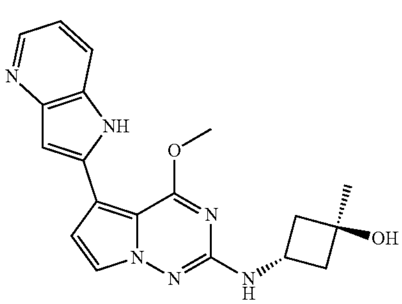

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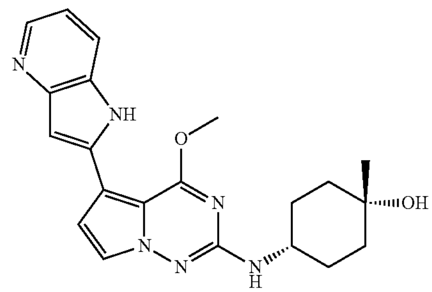

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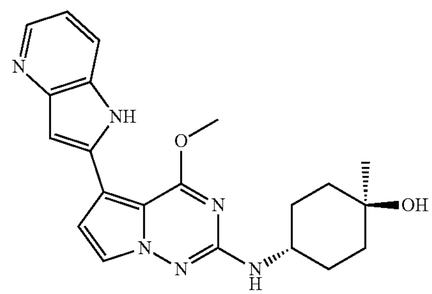

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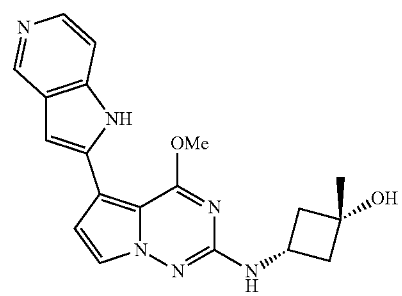

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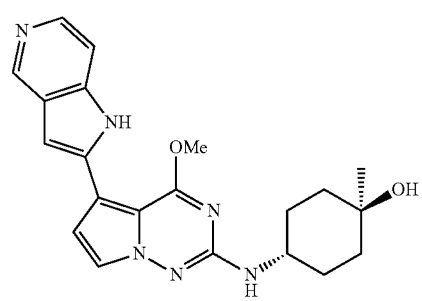

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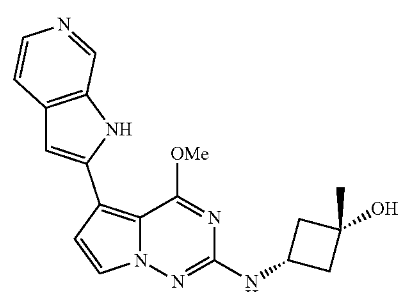

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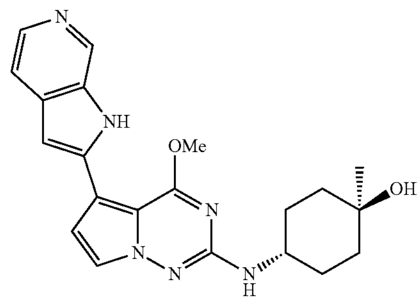

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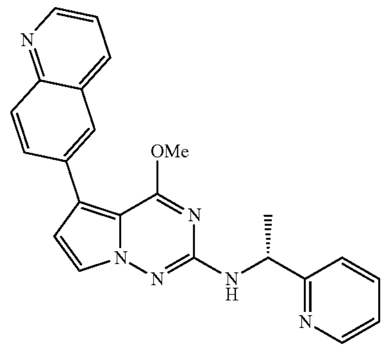

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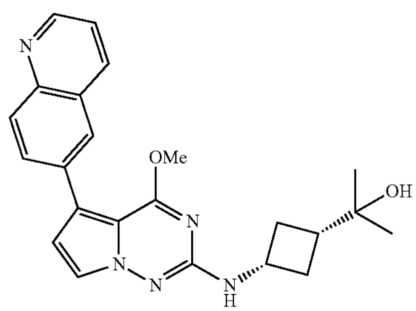

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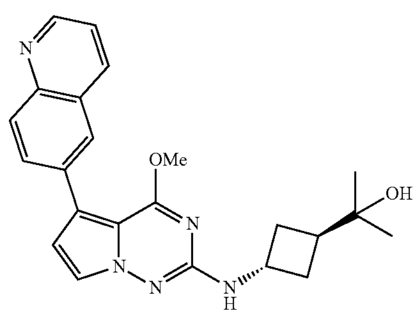

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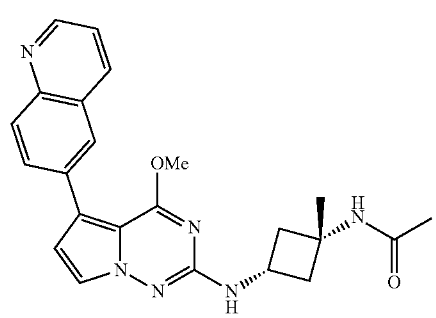

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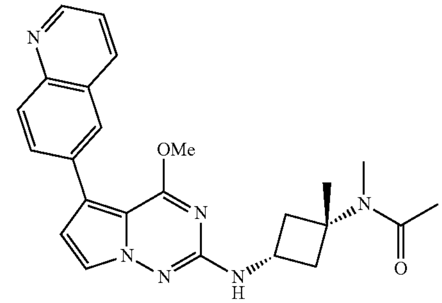

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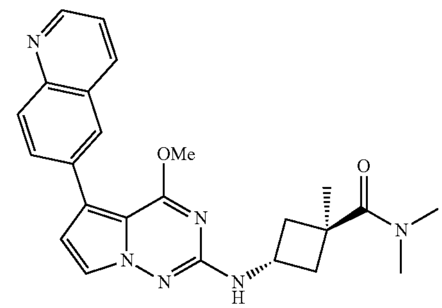

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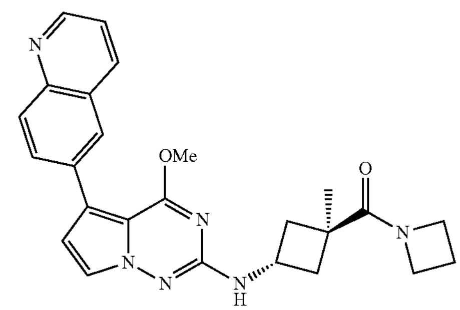

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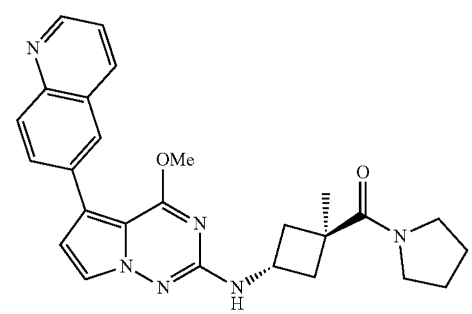

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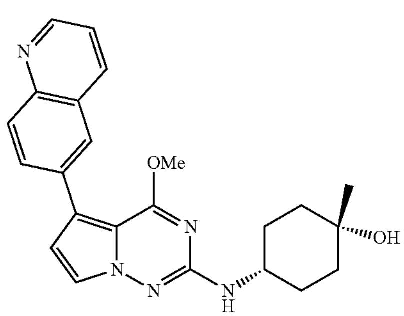

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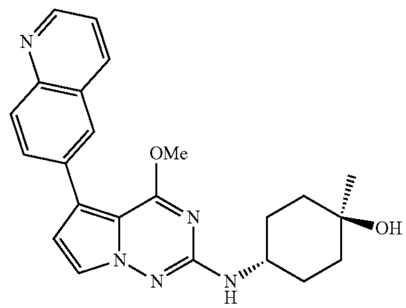

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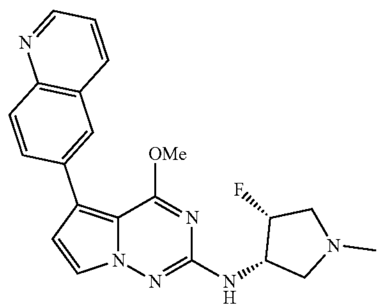

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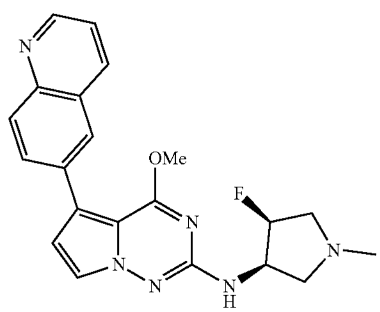

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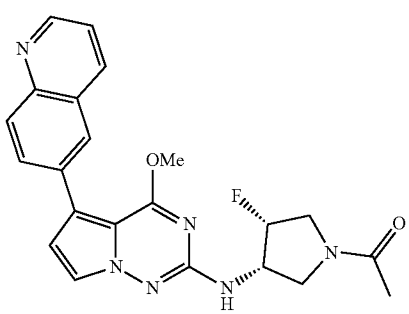

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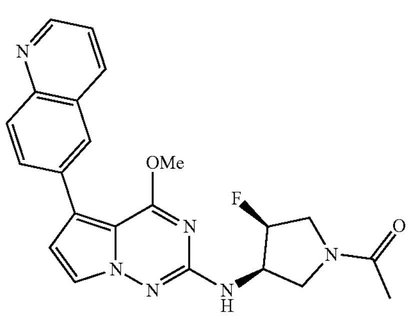

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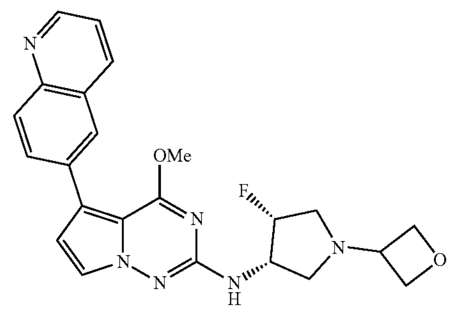

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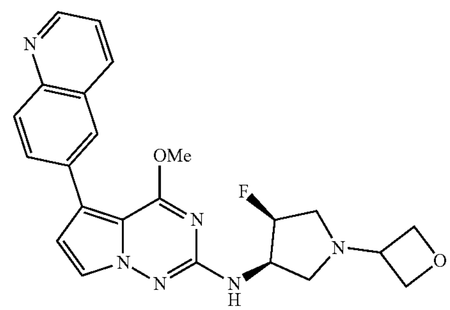

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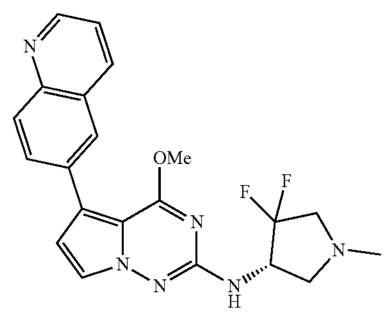

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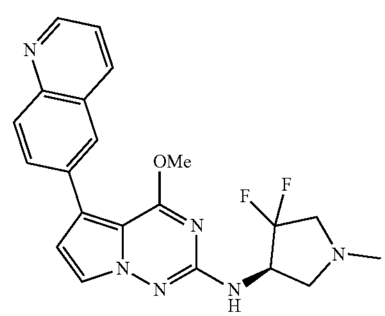

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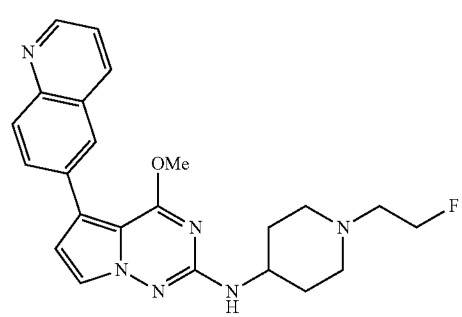

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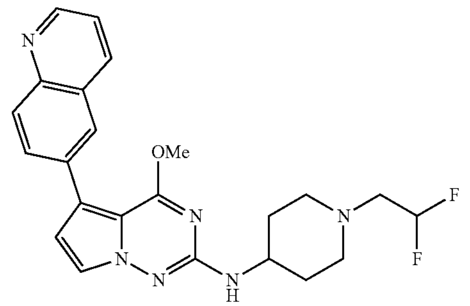

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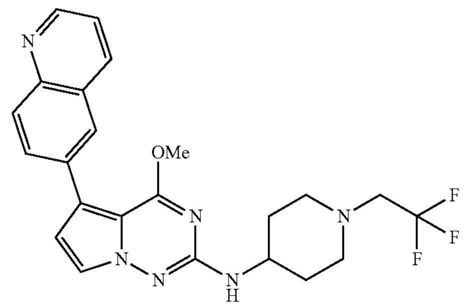

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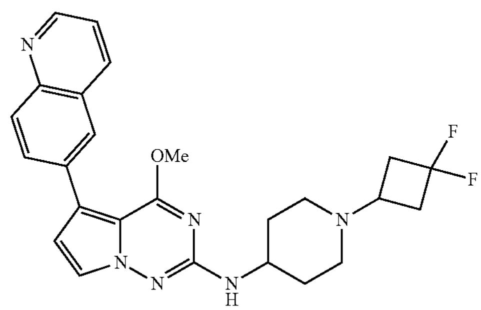

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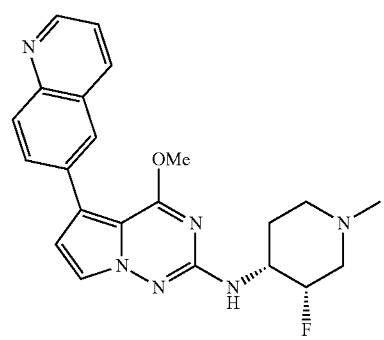

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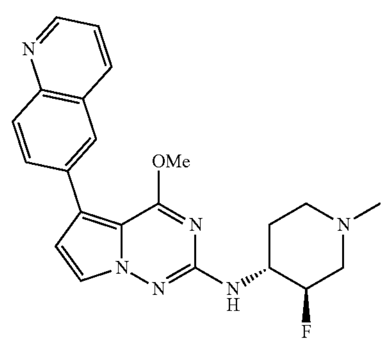

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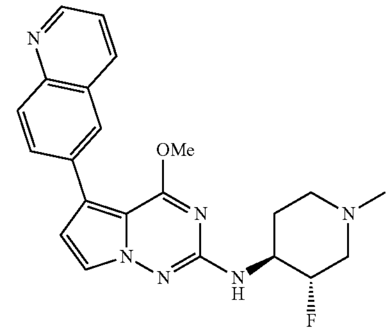

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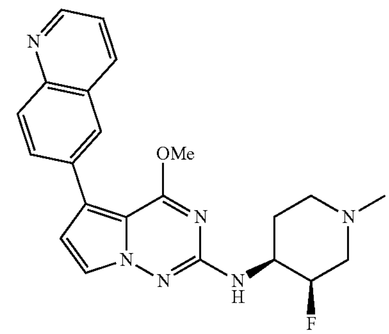

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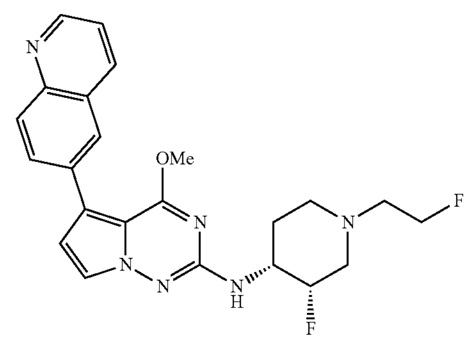

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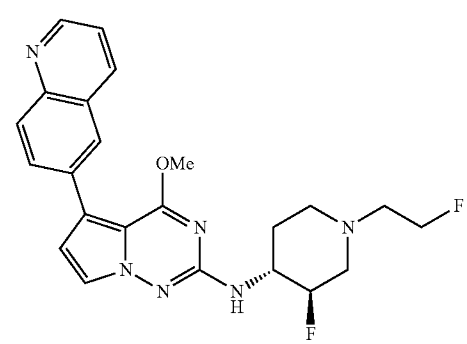

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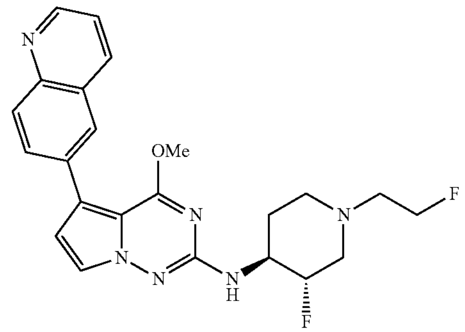

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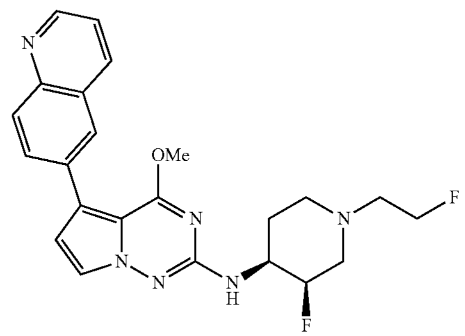

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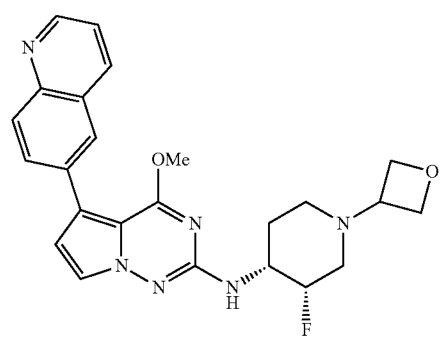

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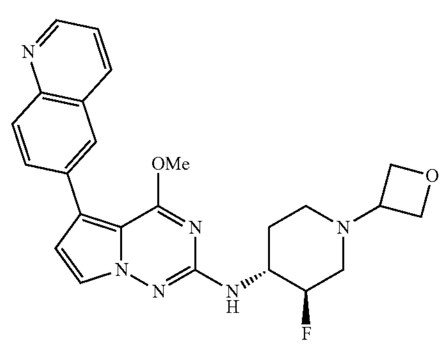

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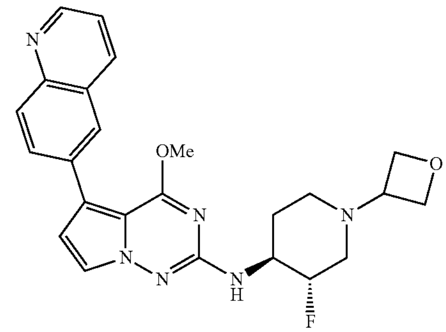

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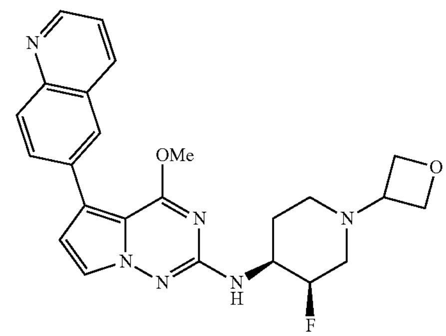

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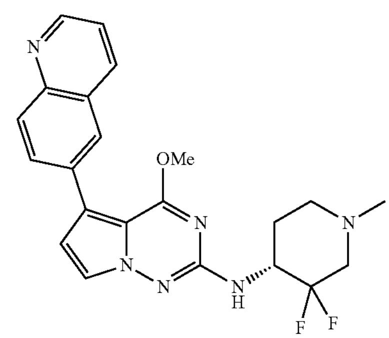

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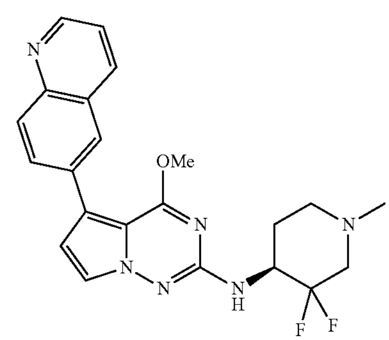

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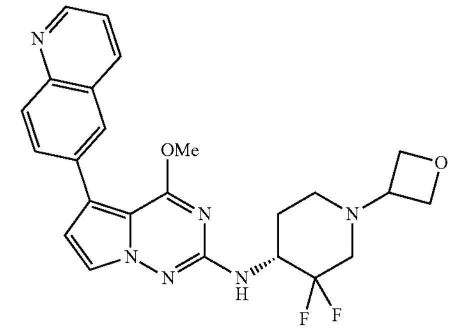

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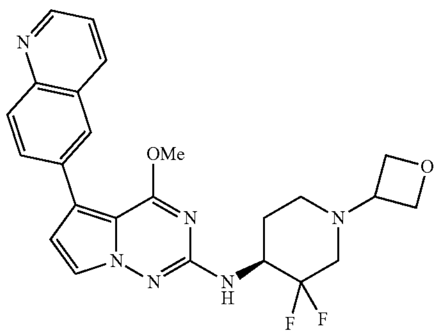

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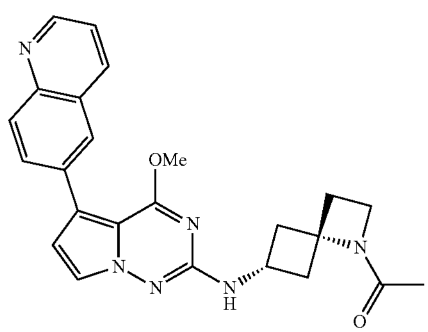

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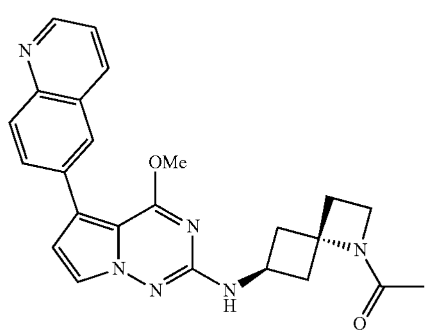

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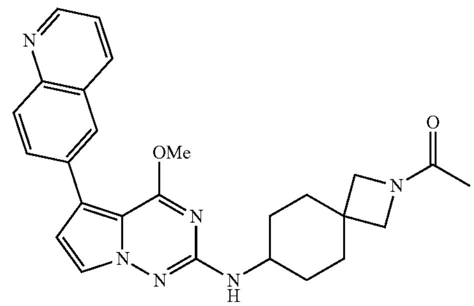

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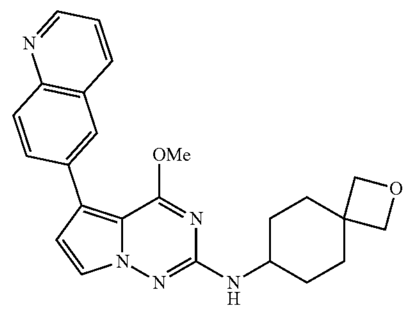

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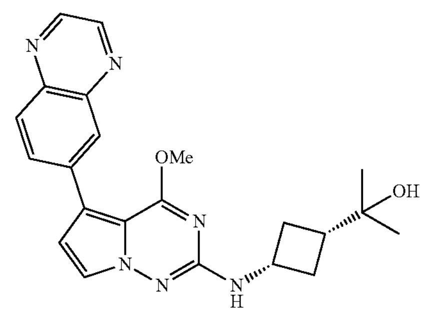

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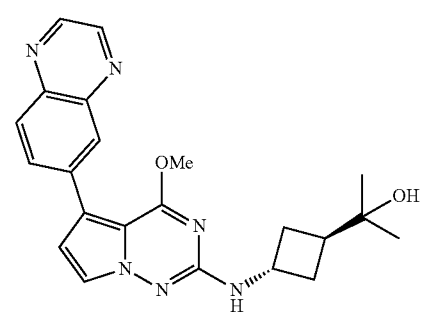

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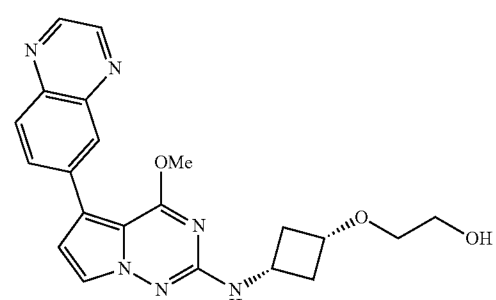

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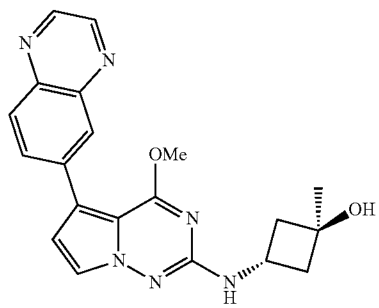

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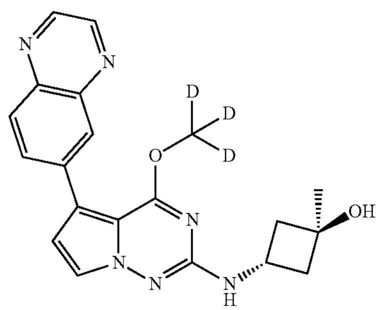

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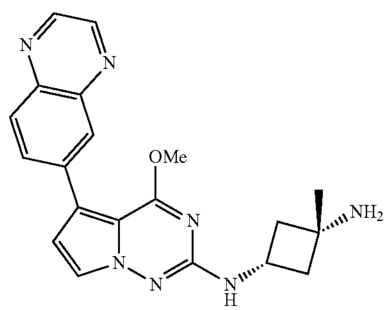

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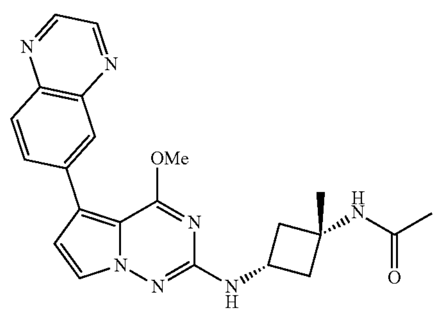

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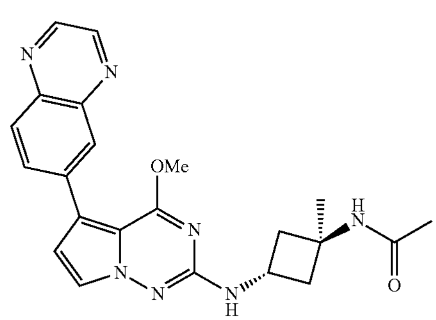

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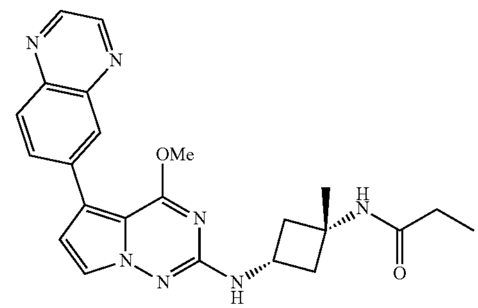

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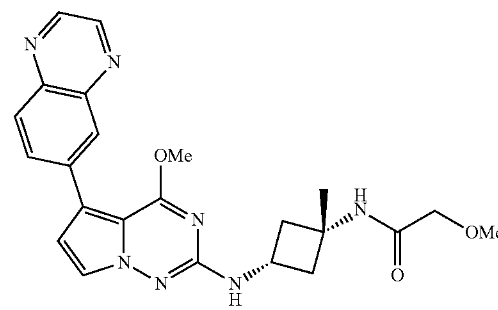

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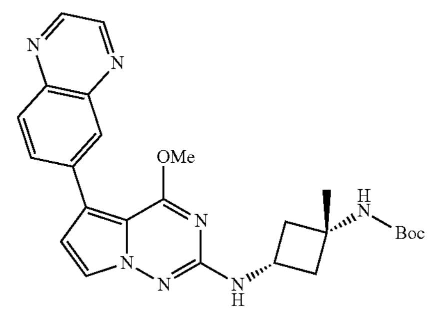

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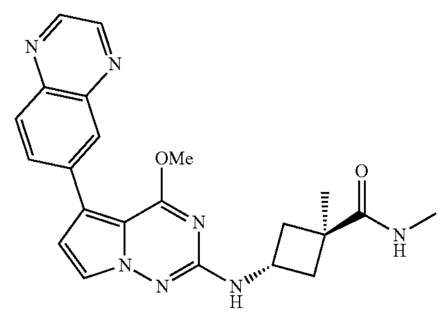

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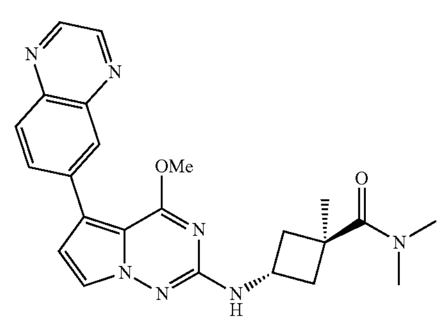

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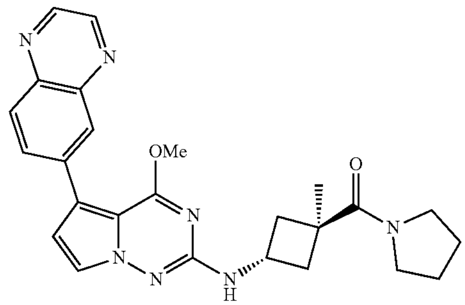

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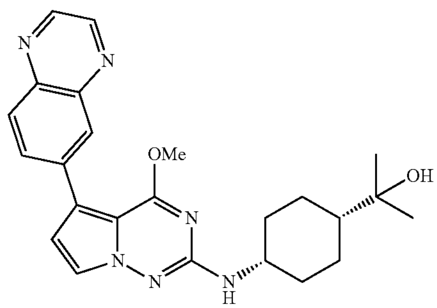

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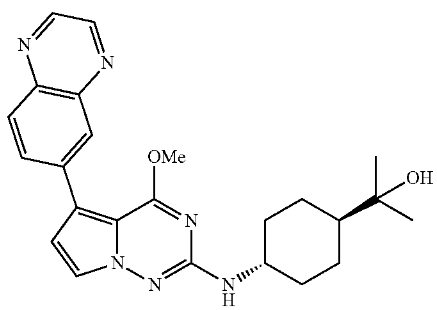

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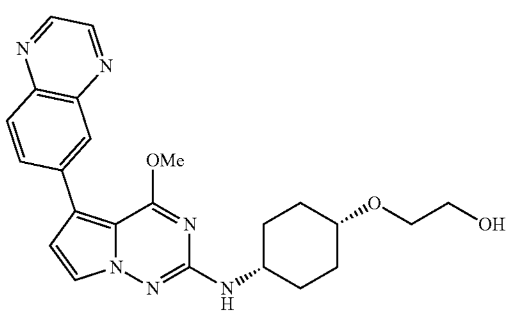

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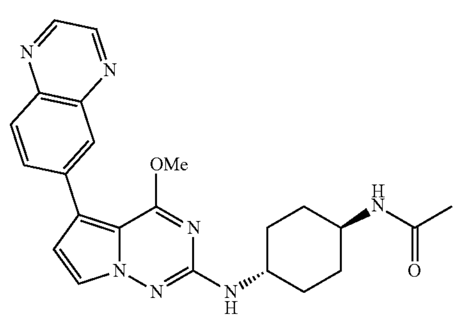

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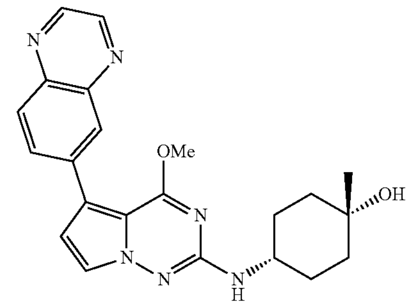

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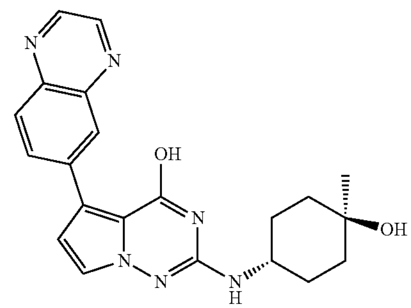

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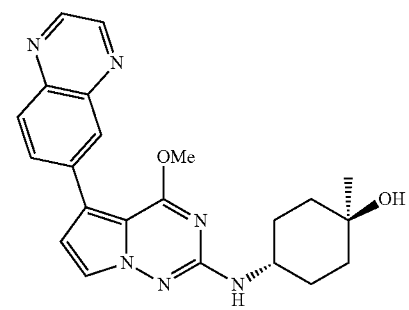

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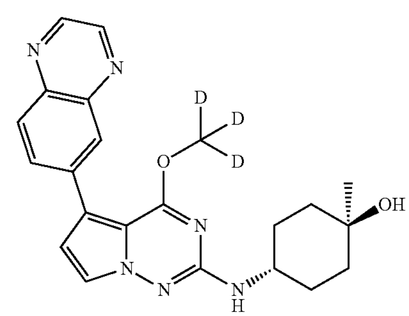

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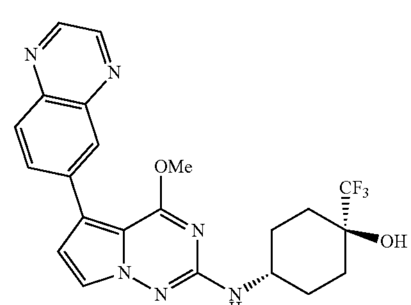

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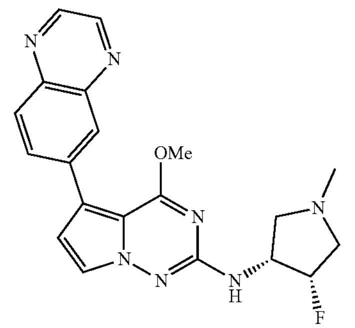

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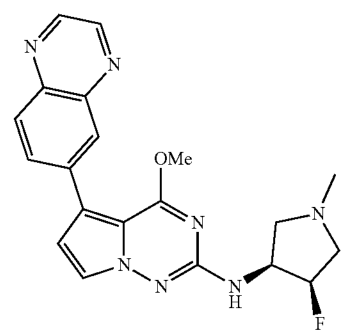

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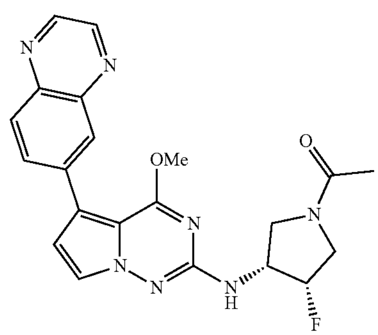

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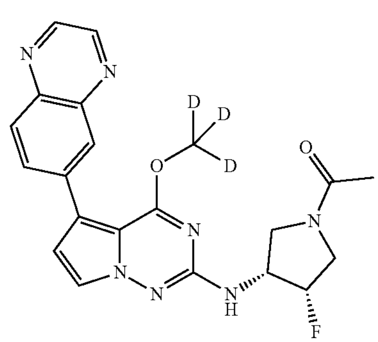

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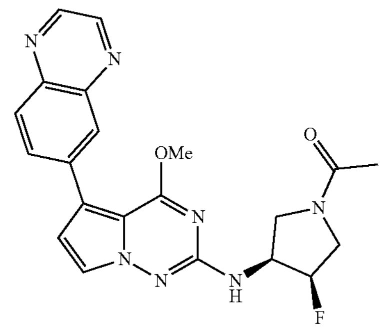

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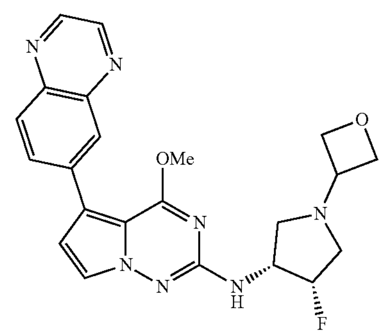

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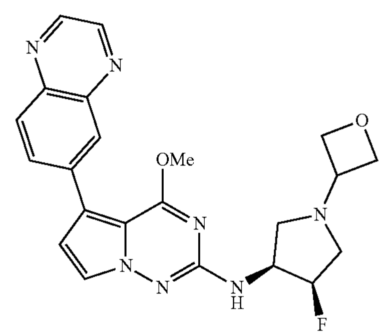

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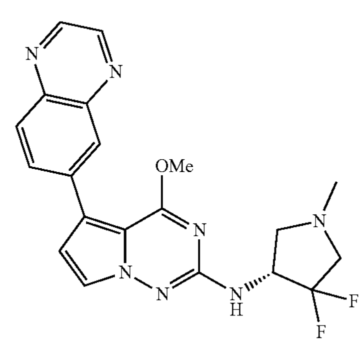

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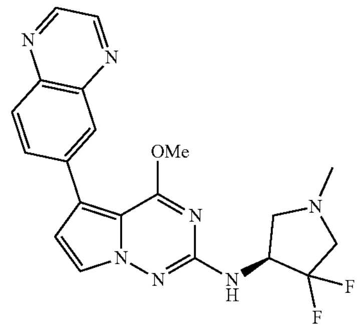

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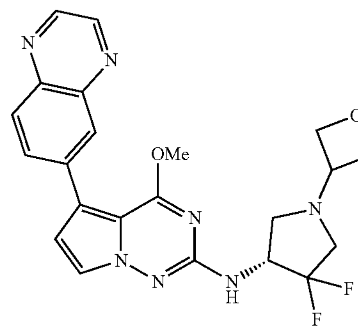

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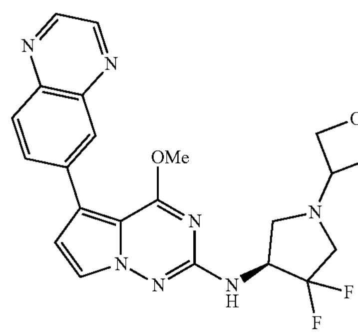

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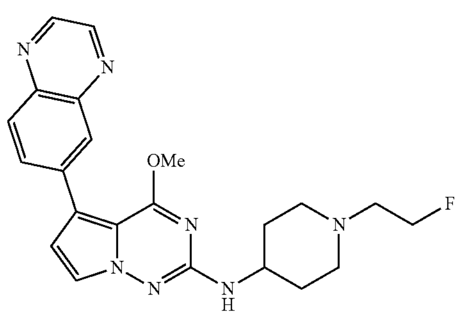

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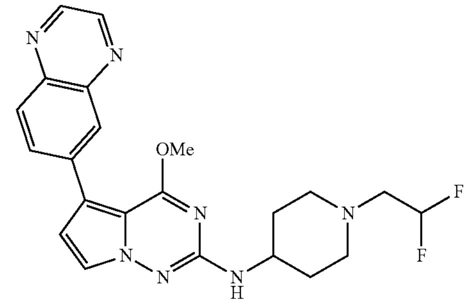

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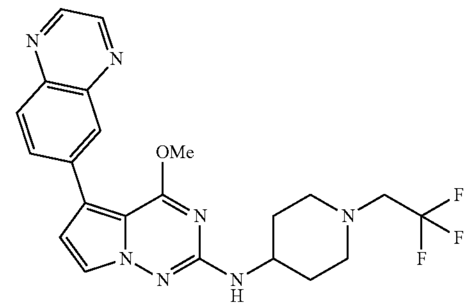

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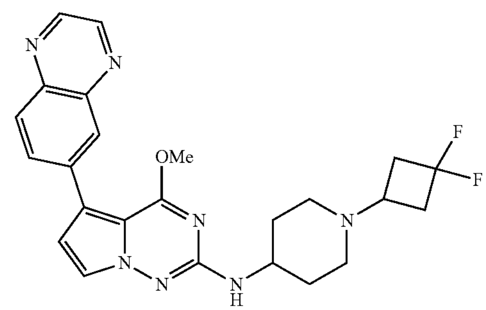

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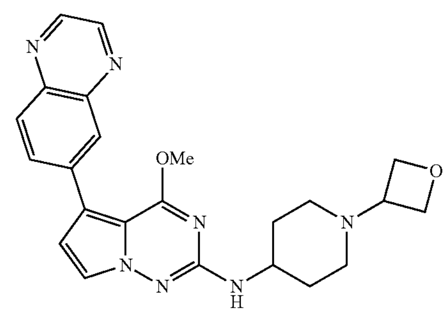

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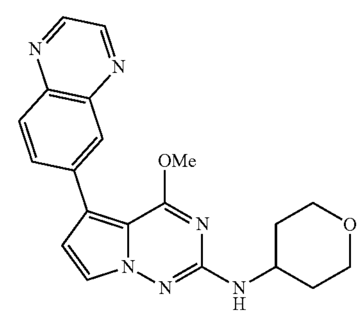

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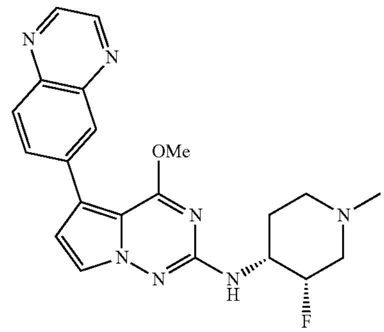

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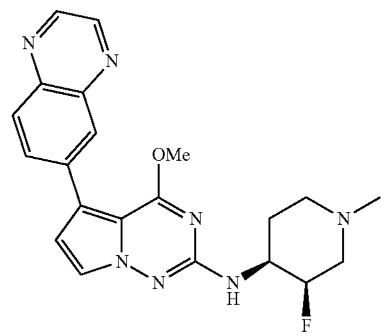

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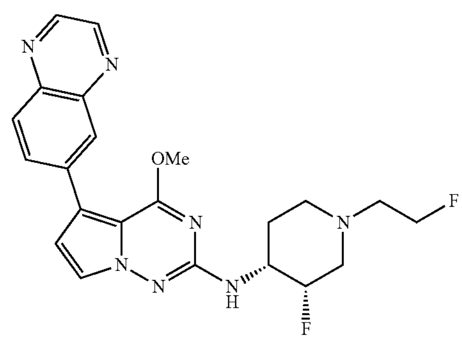

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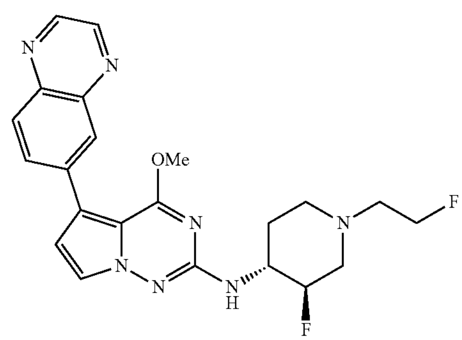

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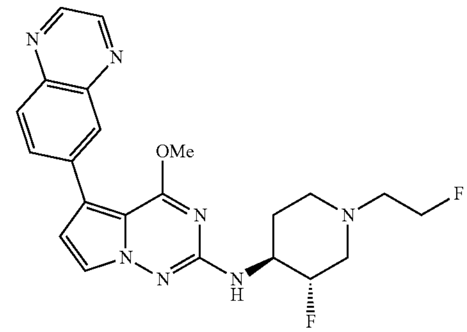

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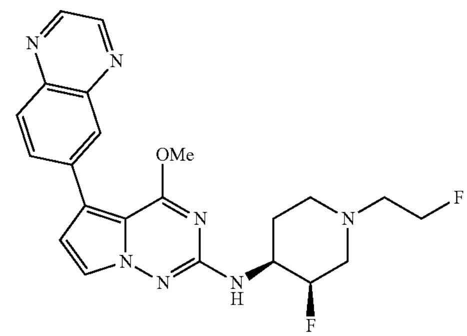

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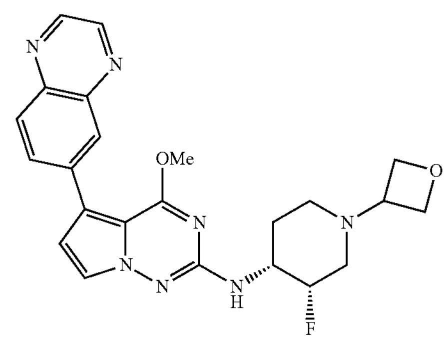

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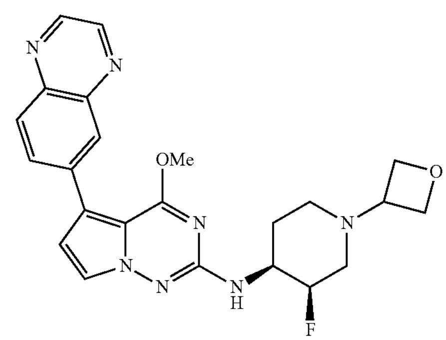

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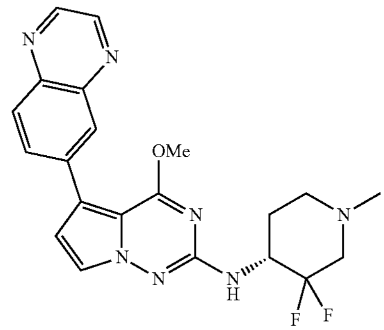

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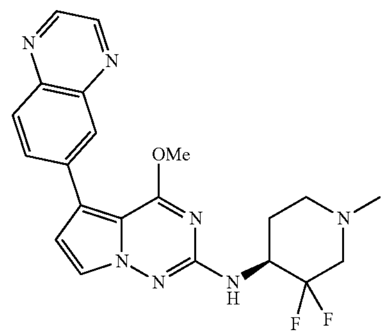

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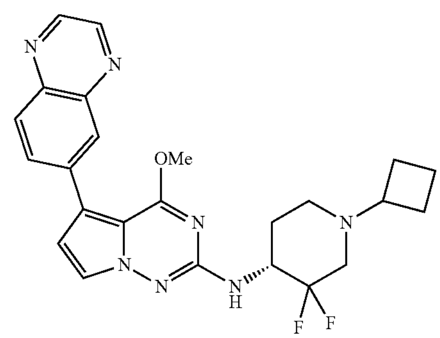

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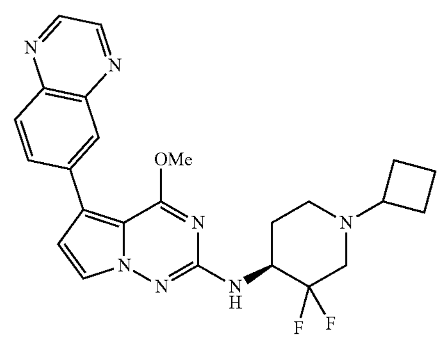

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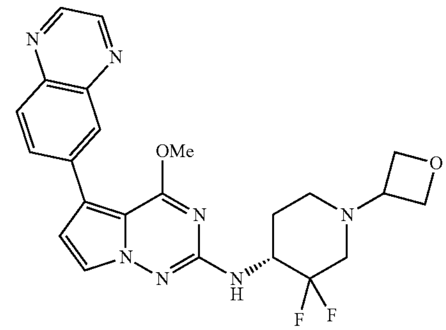

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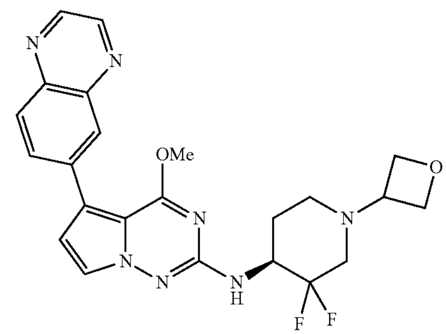

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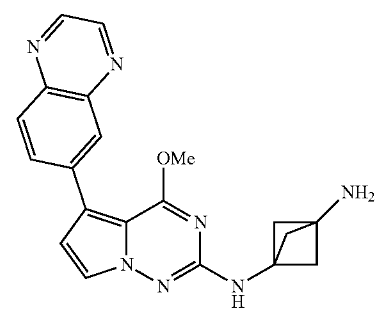

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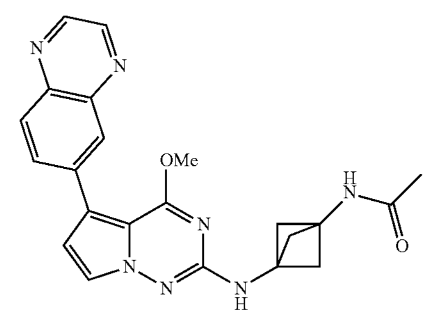

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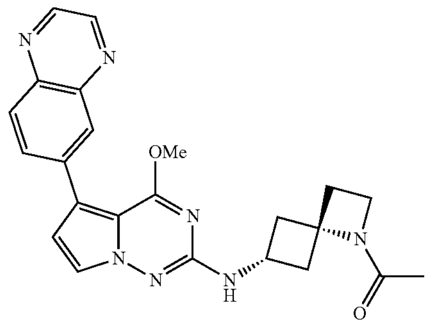

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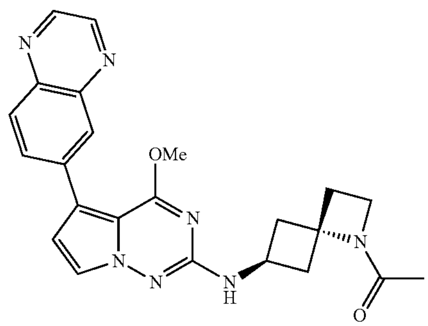

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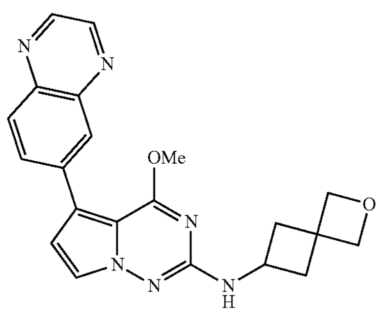

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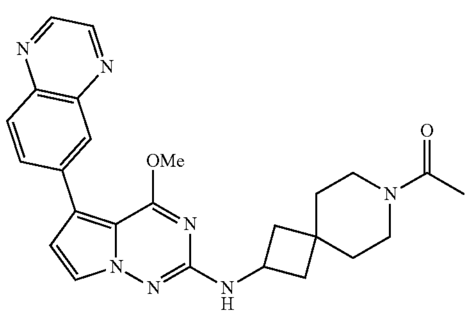

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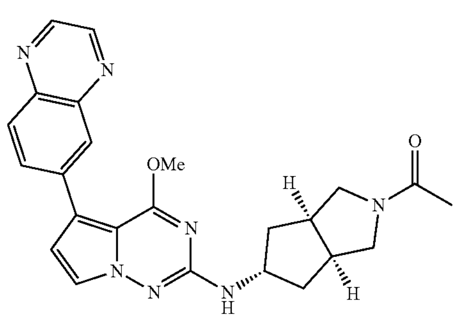

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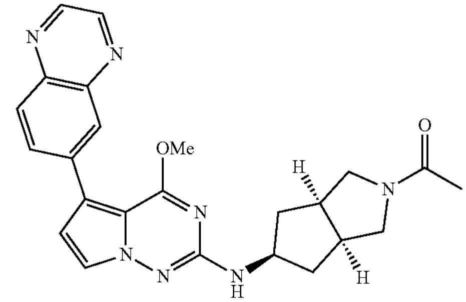

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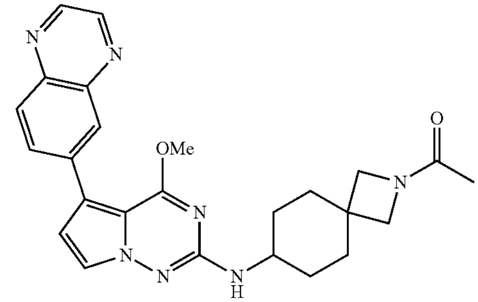

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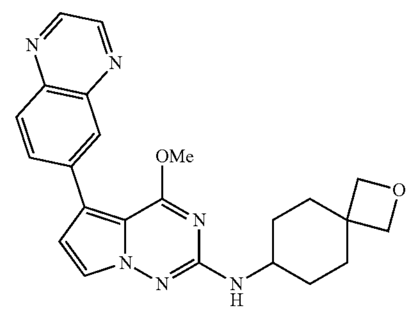

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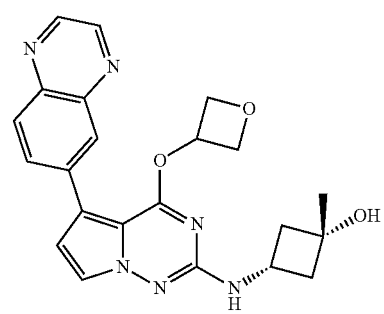

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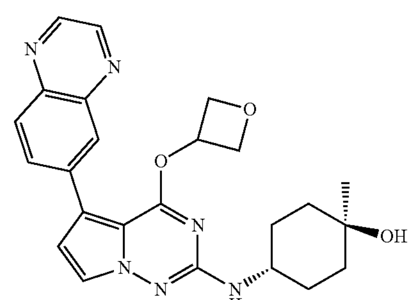

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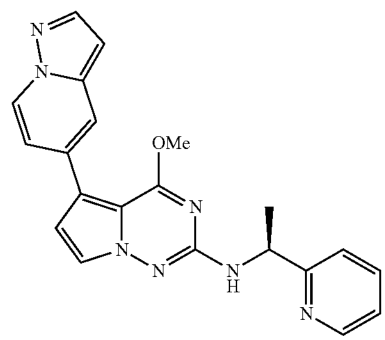

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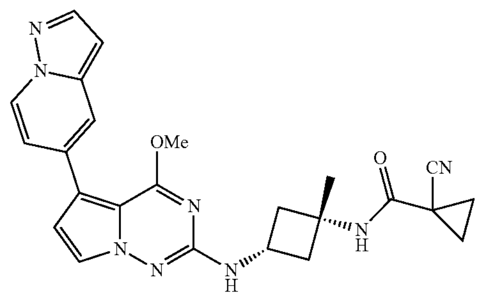

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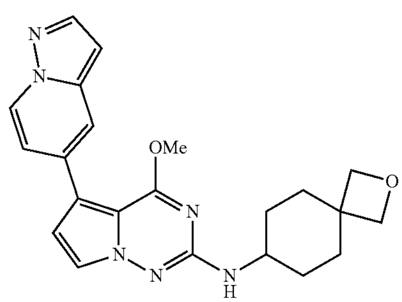

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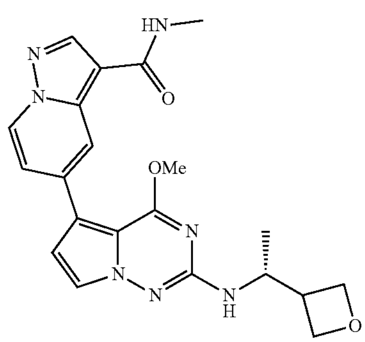

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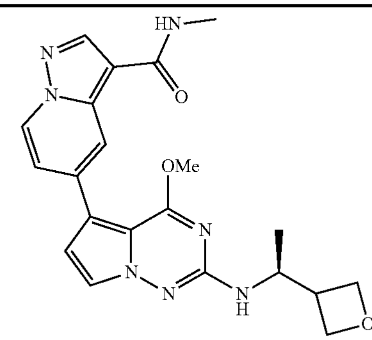

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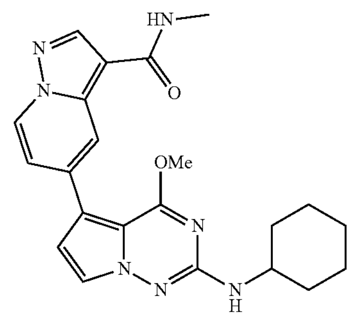

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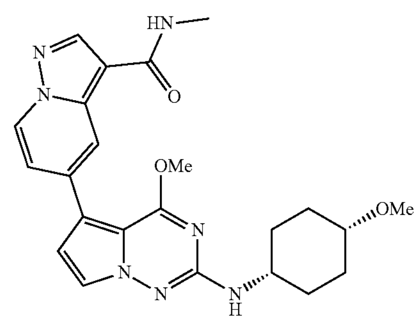

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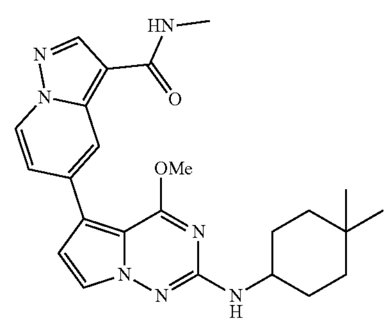

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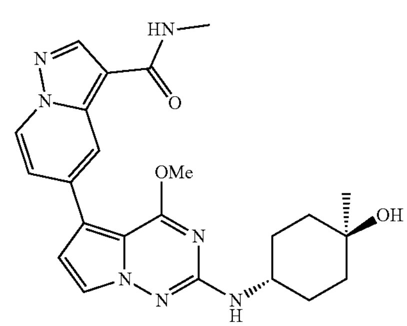

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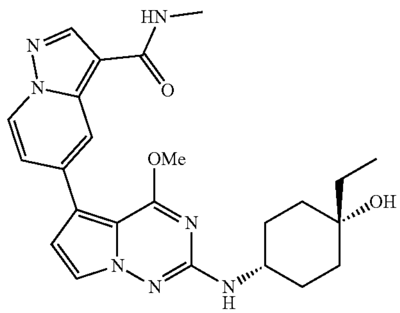

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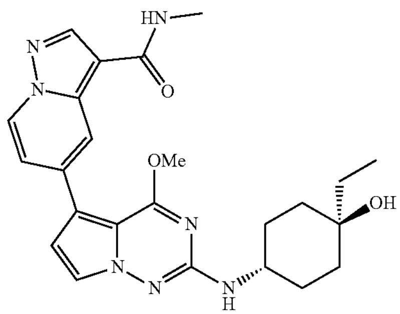

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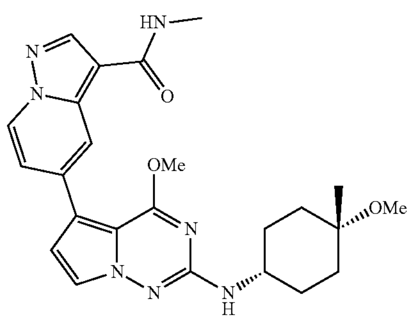

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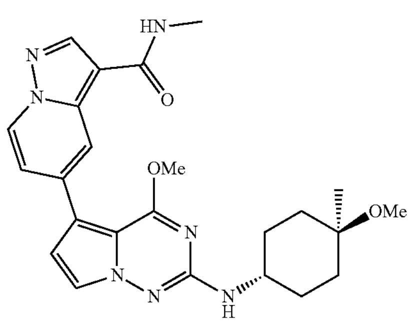

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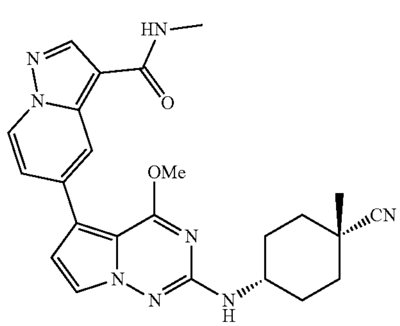

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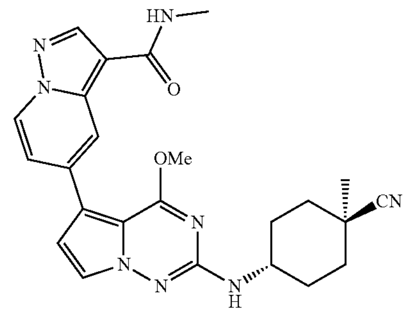

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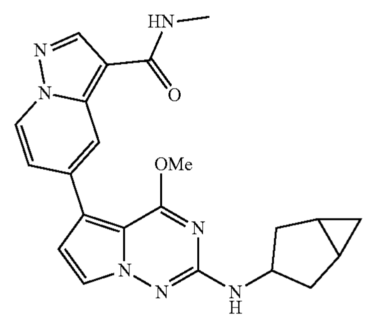

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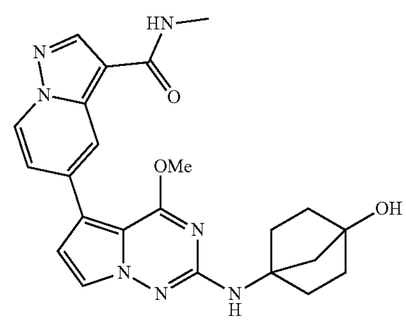

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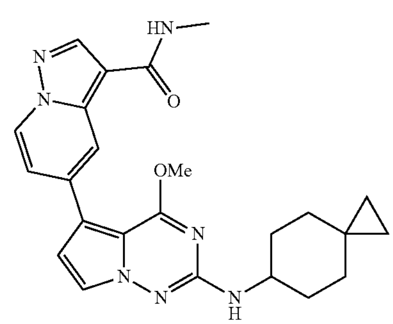

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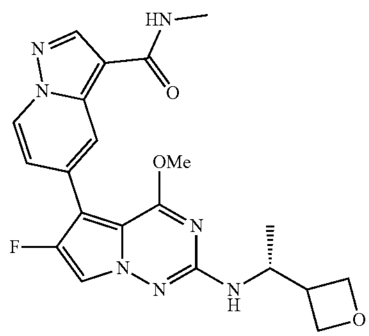

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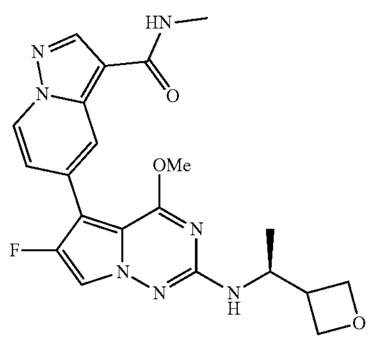

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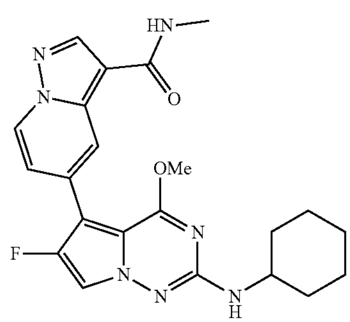

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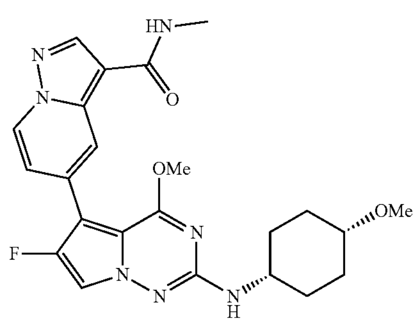

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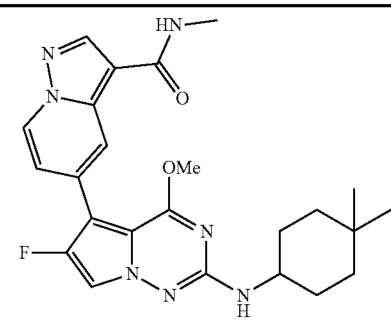

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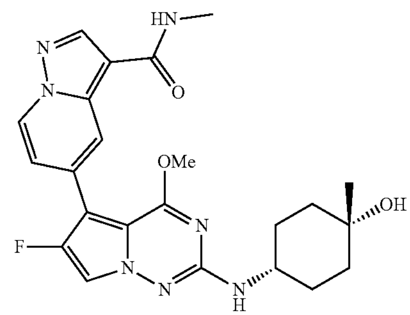

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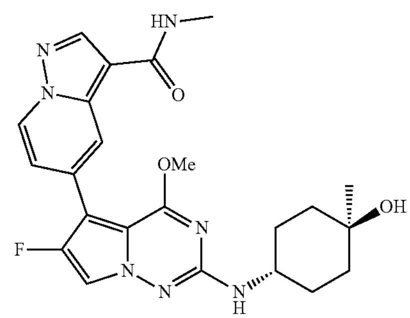

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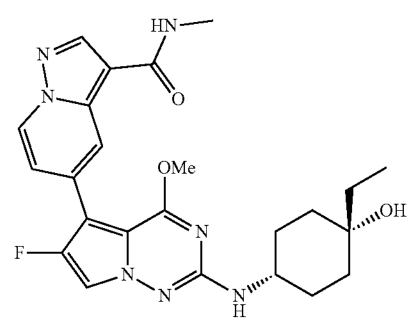

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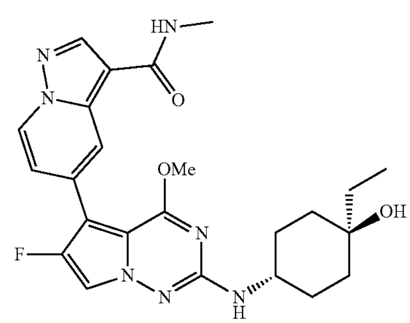

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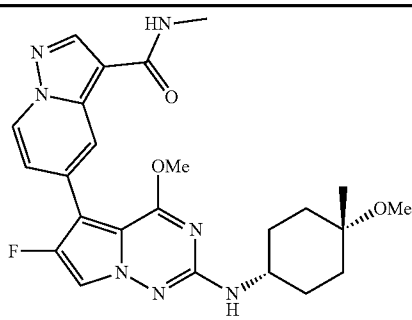
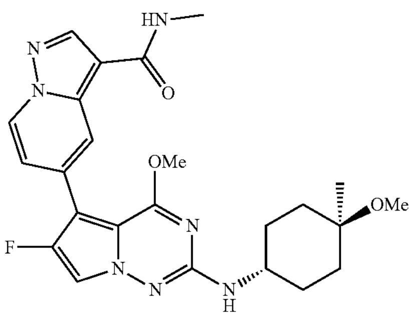
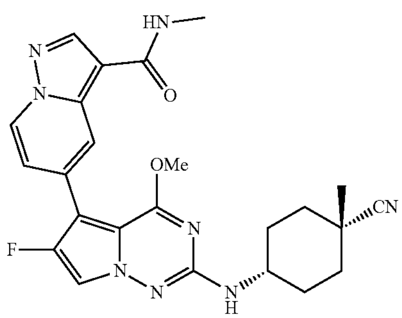
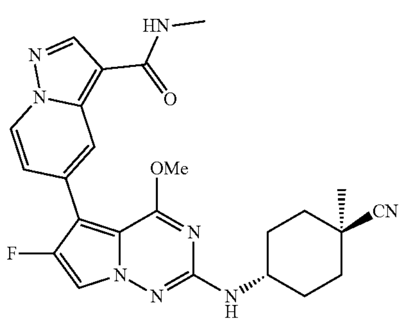
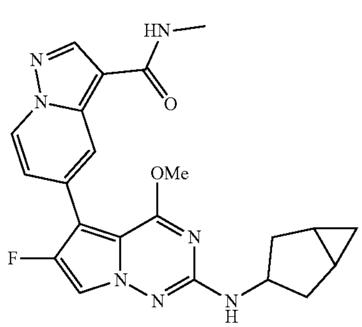
420	
421	
422	
423	
424	

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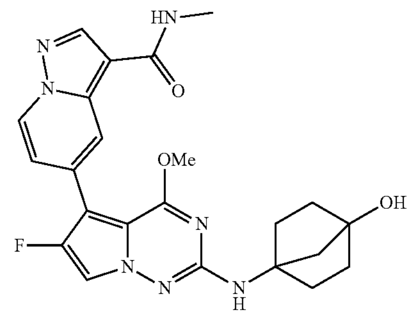
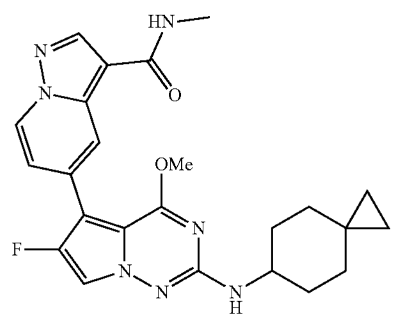
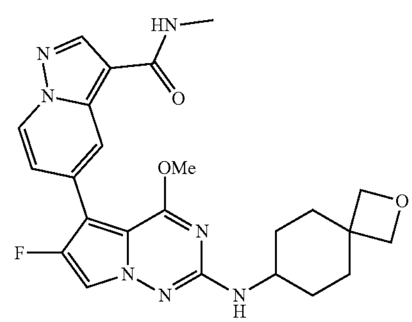
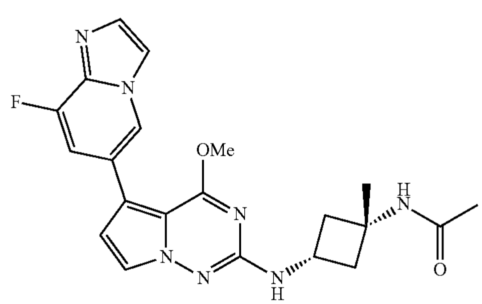
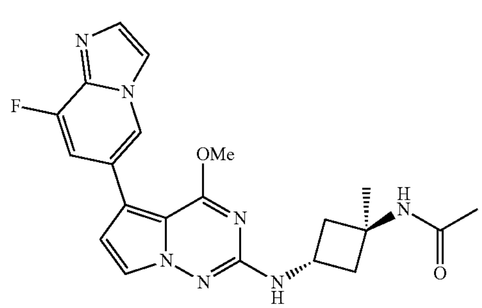
425	
426	
427	
428	
429	

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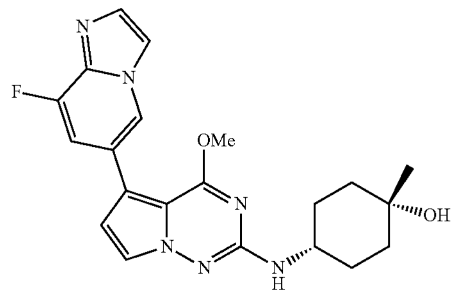

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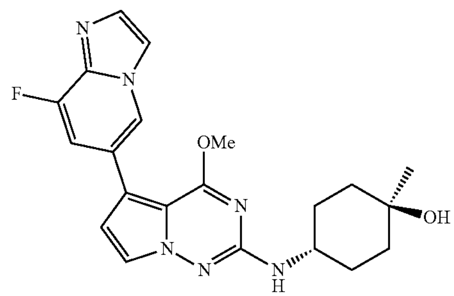

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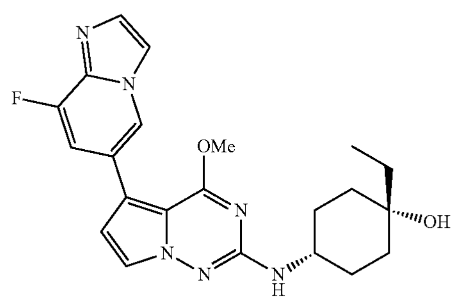

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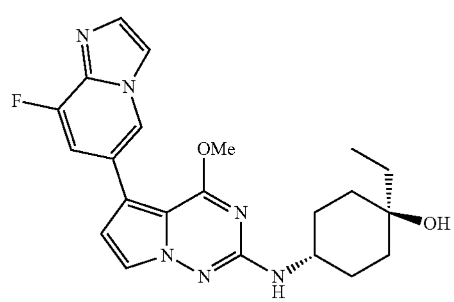

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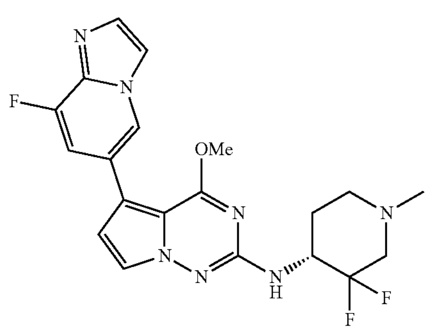

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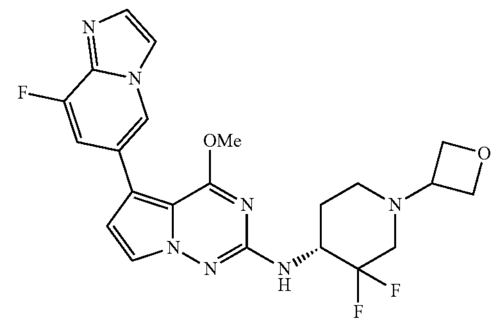

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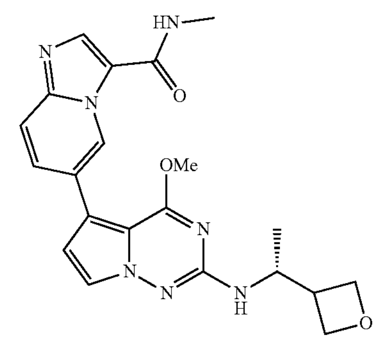

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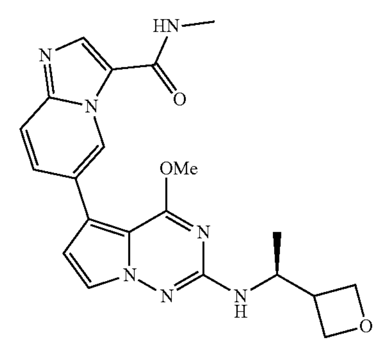

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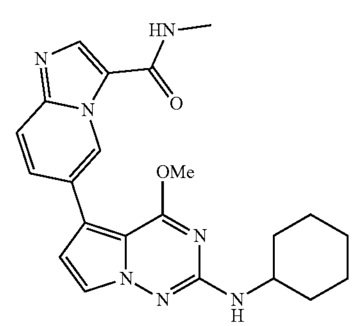

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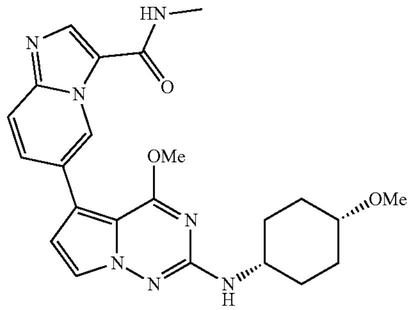
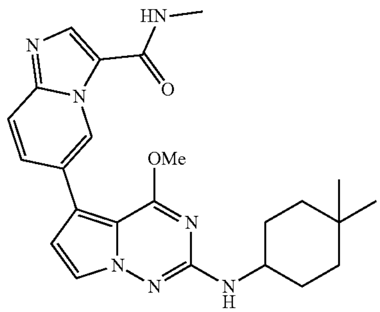
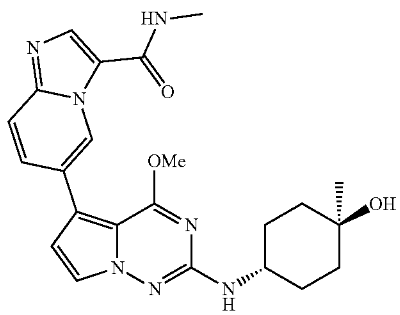
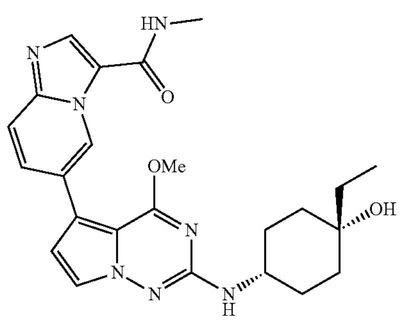
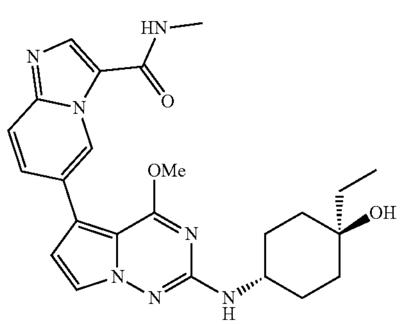
439 

440 

441 

442 

443 

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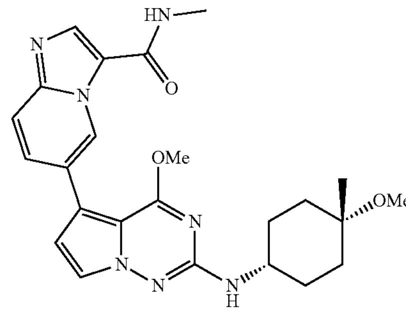
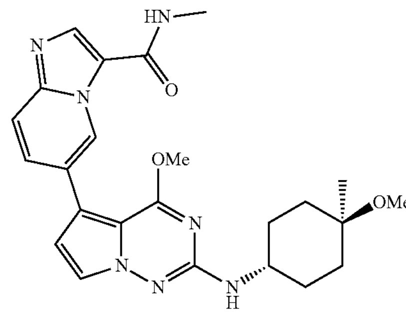
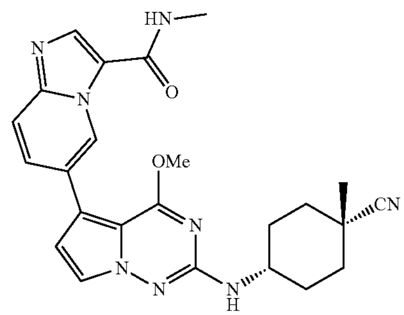
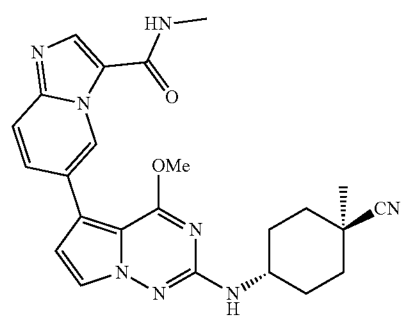
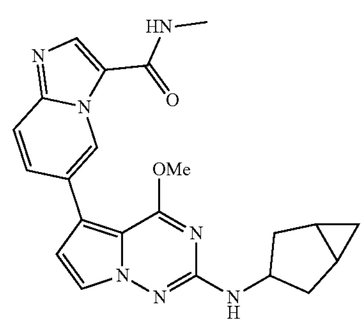
444 

445 

446 

447 

448 

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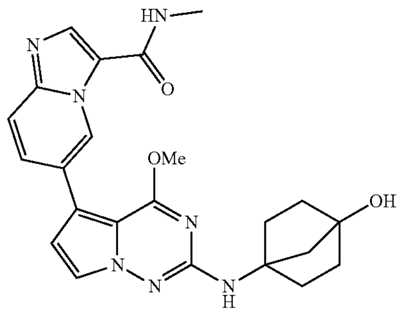

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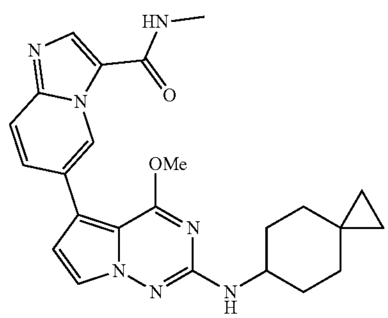

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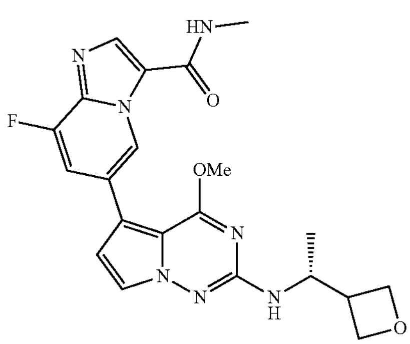

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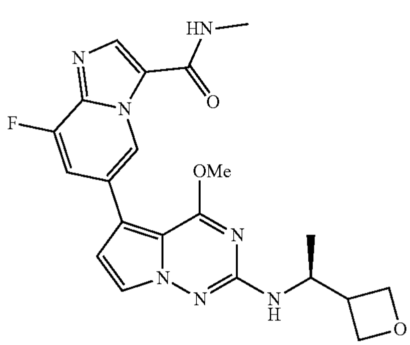

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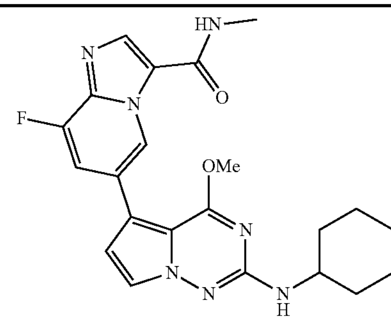

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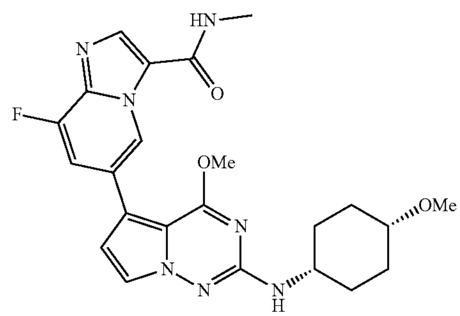

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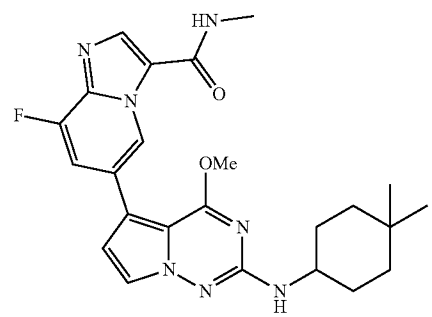

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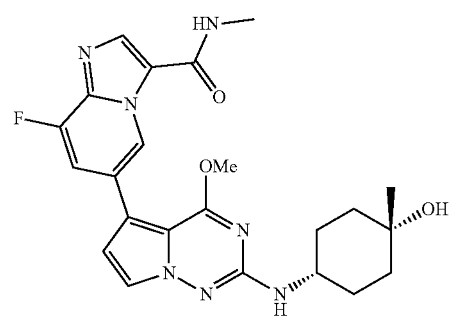

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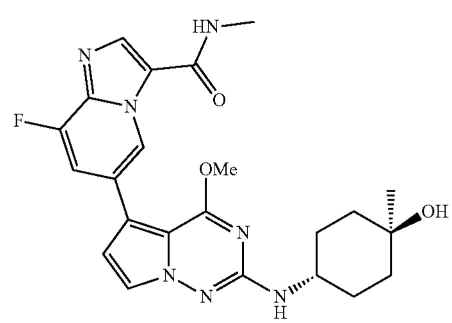

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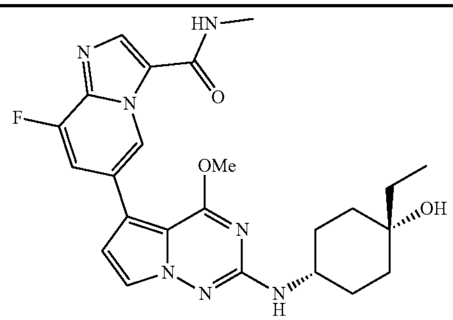

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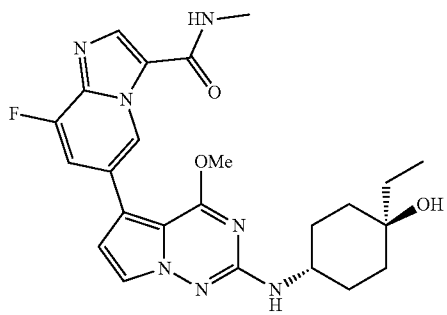

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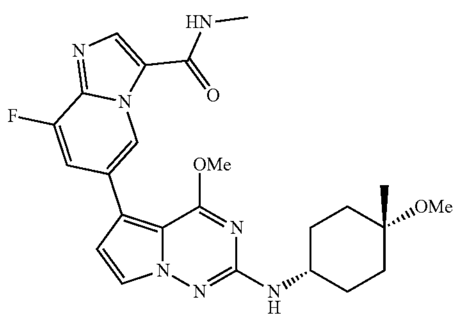

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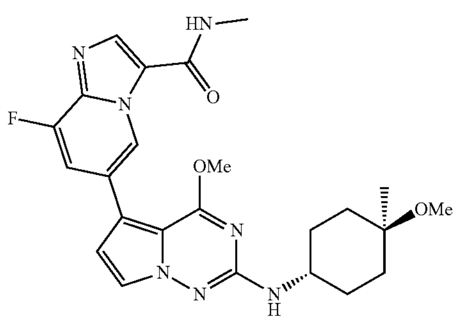

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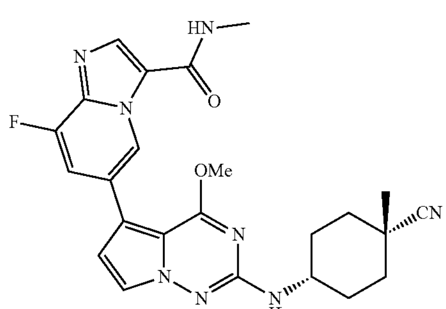

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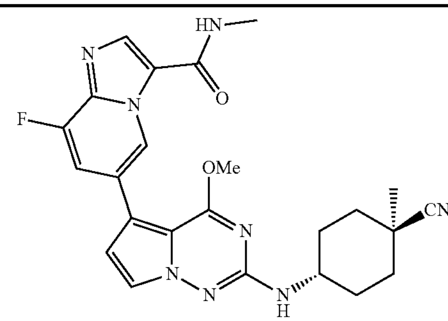

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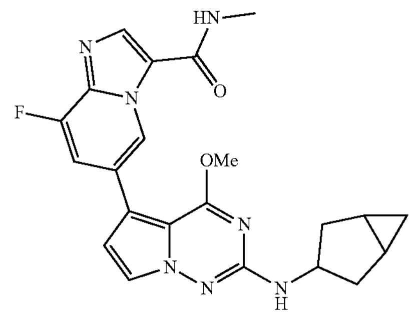

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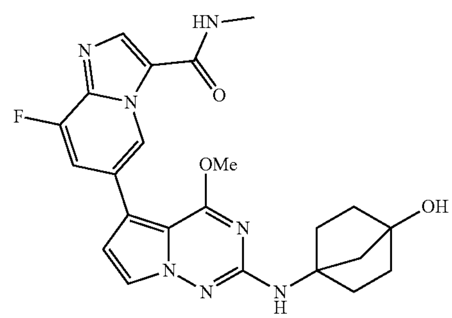

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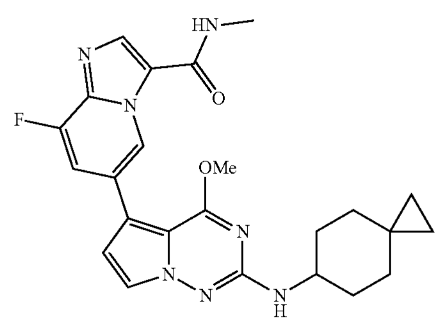

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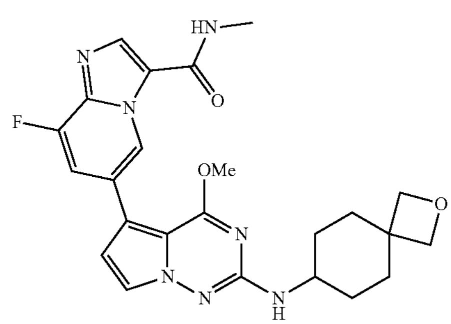

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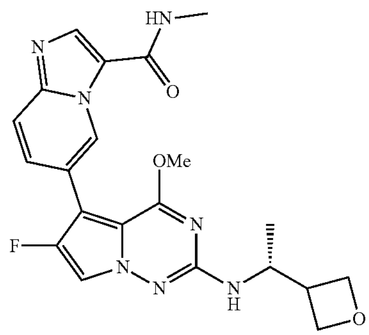

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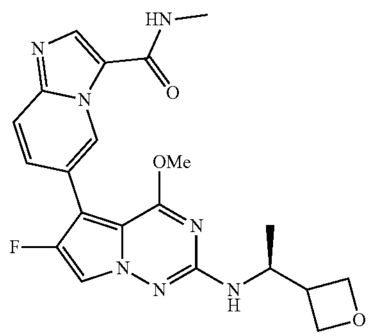

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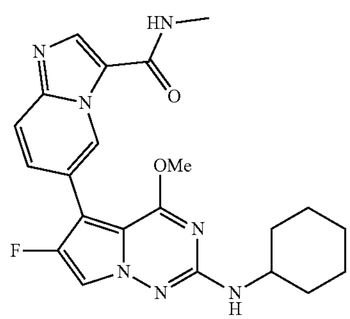

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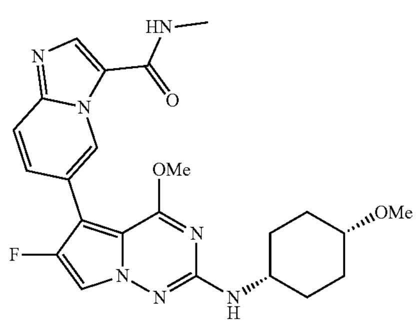

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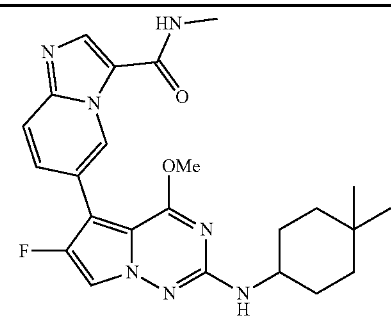

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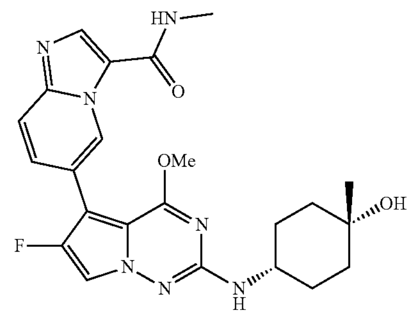

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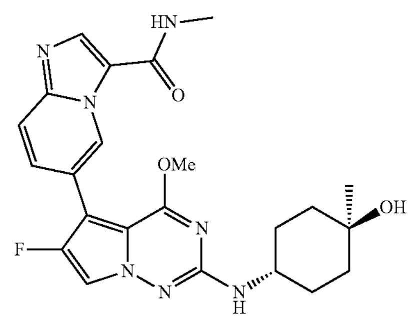

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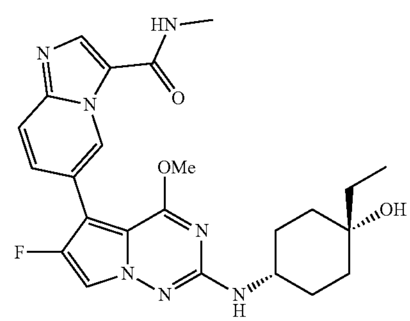

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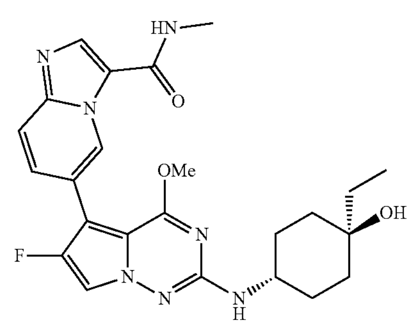

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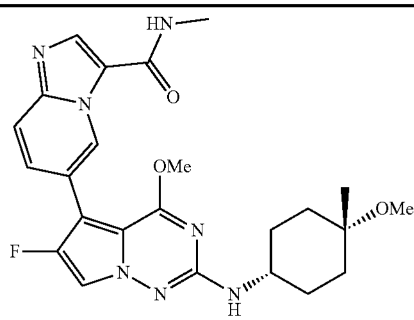

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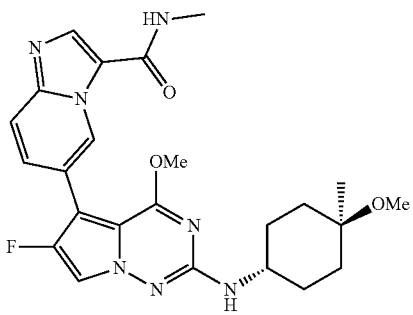

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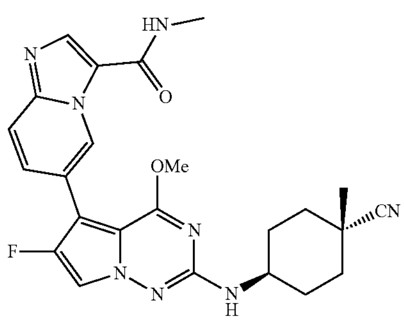

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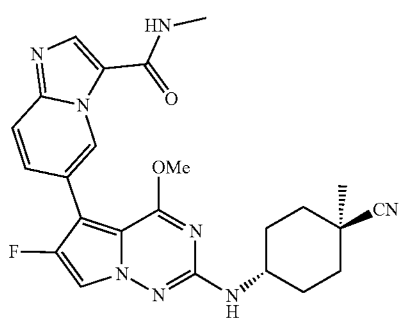

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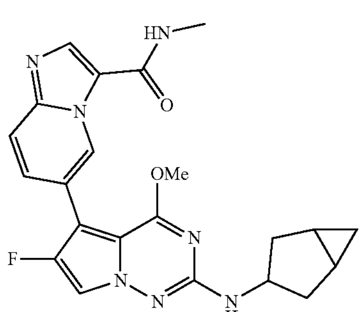

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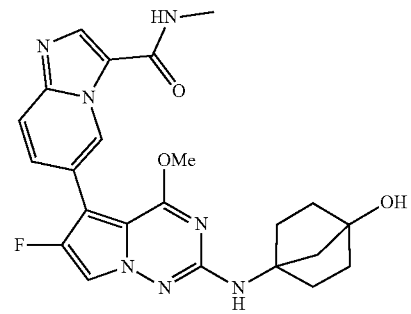

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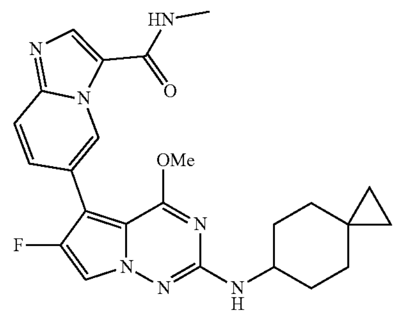

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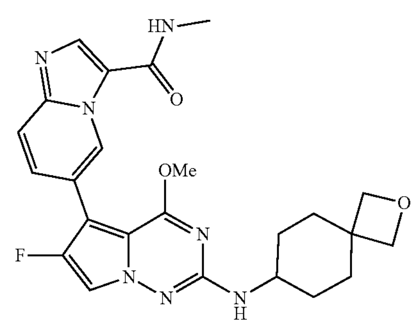

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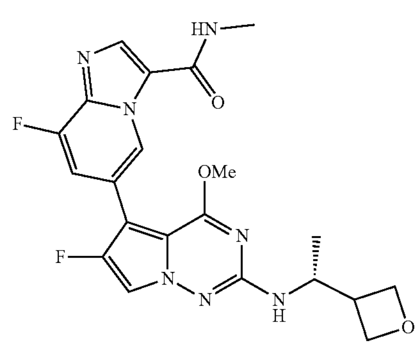

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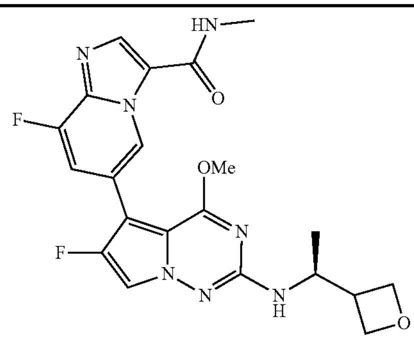

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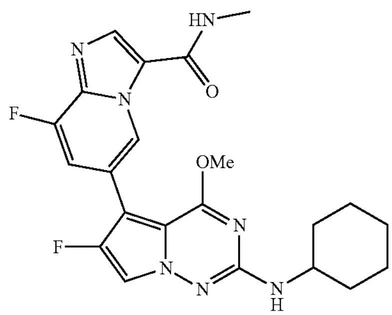

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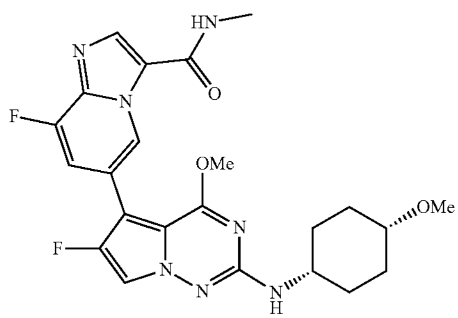

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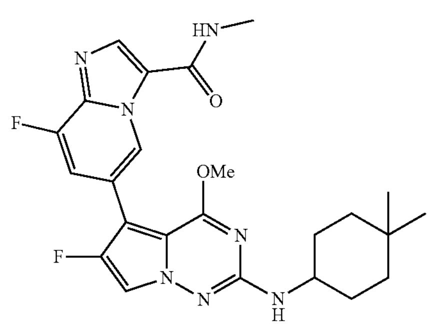

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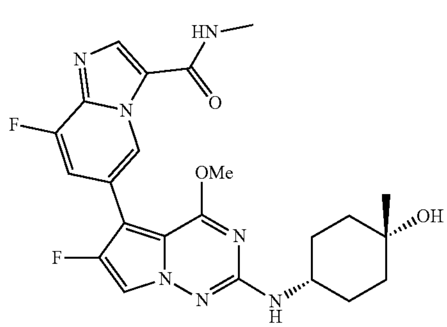

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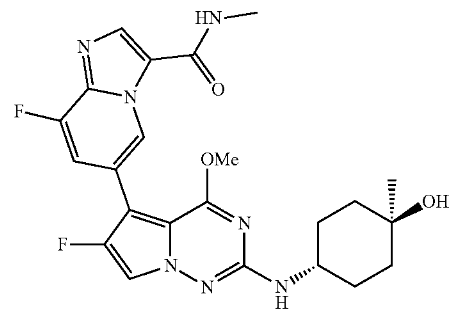

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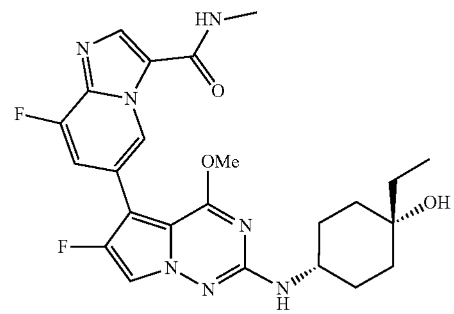

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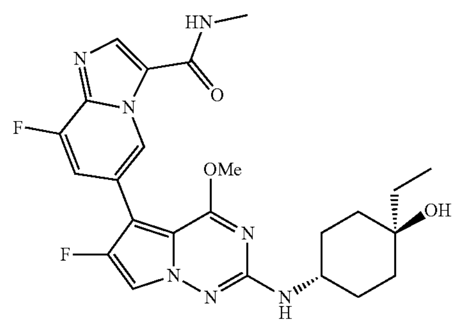

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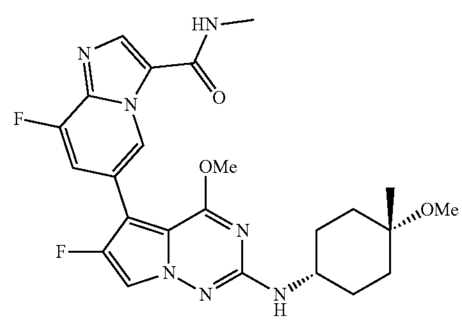

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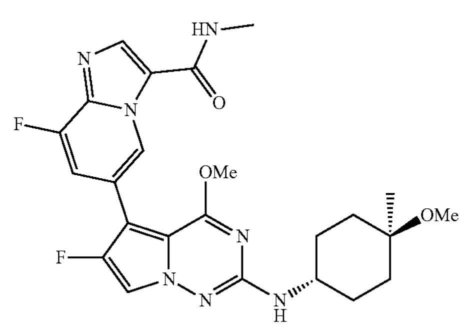

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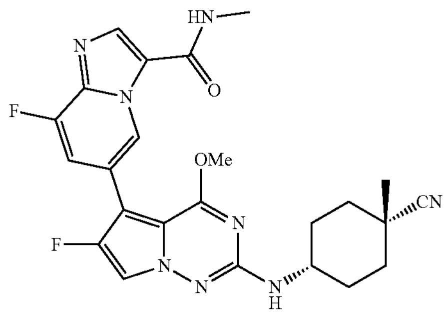

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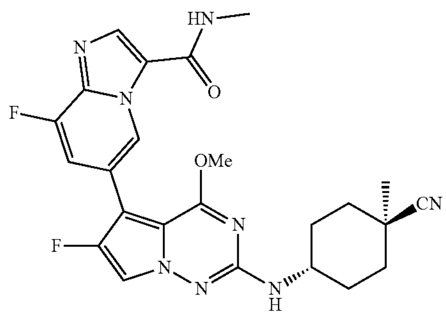

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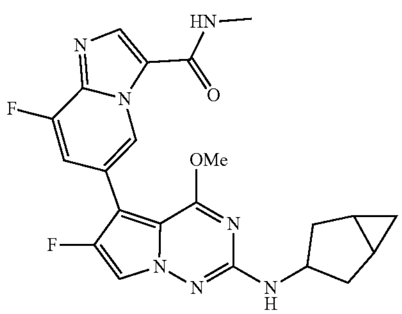

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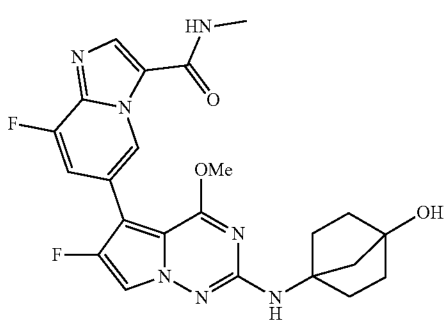

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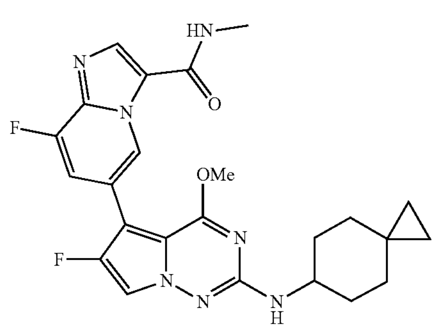

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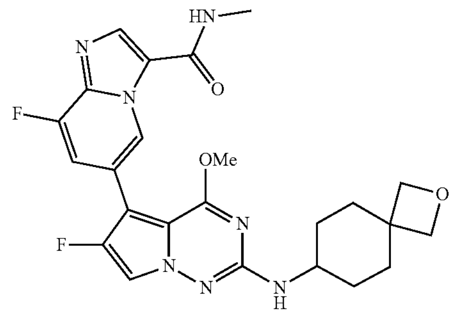

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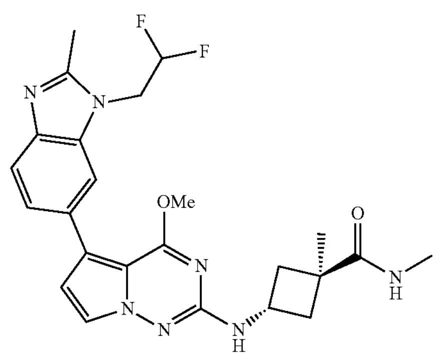

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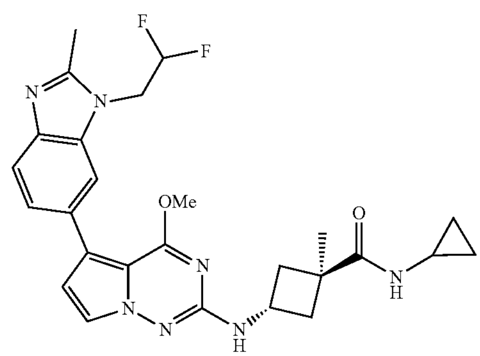

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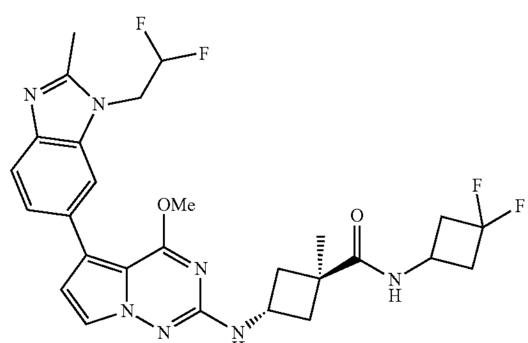

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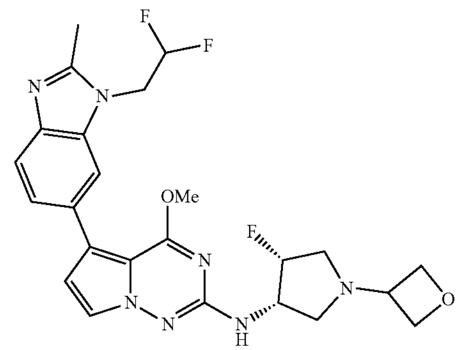

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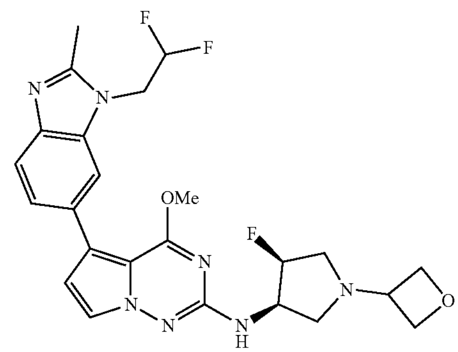

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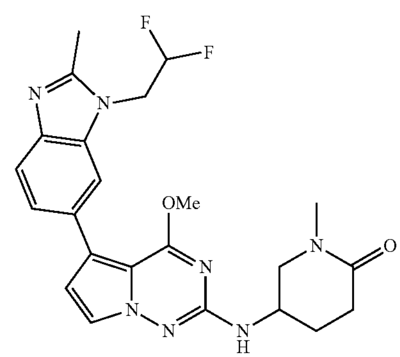

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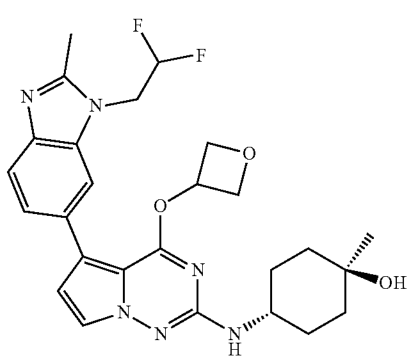

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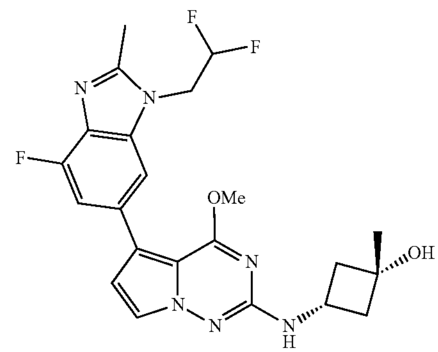

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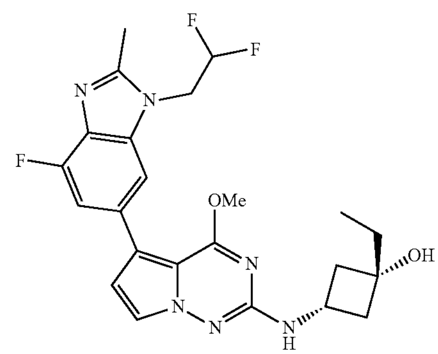

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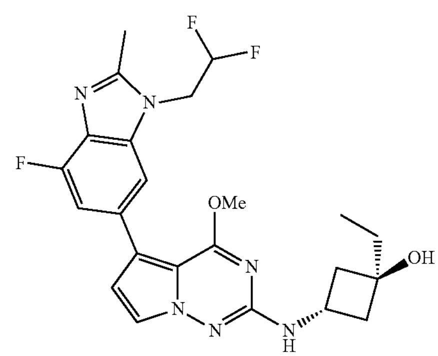

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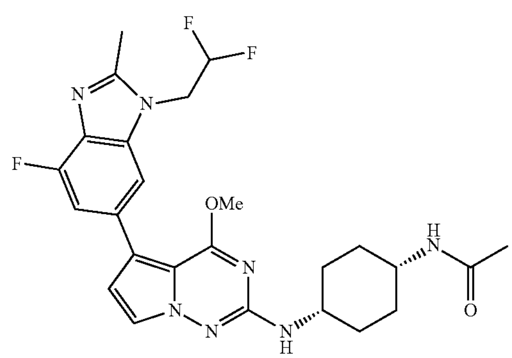

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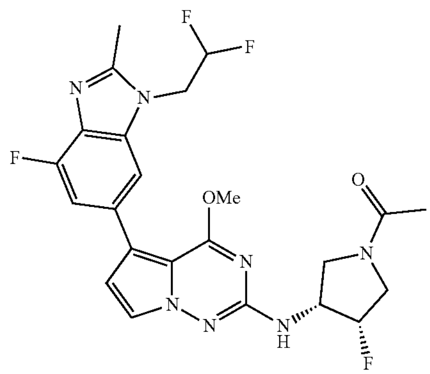

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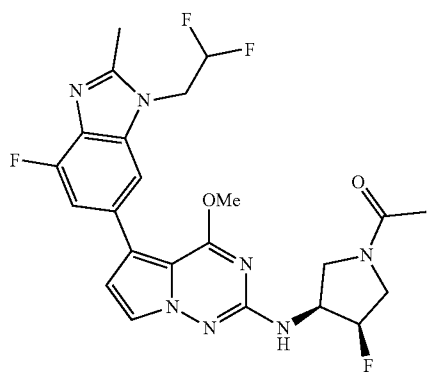

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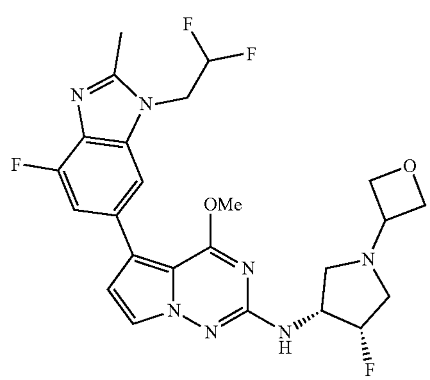

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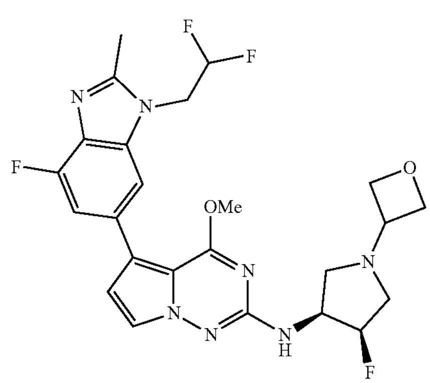

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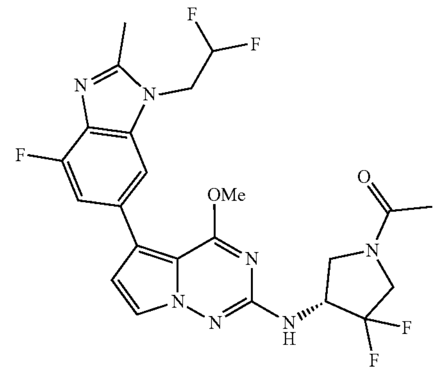

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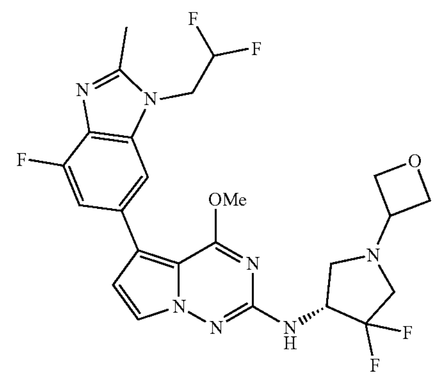

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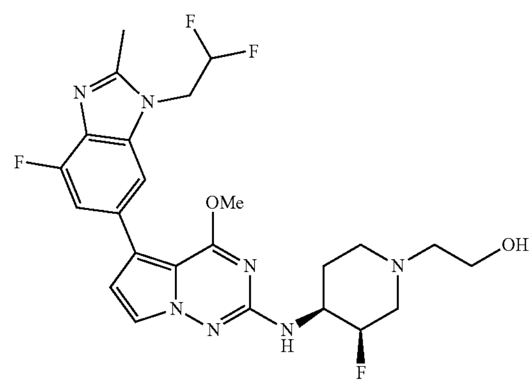

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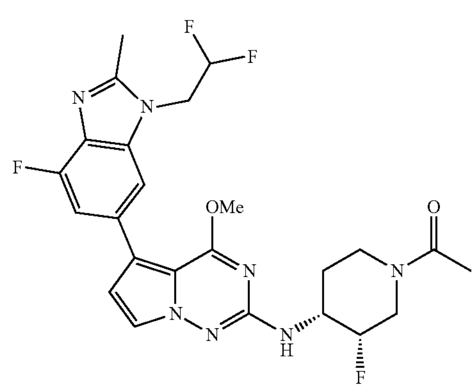

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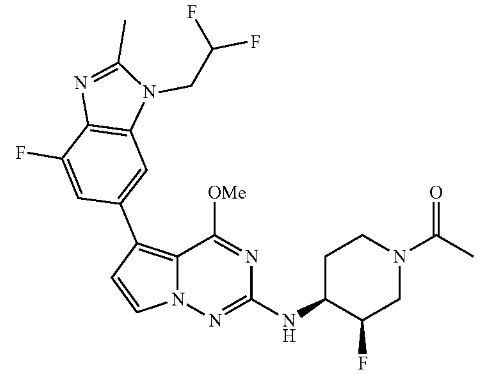

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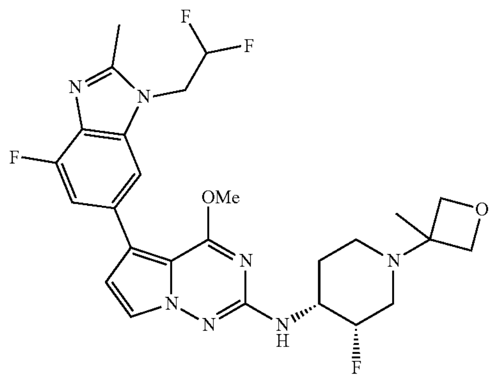

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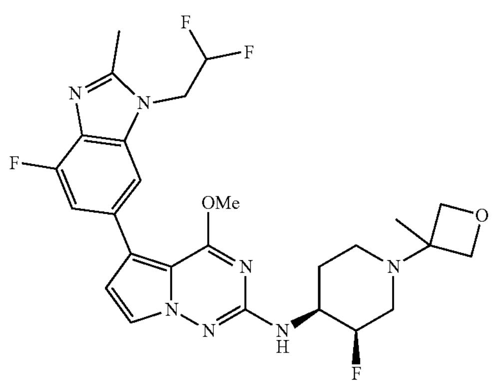

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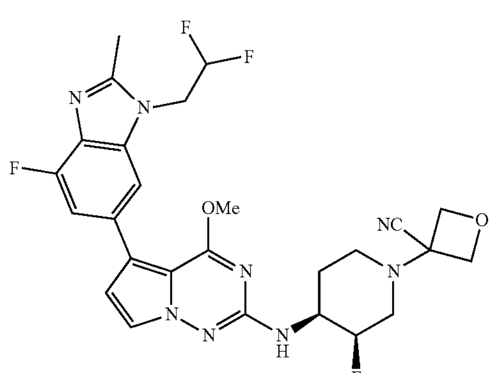

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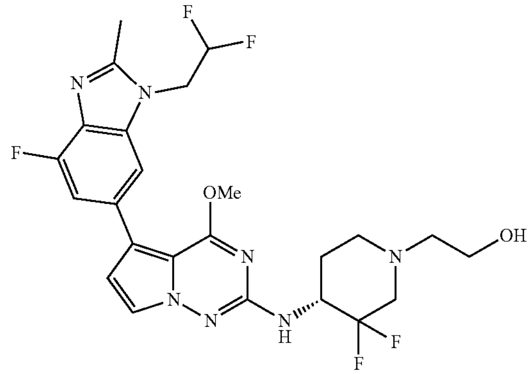

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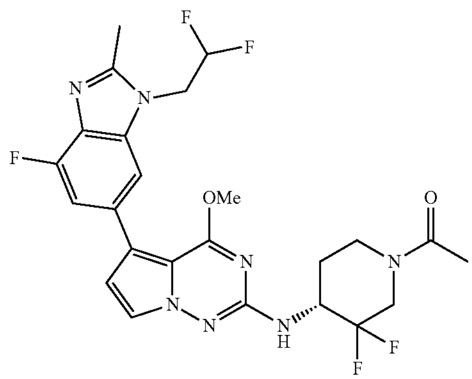

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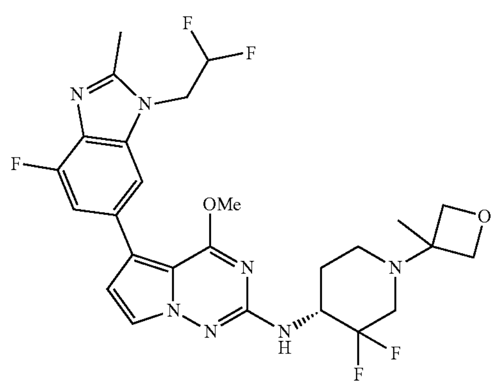

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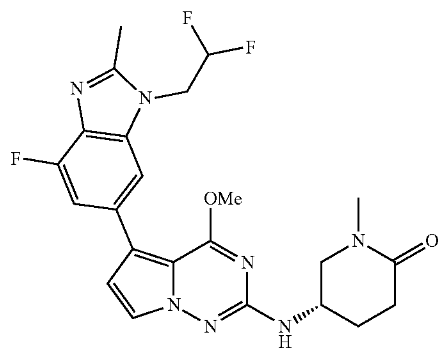

TABLE 1-continued

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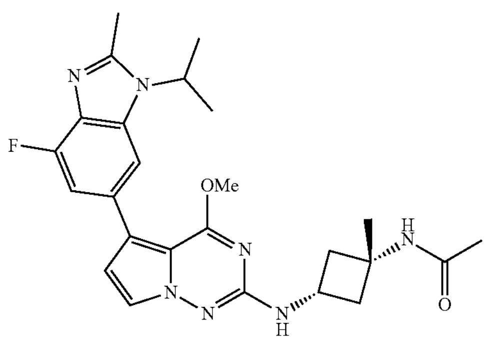

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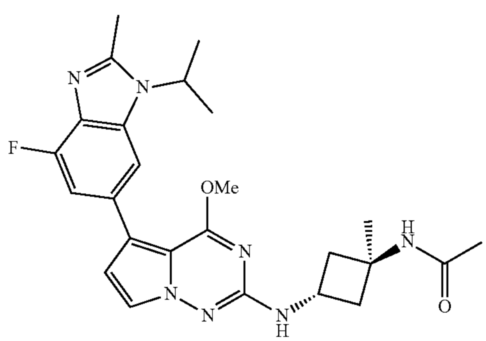

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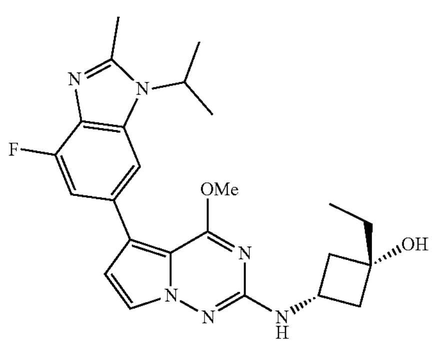

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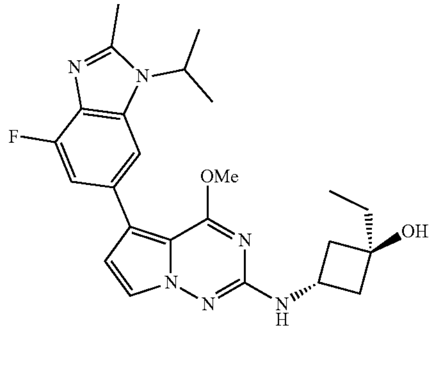

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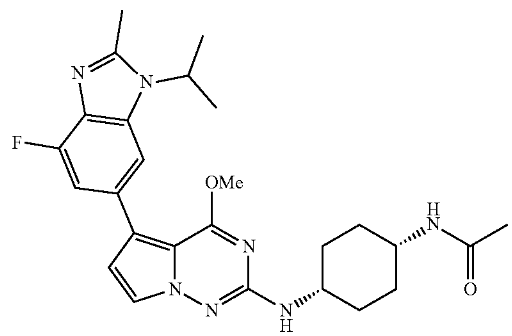

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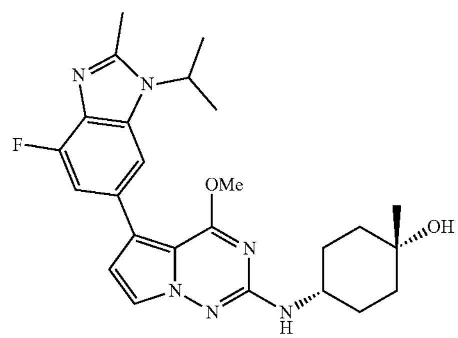

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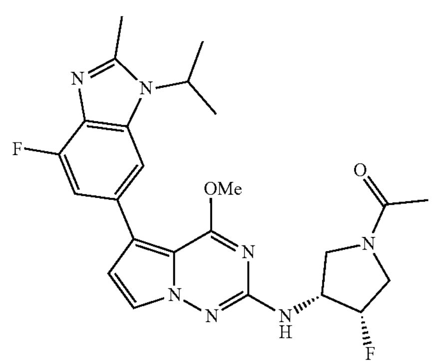

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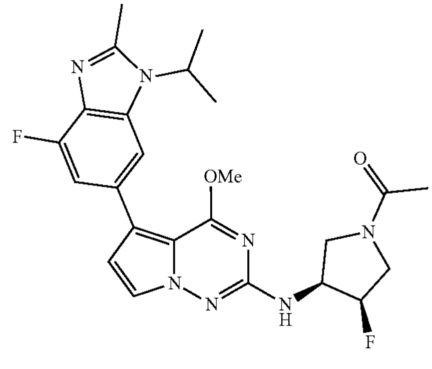

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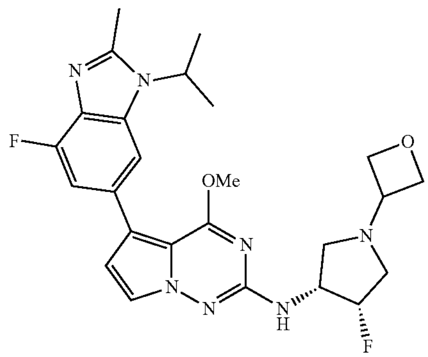

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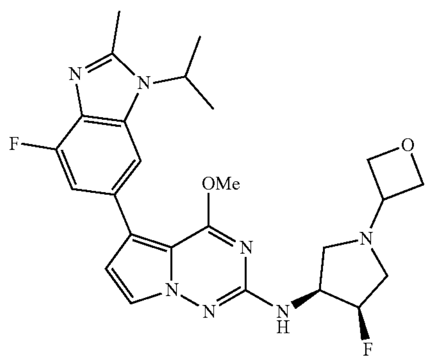

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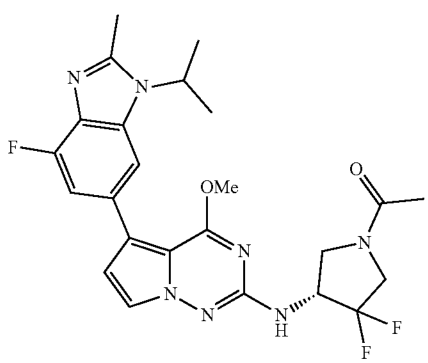

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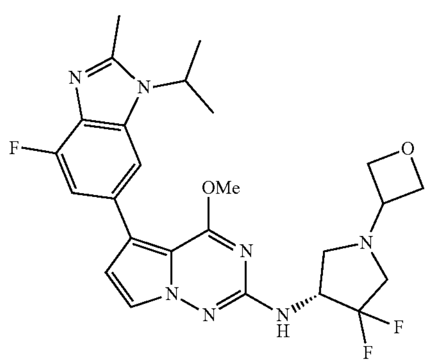

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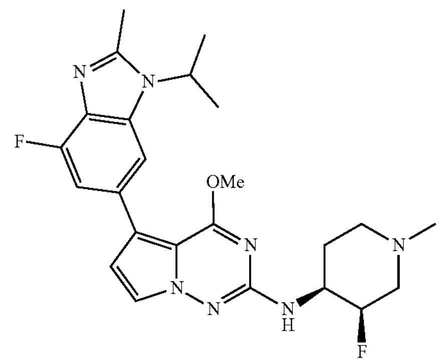

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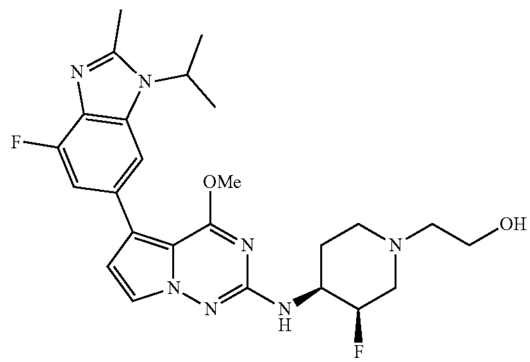

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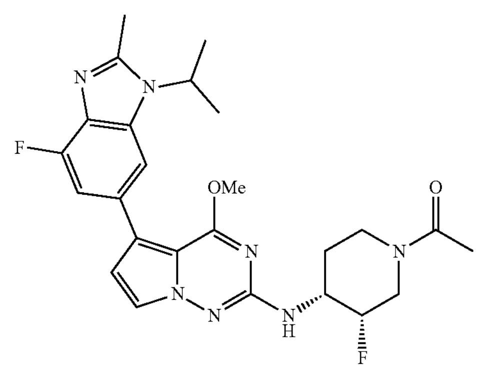

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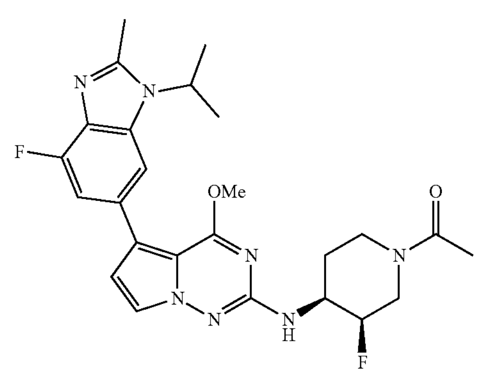

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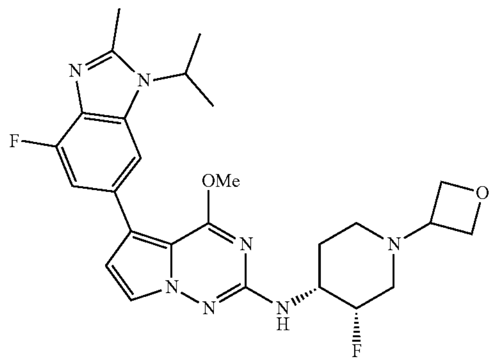

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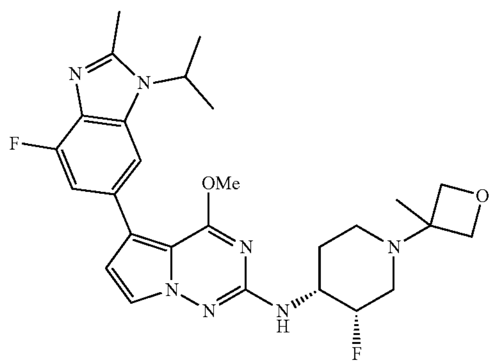

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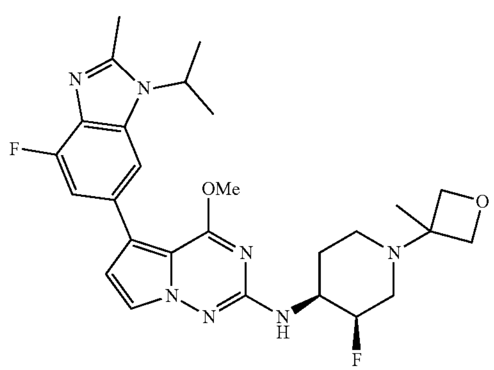

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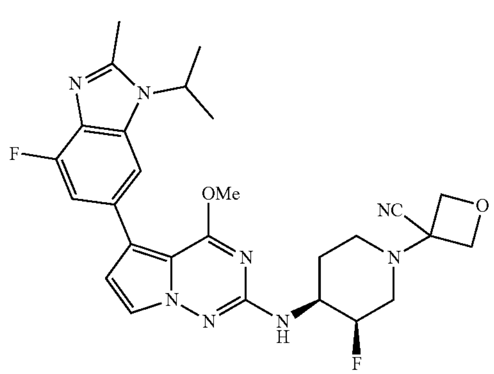

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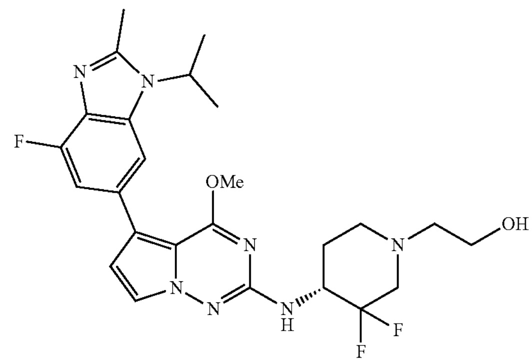

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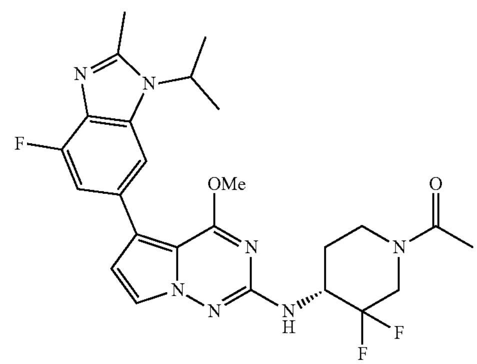

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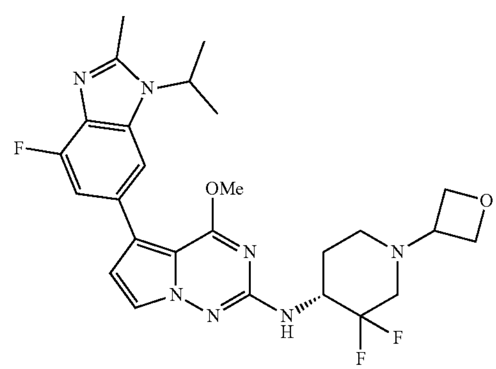

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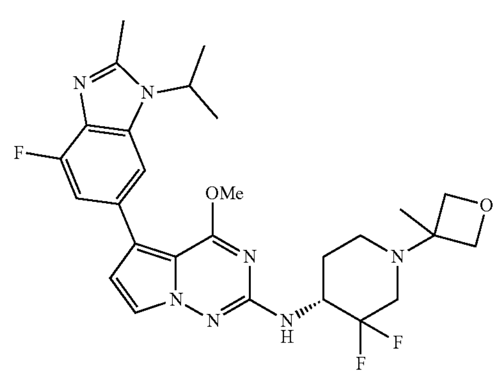

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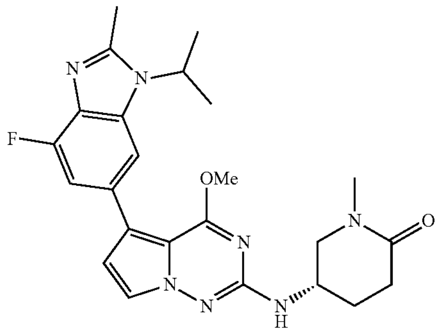

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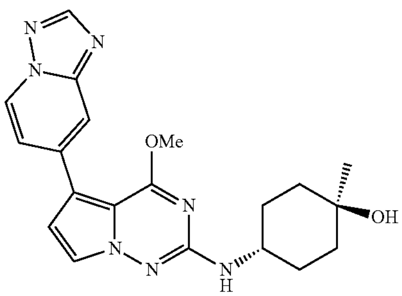

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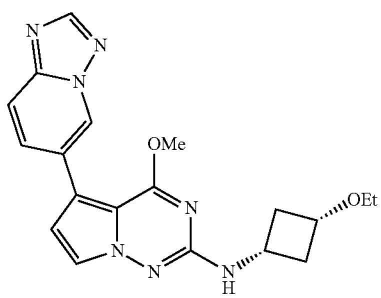

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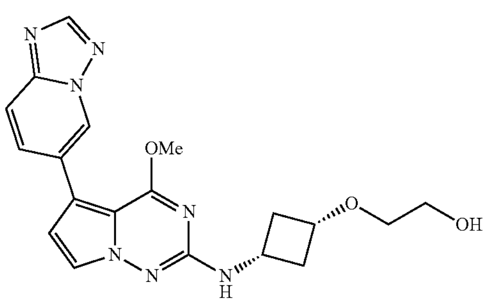

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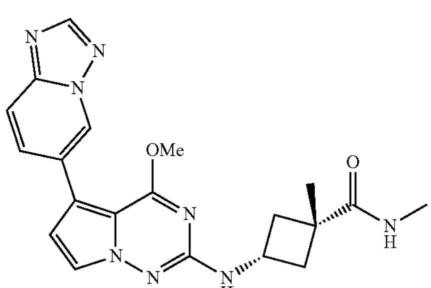

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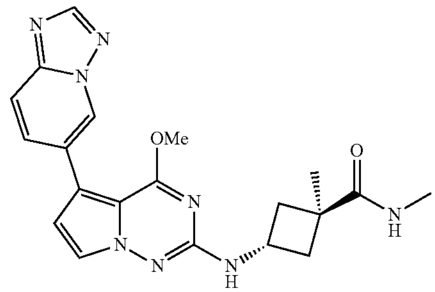

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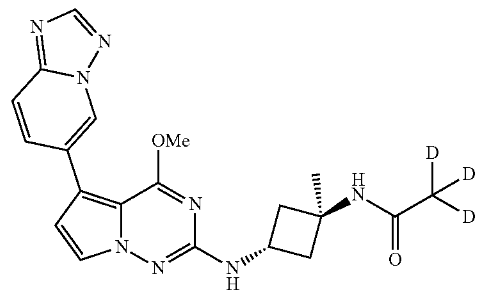

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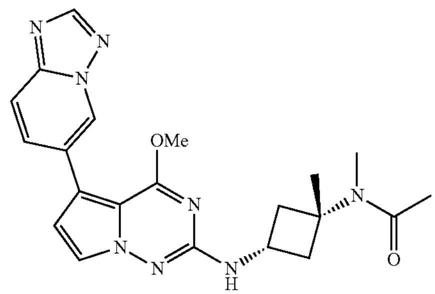

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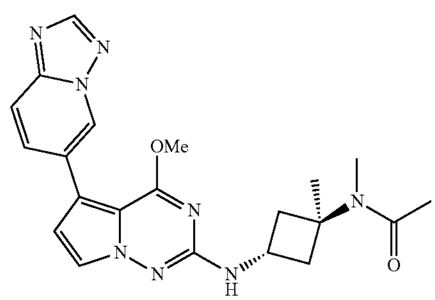

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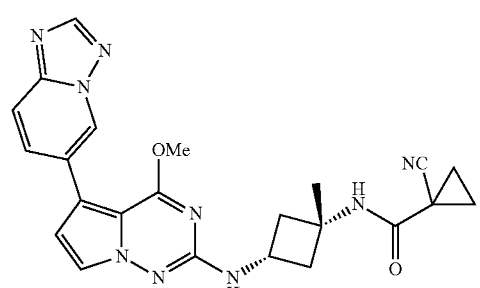

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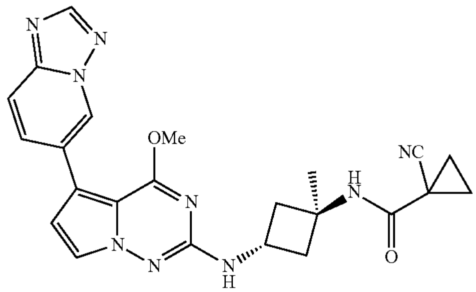

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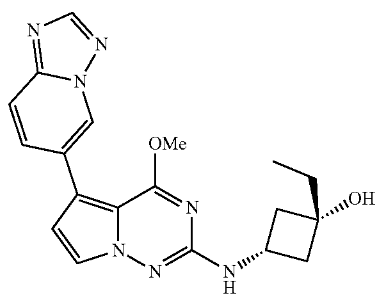

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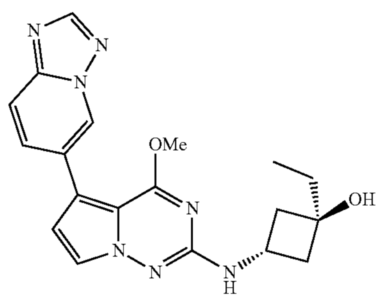

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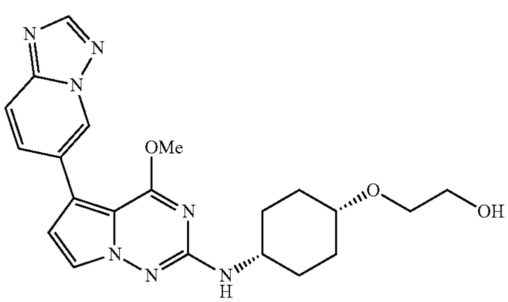

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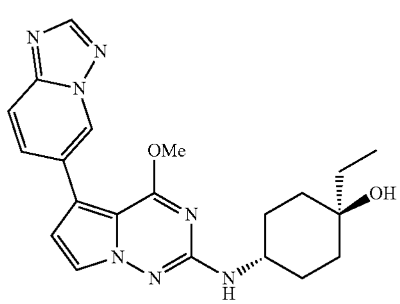

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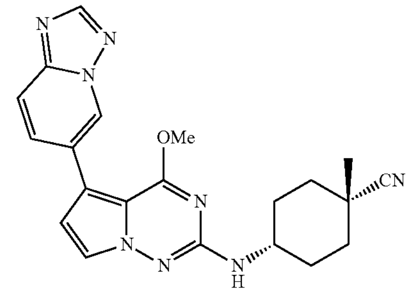

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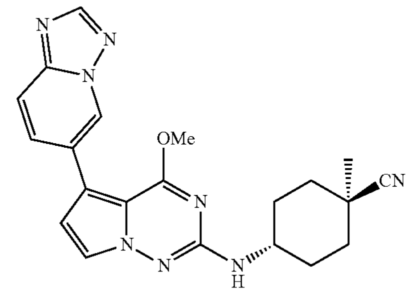

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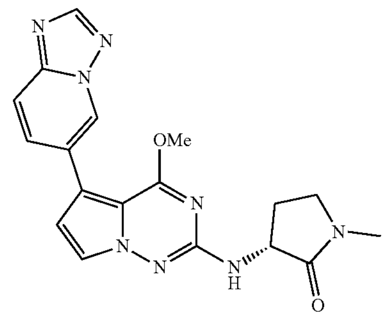

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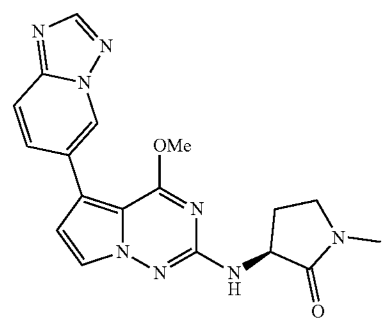

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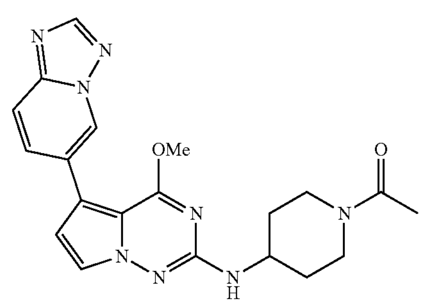

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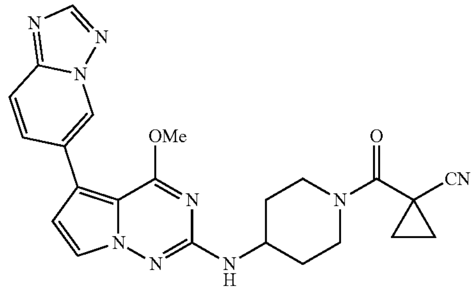

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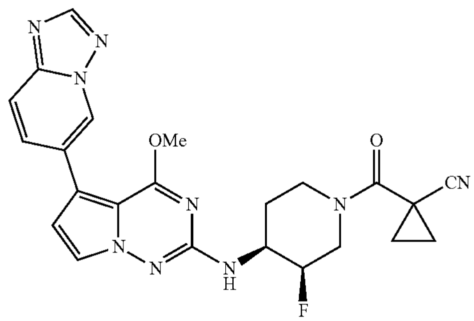

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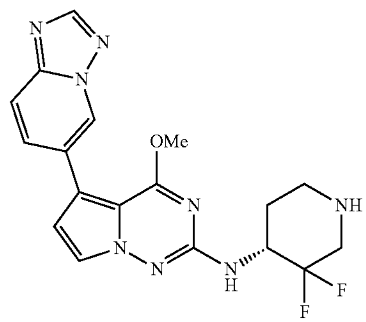

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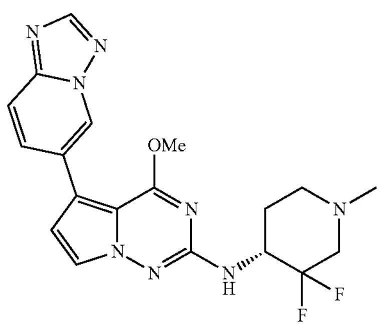

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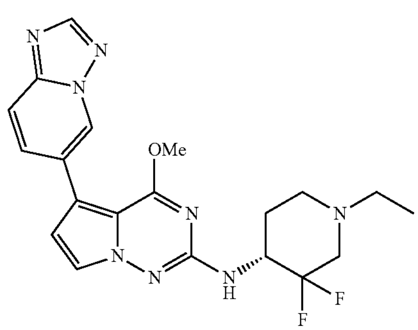

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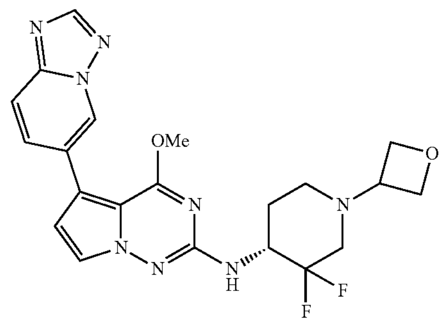

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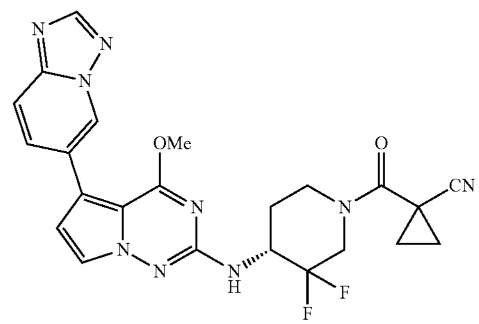

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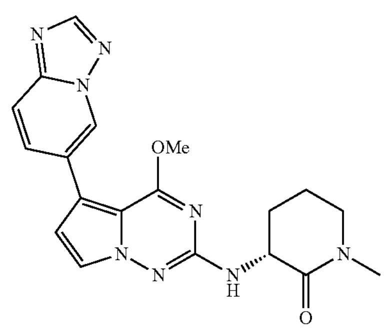

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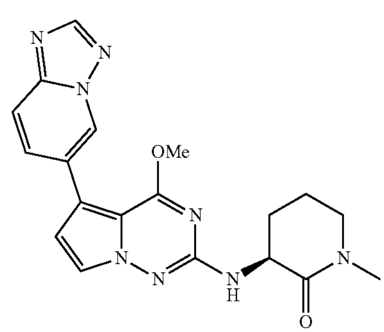

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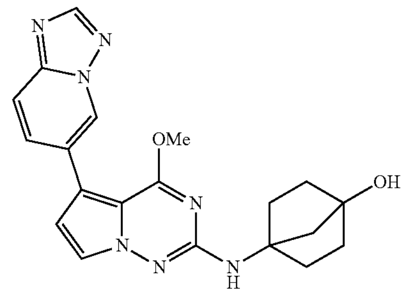

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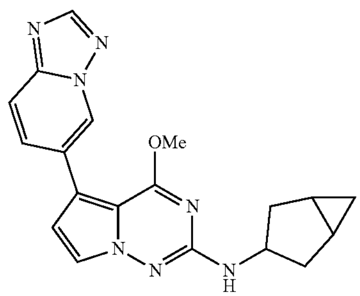

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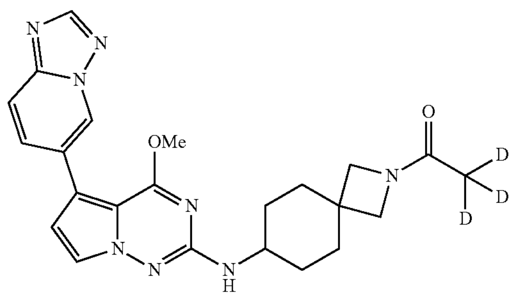

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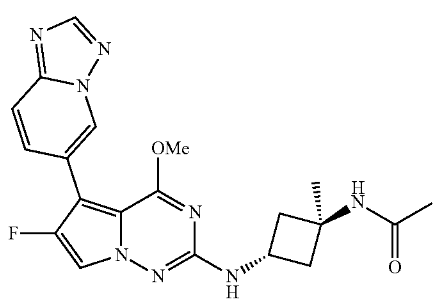

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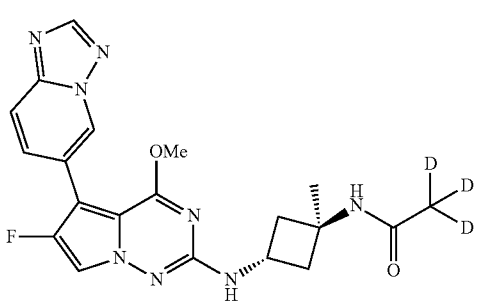

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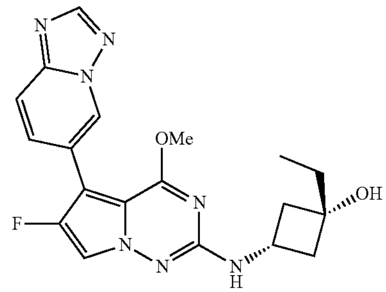

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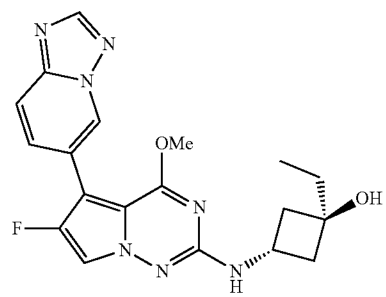

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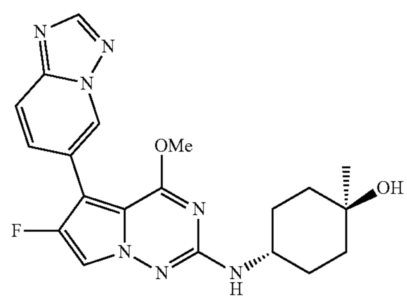

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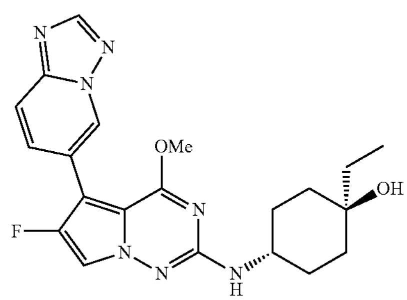

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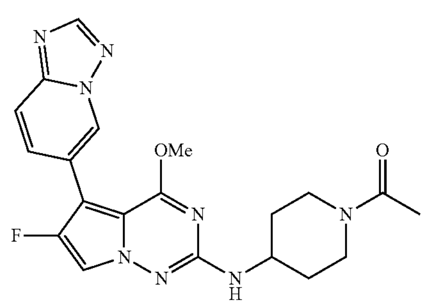

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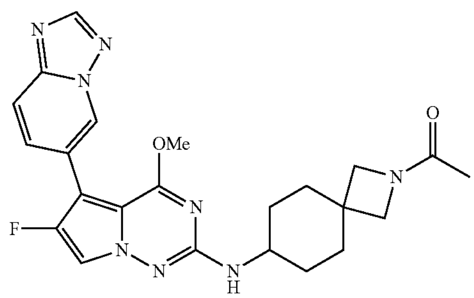

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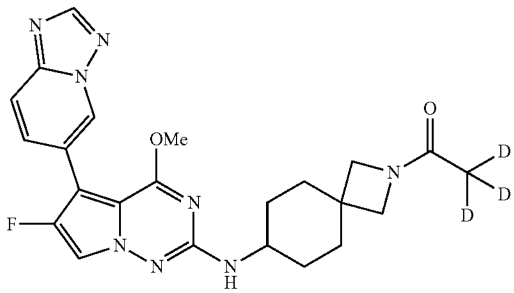

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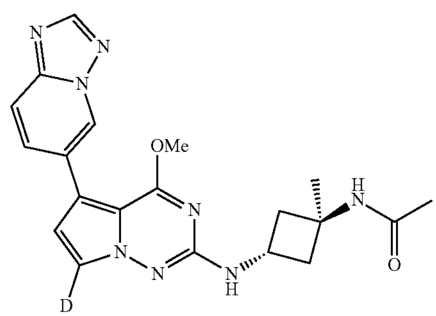

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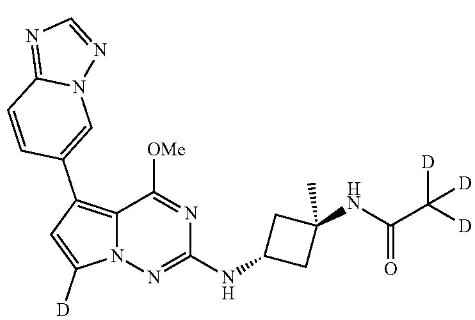

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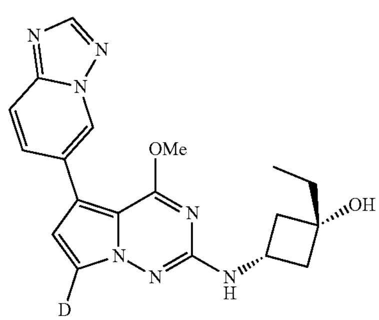

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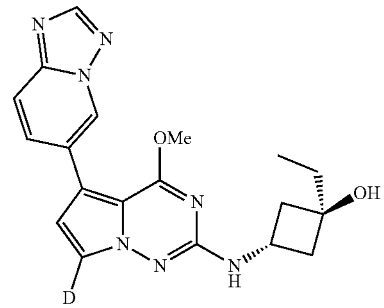

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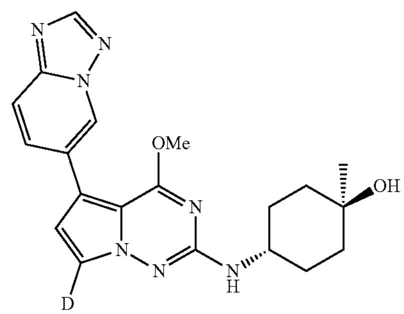

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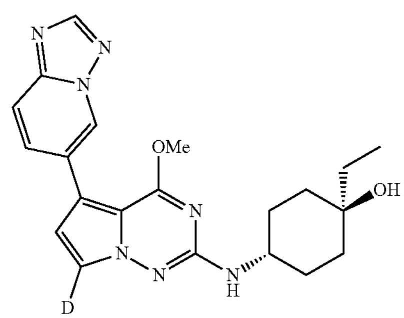

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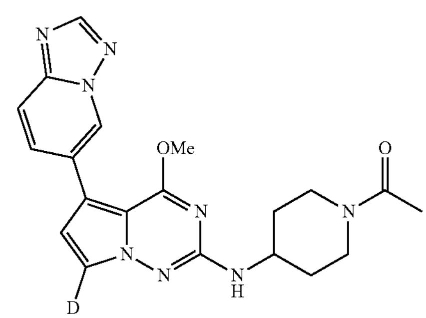

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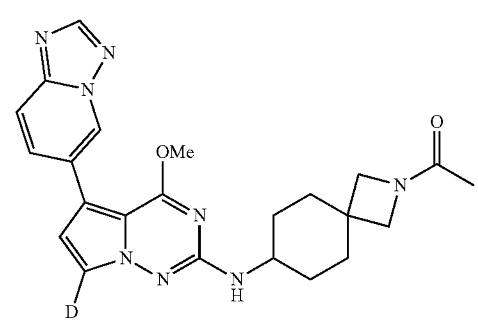

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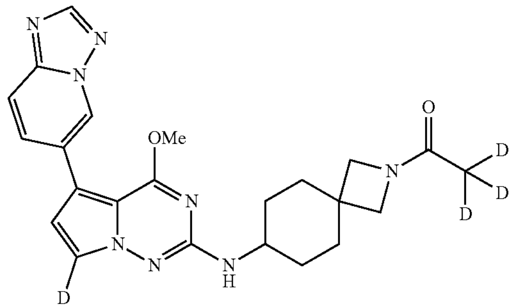

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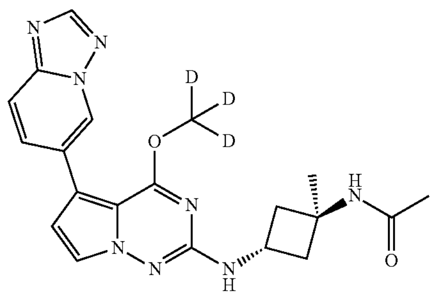

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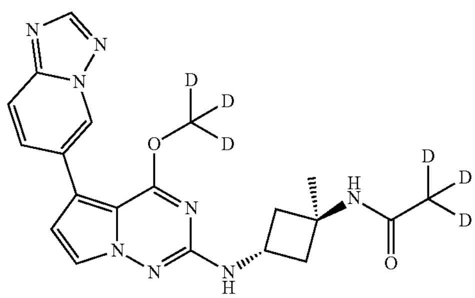

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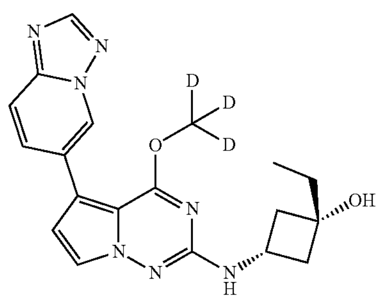

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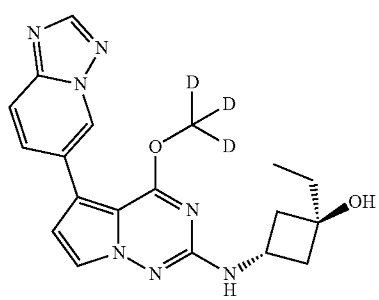

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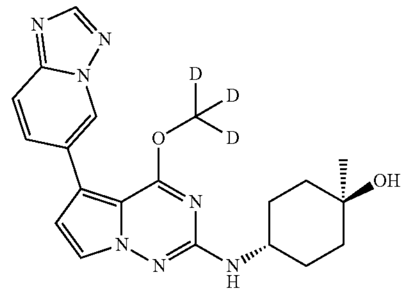

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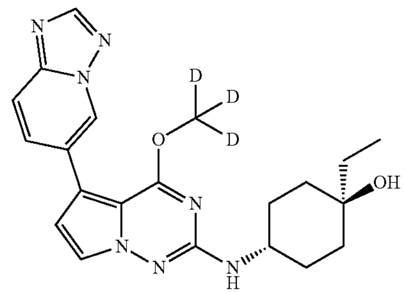

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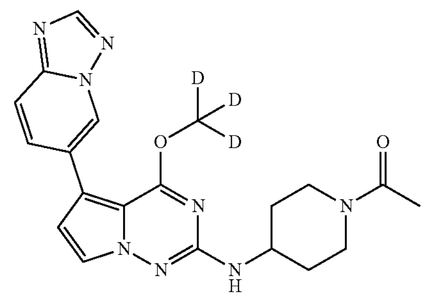

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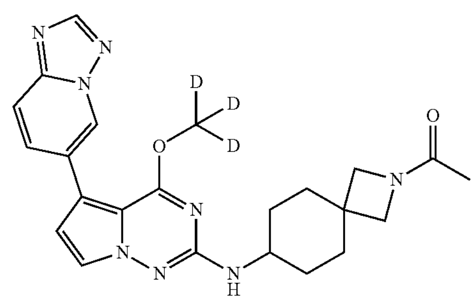

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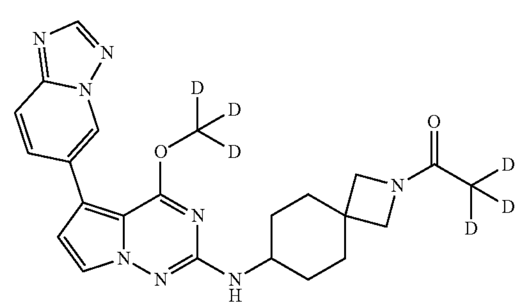

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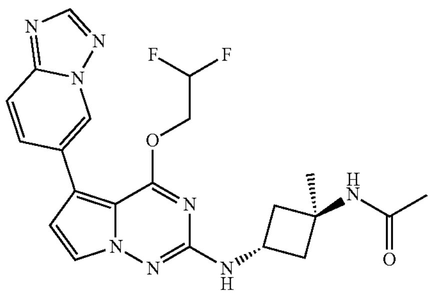

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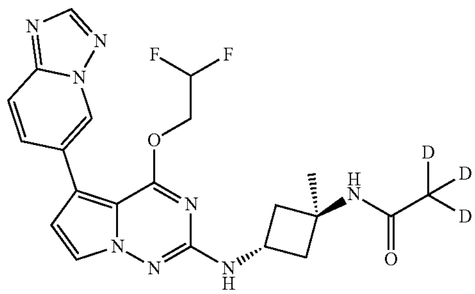

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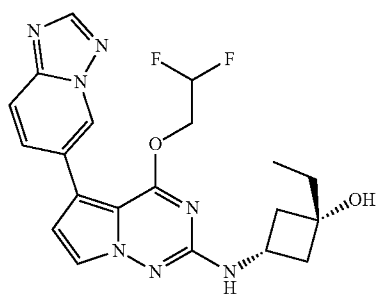

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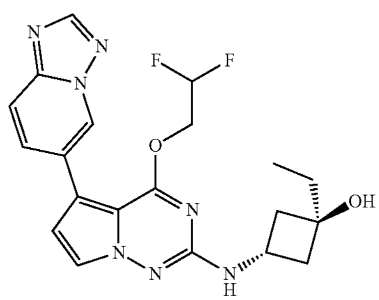

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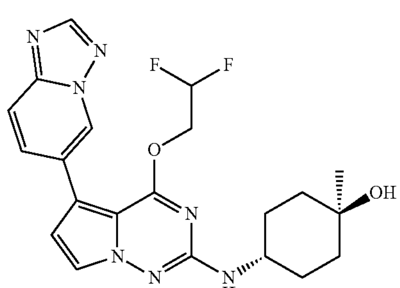

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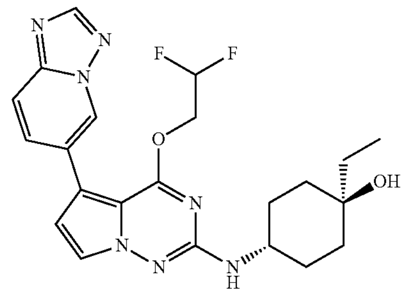

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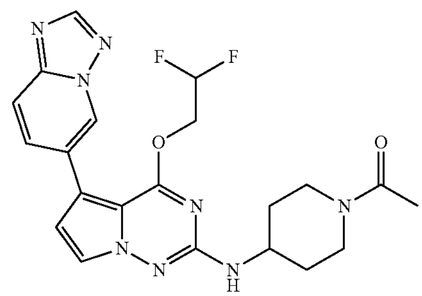

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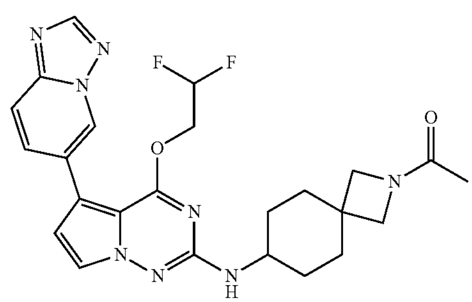

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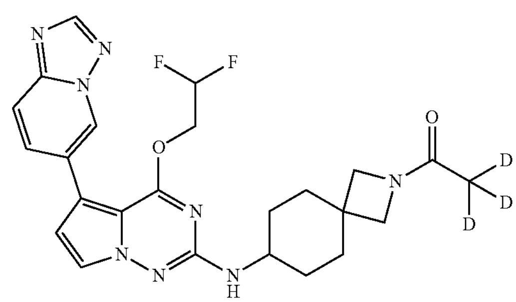

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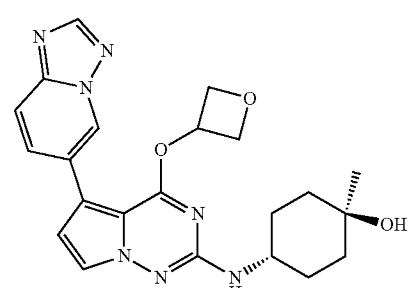

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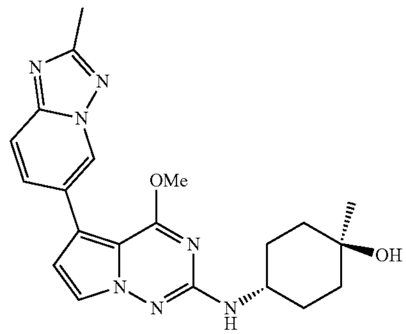

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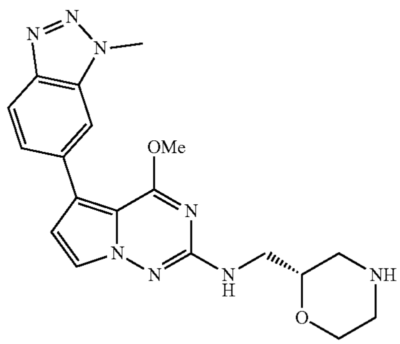

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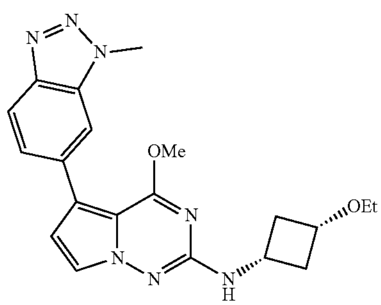

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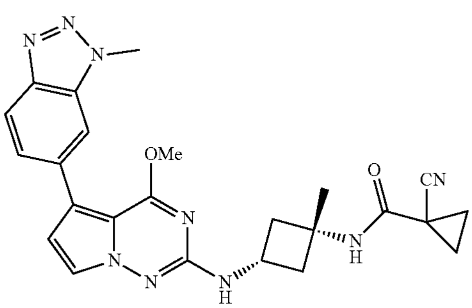

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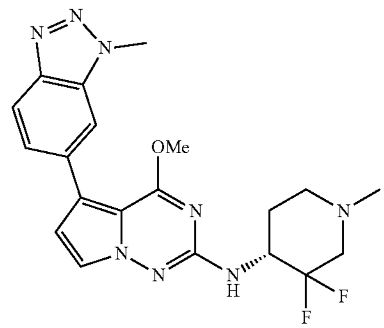

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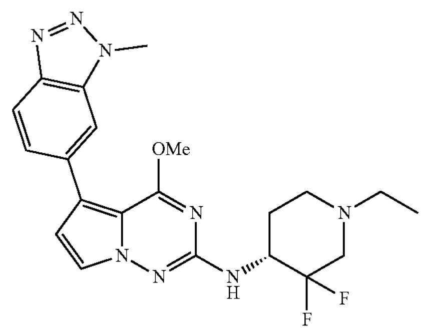

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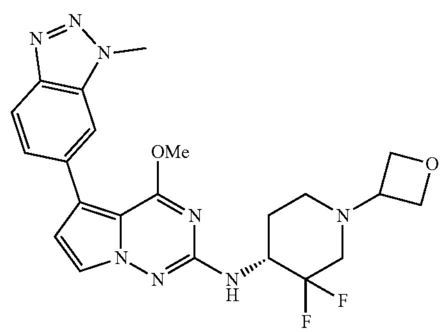

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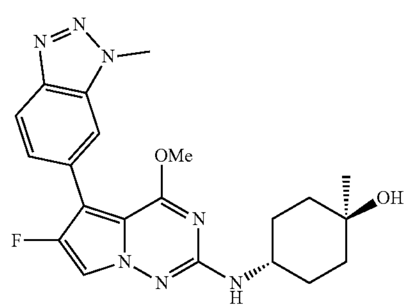

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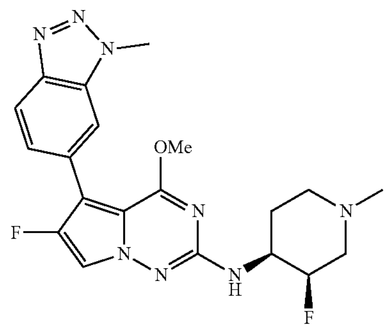

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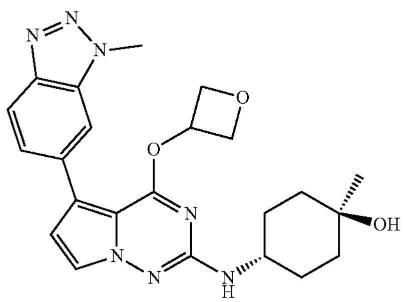

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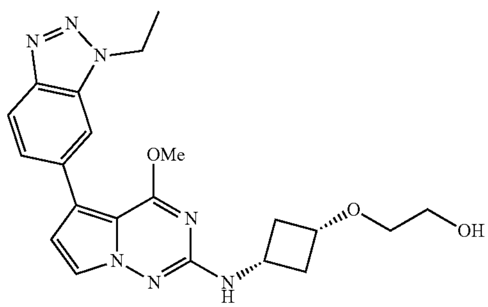

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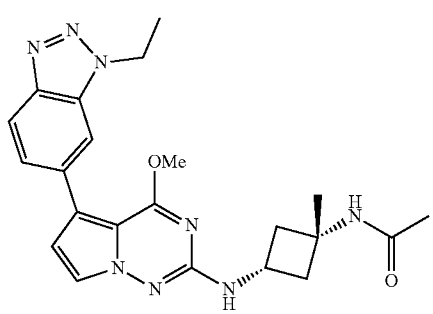

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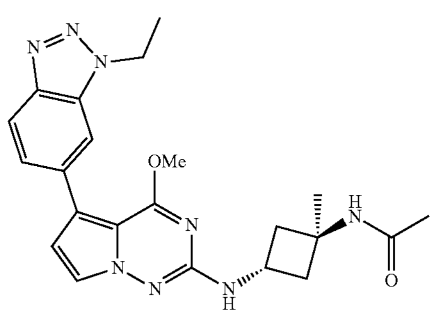

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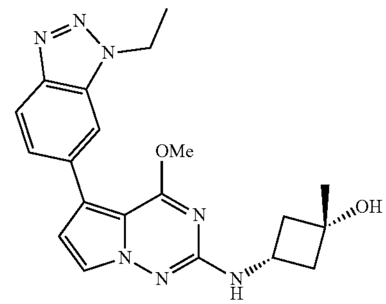

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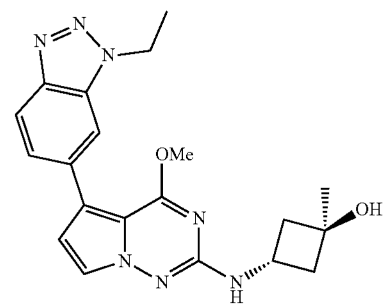

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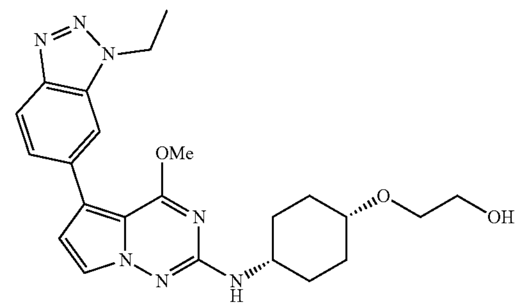

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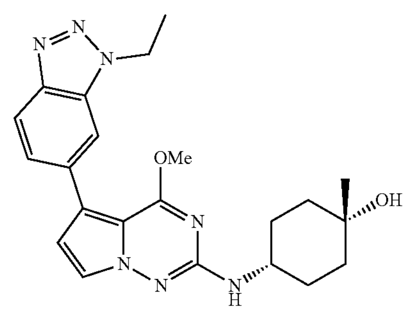

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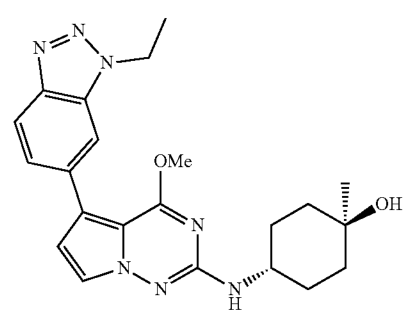

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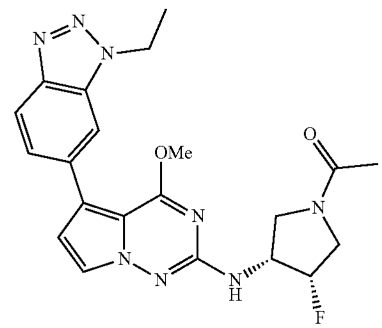

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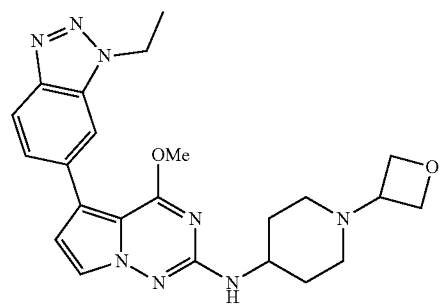

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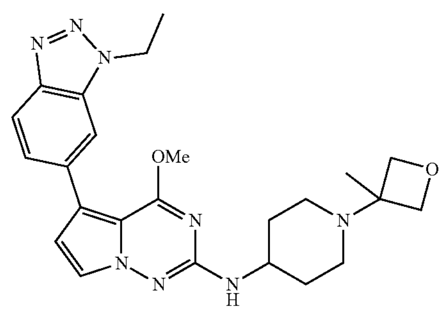

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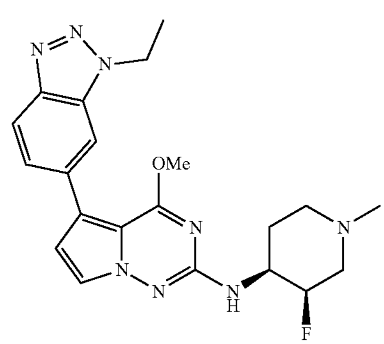

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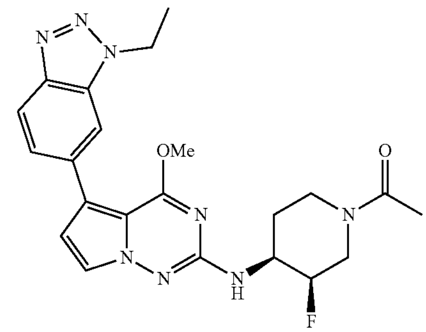

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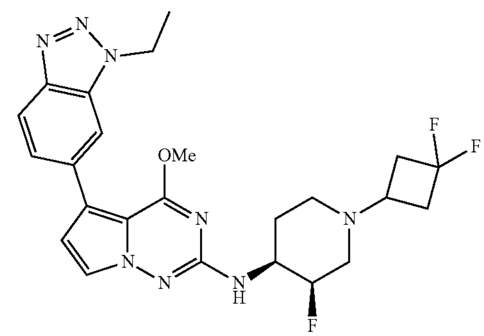

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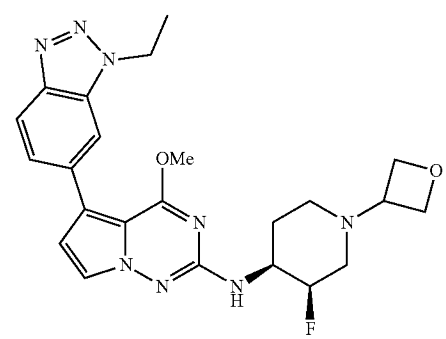

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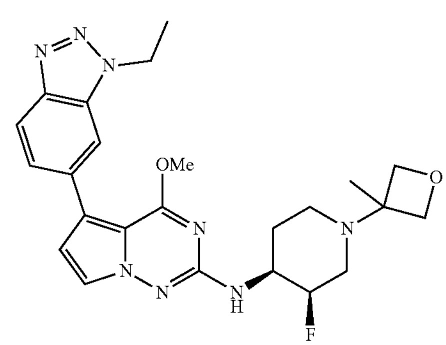

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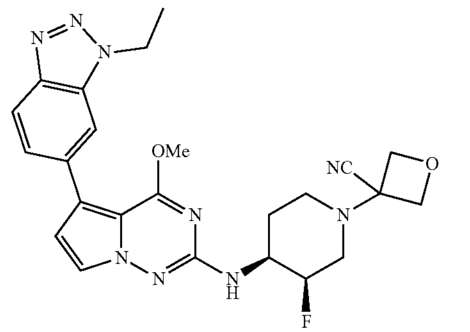

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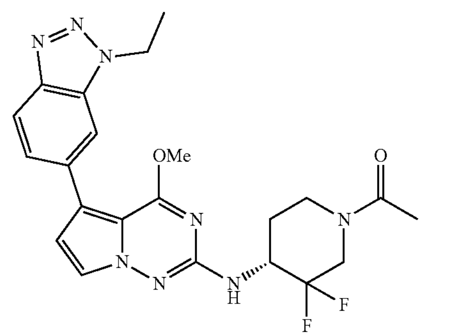

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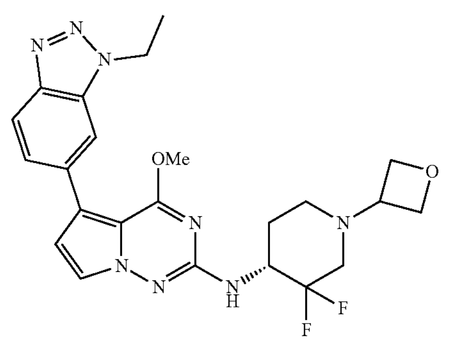

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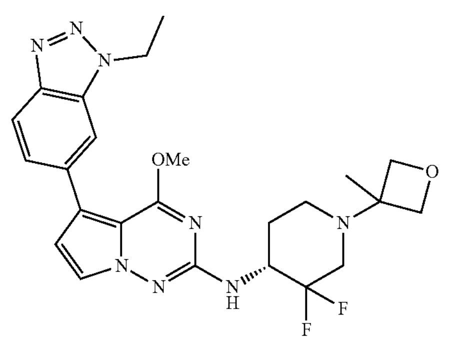

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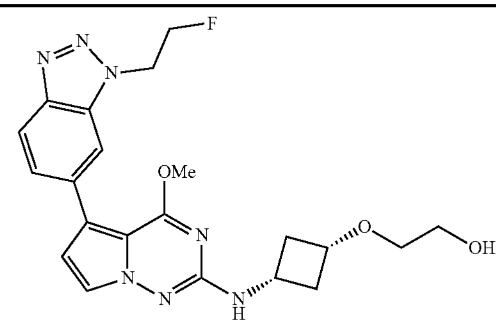

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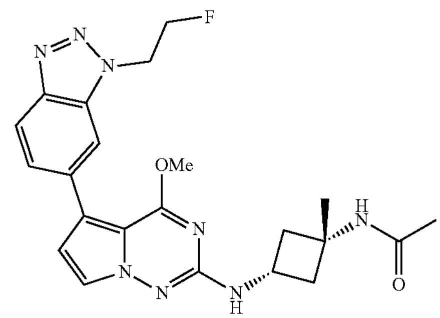

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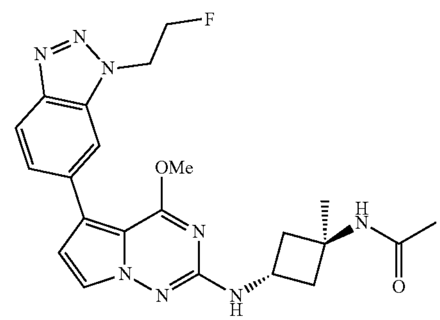

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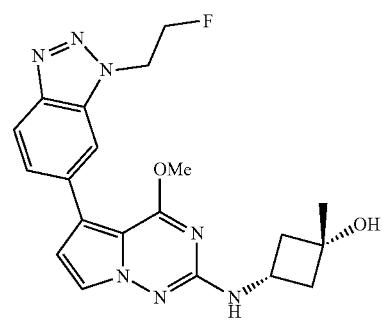

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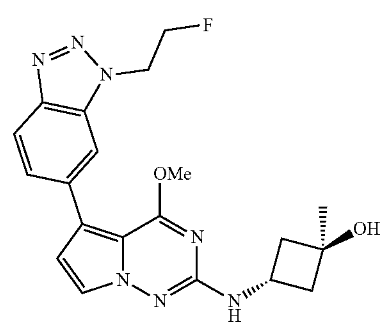

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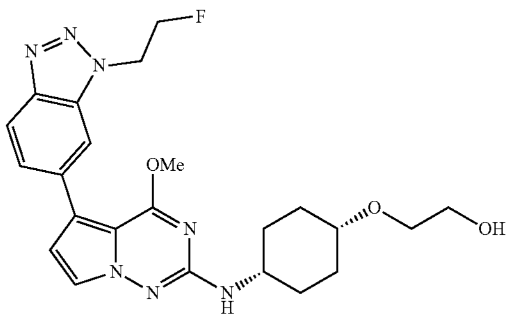

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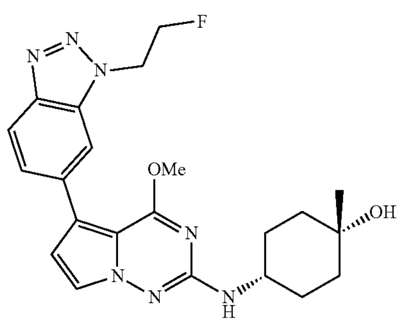

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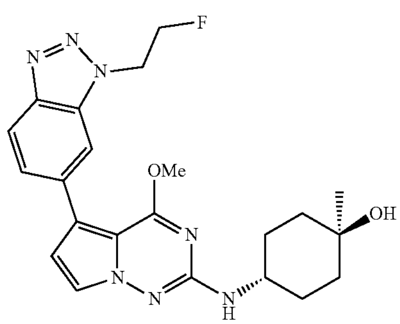

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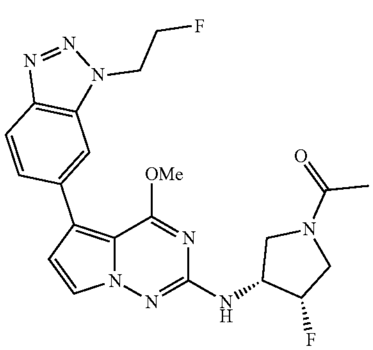

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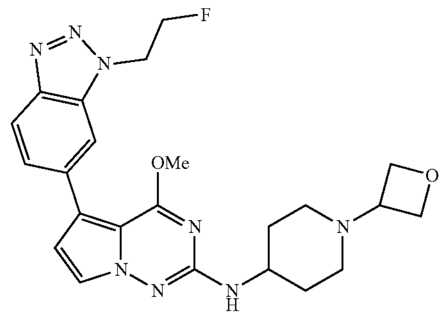

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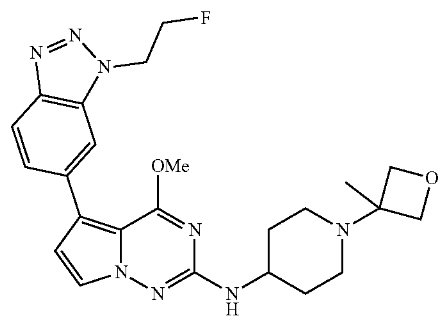

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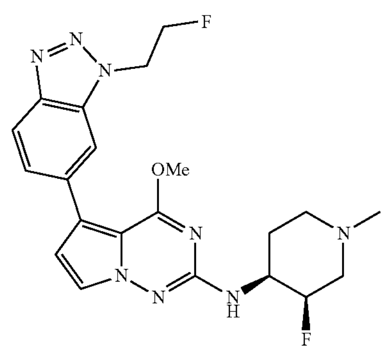

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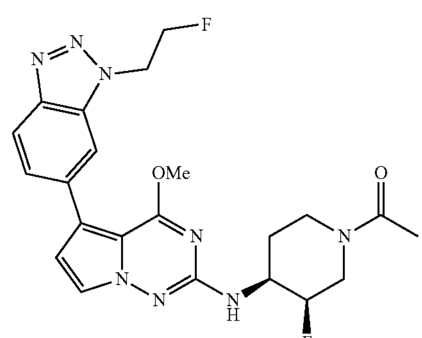

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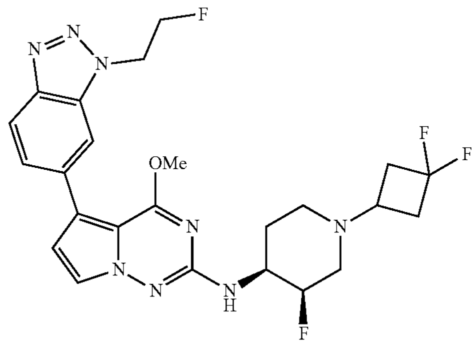

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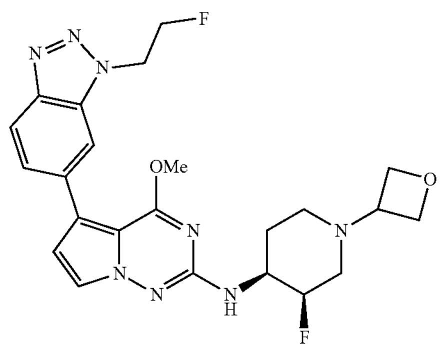

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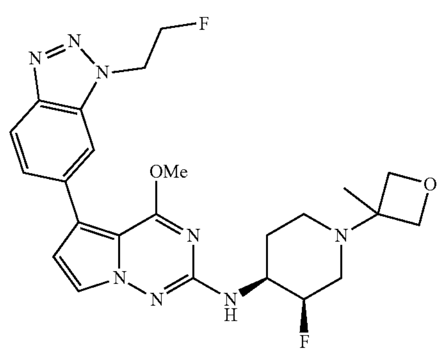

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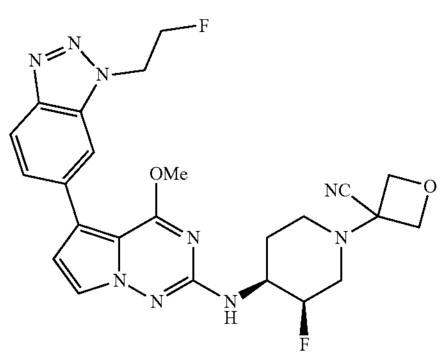

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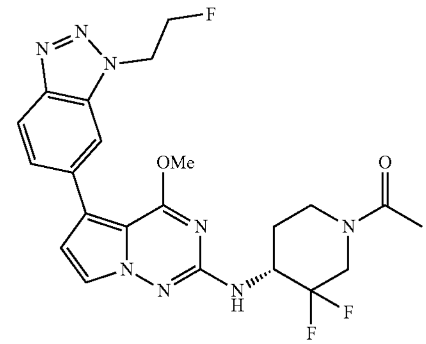

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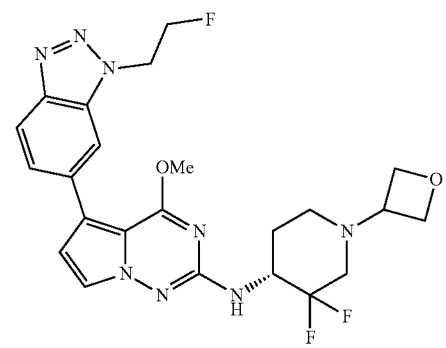

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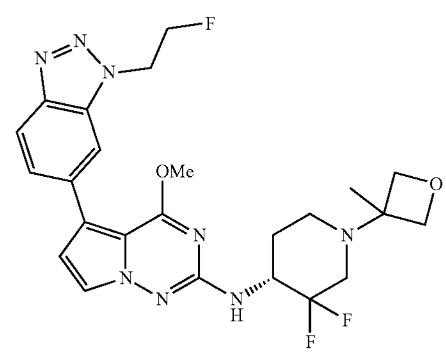

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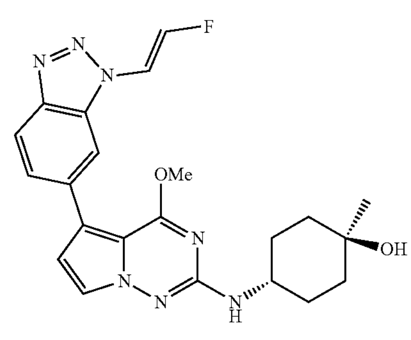

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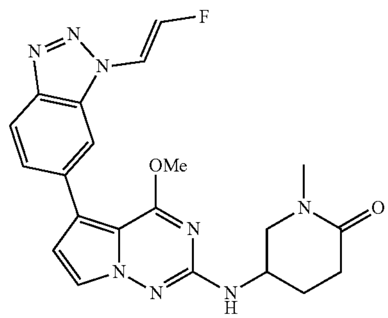

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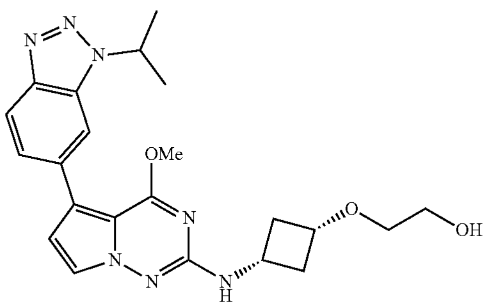

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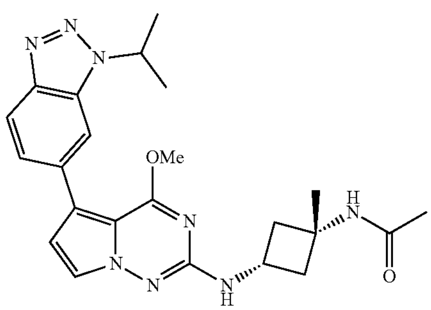

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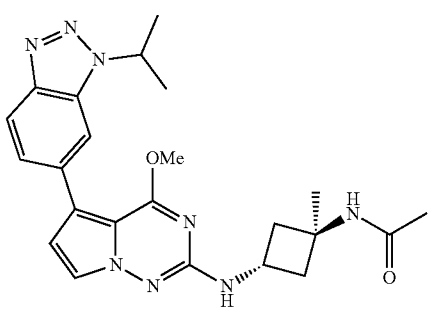

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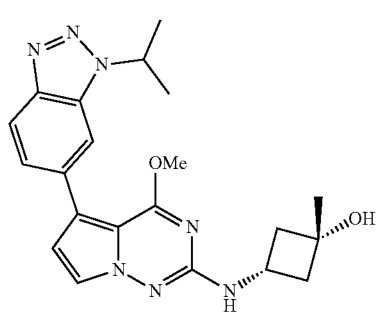

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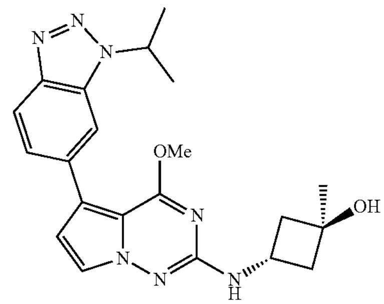

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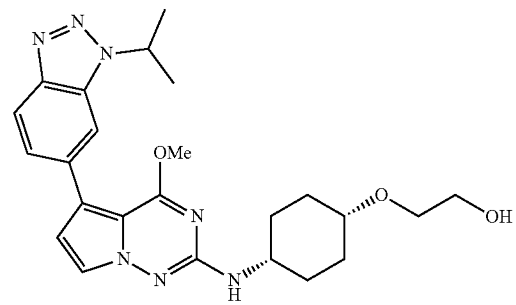

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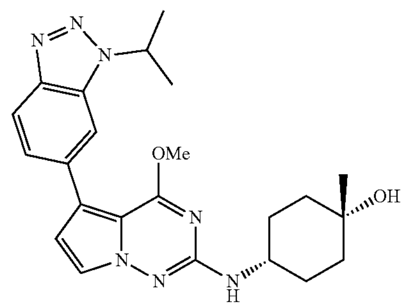

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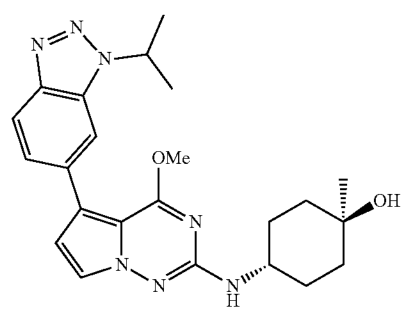

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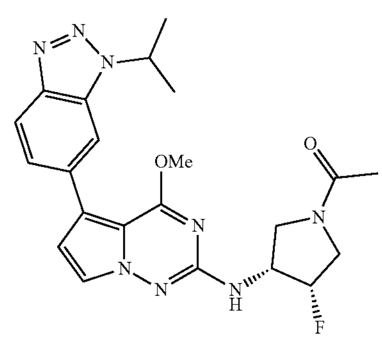

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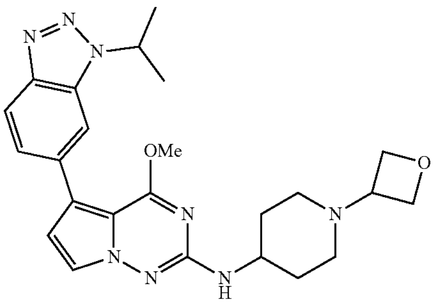

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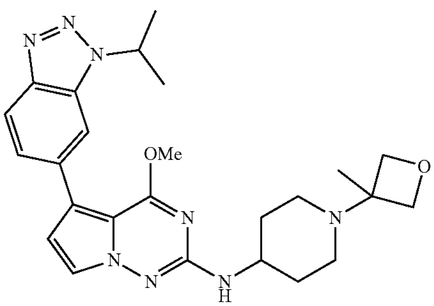

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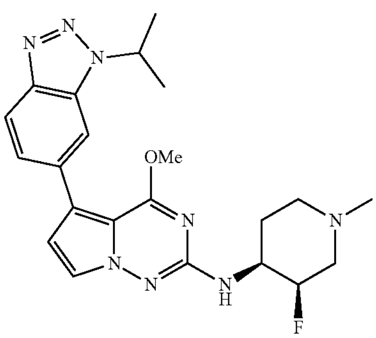

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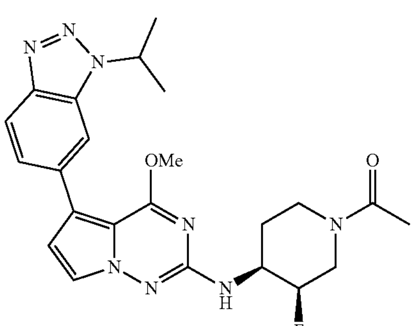

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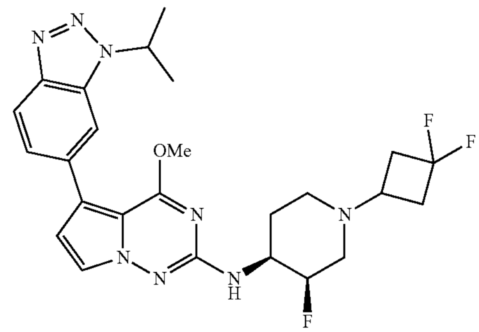

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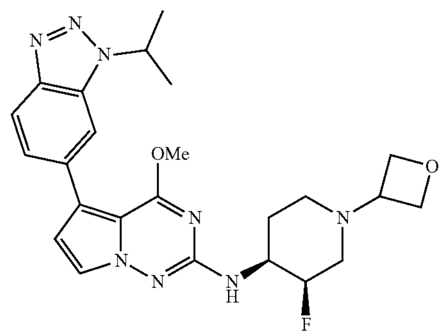

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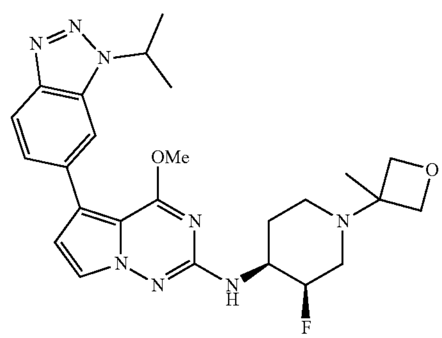

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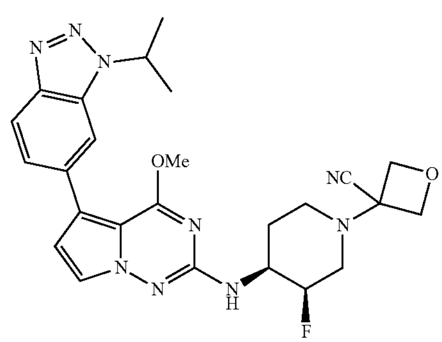

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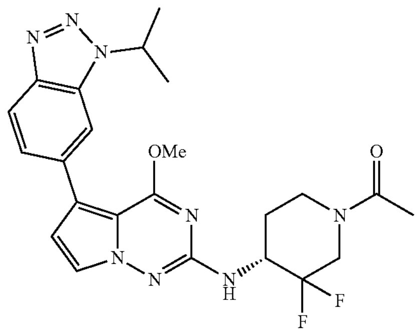

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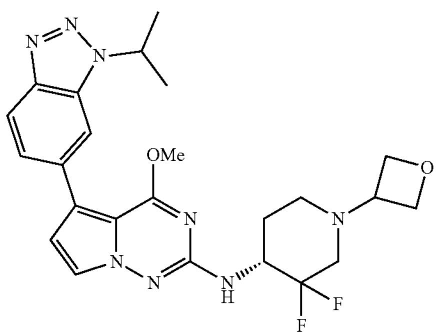

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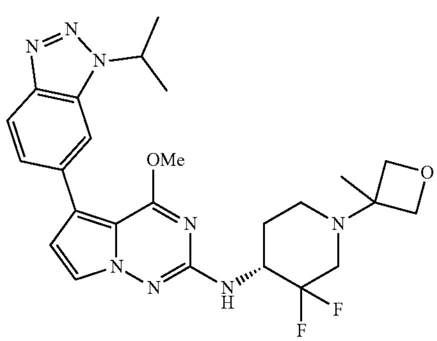

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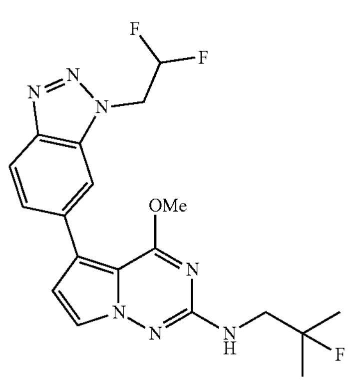

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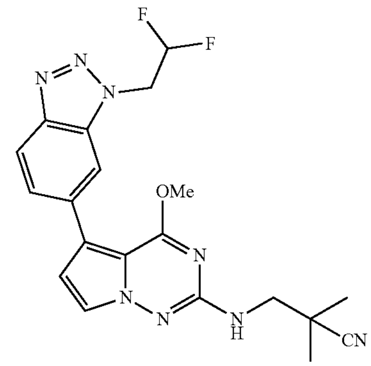

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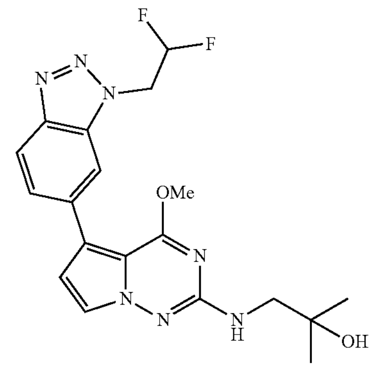

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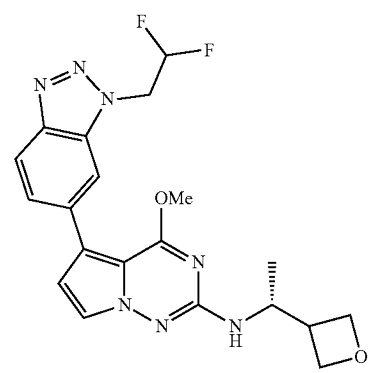

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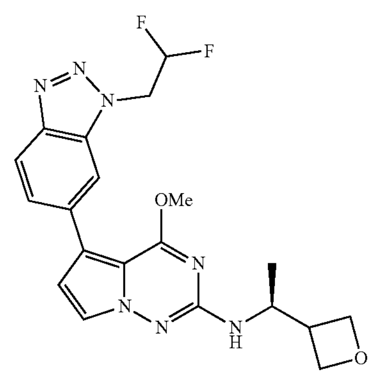

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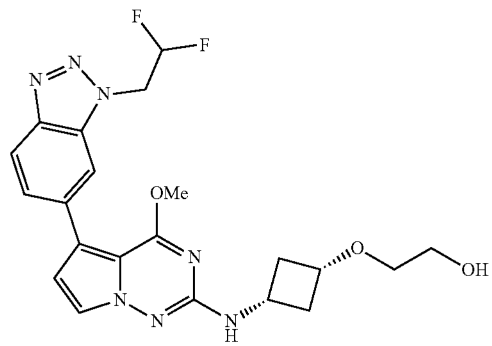

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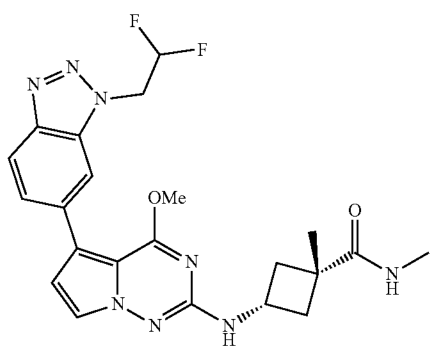

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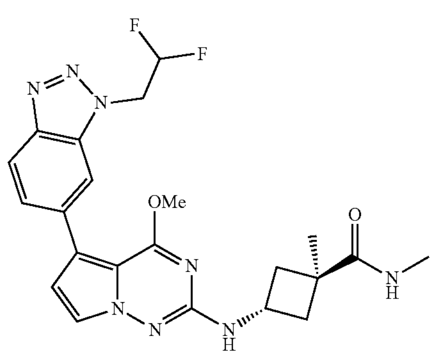

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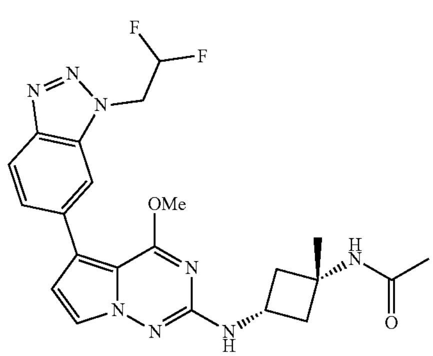

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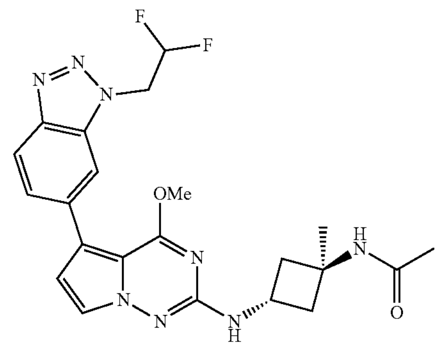

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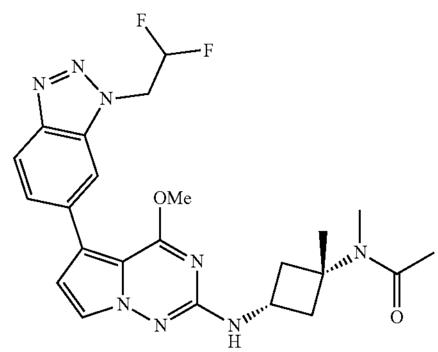

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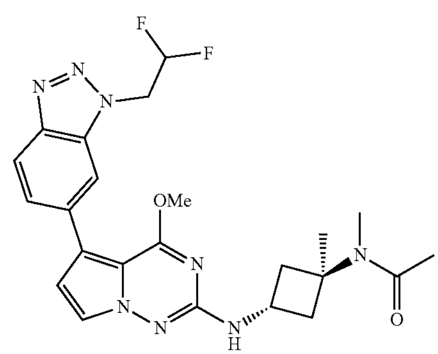

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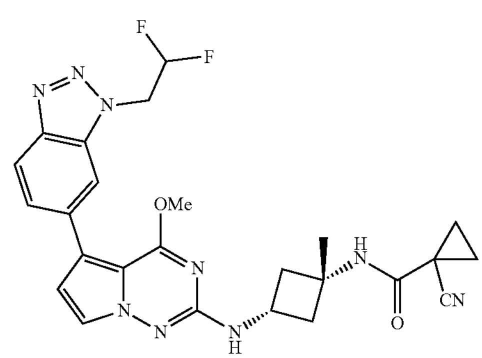

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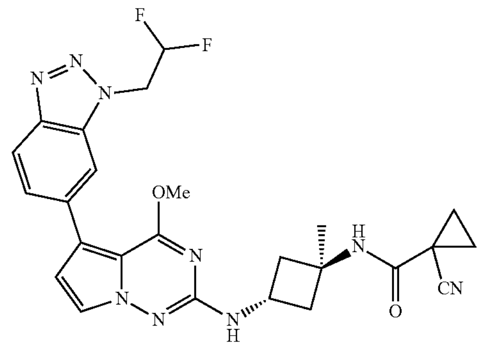

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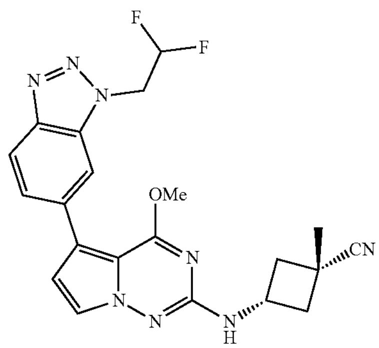

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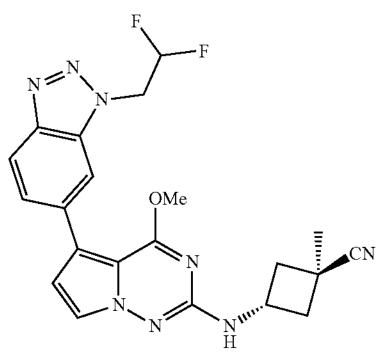

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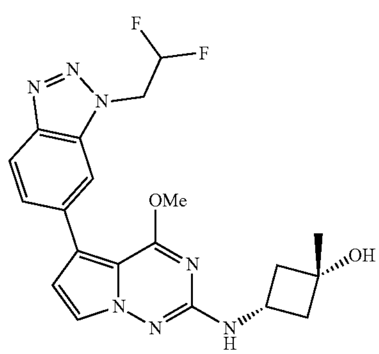

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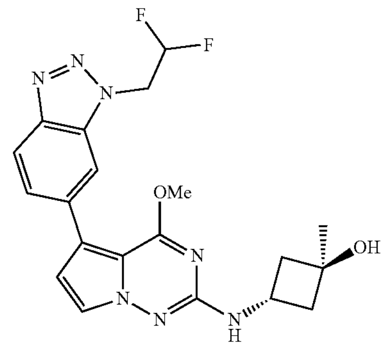

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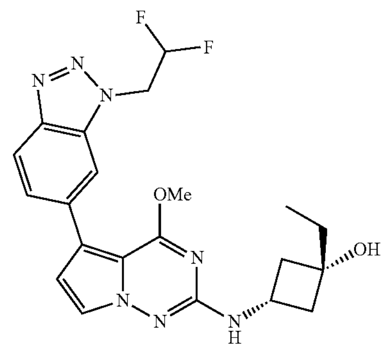

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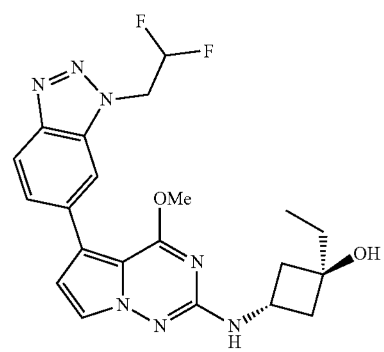

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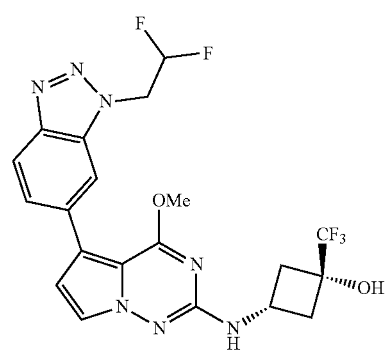

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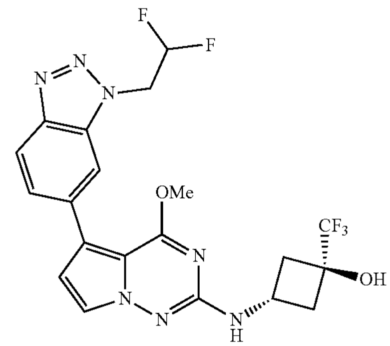

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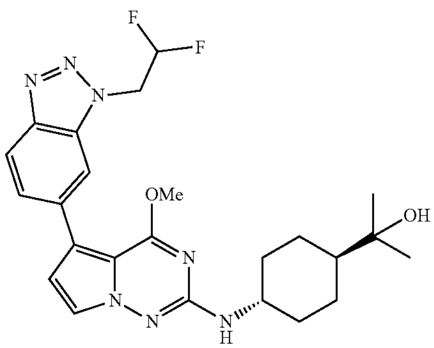

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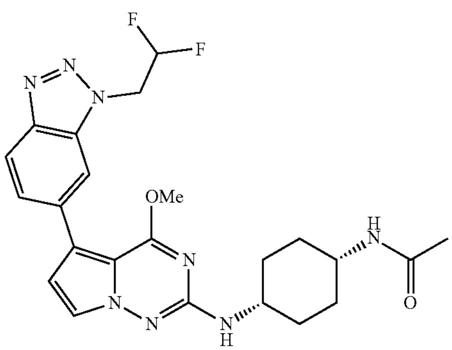

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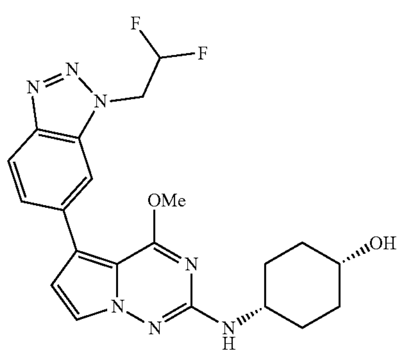

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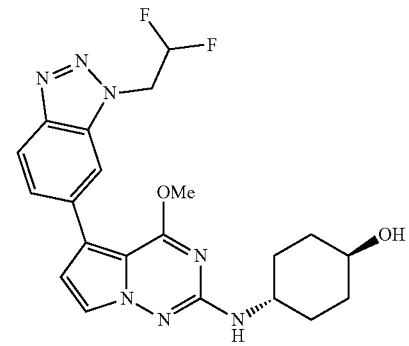

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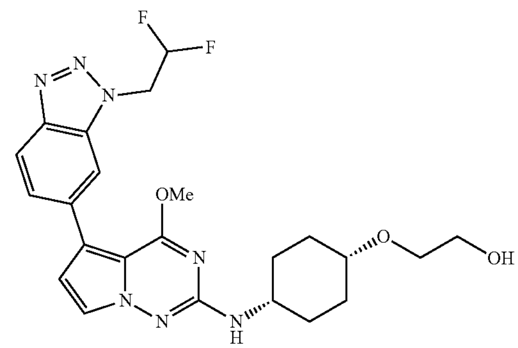

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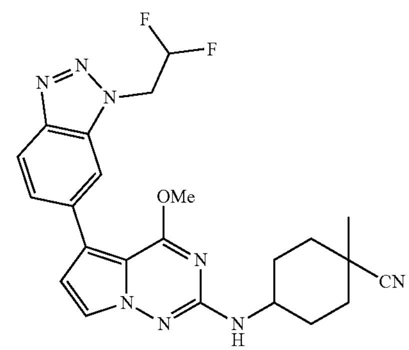

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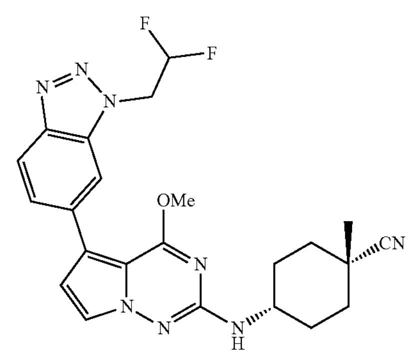

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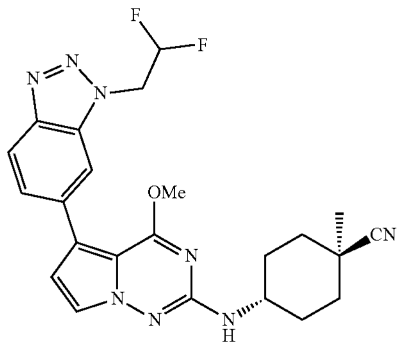

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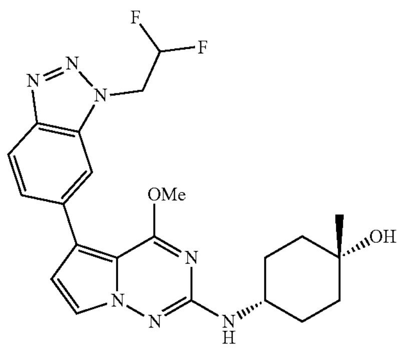

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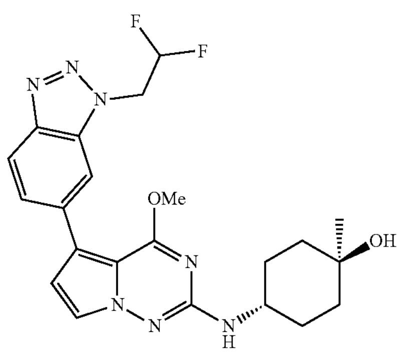

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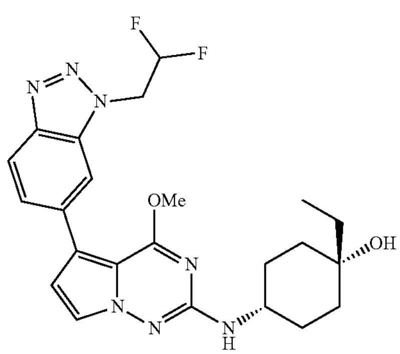

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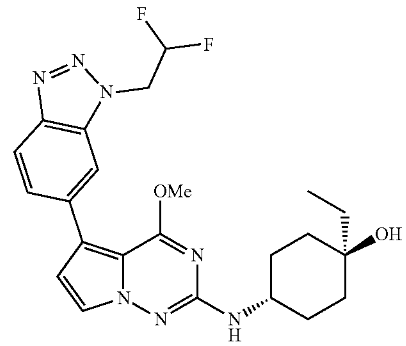

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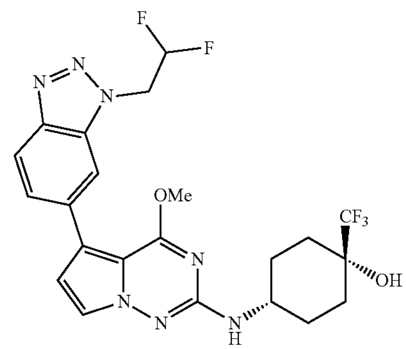

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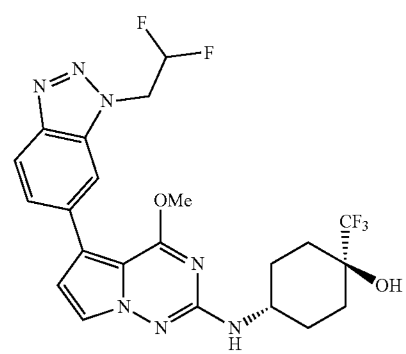

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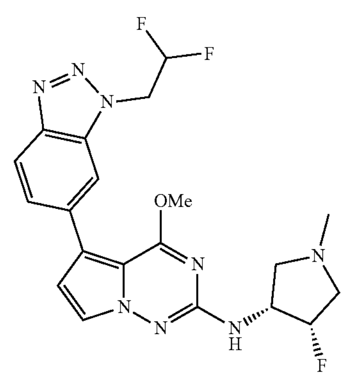

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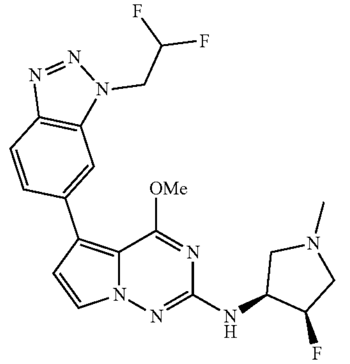

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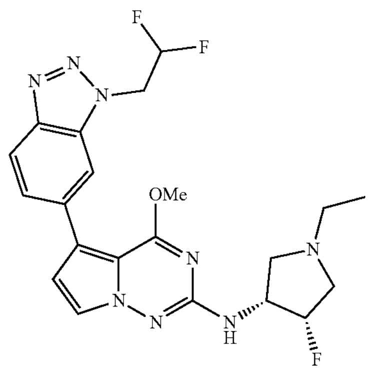

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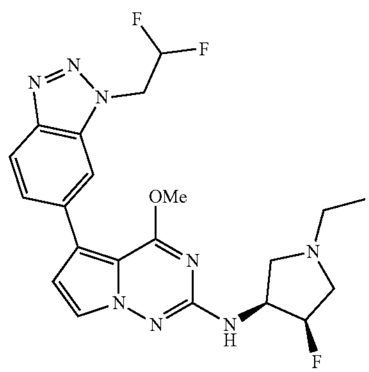

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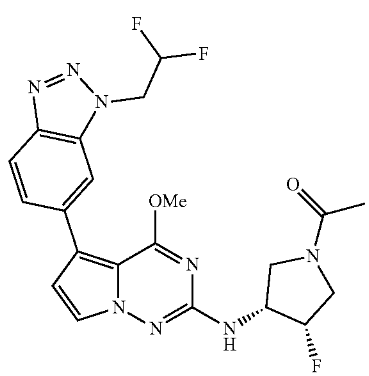

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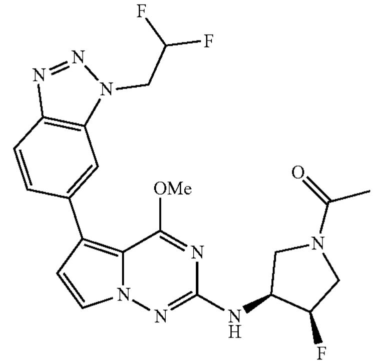

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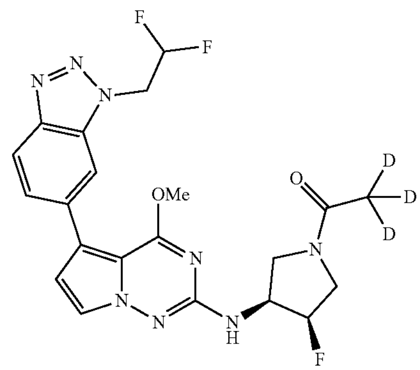

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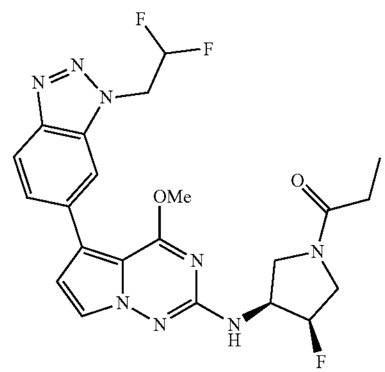

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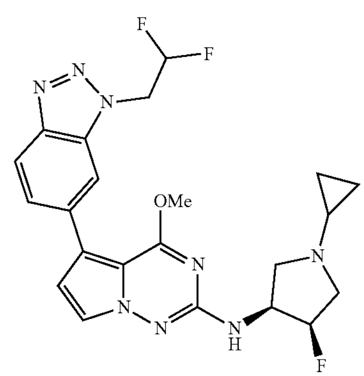

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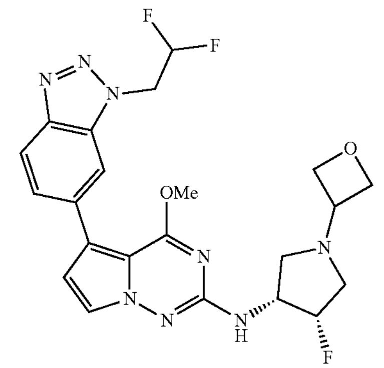

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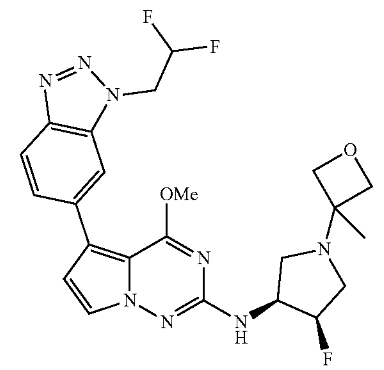

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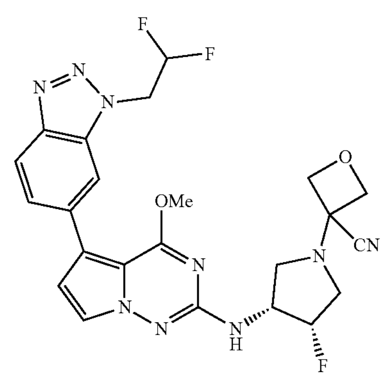

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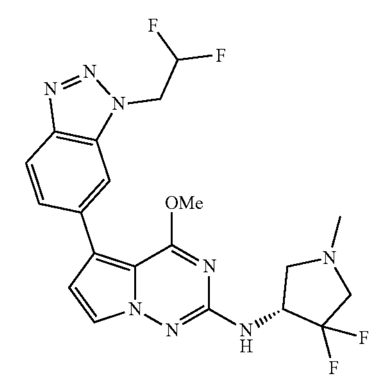

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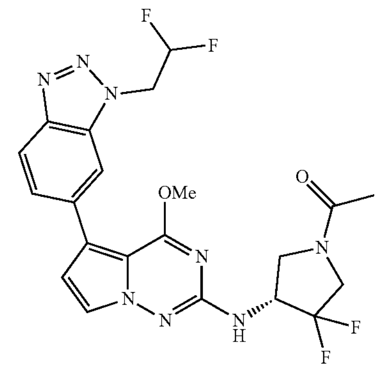

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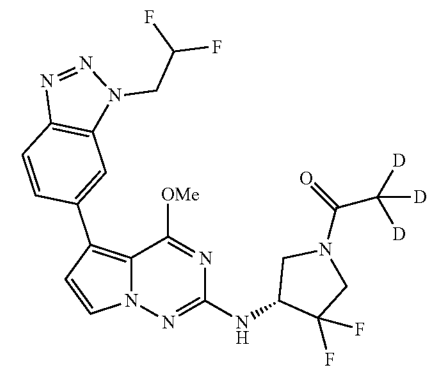

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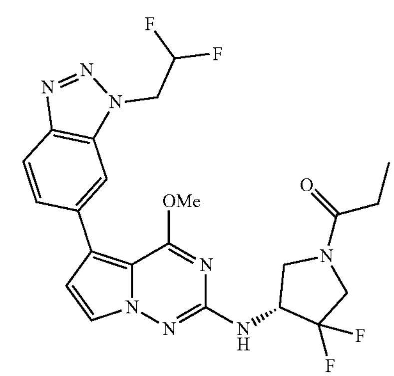

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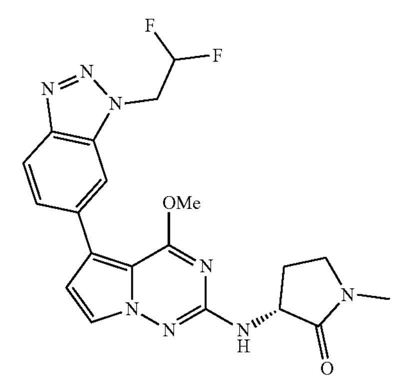

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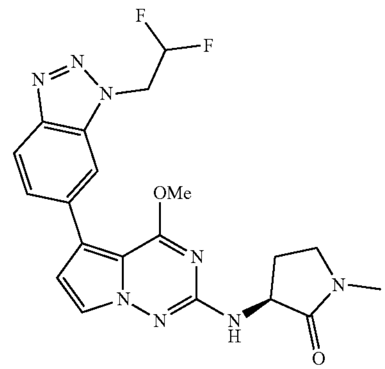

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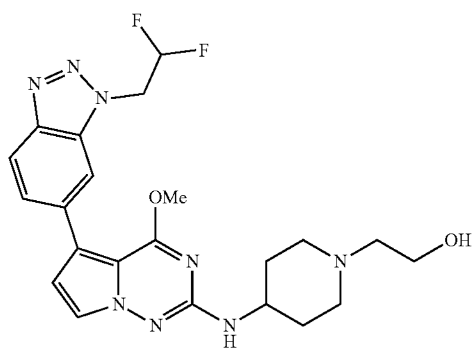

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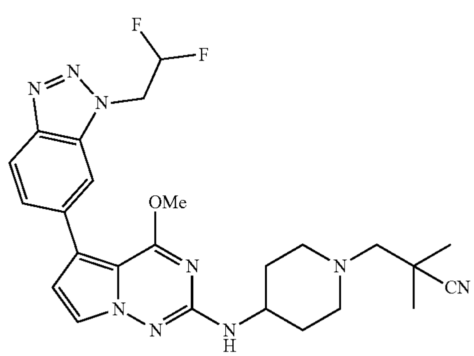

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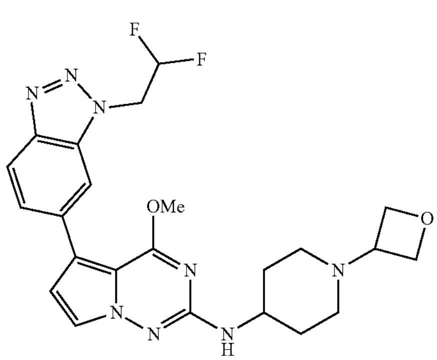

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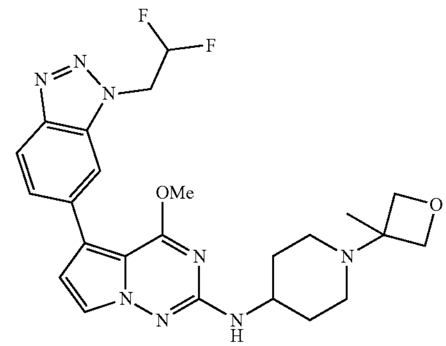

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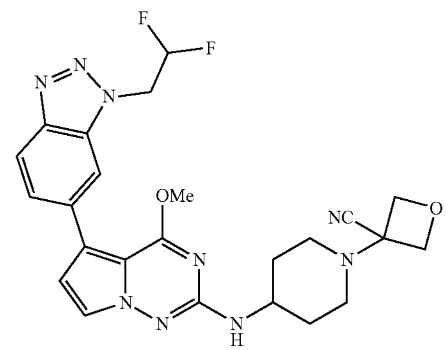

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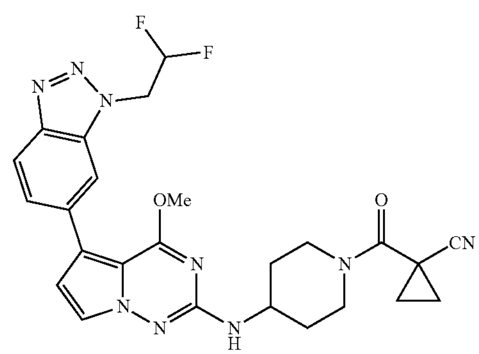

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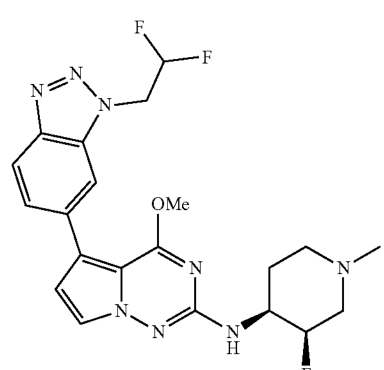

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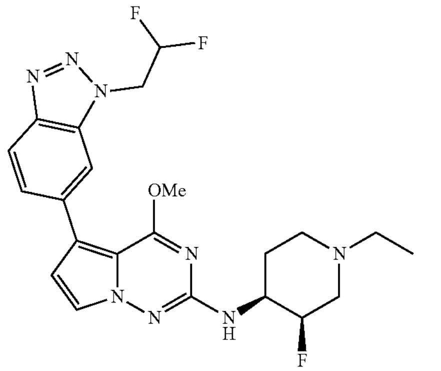

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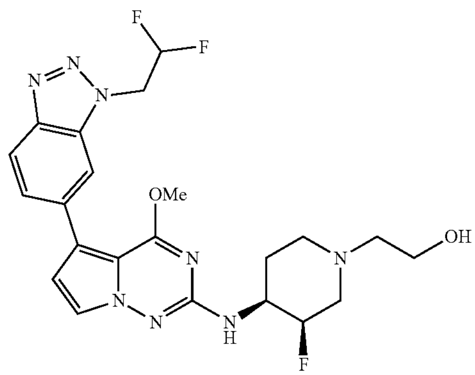

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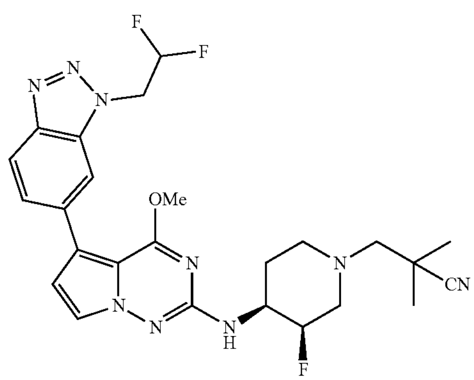

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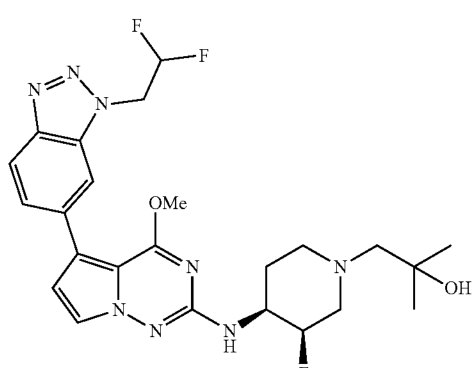

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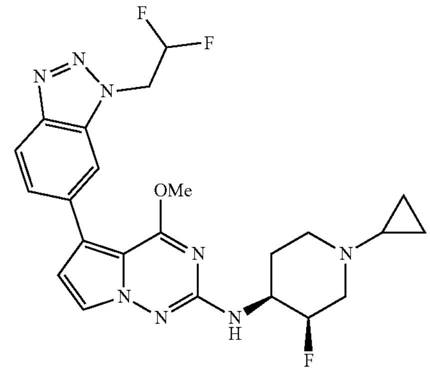

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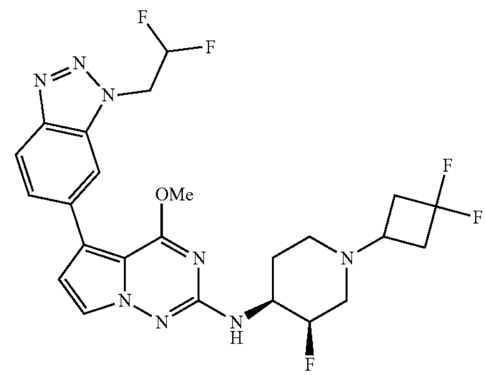

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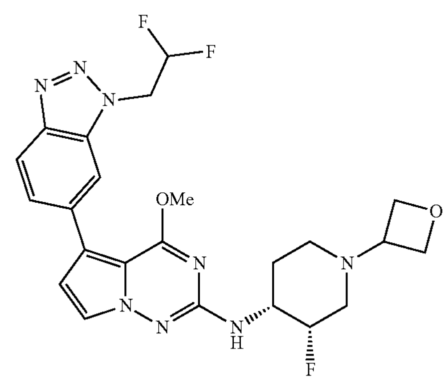

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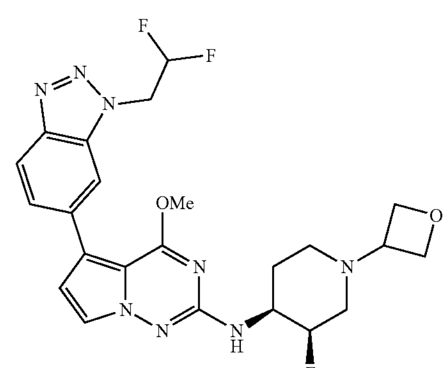

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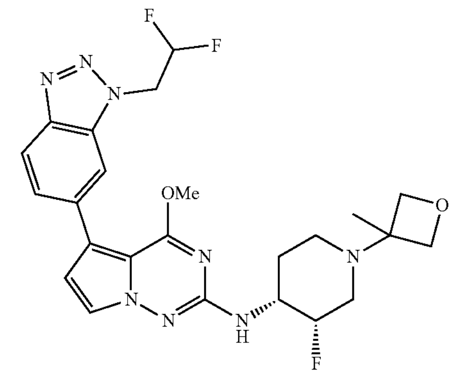

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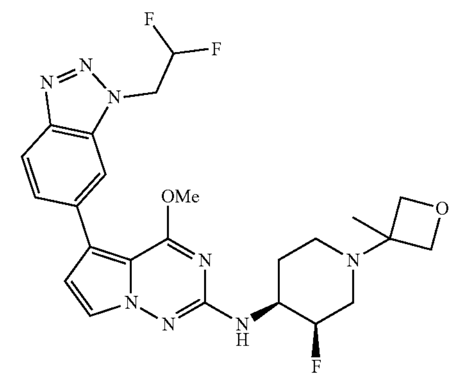

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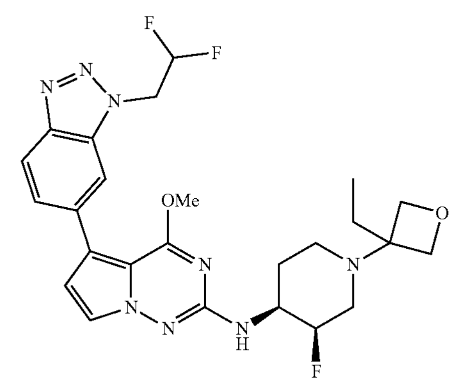

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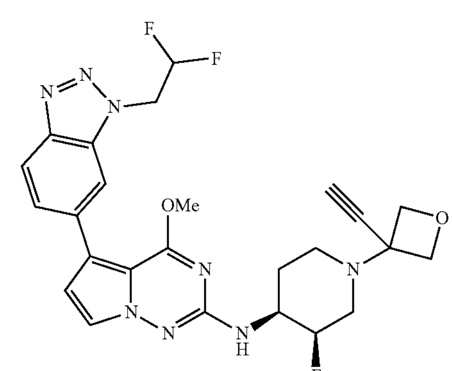

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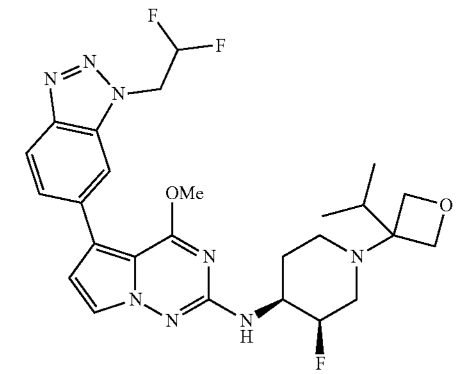

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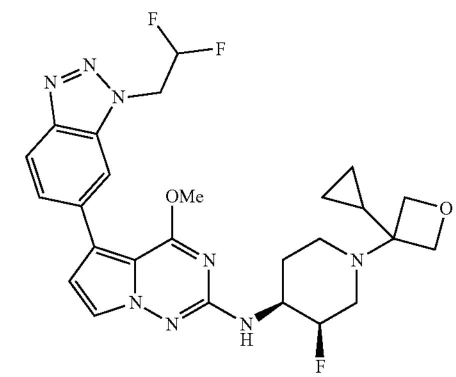

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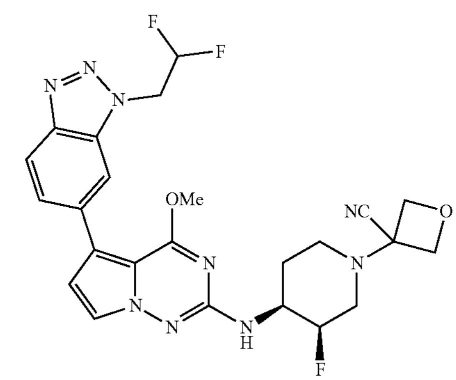

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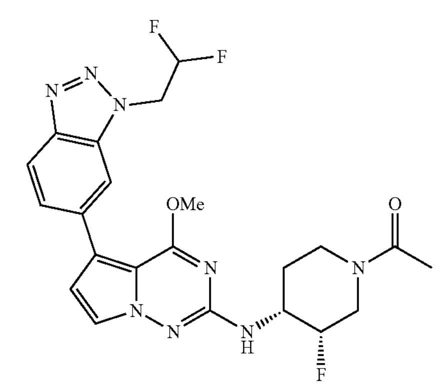

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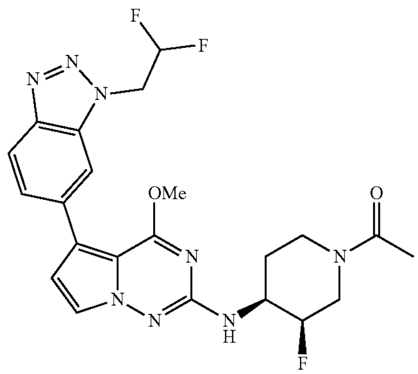

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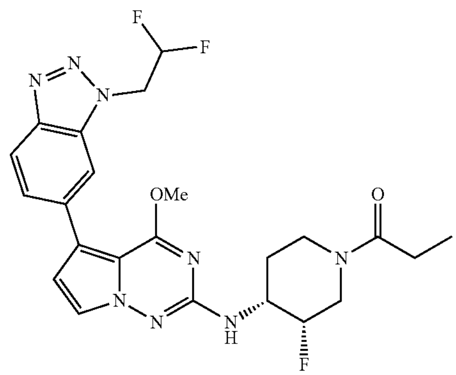

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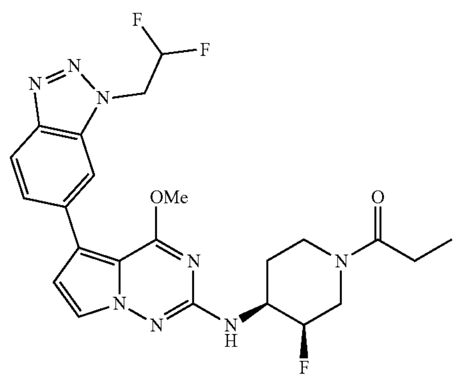

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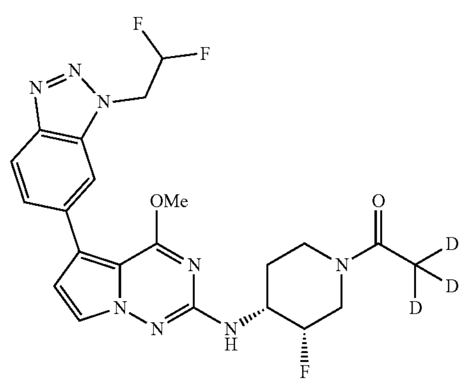

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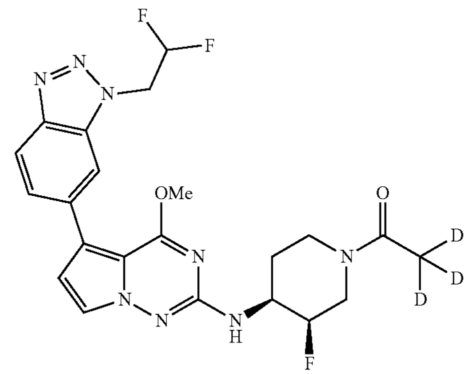

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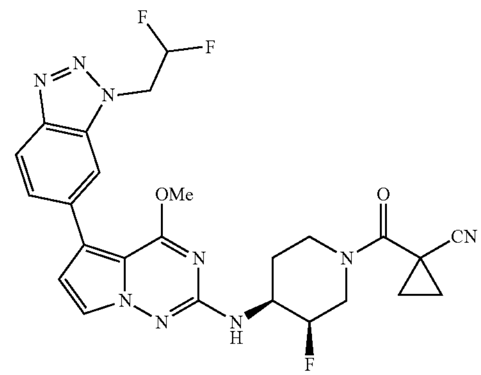

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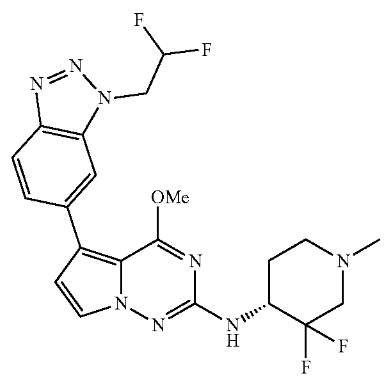

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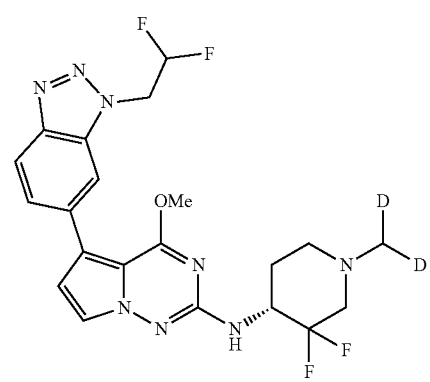

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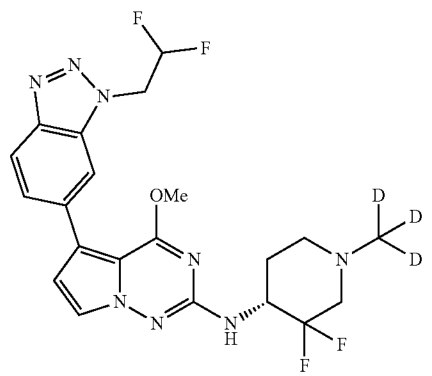

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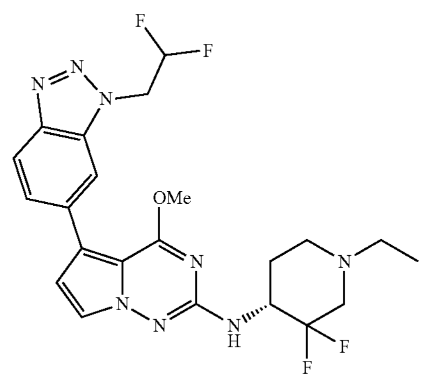

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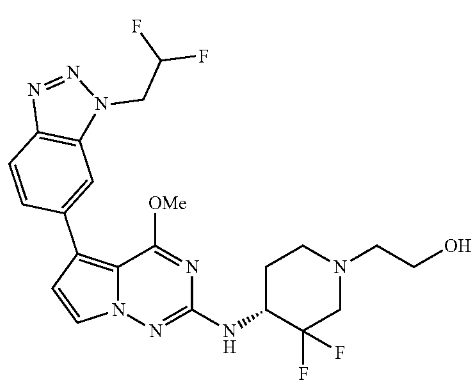

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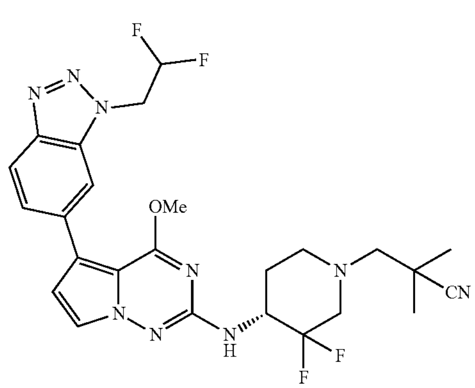

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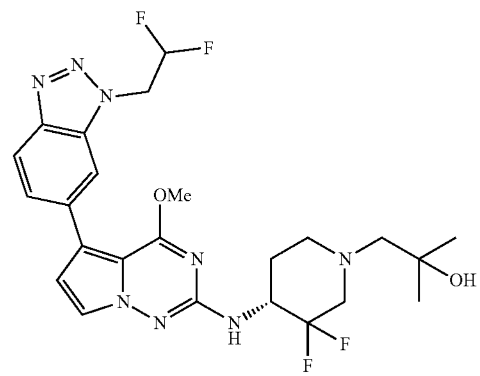

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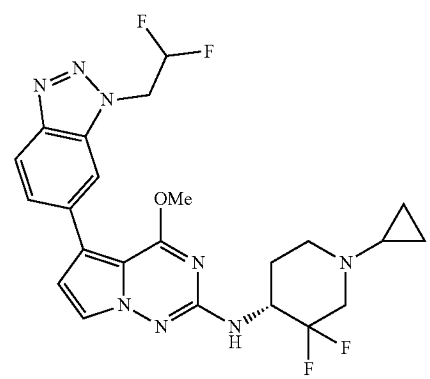

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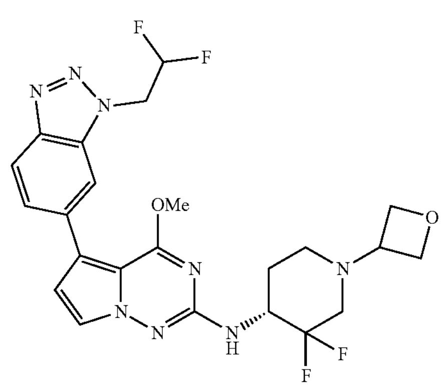

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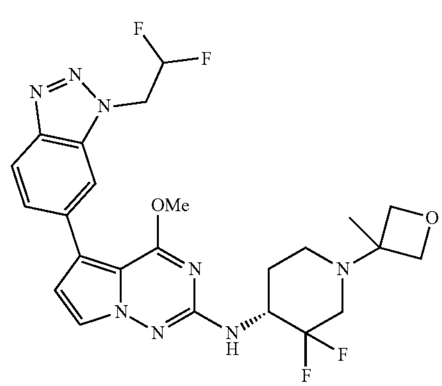

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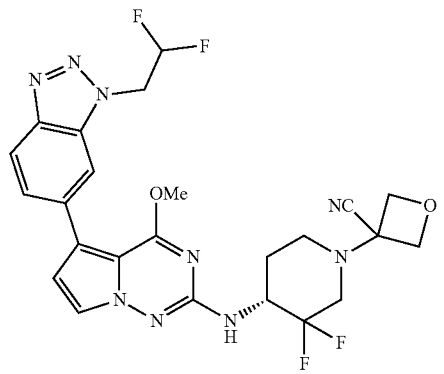

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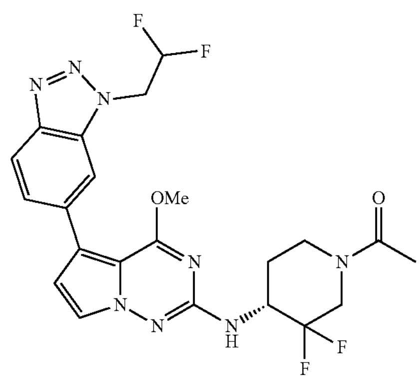

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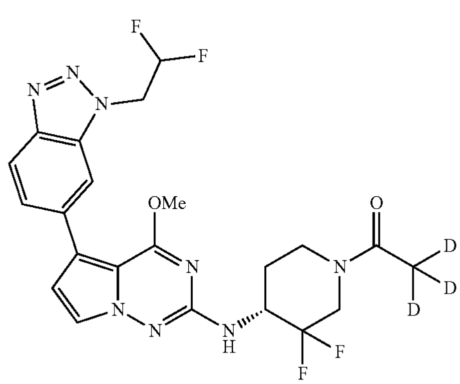

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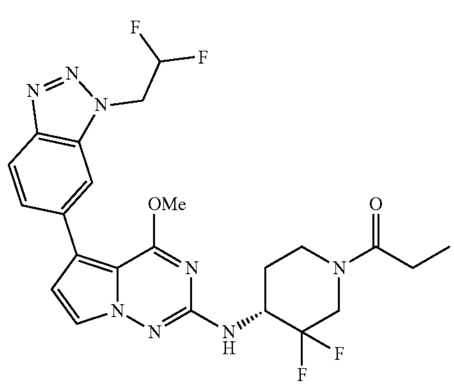

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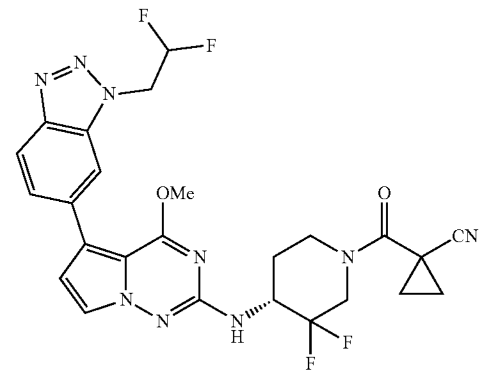

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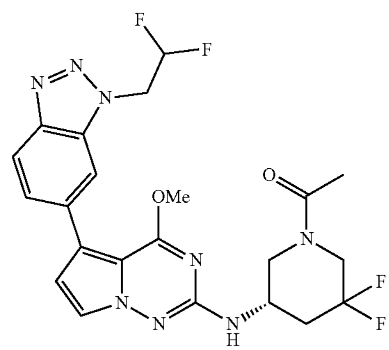

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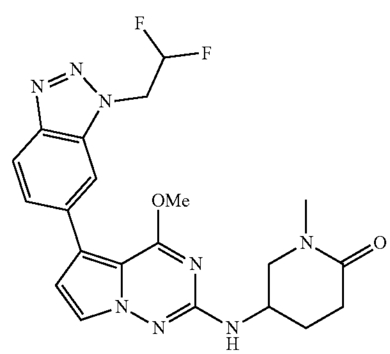

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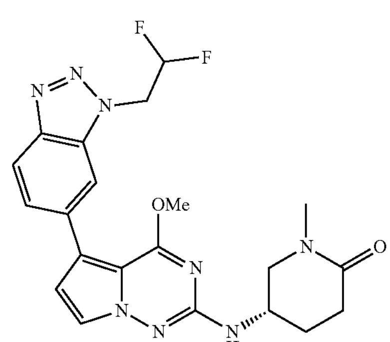

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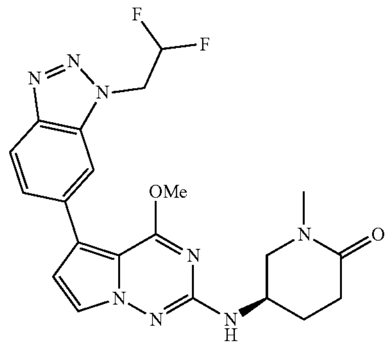

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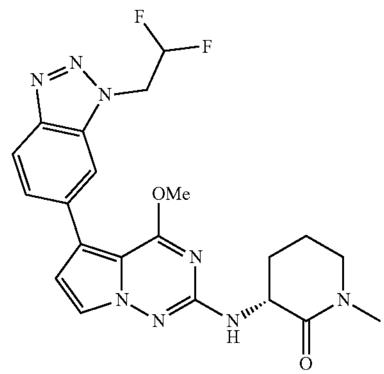

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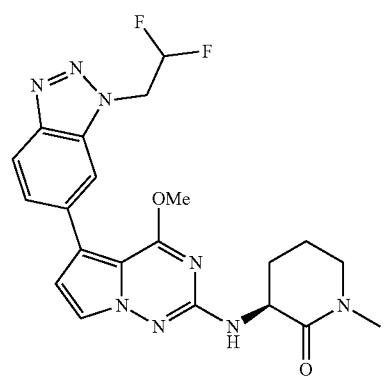

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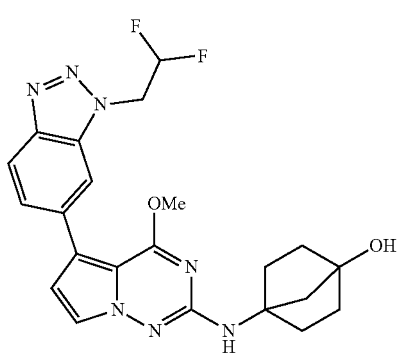

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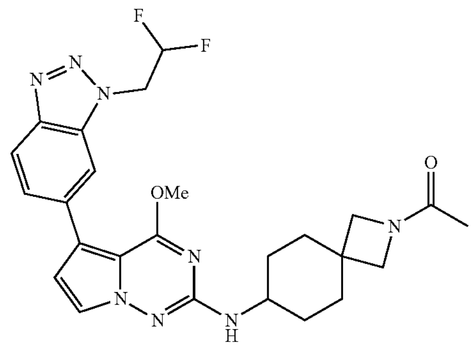

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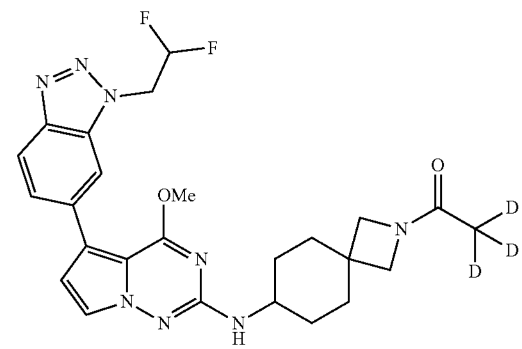

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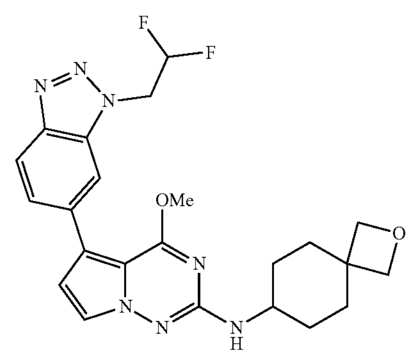

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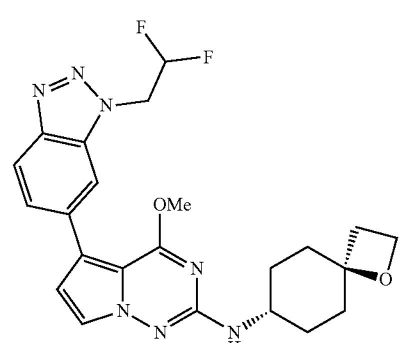

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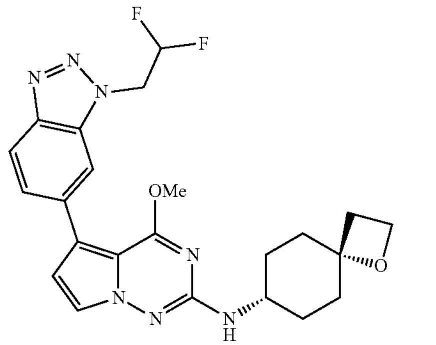

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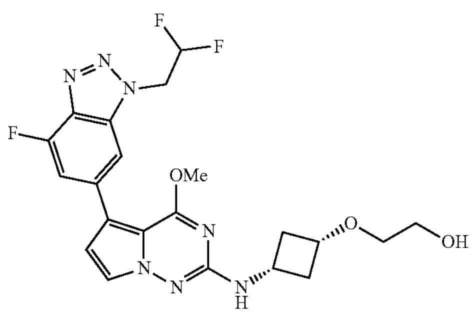

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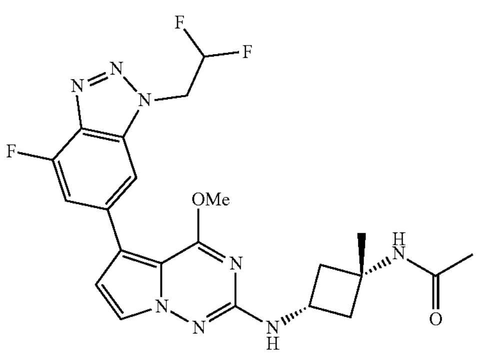

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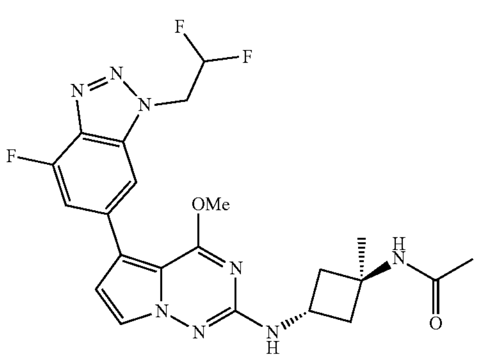

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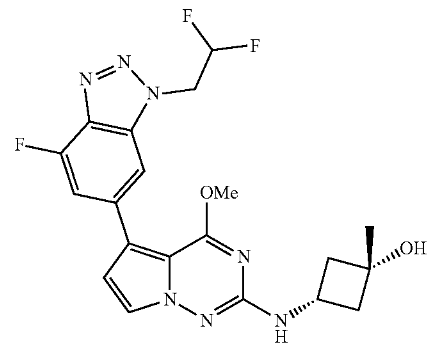

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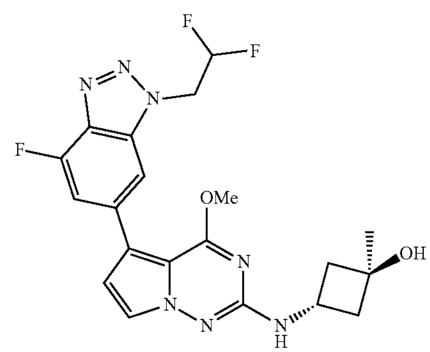

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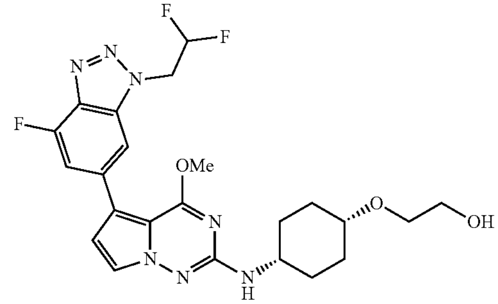

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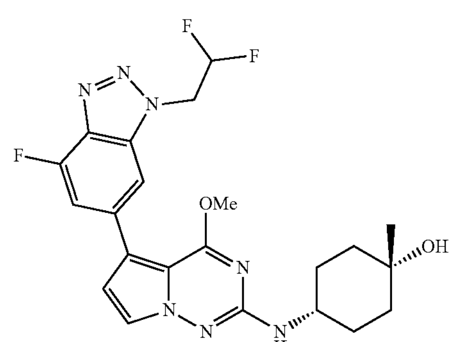

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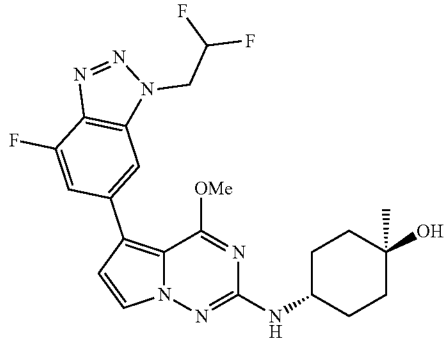

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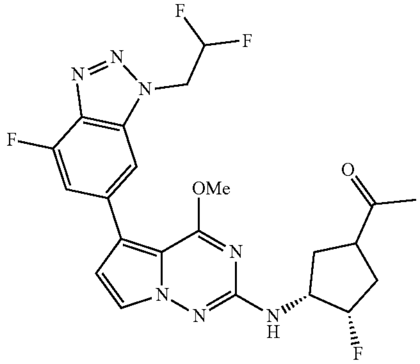

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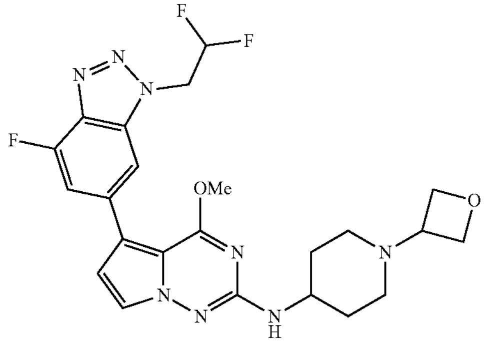

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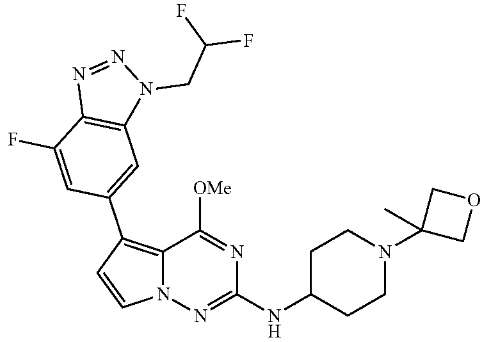

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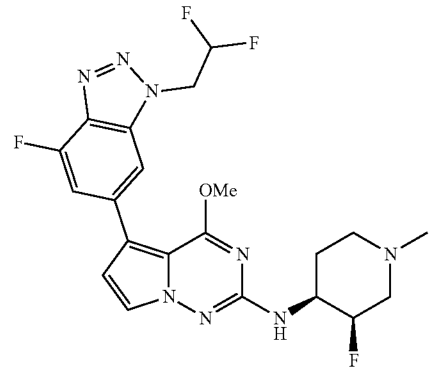

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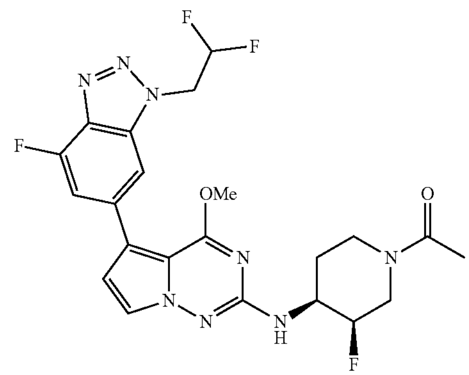

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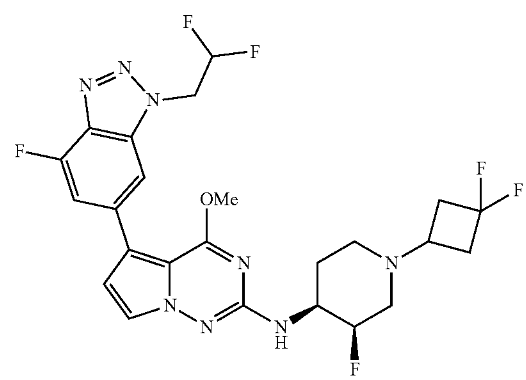

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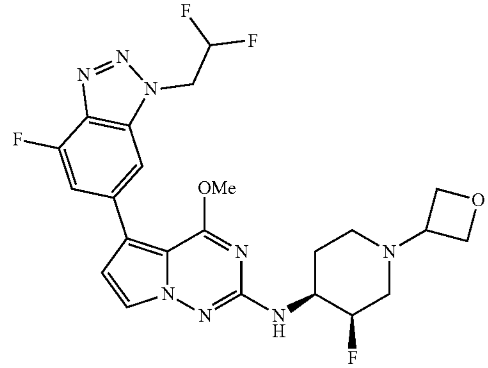

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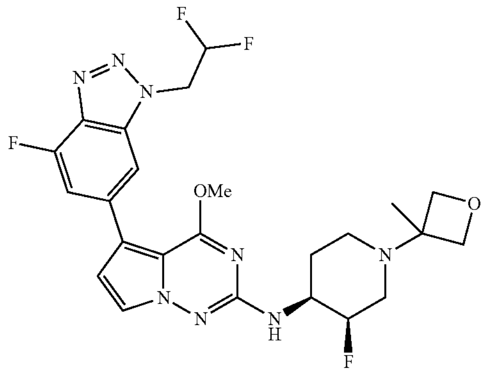

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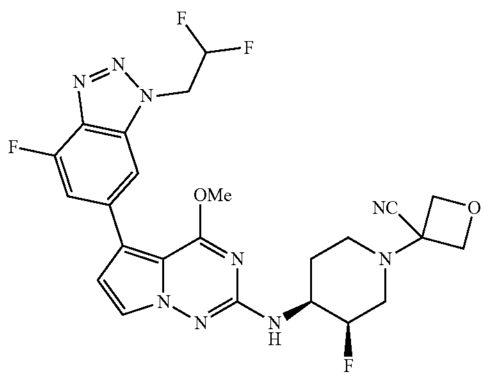

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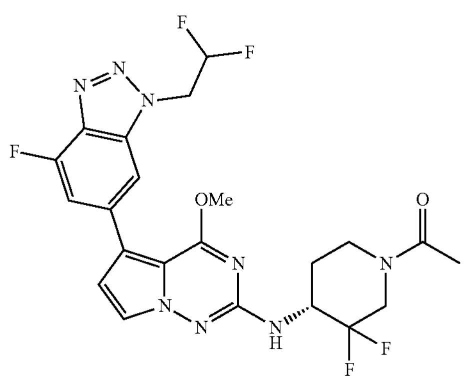

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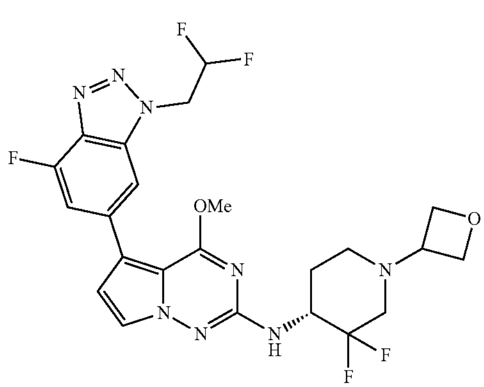

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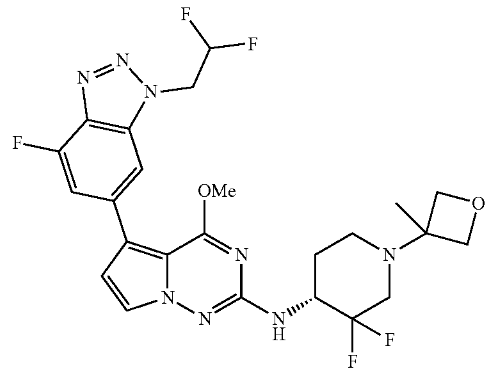

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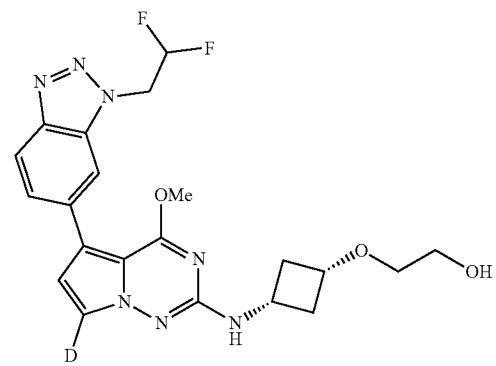

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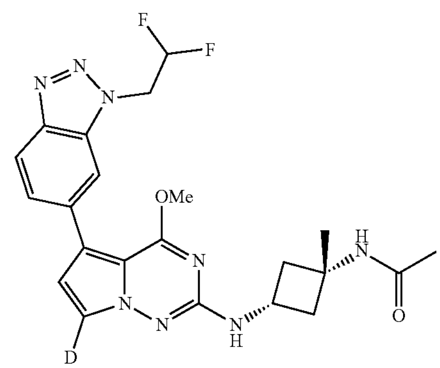

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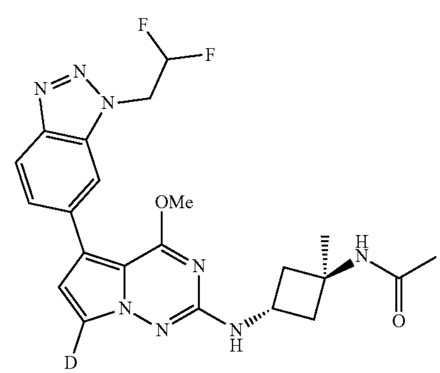

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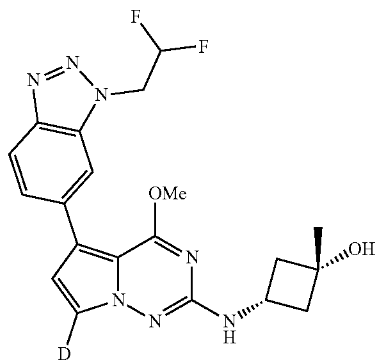

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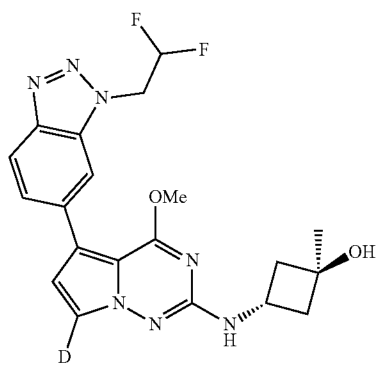

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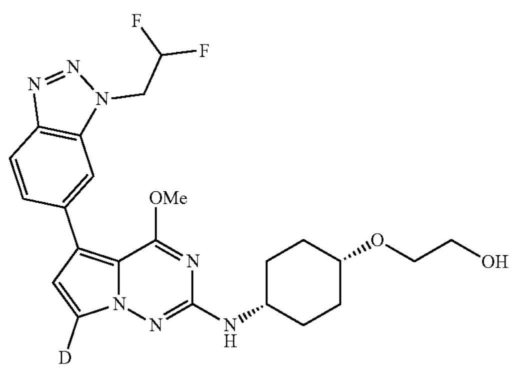

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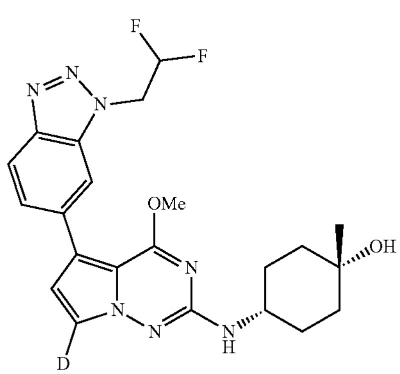

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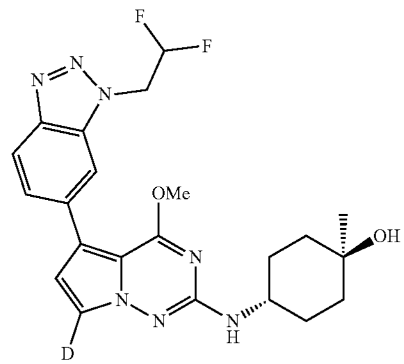

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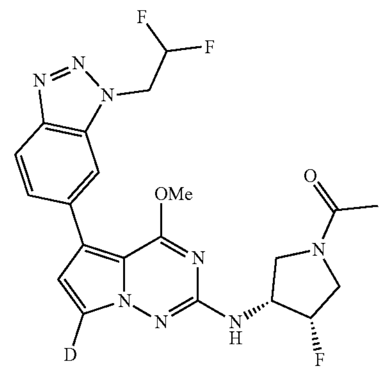

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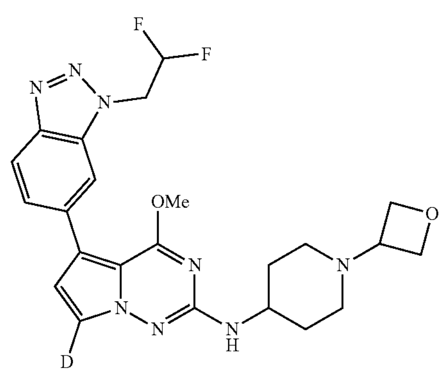

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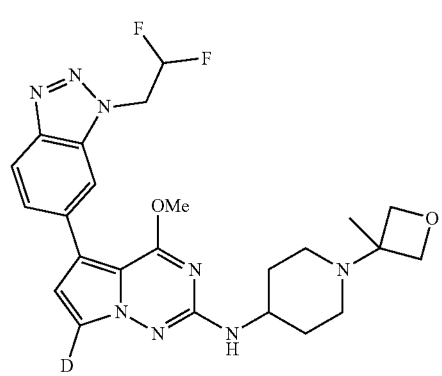

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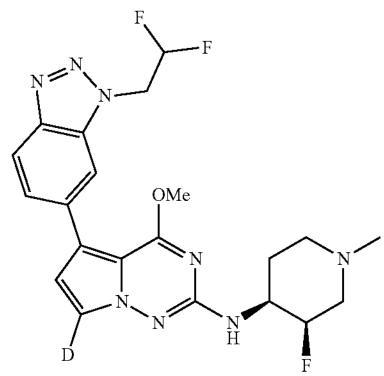

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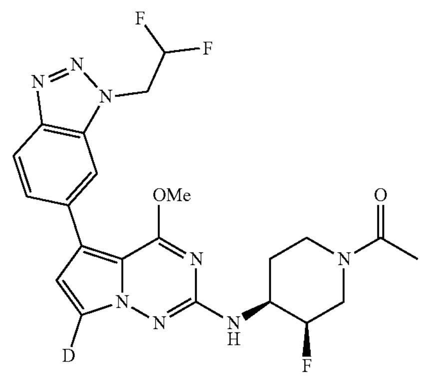

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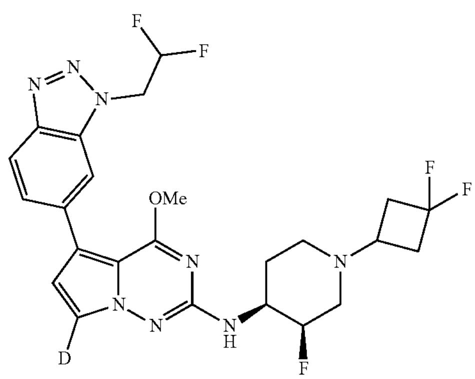

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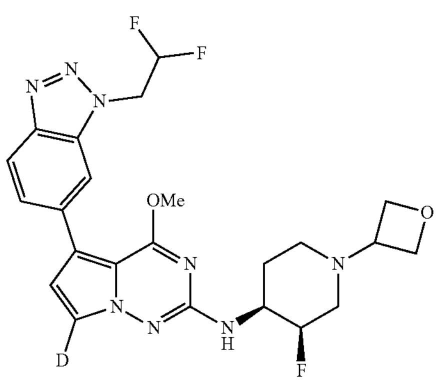

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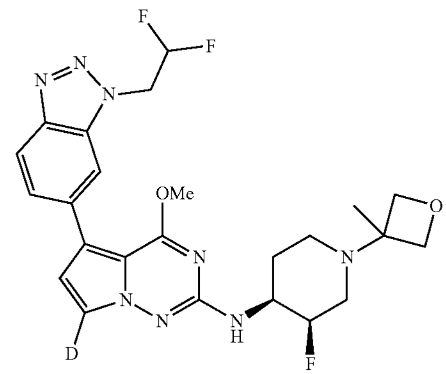

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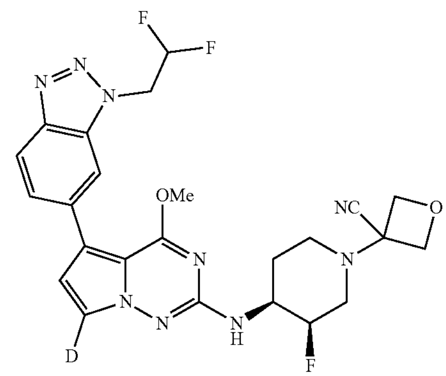

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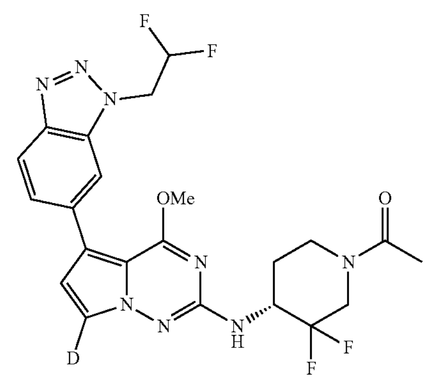

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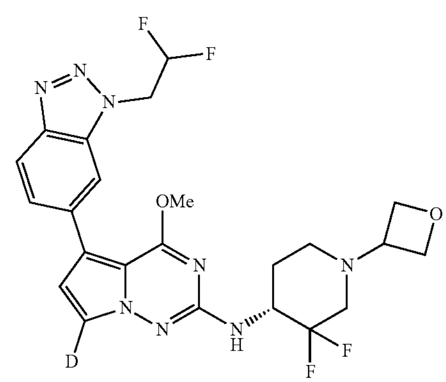

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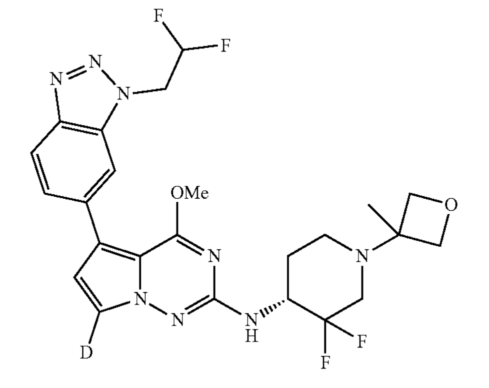

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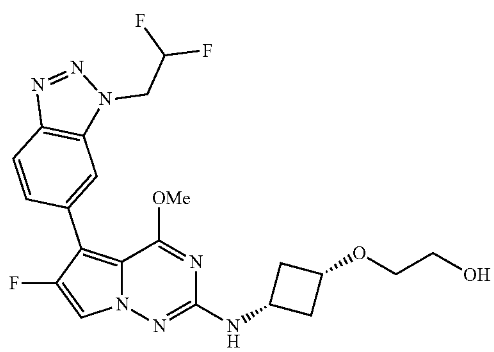

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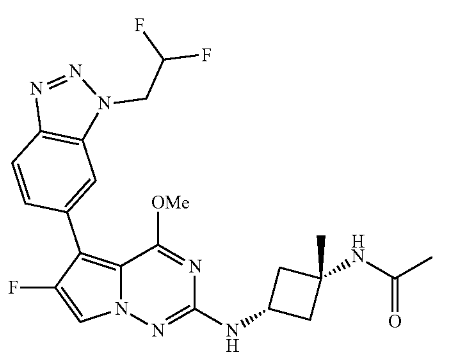

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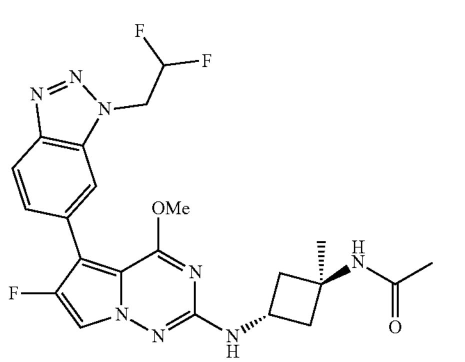

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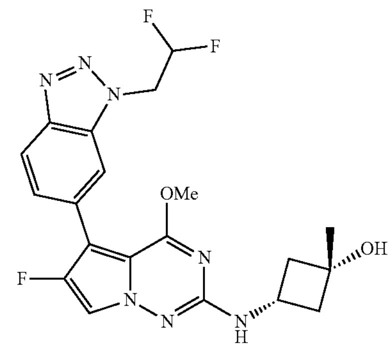

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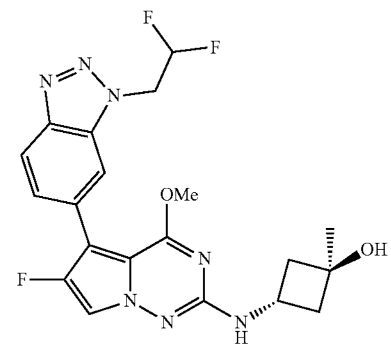

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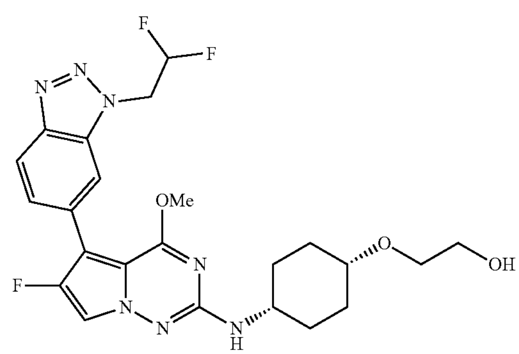

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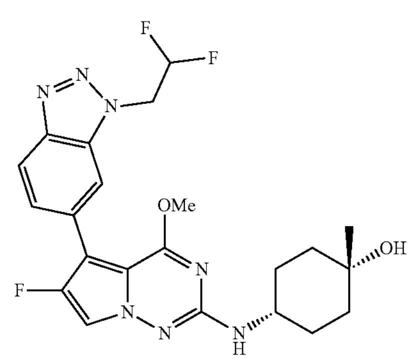

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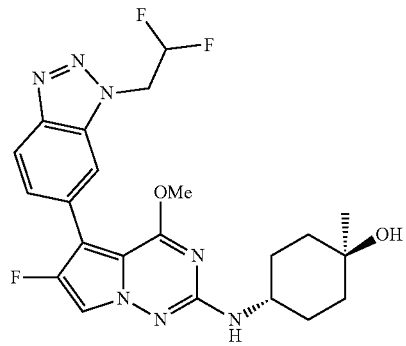

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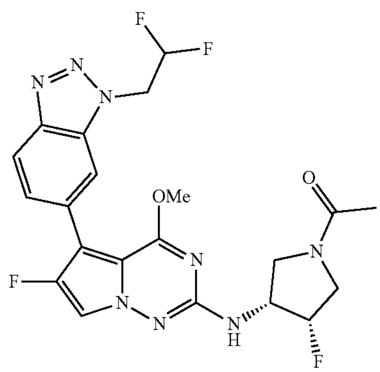

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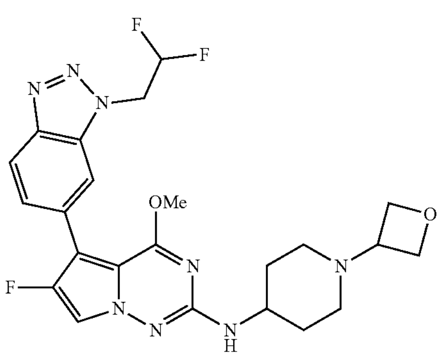

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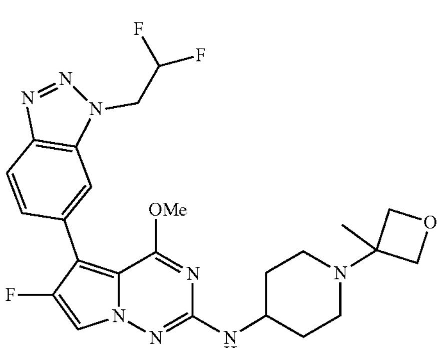

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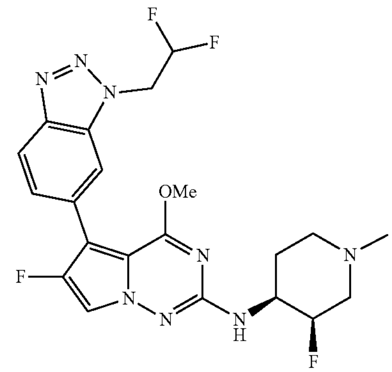

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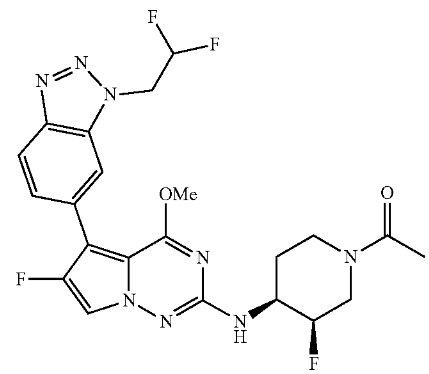

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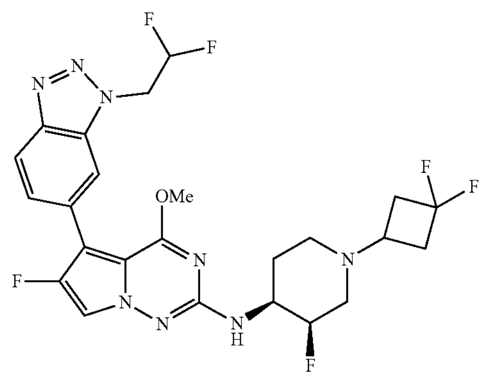

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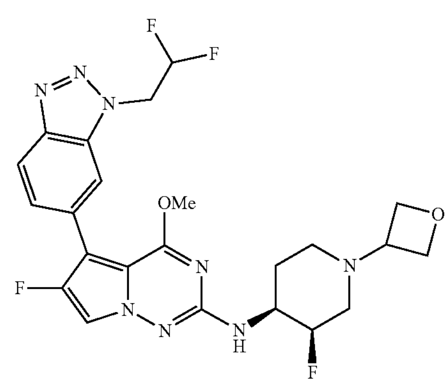

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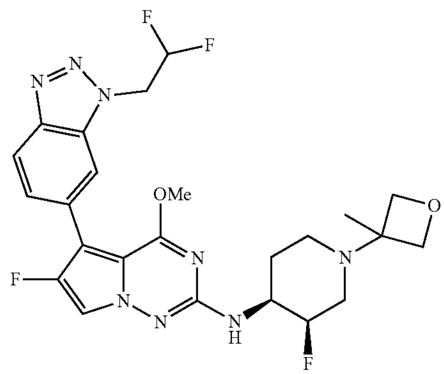

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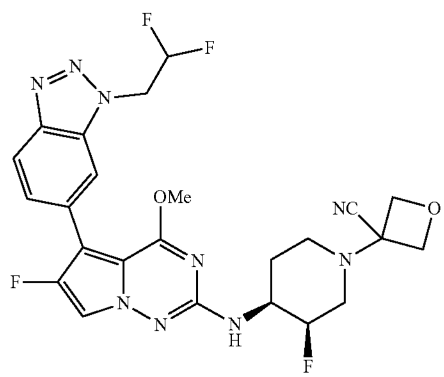

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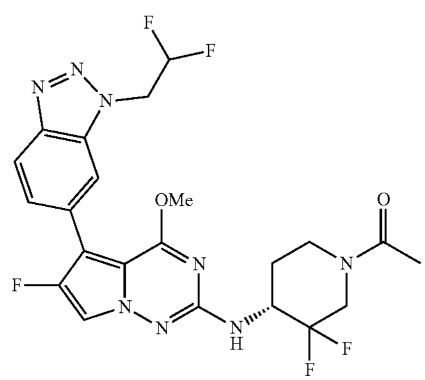

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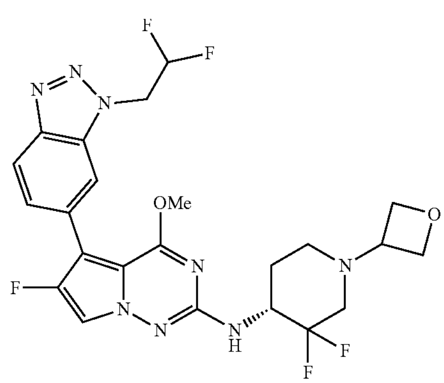

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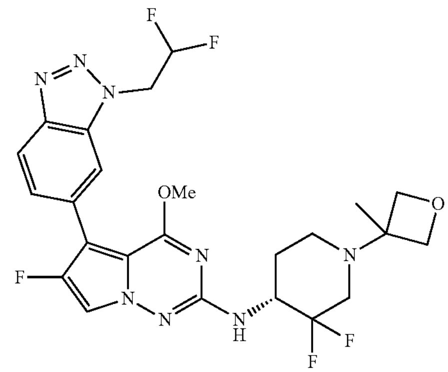

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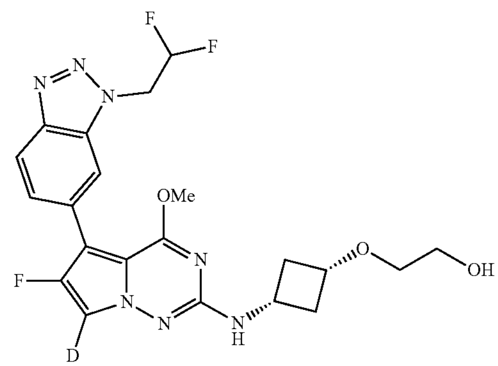

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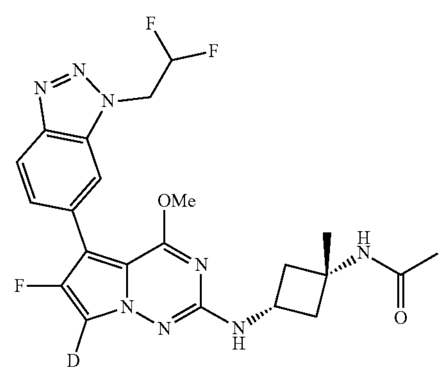

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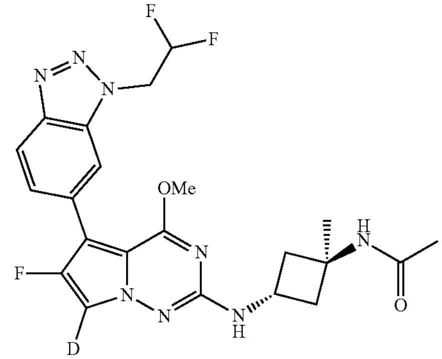

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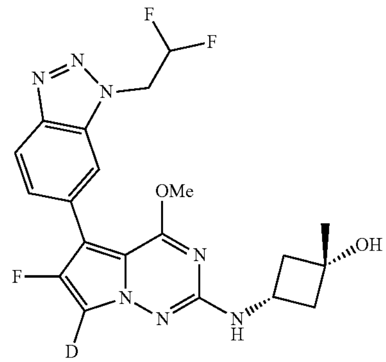

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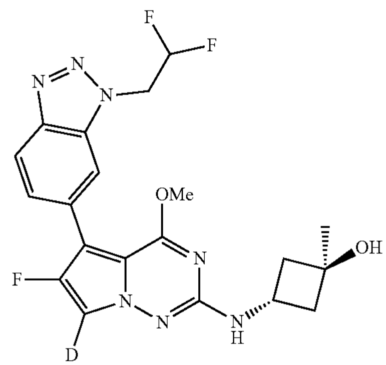

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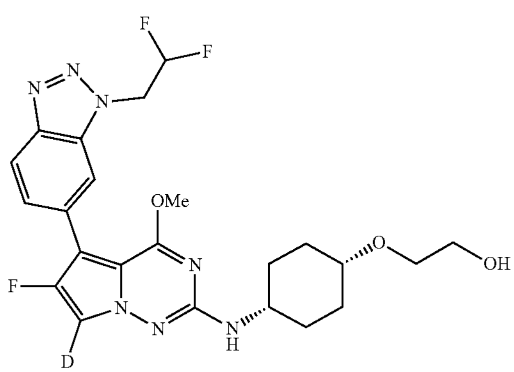

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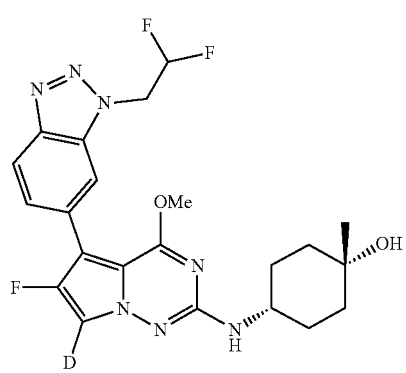

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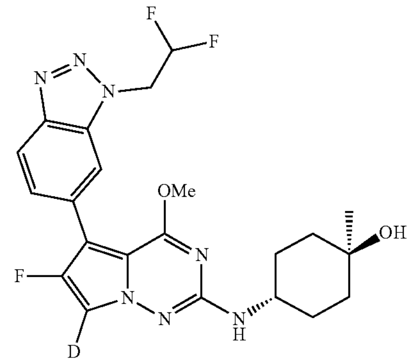

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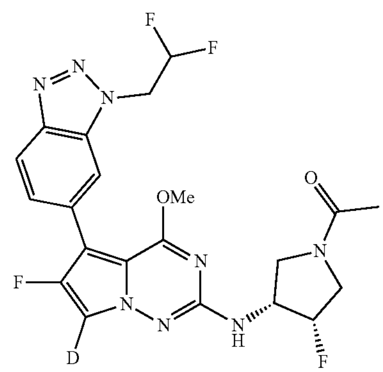

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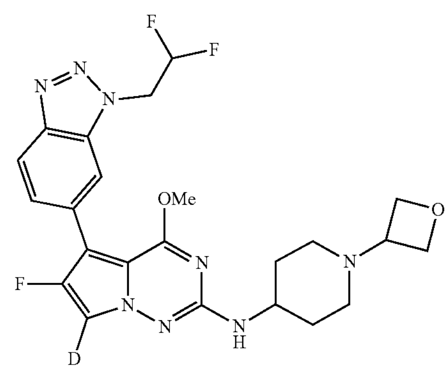

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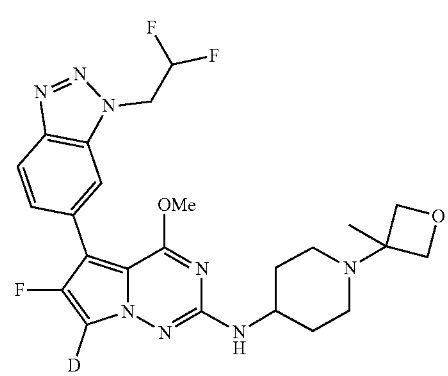

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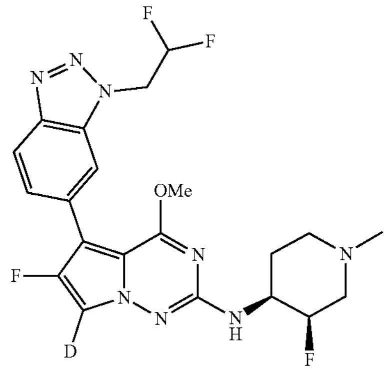

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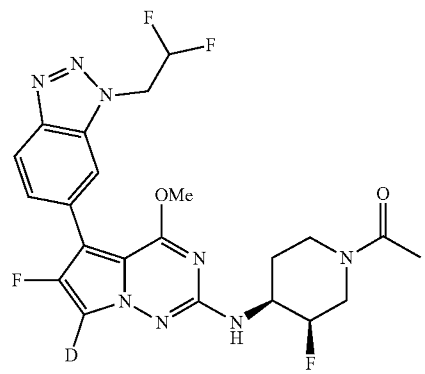

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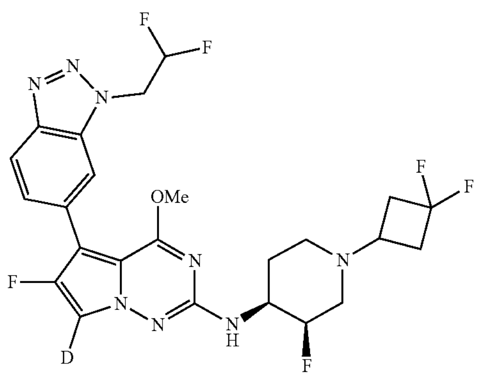

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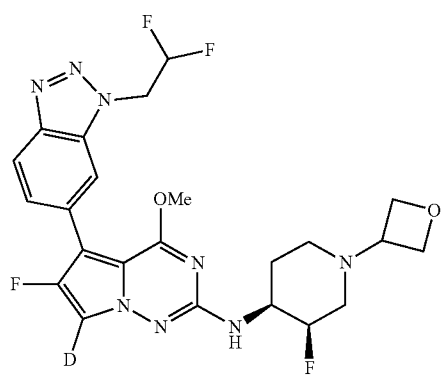

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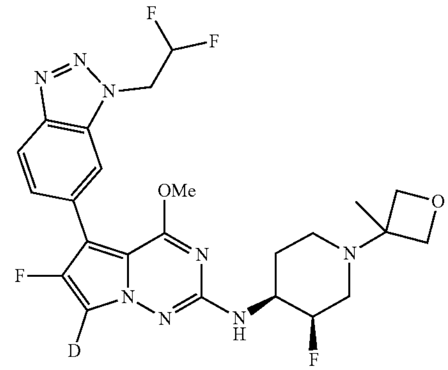

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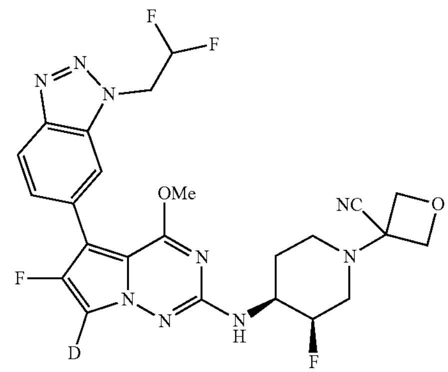

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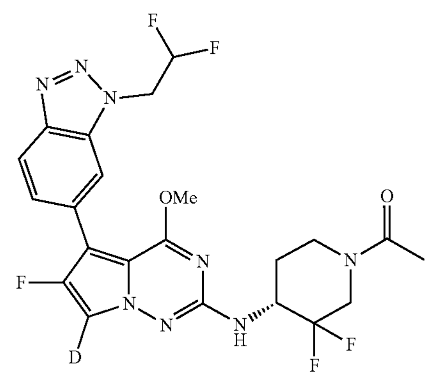

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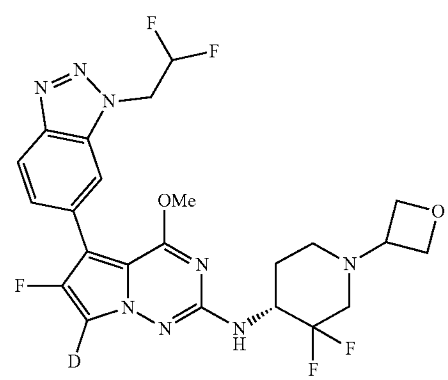

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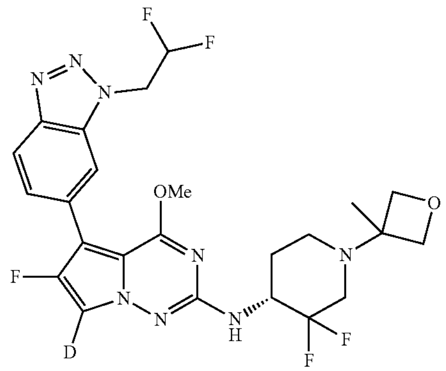

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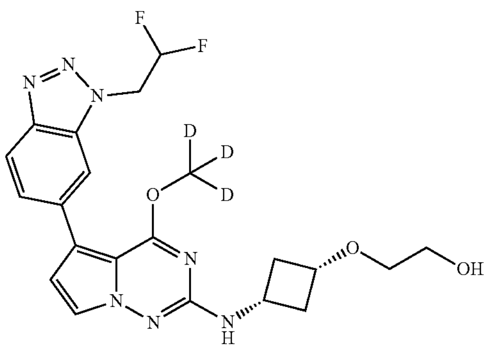

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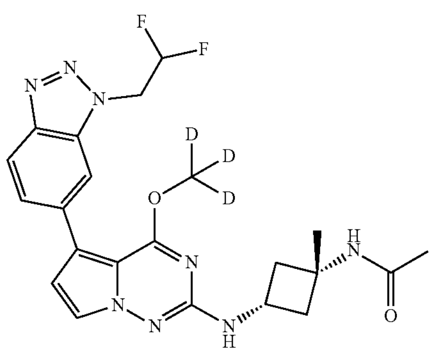

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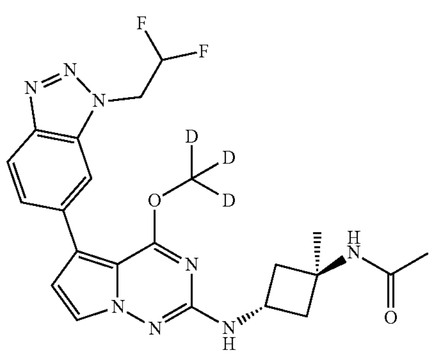

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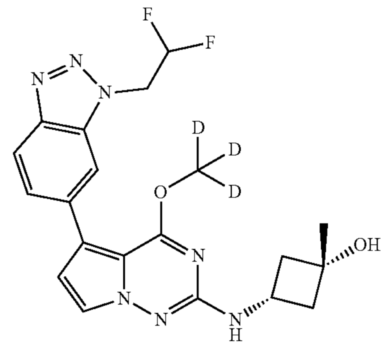

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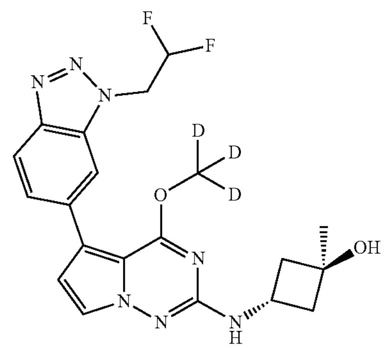

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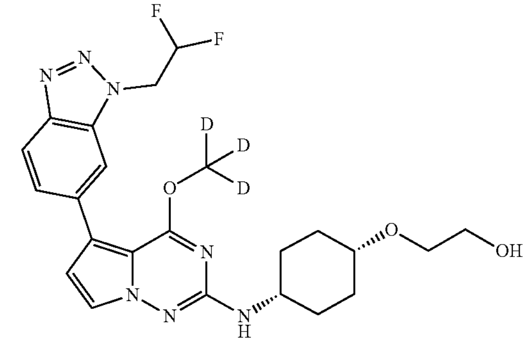

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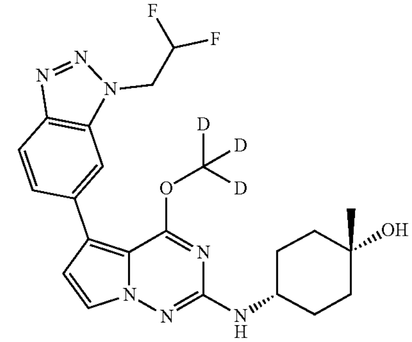

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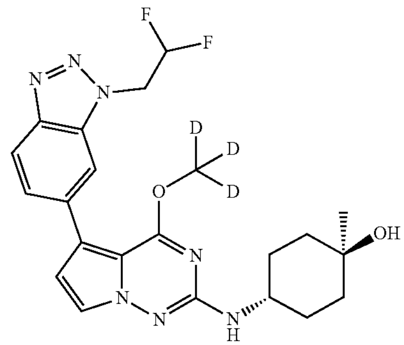

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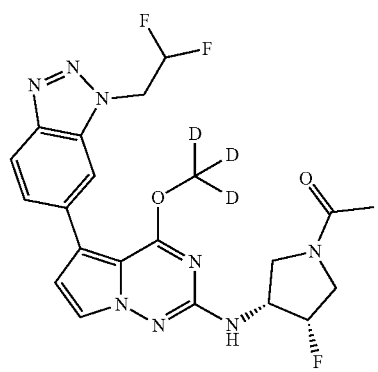

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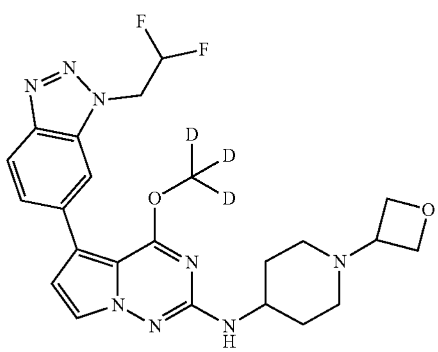

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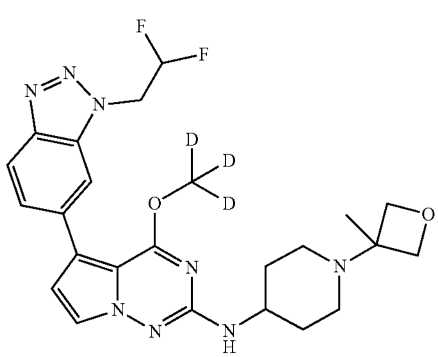

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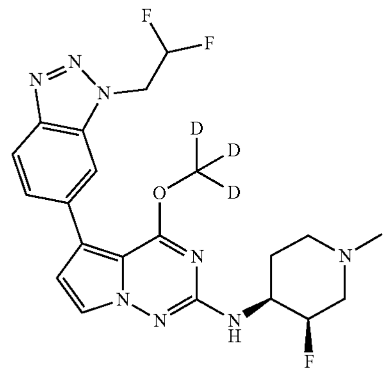

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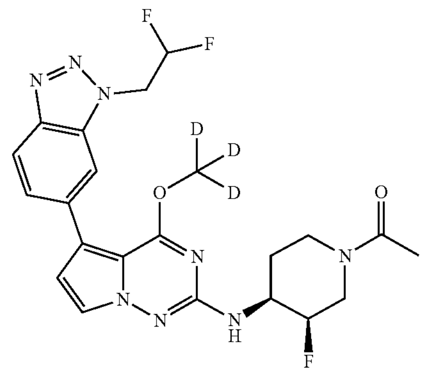

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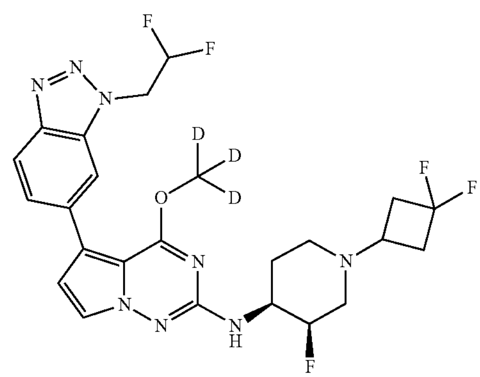

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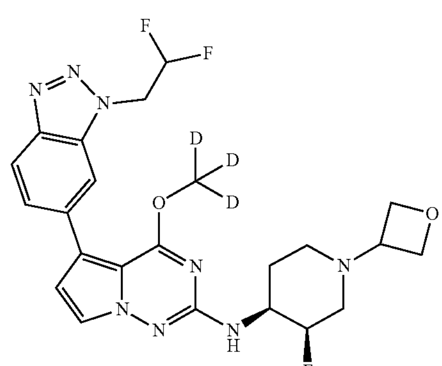

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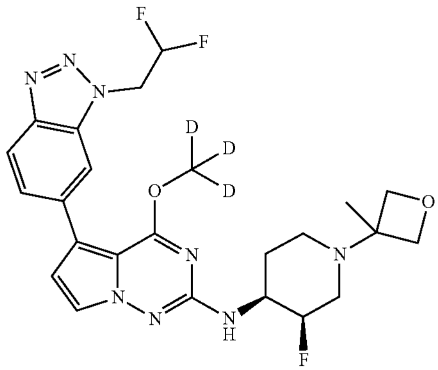

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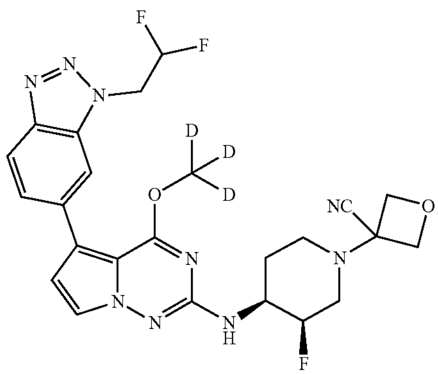

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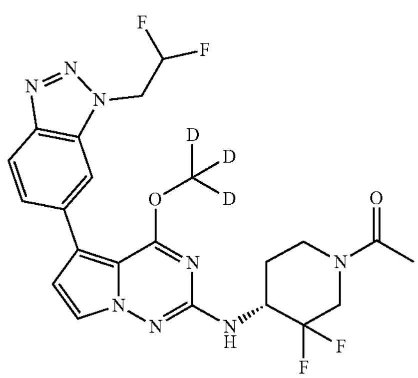

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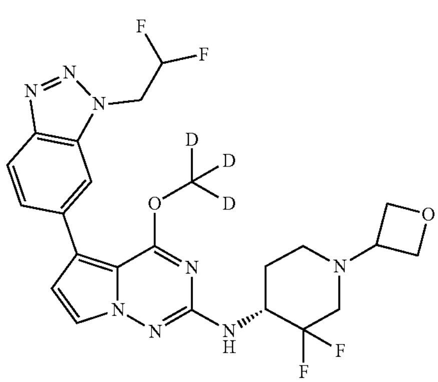

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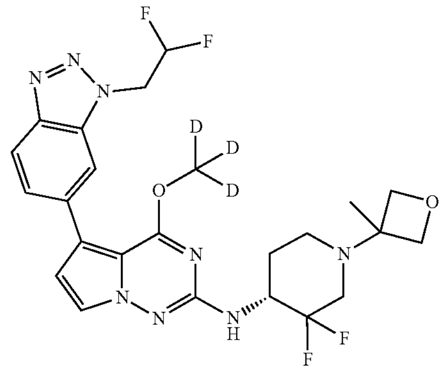

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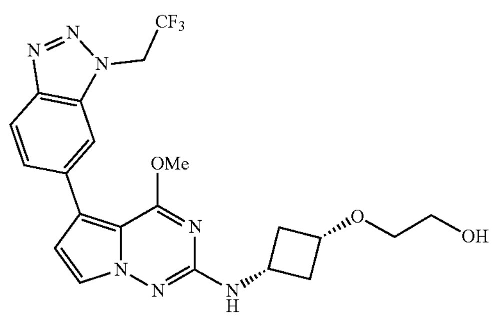

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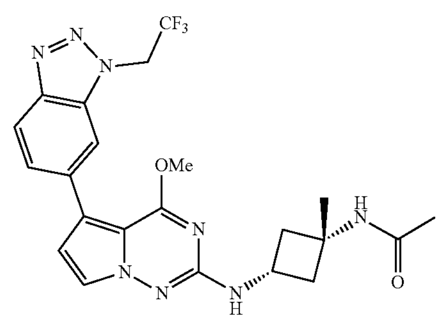

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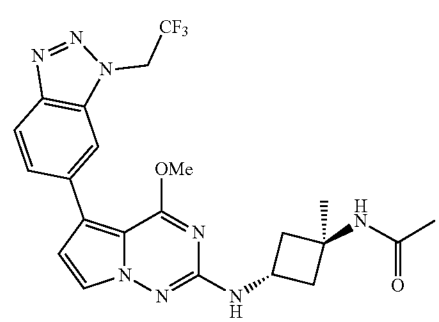

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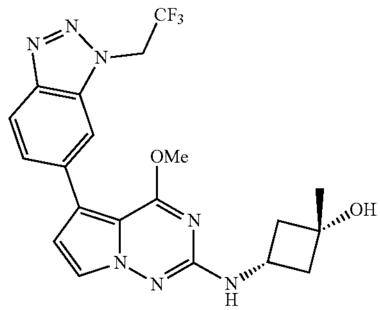

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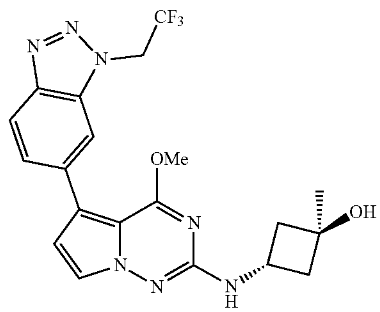

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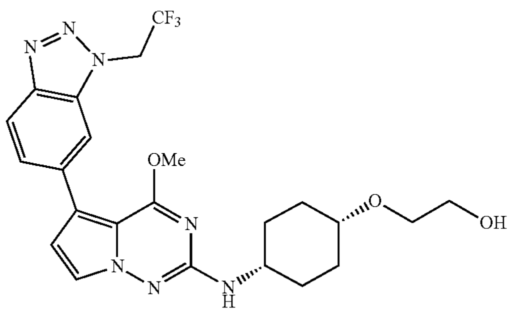

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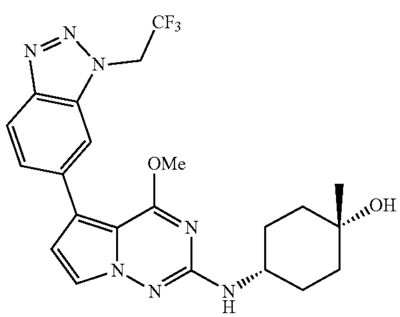

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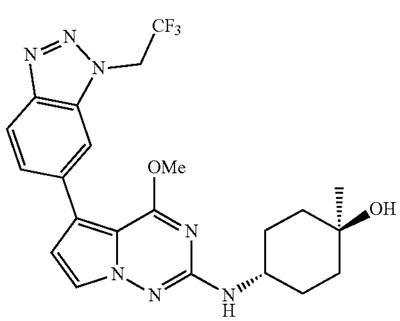

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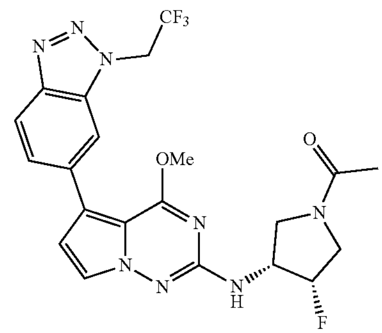

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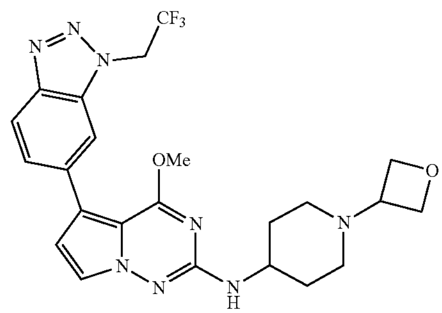

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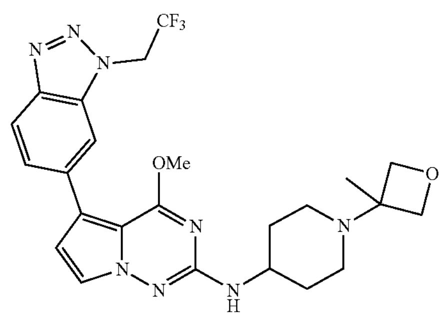

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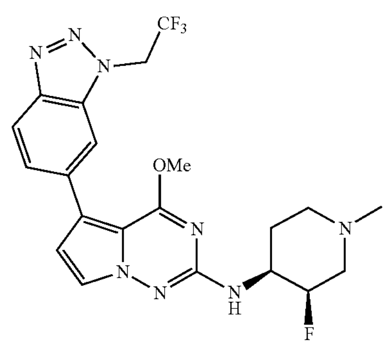

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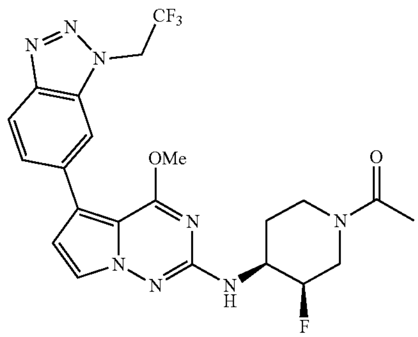

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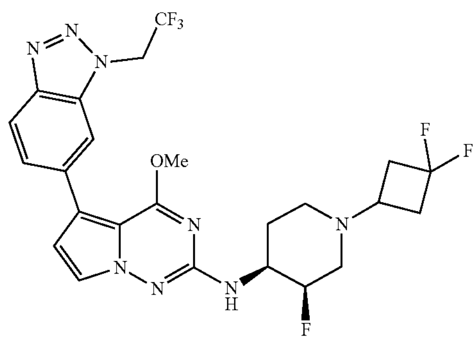

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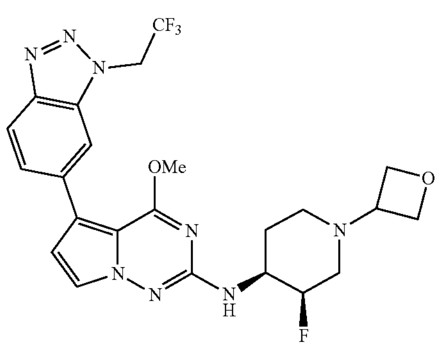

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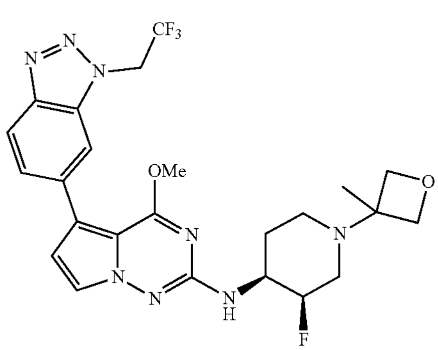

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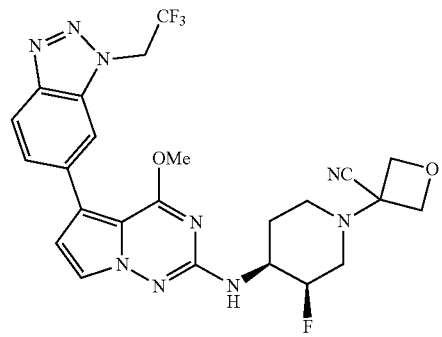

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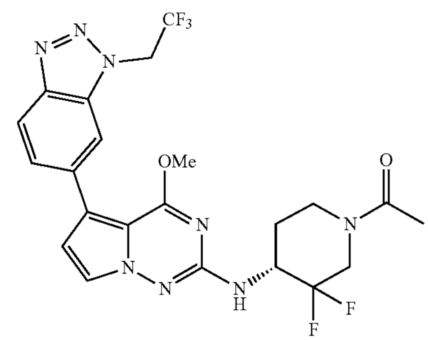

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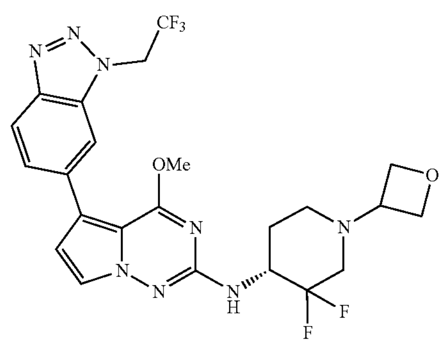

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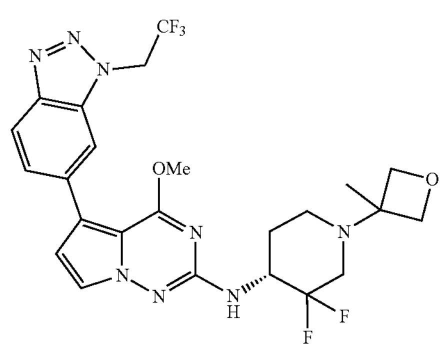

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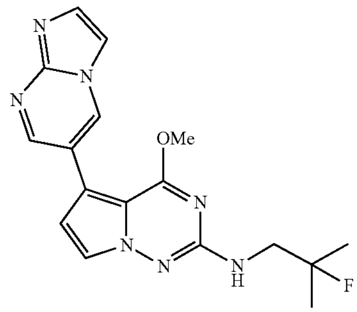

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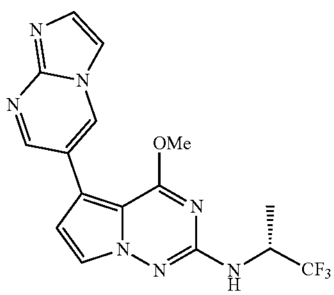

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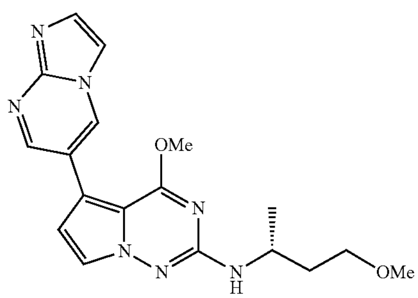

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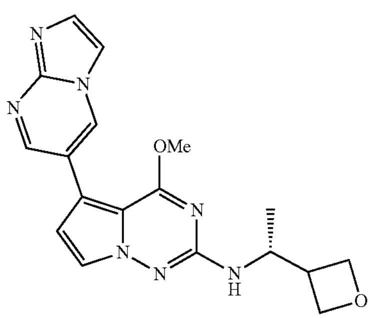

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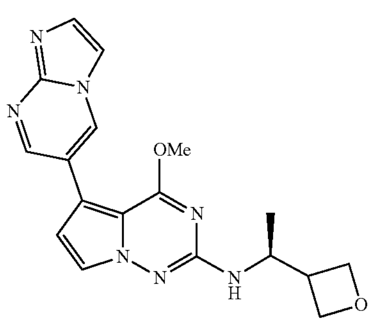

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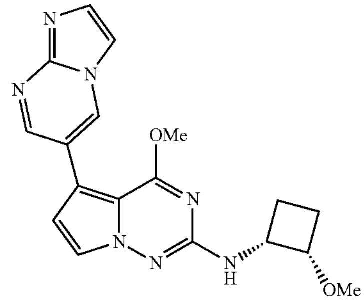

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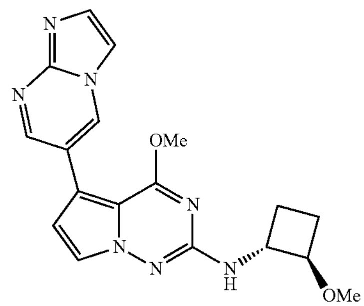

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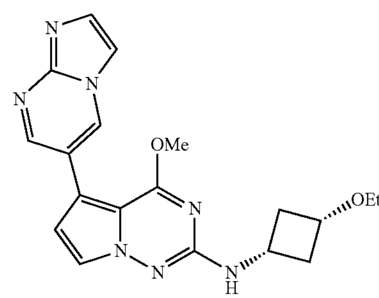

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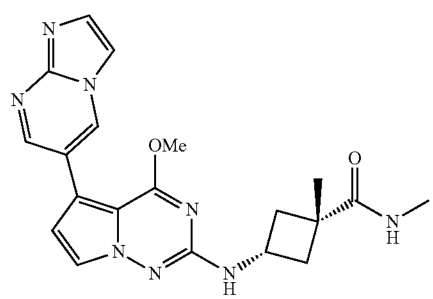

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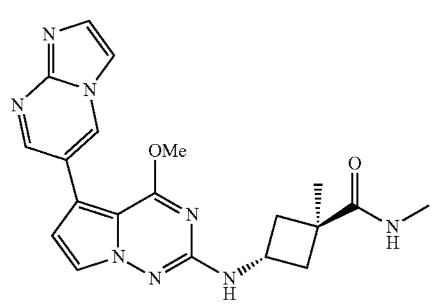

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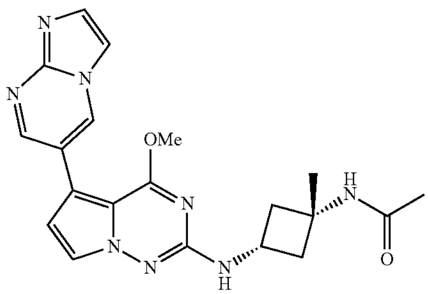

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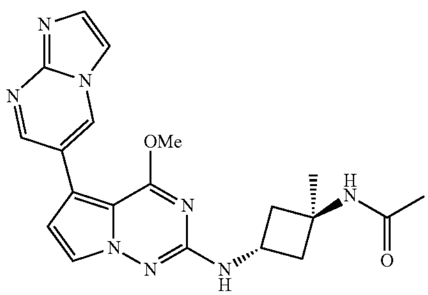

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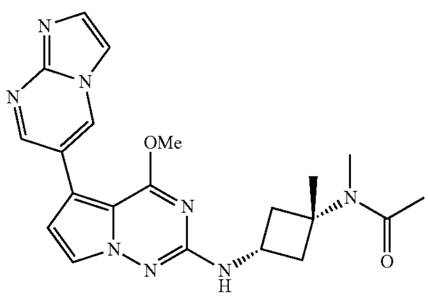

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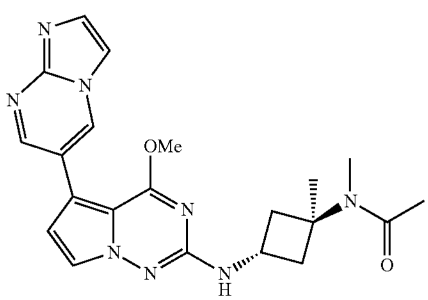

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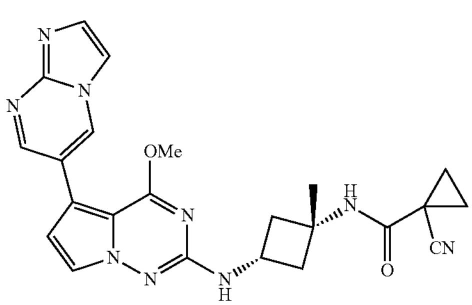

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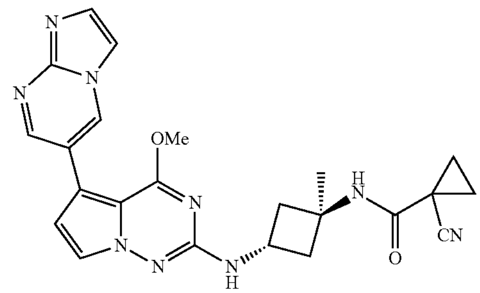

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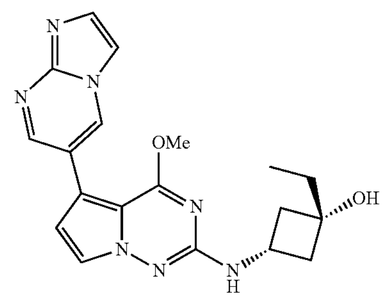

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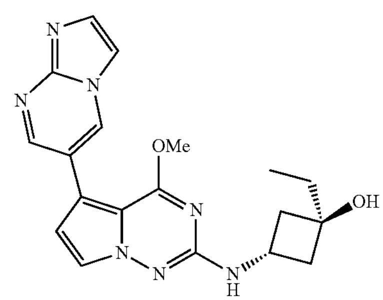

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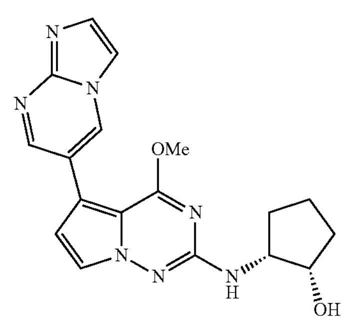

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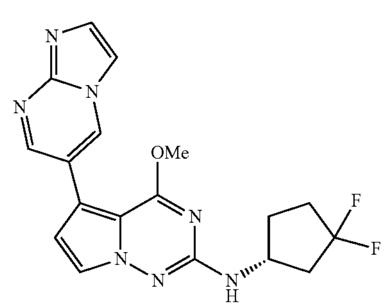

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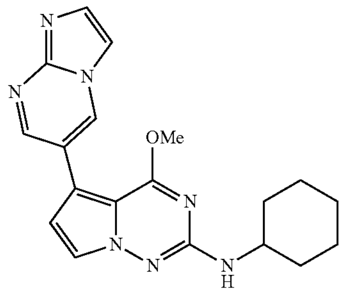

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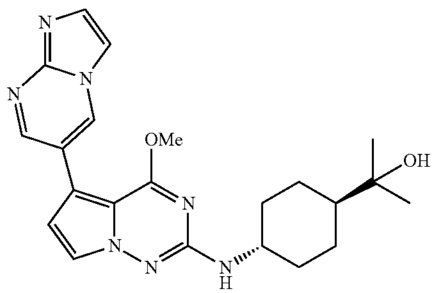

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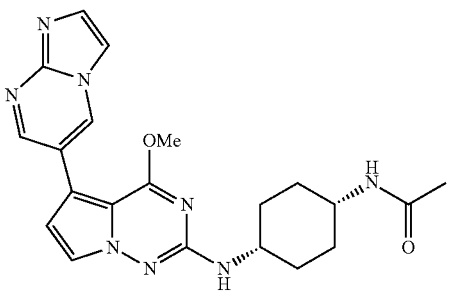

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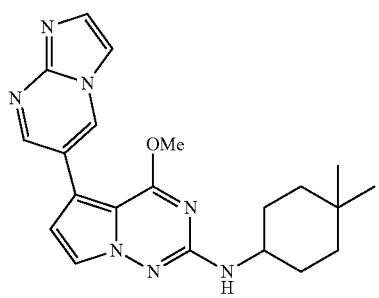

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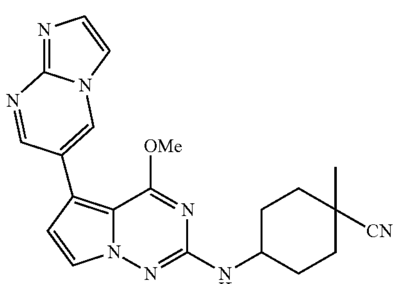

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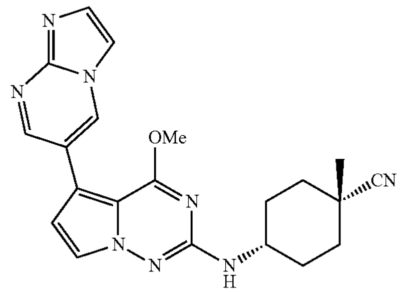

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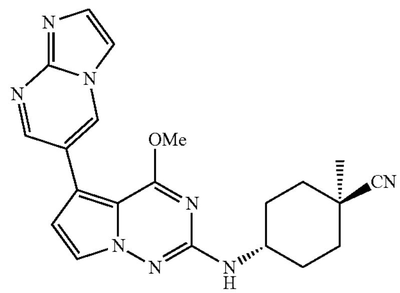

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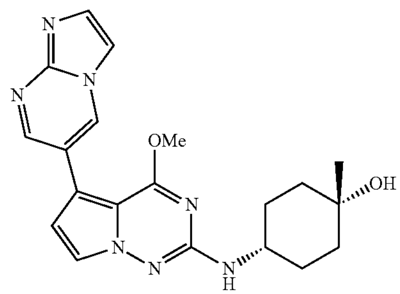

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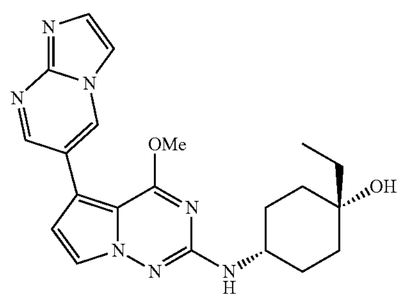

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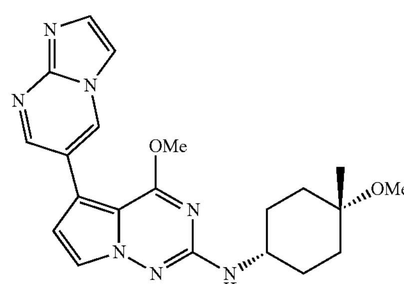

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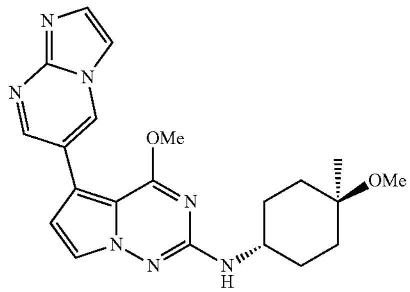

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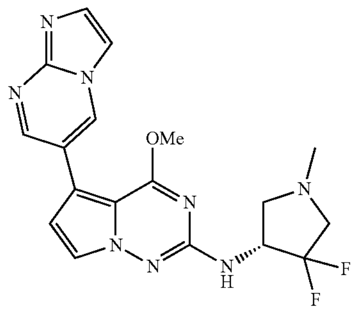

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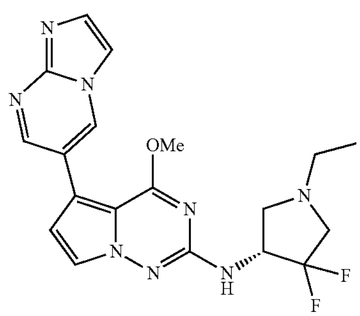

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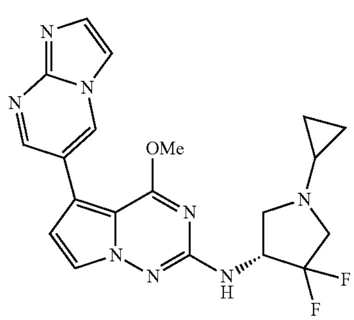

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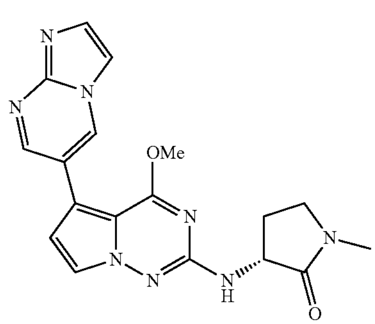

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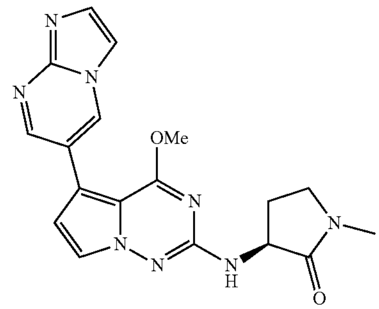

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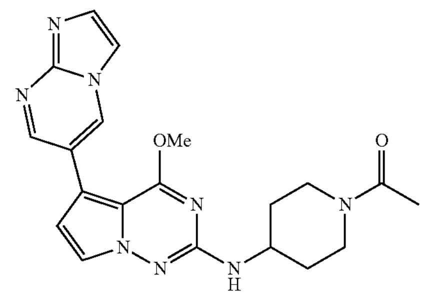

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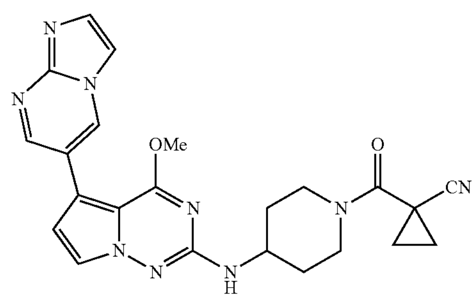

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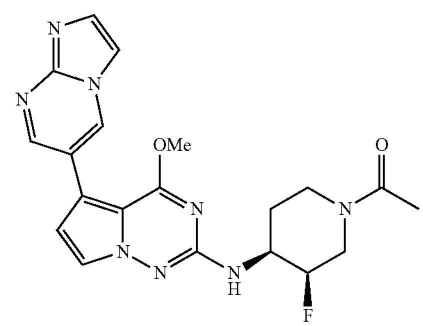

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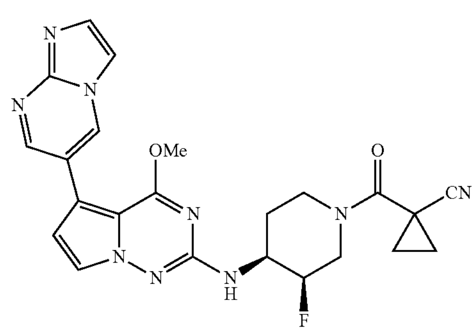

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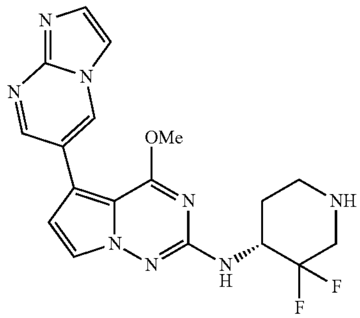

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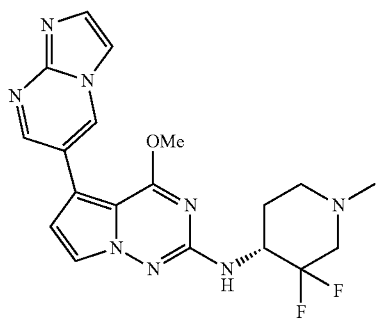

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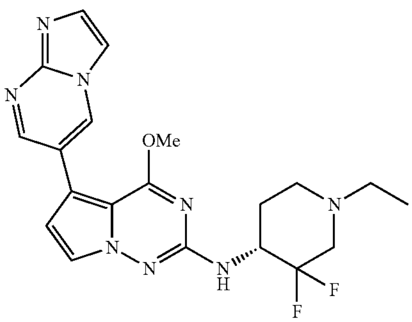

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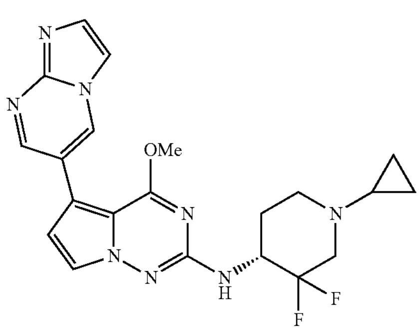

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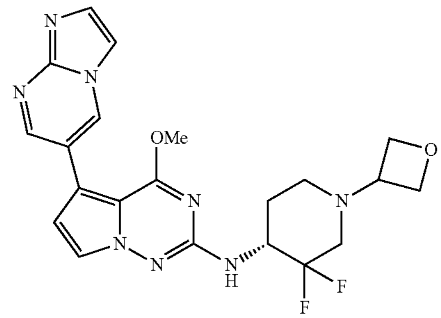

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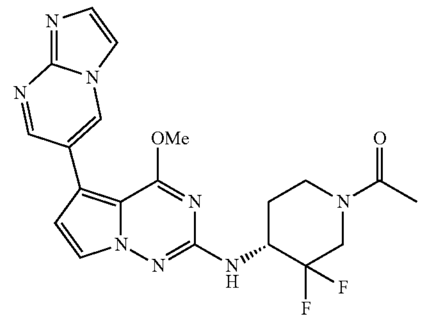

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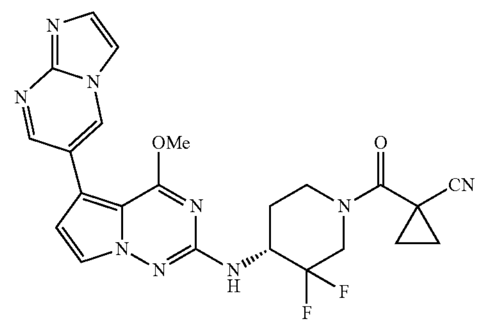

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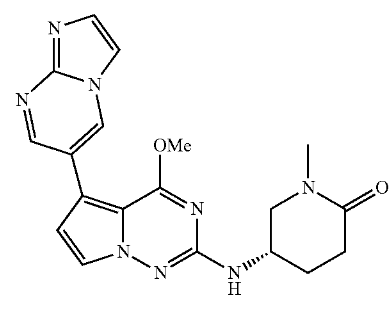

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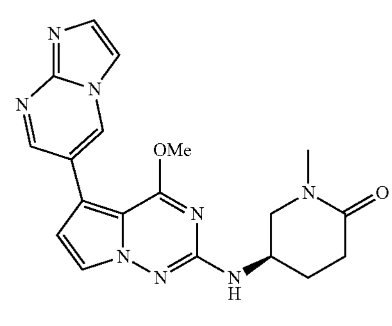

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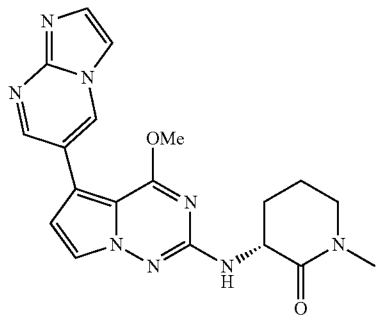

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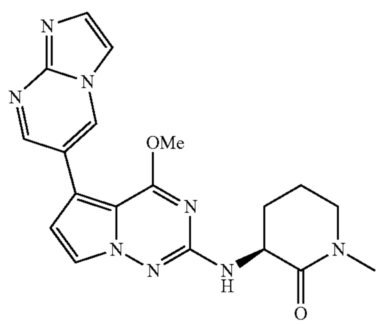

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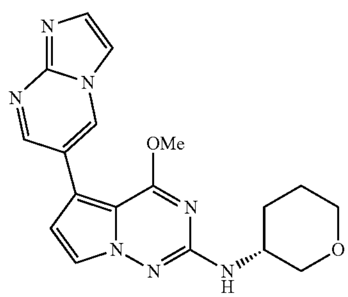

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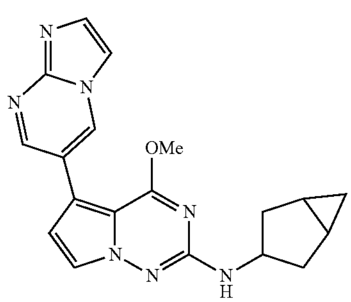

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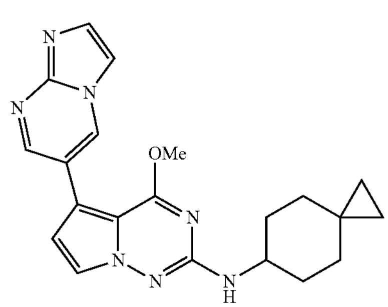

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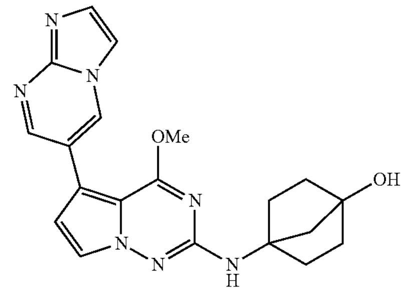

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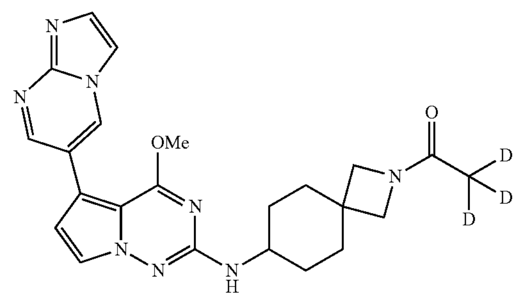

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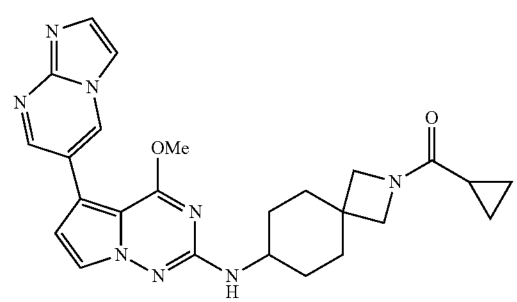

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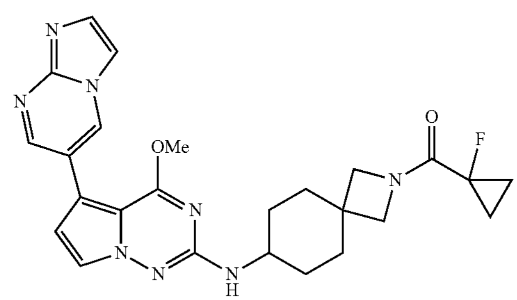

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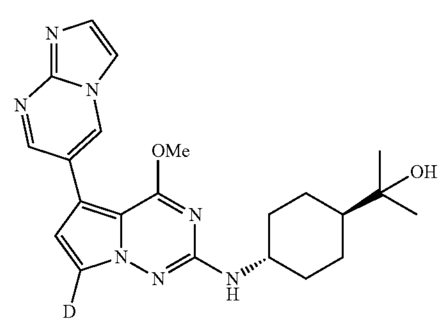

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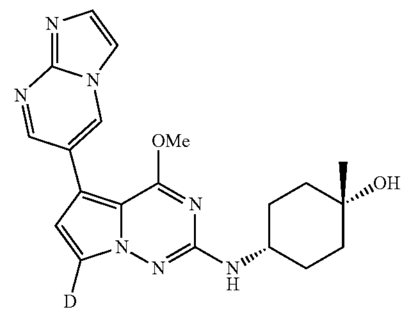

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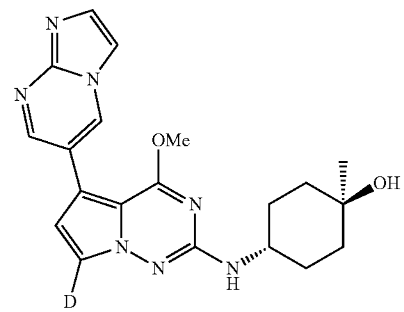

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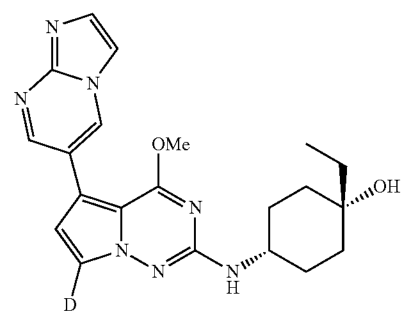

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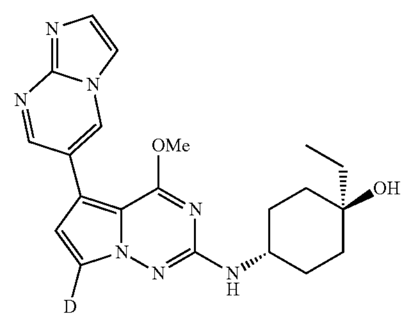

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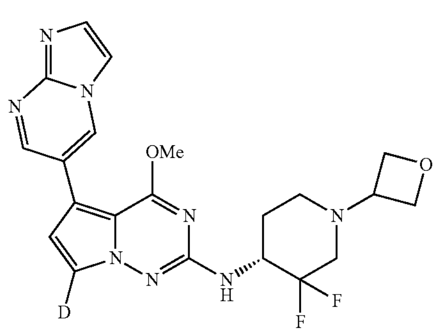

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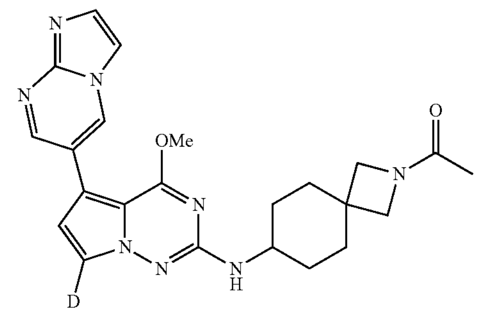

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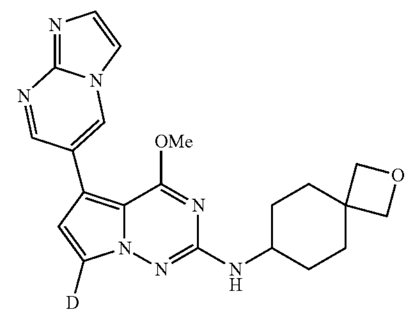

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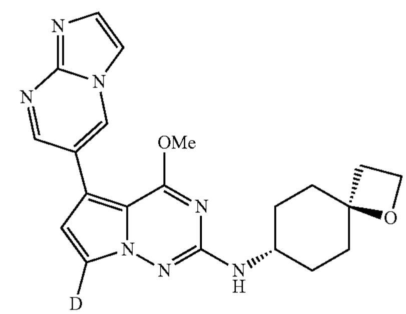

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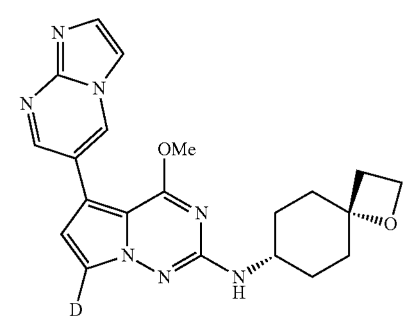

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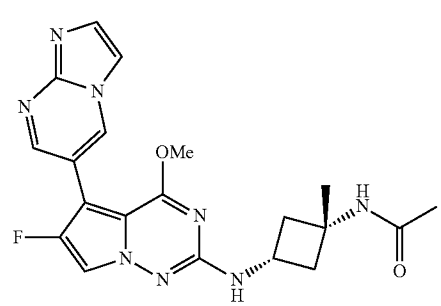

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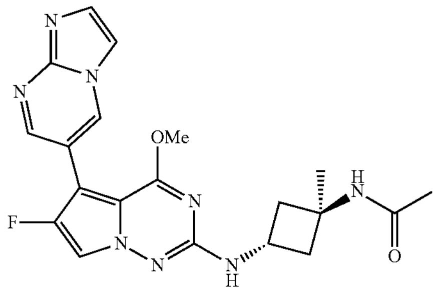

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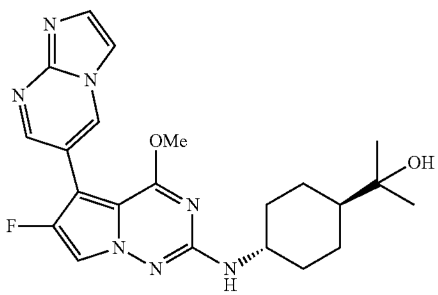

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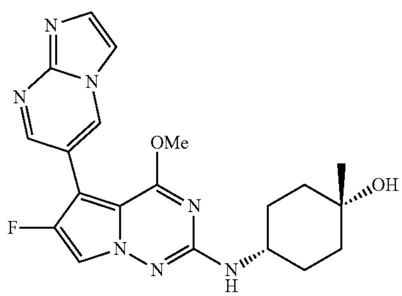

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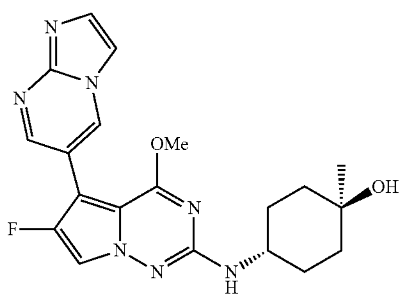

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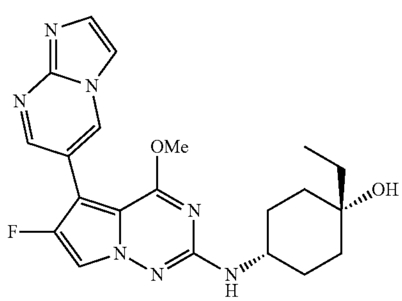

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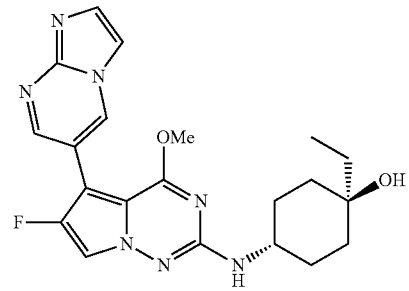

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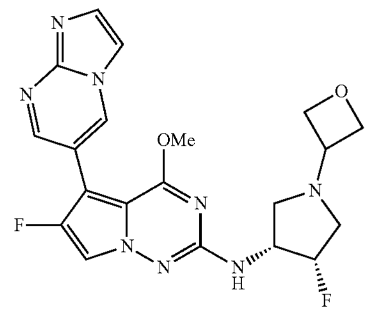

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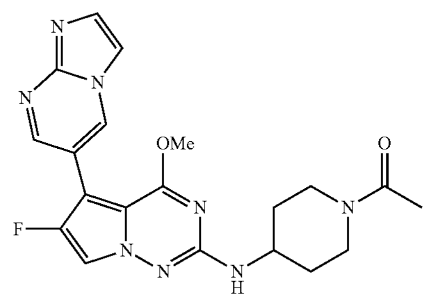

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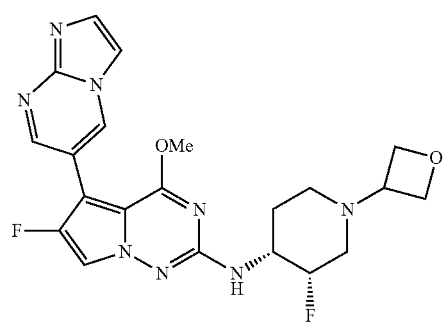

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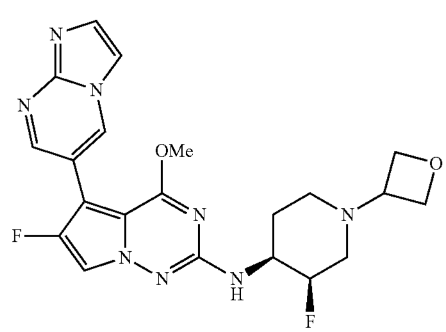

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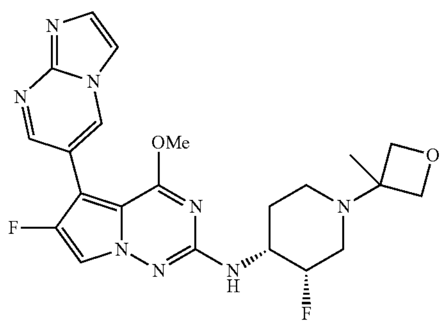

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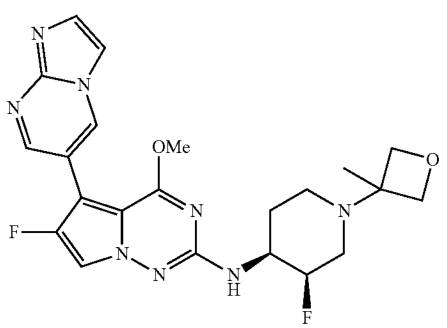

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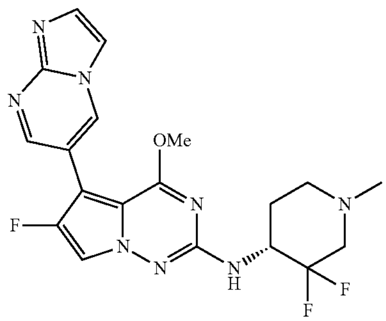

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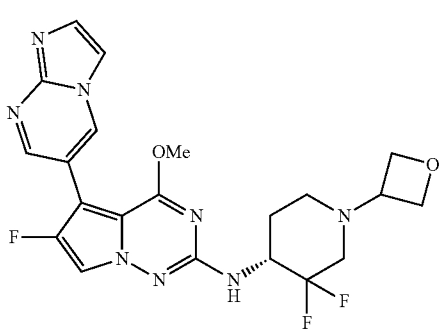

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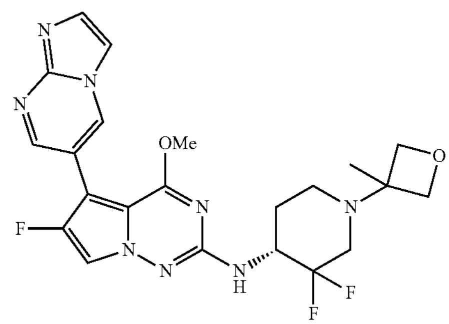

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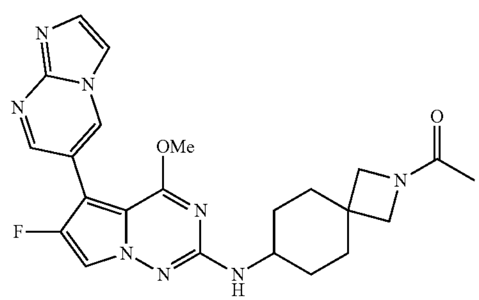

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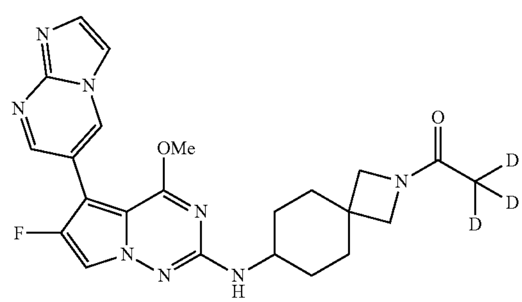

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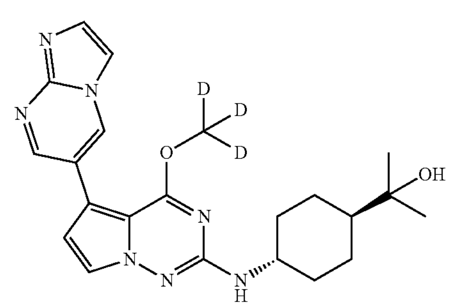

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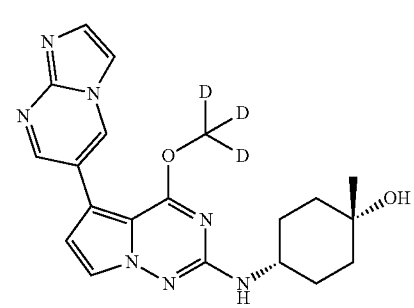

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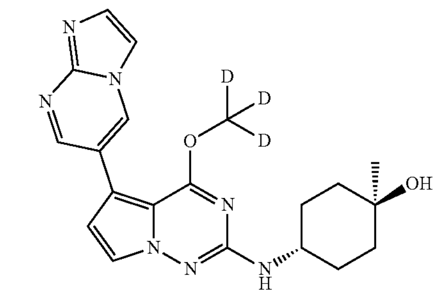

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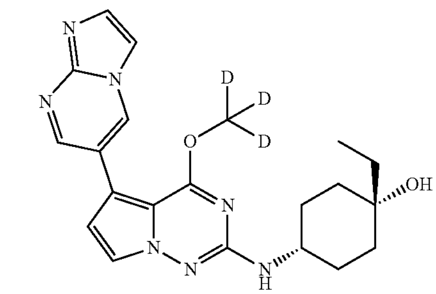

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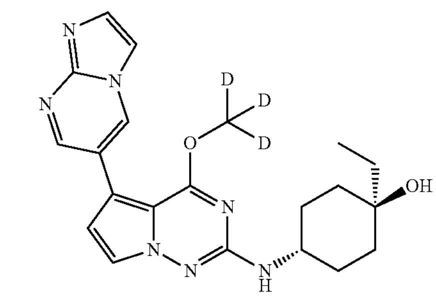

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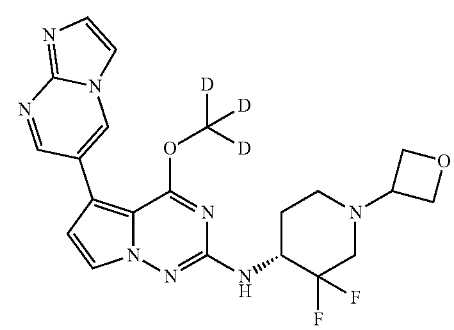

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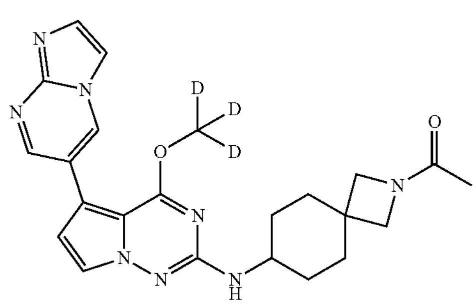

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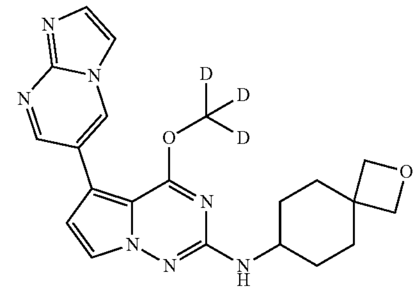

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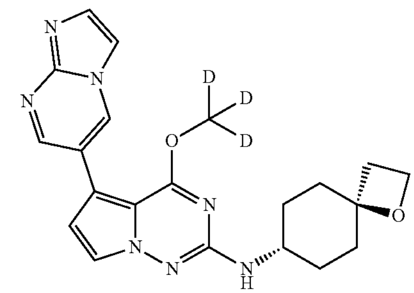

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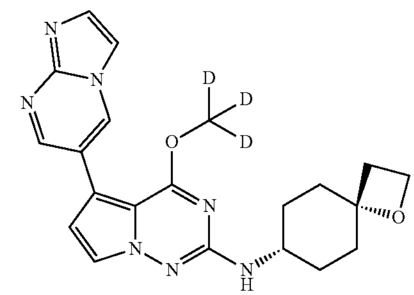

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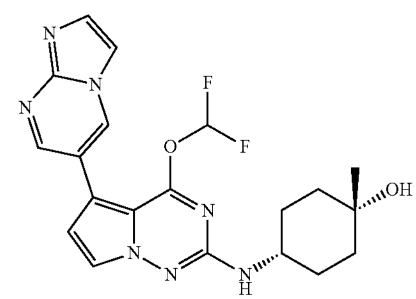

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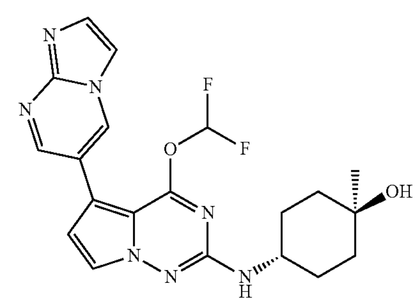

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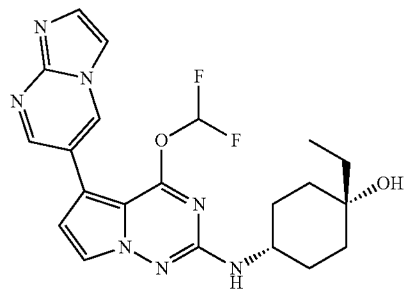

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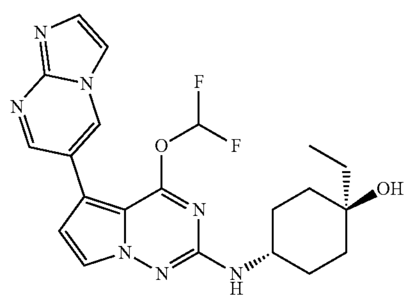

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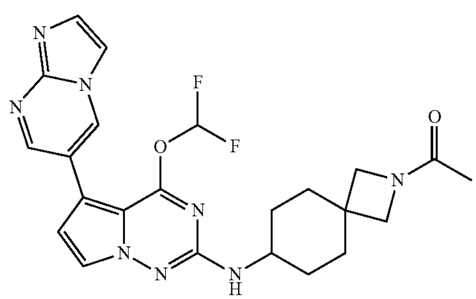

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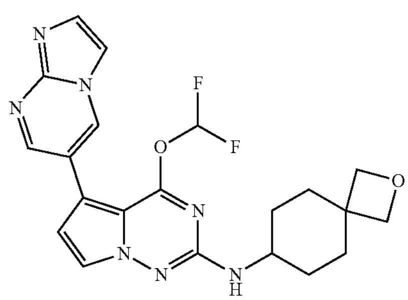

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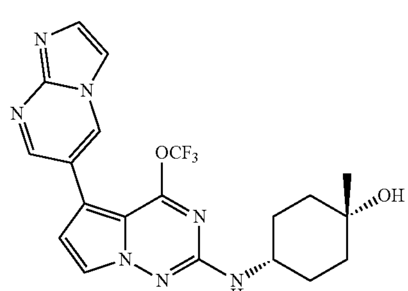

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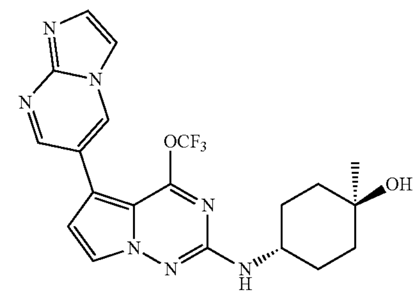

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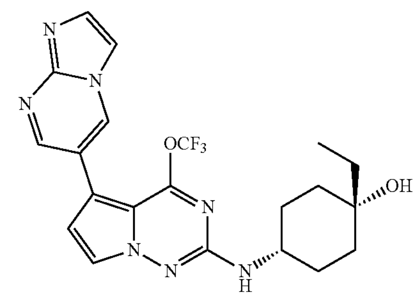

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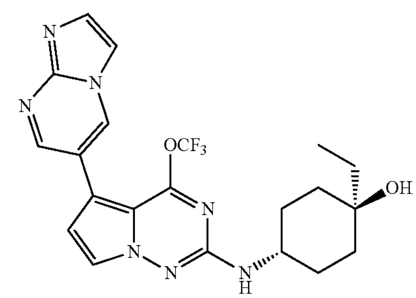

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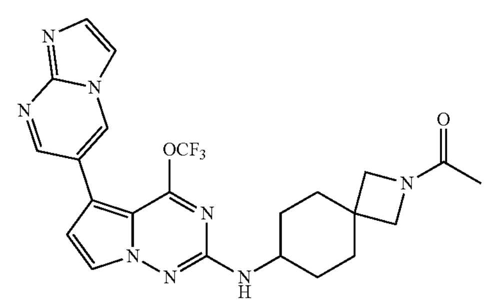

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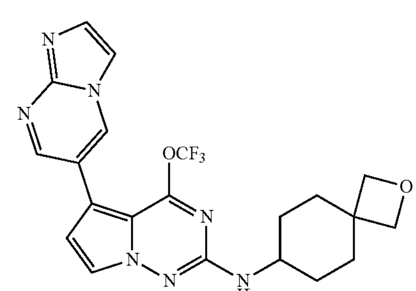

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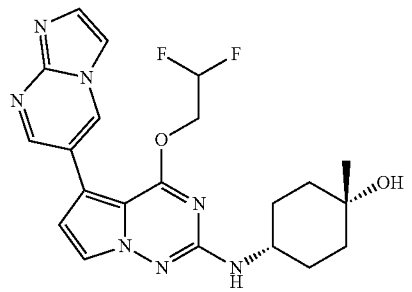

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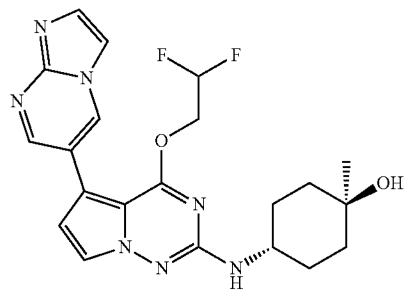

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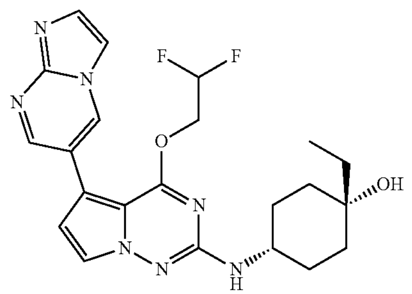

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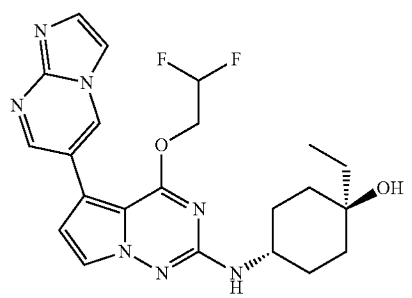

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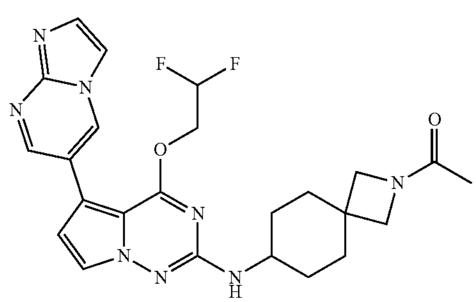

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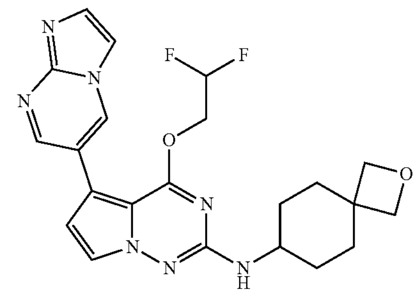

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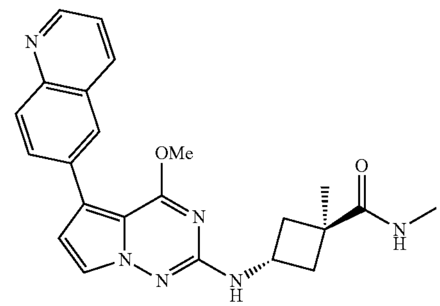

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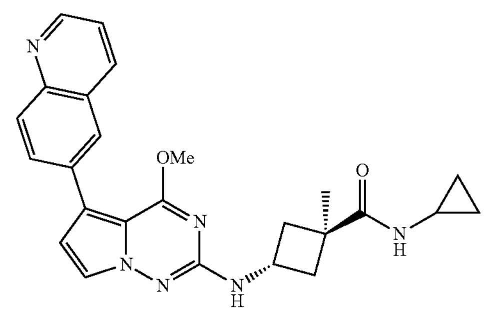

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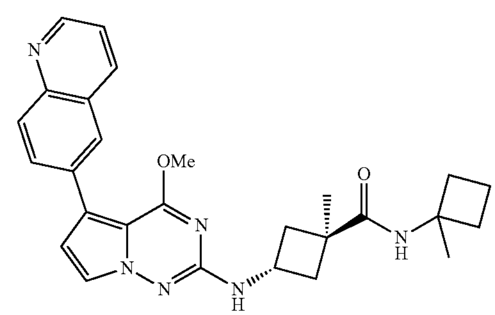

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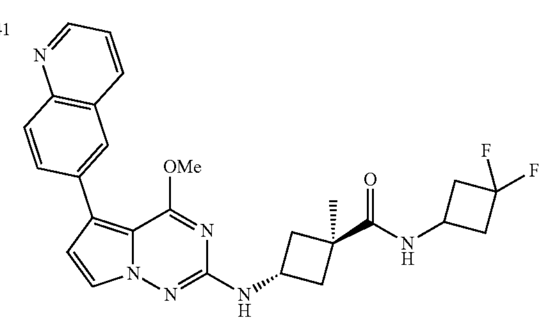

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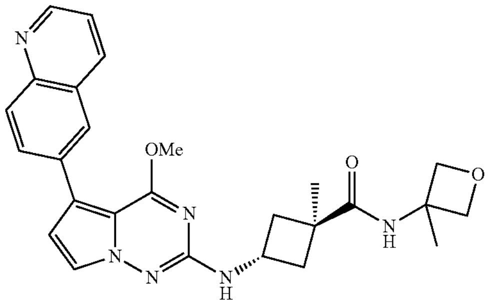
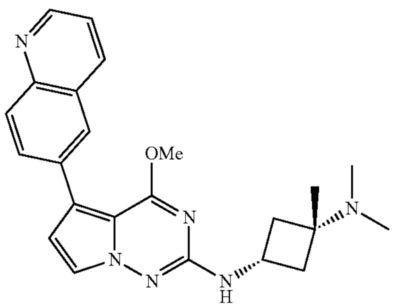
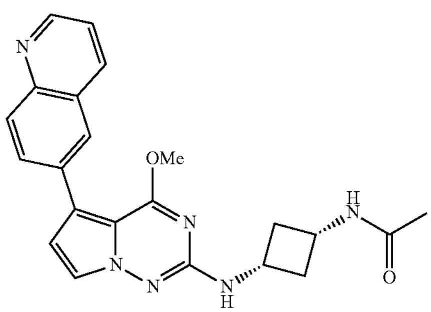
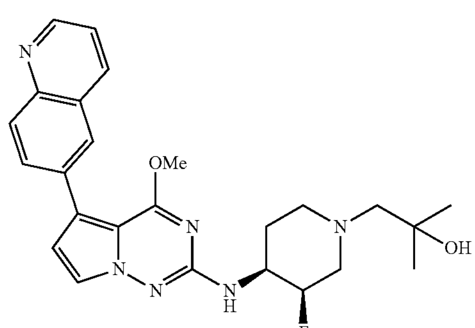
1042 

1043 

1044 

1045 

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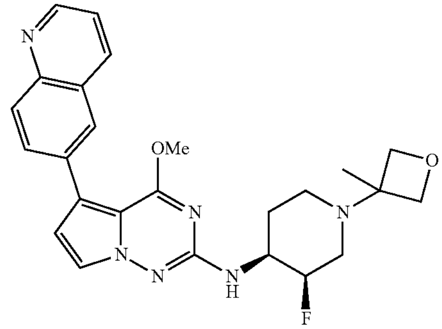
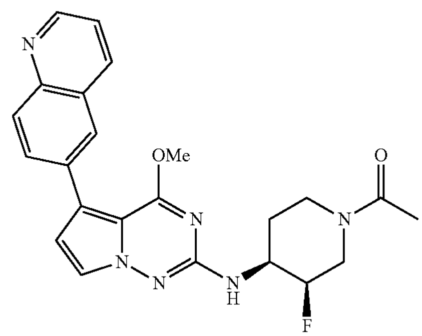
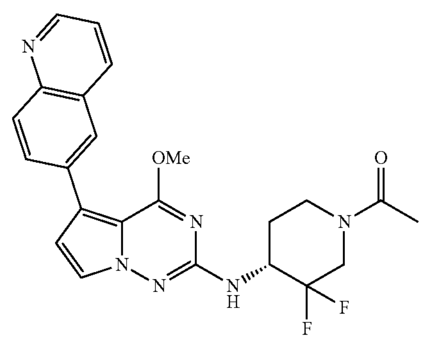
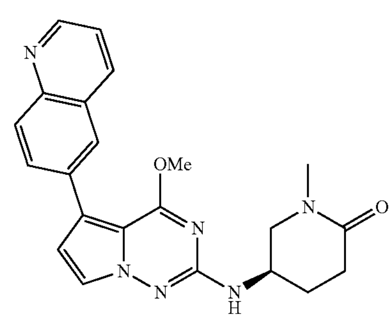
1046 

1047 

1048 

1049 

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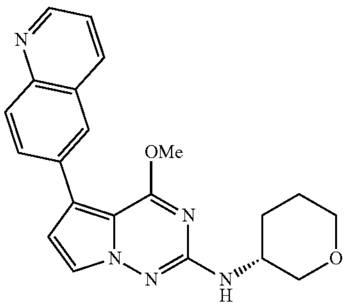

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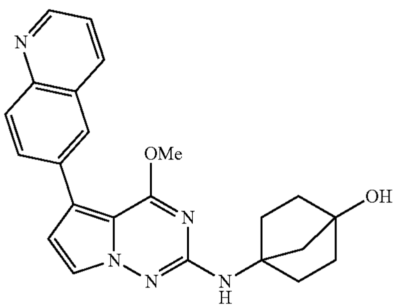

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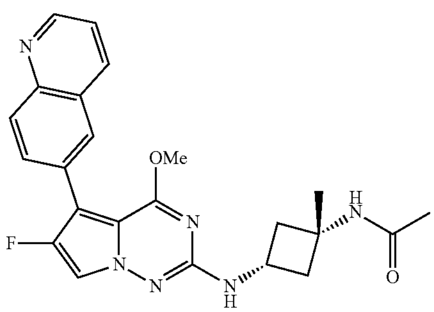

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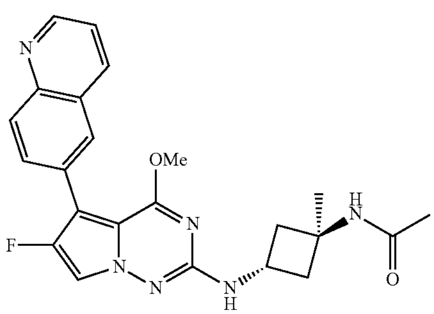

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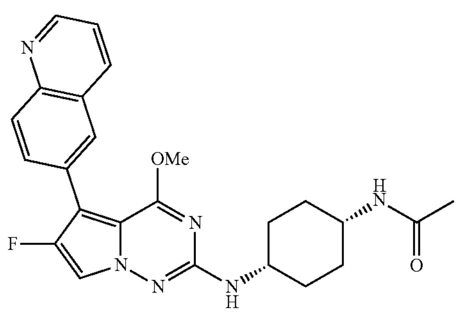

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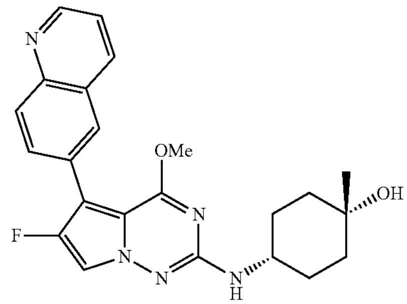

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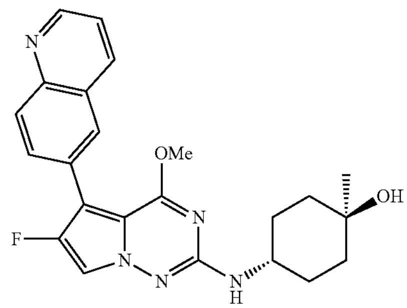

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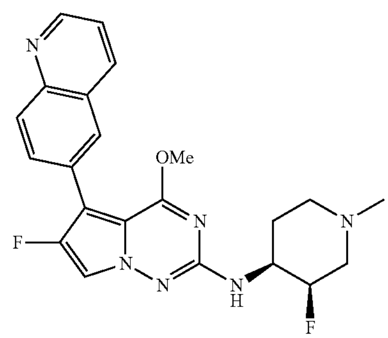

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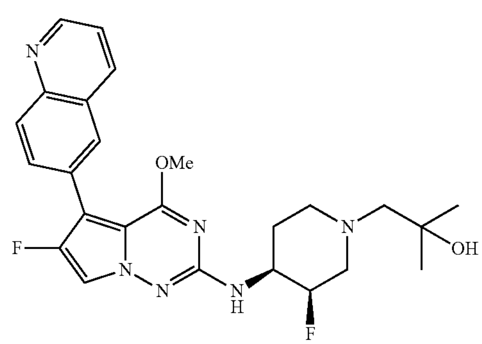

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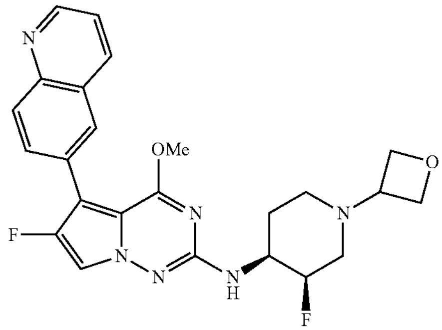

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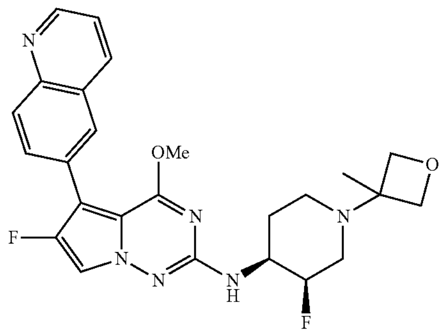

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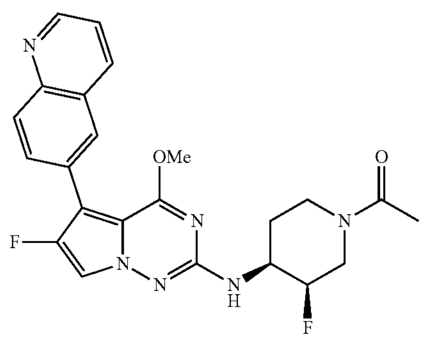

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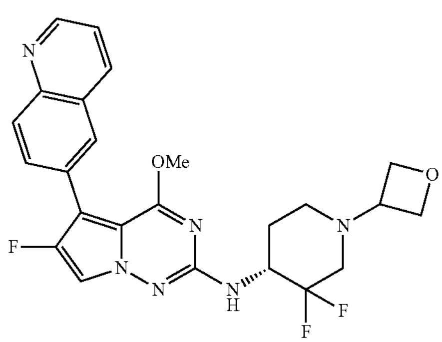

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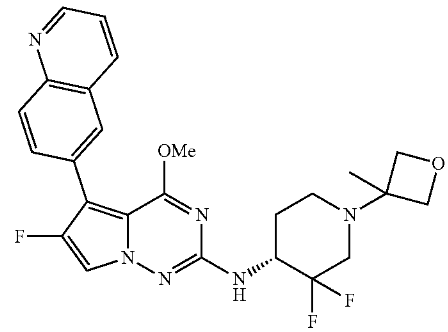

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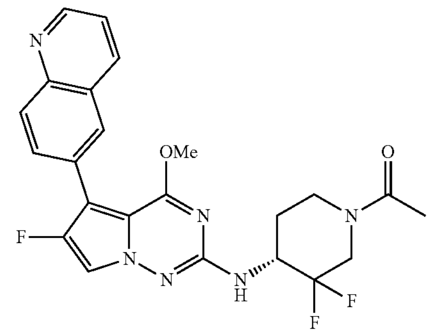

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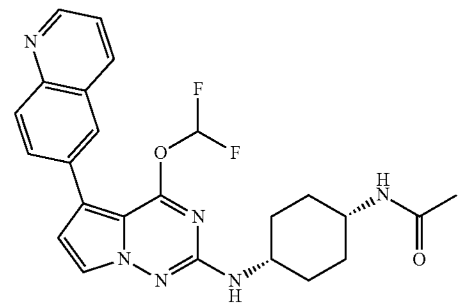

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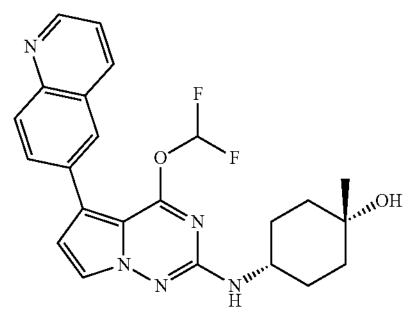

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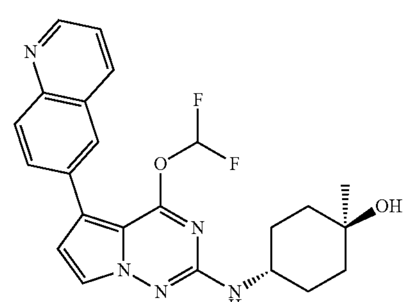

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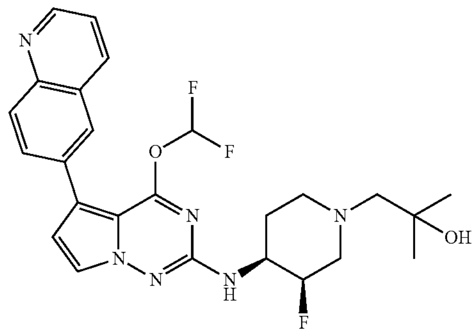

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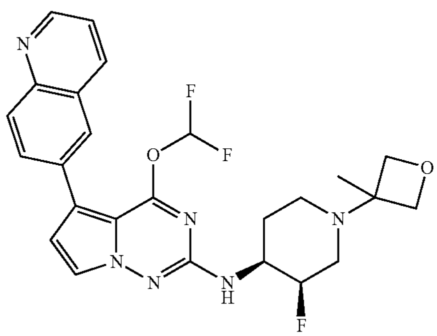

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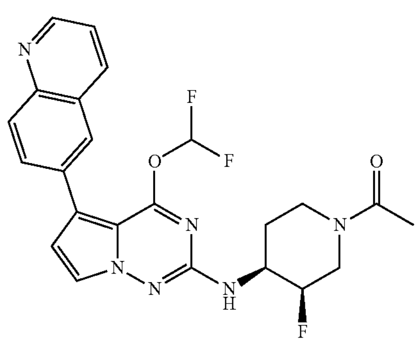

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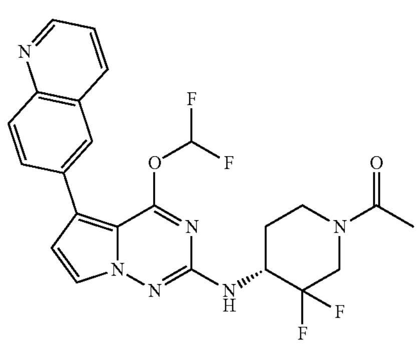

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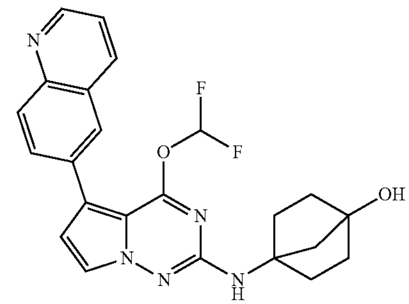

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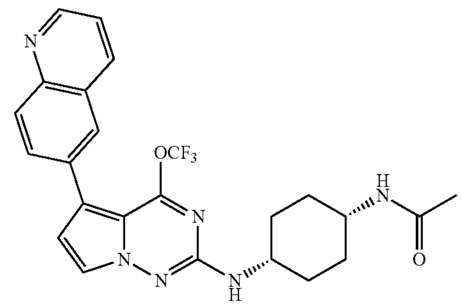

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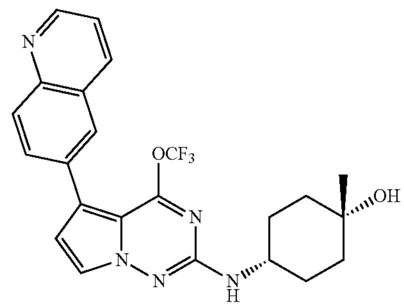

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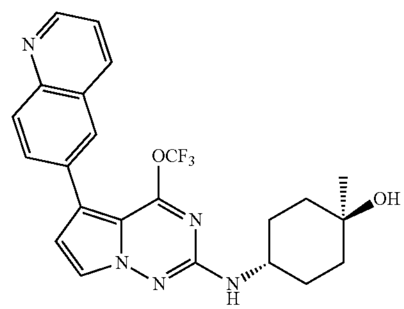

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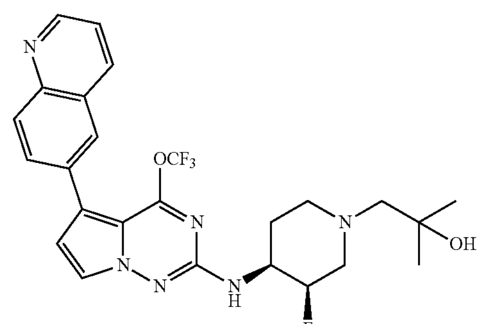

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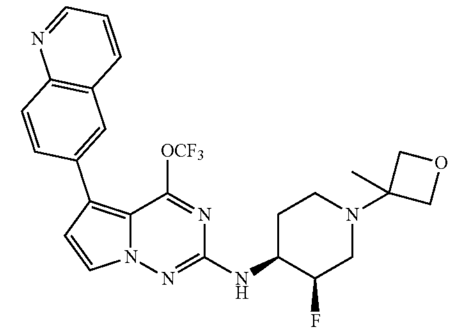

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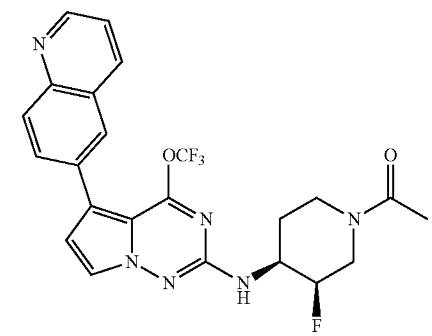

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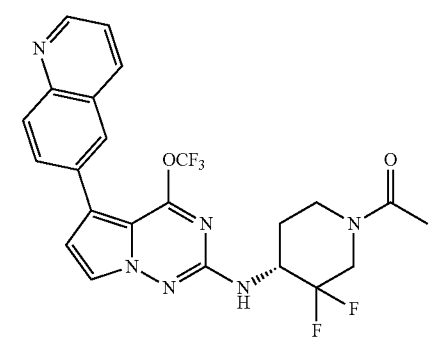

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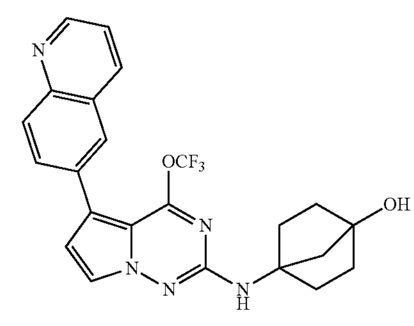

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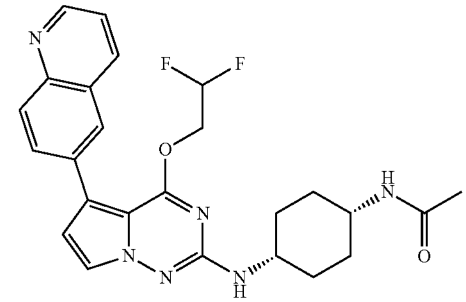

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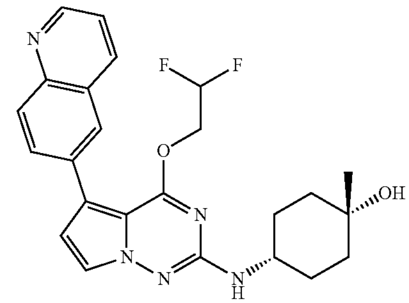

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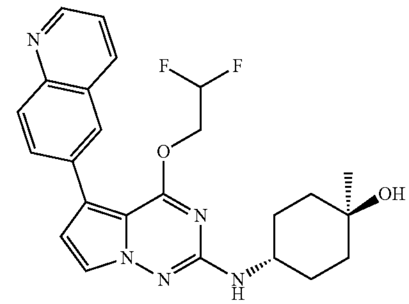

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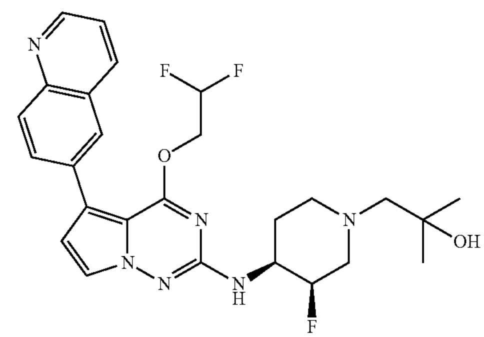

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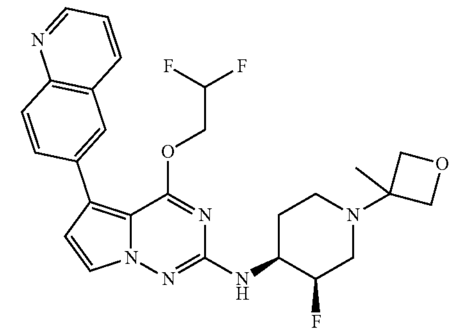
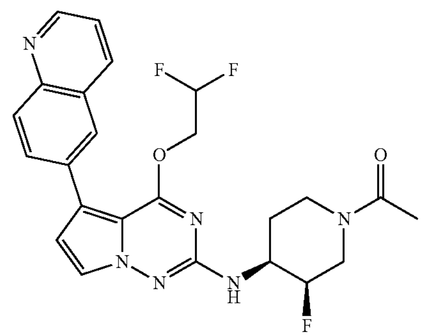
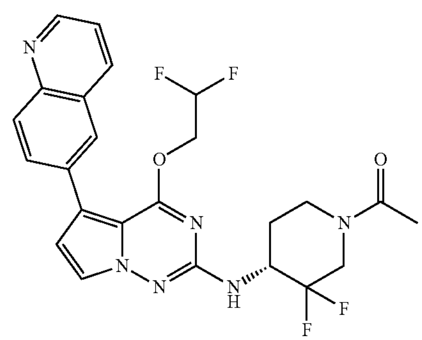
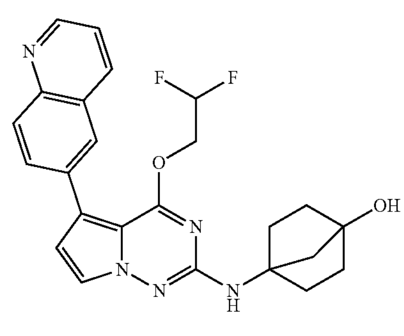
1085 

1086 

1087 

1088 

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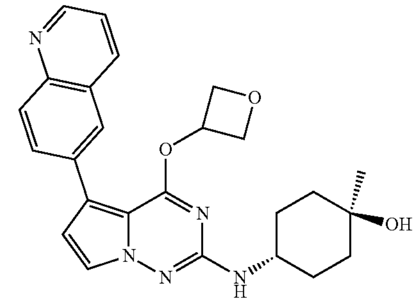
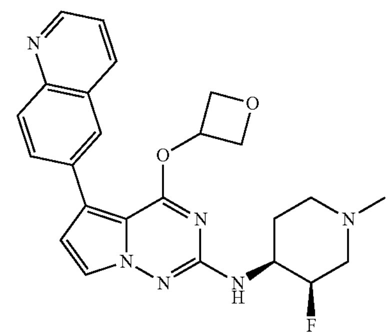
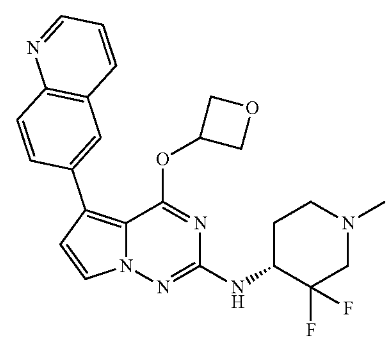
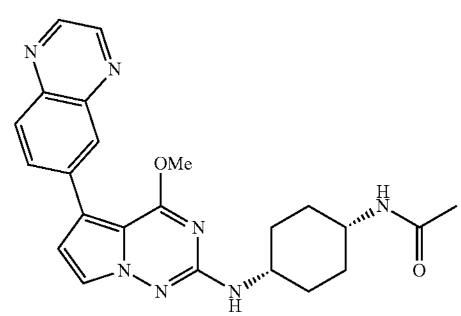
1089 

1090 

1091 

1092 

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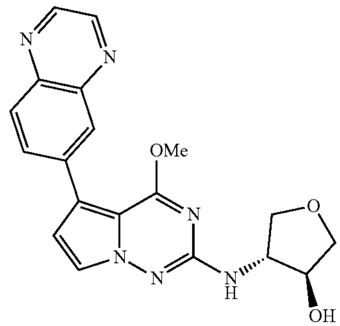

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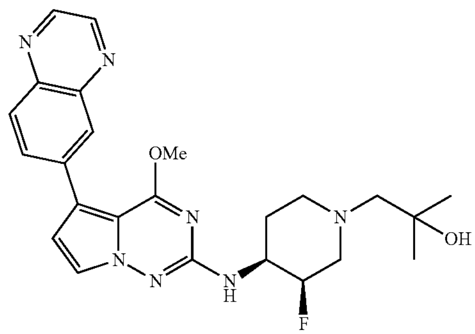

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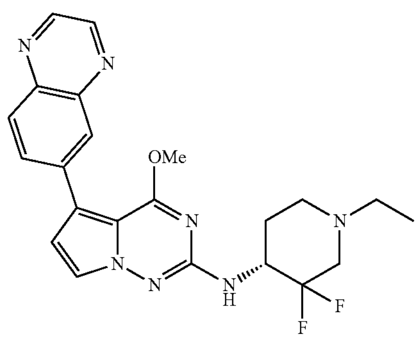

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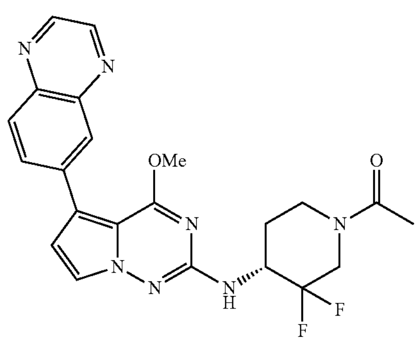

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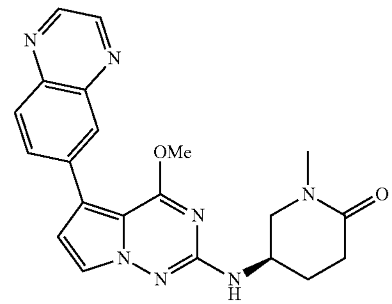

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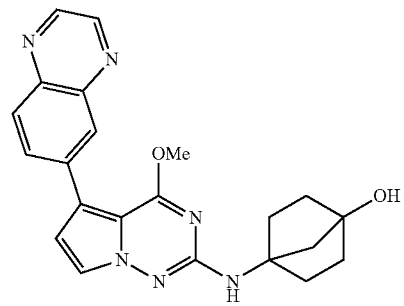

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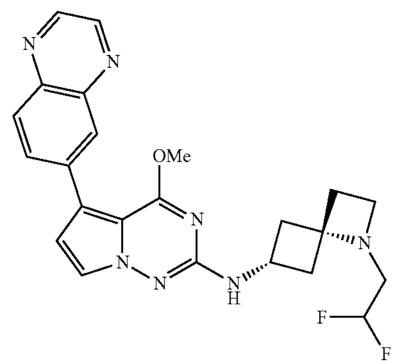

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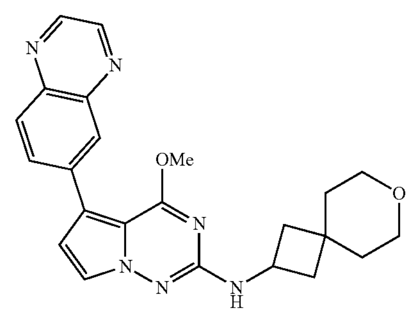

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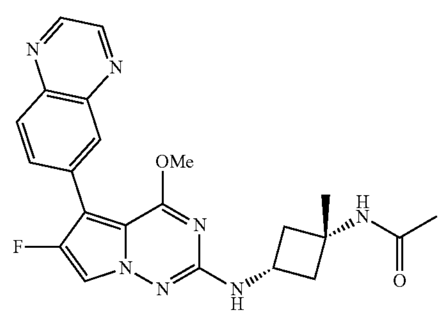

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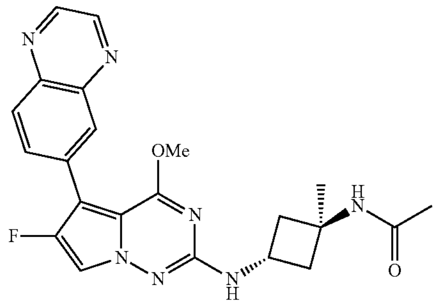

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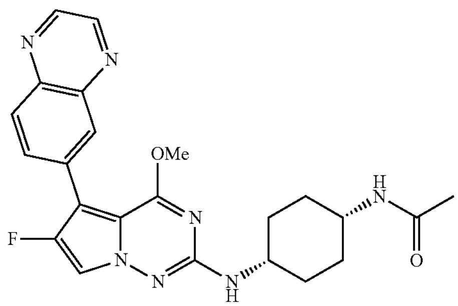

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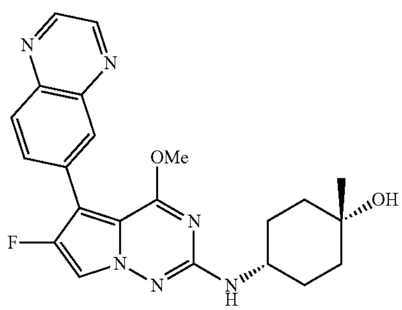

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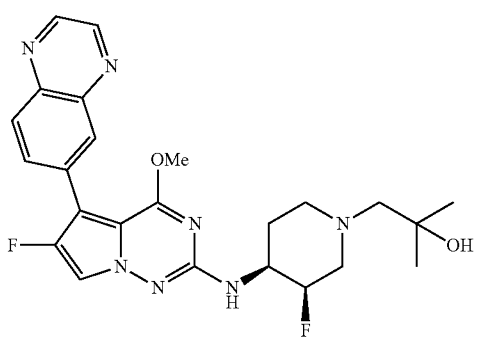

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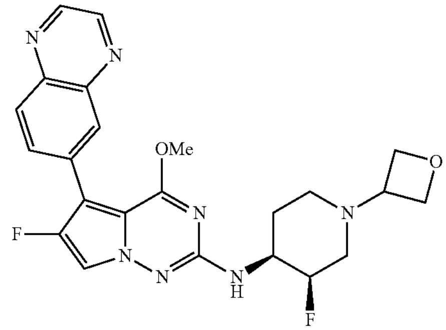

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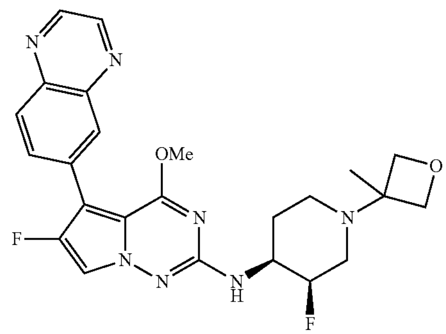

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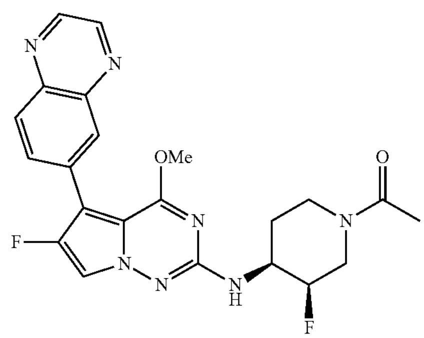

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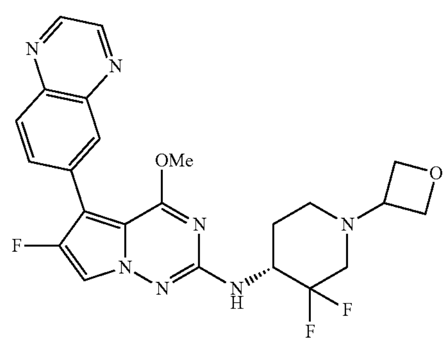

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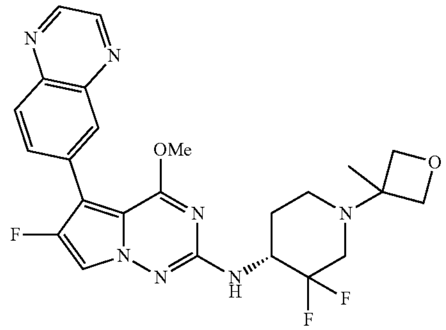
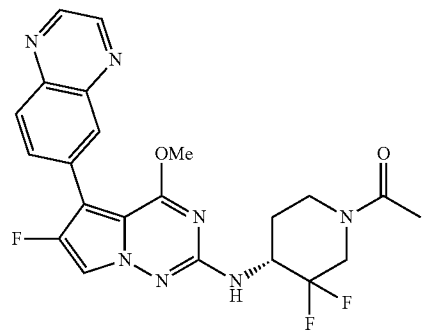
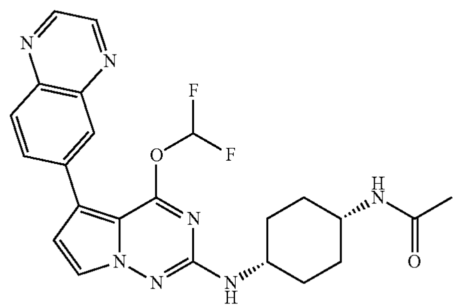
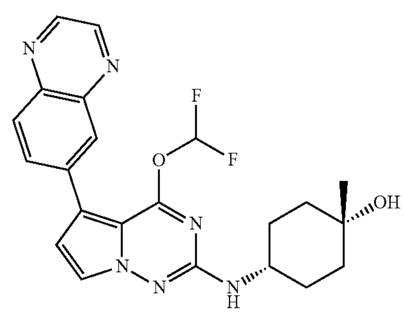
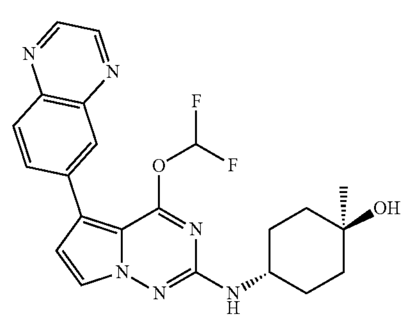
1110 

1111 

1112 

1113 

1114 

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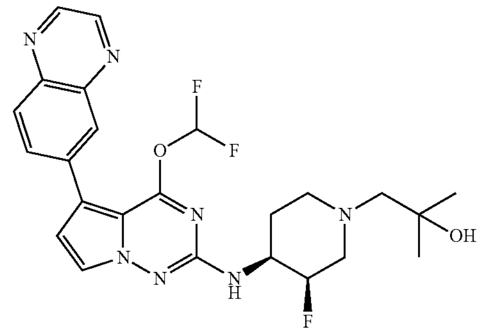
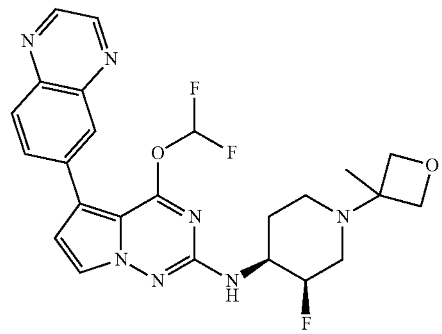
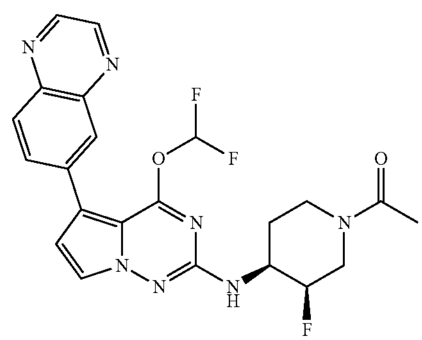
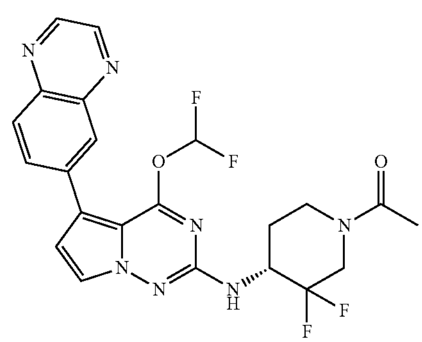
1115 

1116 

1117 

1118 

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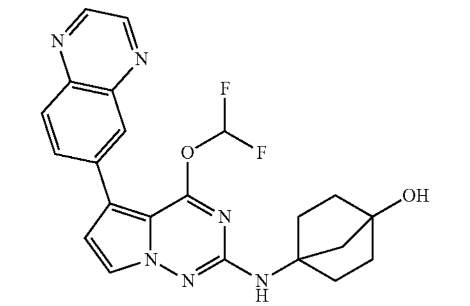

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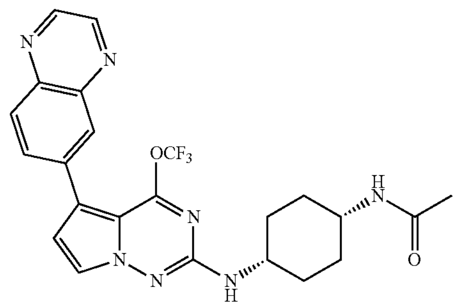

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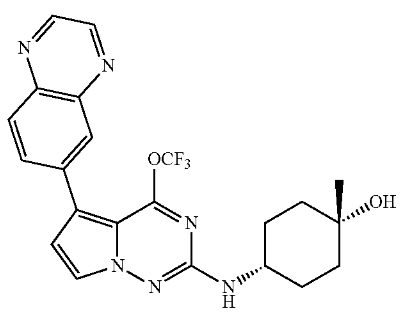

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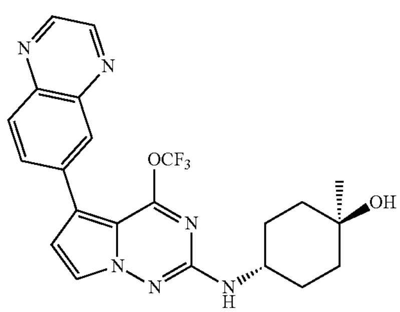

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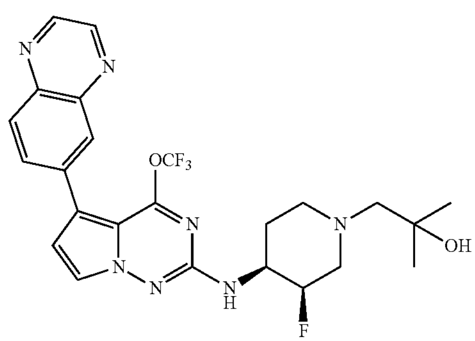

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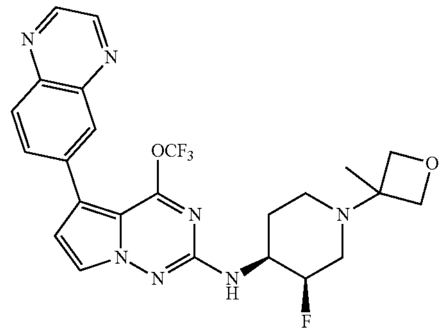

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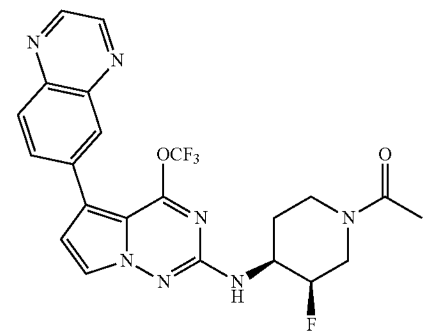

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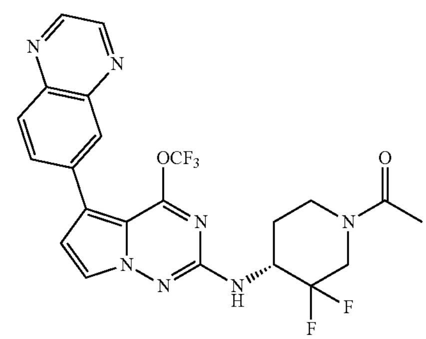

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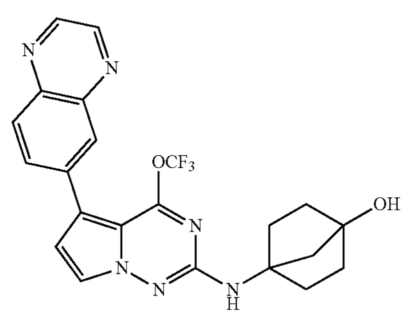

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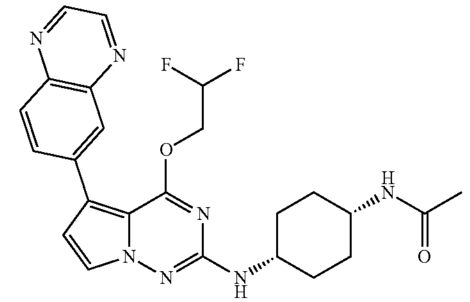

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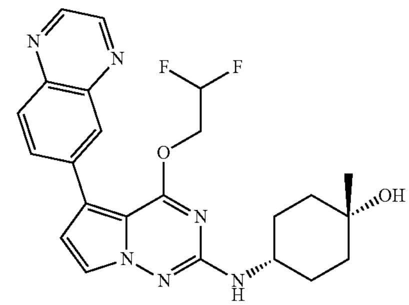

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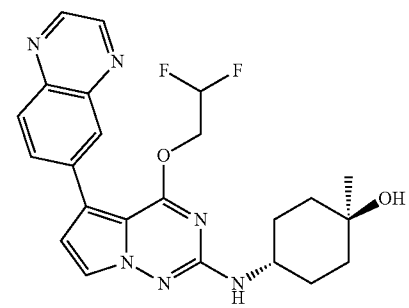

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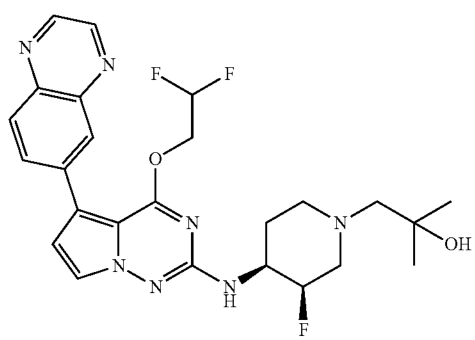

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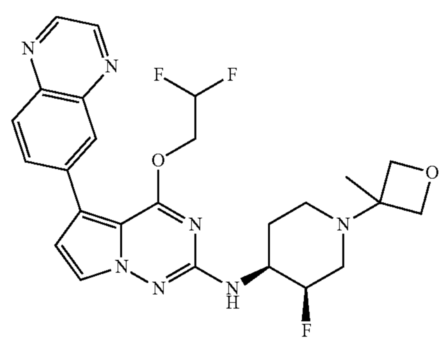

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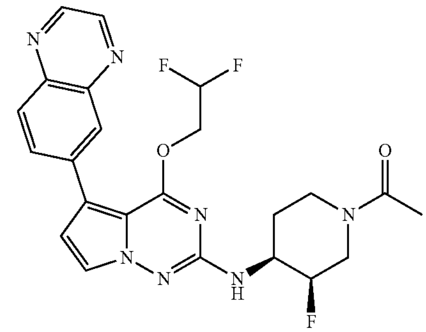

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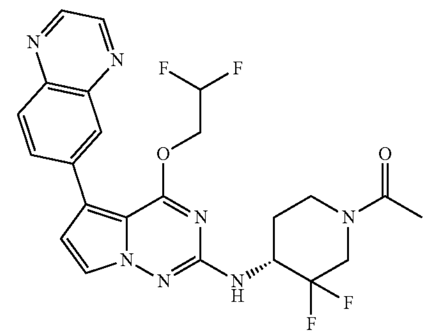

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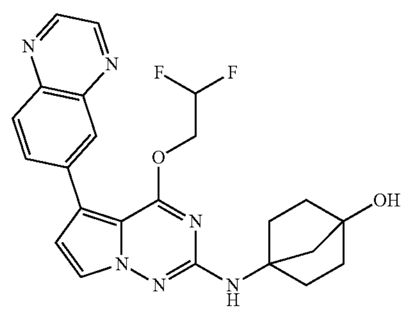

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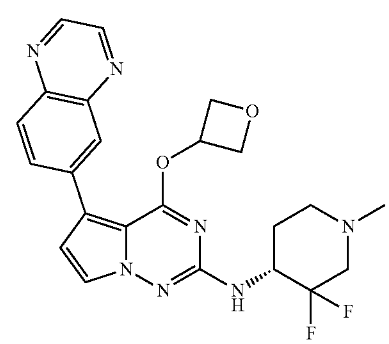

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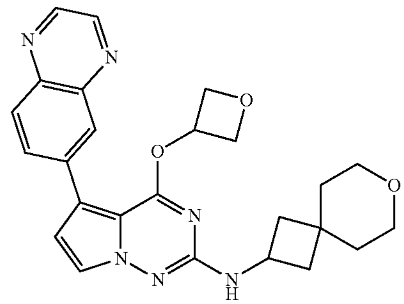

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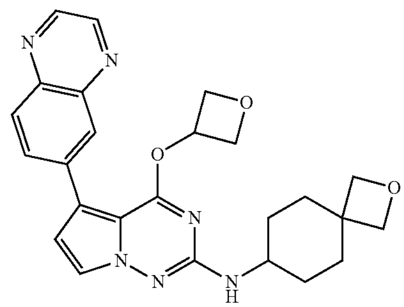

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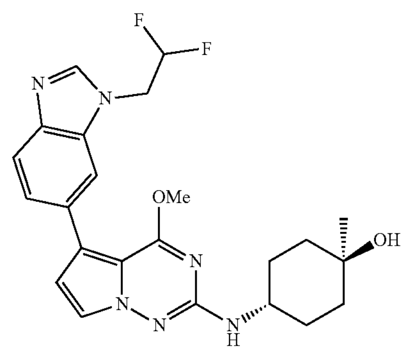

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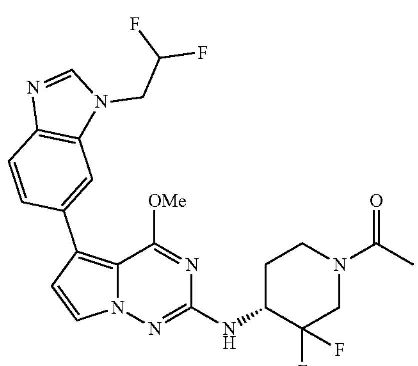

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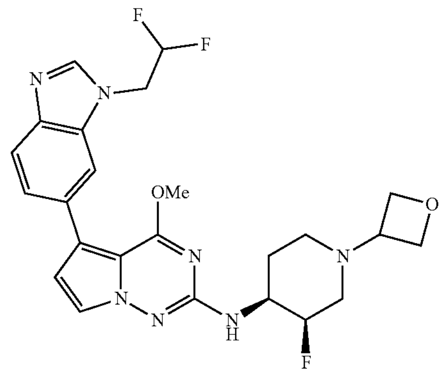

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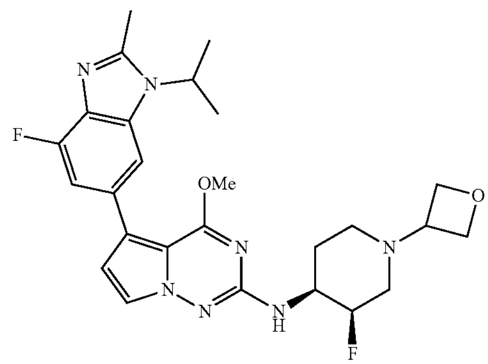

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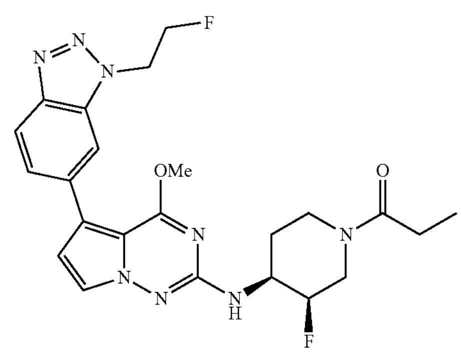

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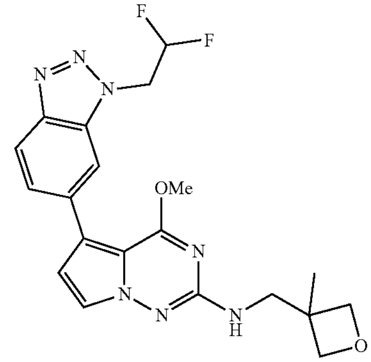

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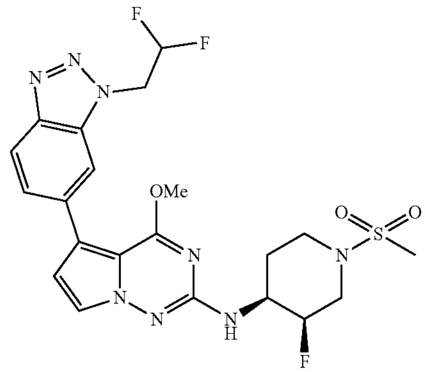

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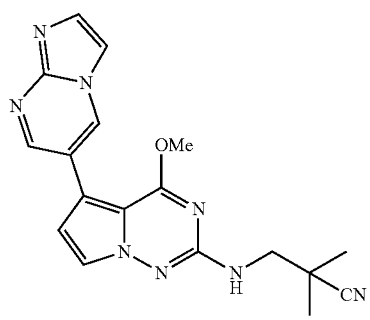

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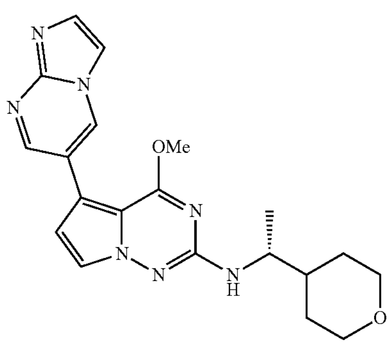

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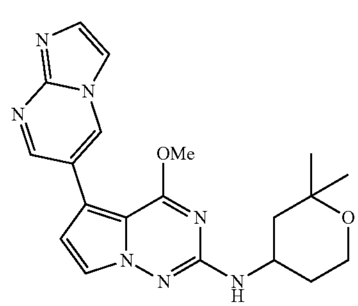

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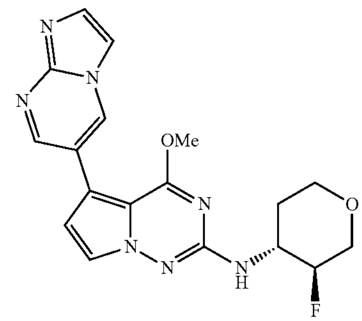

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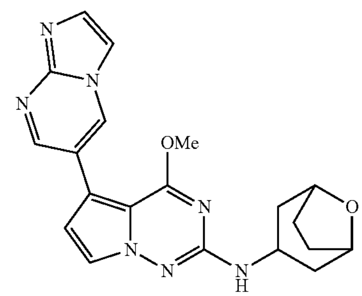

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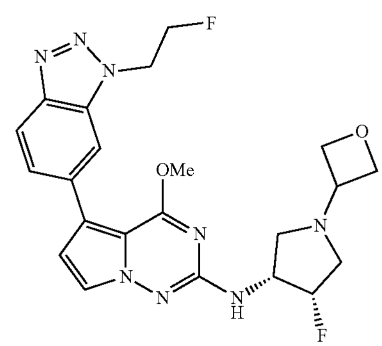

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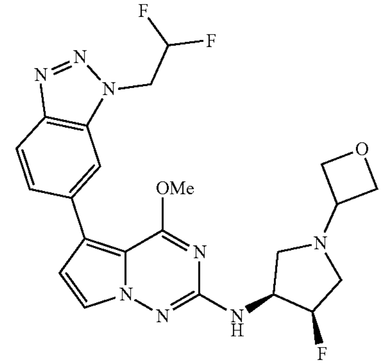

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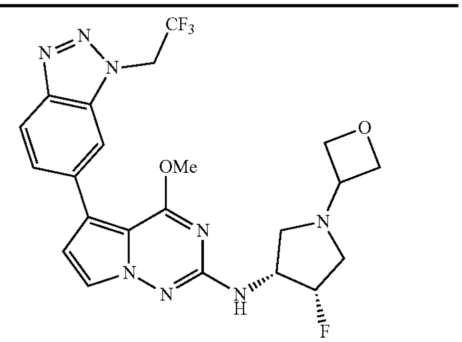


Administration and Pharmaceutical Compositions

[0292] 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.

[0293] The compounds provided herein may also be useful in combination (administered together or sequentially) with other known agents.

[0294] Non-limiting examples of diseases which can be treated with a combination of a compound of Formula I and another active agent are colorectal cancer, ovarian cancer, hepatocellular carcinoma, head and neck squamous cell carcinoma, acute lymphoblastic leukemia (ALL), pancreatic cancer, brain tumors, acute megakaryoblastic leukemia (AMKL), and osteoarthritis. For example, a compound of Formula I can be combined with one or more chemotherapeutic compounds.

[0295] In some embodiments, hepatocellular carcinoma can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: sorafenib (Nexavar®); regorafenib (Stivarga®, Regonix®), nivolumab (Opdivo®); lenvatinib (Lenvima®); pembrolizumab (Keytruda®); cabozantinib (Cometriq®, Cabometyx®); 5-fluorouracil (5-FU®); ramucirumab (Cyramza®); combination of gemcitabine and oxaliplatin (GEMOX). Other therapies that can be performed in combination with a compound of Formula I are i) transcatheter arterial chemoembolization (TACE) in combination with doxorubicin (DOXIL®), cisplatin, or mitomycin C (Mitosol®, Mutamycin®, Jelmyto®); ii) low-dose brachytherapy.

[0296] In some embodiments, head and neck squamous cell carcinoma can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: TransOral Robotic Surgery (TORS); TORS with radiation therapy; larotrectinib (Vitrakvi®); EGFR inhibitors, e.g., erlotinib (Tarceva®), osimertinib (Tagrisso®), neratinib (Nerlynx®), gefitinib (Iressa®), cetuximab (Erbitux®), panitumumab (Vectibix®), dacomitinib (Vizimpro®), lapatinib (Tykerb®), necitumumab (Portrazza), and vandetanib (Caprelsa®).

[0297] In some embodiments, acute lymphoblastic leukemia (ALL) can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: remission induction therapy; consolidation therapy; nelarabine (Arranon®); asparaginase *Erwinia chrysanthemi* (Erwinaze®); asparaginase *Erwinia chrysanthemi* (recombinant)-rywn (Rylaze®); calaspargase Pegol-mknl (Asparlas®); inotuzumab ozogamicin (Besponsa®); blinatumomab (Blincyto®); daunorubicin hydrochloride (Cerubidine®); clofarabine (Clolar®); cyclophosphamide; methotrexate sodium (Trexall®); cytarabine (Cytosar-U®); dasatinib (Sprycel®); dexamethasone; imatinib mesylate (Gleevec®); ponatinib hydrochloride (Iclusig®); mercaptopurine (Purinethol®, Purixan®); tisagenlecleucel (Kymriah®); vincristine sulfate liposome (Marqibo®); pegaspargase (Oncaspar®); prednisone; daunorubicin hydrochloride (Rubidomycin®); and vincristine sulfate.

[0298] In some embodiments, pancreatic cancer can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: ablation and embolization treatment; gemcitabine (Gemzar®); 5-fluorouracil (5-FU®); oxaliplatin (Eloxatin®); albumin-bound paclitaxel (Abraxane®); capecitabine (Xeloda®); cisplatin; irinotecan (Camptosar®); liposomal irinotecan (Onivyde®); paclitaxel (Taxol®), and docetaxel (Taxotere®).

[0299] In some embodiments, brain tumors can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: carmustine can be administered by way of a gliadel wafer; for glioblastoma and high-grade glioma, radiation therapy with daily low-dose temozolomide (Temodar®) followed by monthly doses of temozolomide after radiation therapy for 6 months to 1 year; lomustine (Gleostine®), procarbazine (Matulane®), and vincristine (Vincasar®), have been used along with radiation therapy; anti-angiogenesis therapy with bevacizumab (Avastin®, Mvasi®); and targeted therapy using larotrectinib (Vitrakvi®).

[0300] In some embodiments, acute megakaryoblastic leukemia (AMKL) can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: cytarabine (Cytosar-U®), etoposide (Vepesid®), and anthracycline drugs. Anthracyclines include daunorubicin (Cerubidine®), idarubicin (Idamycin®), and mitoxantrone (Novantrone®).

[0301] In some embodiments, acute myeloid leukemia (AML) can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: venetoclax and hypomethylating agents (e.g., decitabine, azacitidine), induction chemotherapy (cytarabine and an anthracycline (e.g., daunorubicin or idarubicin), all-trans-retinoic acid (ATRA) and either arsenic trioxide (ATO) monotherapy or an anthracycline), consolidation therapy (cytarabine).

[0302] In some embodiments, myelodysplastic syndrome (MDS) can be treated with a combination of a compound of Formula I and one or more of the following drugs/therapies: 5-azacytidine, decitabine, lenalidomide, and decitabine/cedazuridine (Ingovi®).

[0303] 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).

[0304] 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). Ovarian cancer can also be treated with a combination of a compound of Formula I and immune checkpoint blockade (ICB) therapy.

[0305] 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, navitoclax (ABT-263), oblimersen (G3139), venetoclax (ABT-199), Gossypol), PARP inhibitors (e.g., iniparib, olaparib, rucaparib, niraparib, talazoparib), PI3K inhibitors (e.g., 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®); (k) chemotherapy using KRAS G12C inhibitors such as sotorasib (Lumakras® and Lumykras®), adagrasib (MRTX849), and ARS-3248 (Wellspring Biosciences); (1) chemotherapy using checkpoint inhibitor therapy such as ipilimumab (Yervoy®), nivolumab (Opdivo®), pembrolizumab (Keytruda®), atezolizumab (Tecentriq®), avelumab (Bavencio), durvalumab (Imfinzi), cemiplimab (Libtayo®), and spartalizumab (PDR001); (m) chemotherapy using antibody-drug conjugates (ADC) such as gemtuzumab ozogamicin, brentuximab vedotin, trastuzumab emtansine, inotuzumab ozogamicin, polatuzumab vedotin, enfortumab vedotin, trastuzumab deruxtecan, sacituzumab govitecan, belantamab mafodotin, moxetumomab pasudotox, and loncastuximab tesirine; (n) chemotherapy using proteasome inhibitors such as carfilzomib, lactacystin, disulfiram, salinosporamide A (marizomib), oprozomib, delanzomib, epoxomicin, MG132, β-hydroxy β-methylbutyric acid (HMB), bortezomib, ixazomib (alone or in in combination with lenalidomide and dexamethasone); and (o) radiation therapy.

[0306] In some embodiments, a compound of Formula I, can be used to treat diabetes mellitus in combination with any of the following methods: (a) injections of insulin; (b) biguanides such as metformin (Glucophage), phenformin (DBI), and buformin; (c) thiazolidinediones (TZDs) such as rosiglitazone (Avandia), pioglitazone (Actos), and yroglitazone (Rezulin); (d) lyn kinase activators such as glimepiride (Amaryl®) and tolimidone (MLR-1023); (e) secretagogues such as sulfonylureas (non-limiting examples are acetohexamide, carbutamide, chlorpropamide, glycyclamide (tolcyclamide), metahexamide, tolazamide, tolbutamide, glibenclamide (glyburide), glibornuride, gliclazide, glipizide, gliquidone, glisoxepide, glyclopyramide, and glimepiride) and meglitinides (nonlimiting examples are repaglinide (Prandin), nateglinide (Starlix), and mitiglinide (Glufast)); (f) alpha-glucosidase inhibitors such as acarbose (Glucobay, Precose, Prandase), miglitol (Glyset), and voglibose; (g) injectable incretin mimetics such as glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide (glucose-dependent insulinotropic peptide, GIP), nonlimiting examples of injectable glucagon-like peptide (GLP) analogs and agonists are exenatide (Exendin-4, marketed as Byetta), liraglutide (Victoza, Saxenda), taspoglutide, lixisenatide (Lyxumia), Semaglutide (Ozempic, Rybelsus), dulaglutide (Trulicity), albiglutide (Tanzeum), nonlimiting examples of dipeptidyl peptidase-4 (DPP-4) inhibitors are sitagliptin (Januvia), vildagliptin (Galvus), saxagliptin (Onglyza), linagliptin (Tradjenta), gemigliptin (Zemiglo), anagliptin (Suiny), teneligliptin (Tenelia), alogliptin (Nesina, Vipidia, Kazano, Vipidomet (with metformin), Oseni, Incresync (with pioglitazone)), trelagliptin (Zafatek, Wedica), omarigliptin (MK-3102), evogliptin (Suganon, Evodine), gosogliptin (Saterex), and dutogliptin; (h) injectable amylin analogues such as pramlintide (Symlin); (i) glycosurics (SGLT2 inhibitors) such as canagliflozin (Invokana, Sulisent, Prominad), dapagliflozin (Forxiga, Farxiga, Edistride), empagliflozin (Jardiance, Sciampa-M), ertugliflozin (Steglatro), ipragliflozin (Suglat), luseogliflozin (Lusefi), remogliflozin etabonate (pro-drug of remogliflozin), sergliflozin etabonate (GW869682X), sotagliflozin (Zynquista), and tofogliflozin (CSG452).

[0307] In some embodiments, a compound of Formula I can be used to treat osteoarthritis in combination with any of the following methods: (d) injections of a Wnt signaling pathway inhibitor (e.g., lorecivivint); (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.

[0308] In some embodiments, a compound of Formula I can be used to treat Alzheimer's disease in combination with aducanumab (Aduhelm™); acetylcholinesterase inhibitors, e.g., tacrine, rivastigmine (Exelon*), galantamine (Razadyne® and GalantaMind™), and donepezil (Aricept®); and memantine (Axura®, Ebixa®, Namenda*).

[0309] 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.

[0310] 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.

[0311] 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,* 22^{nd} Edition (Pharmaceutical Press, London, U K. 2012).

[0312] 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.

[0313] 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, co-solvents, 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).

[0314] In some embodiments, the unit dosage of compounds of Formula I is about 0.25 mg/Kg to about 50 mg/Kg in humans.

[0315] In some embodiments, the unit dosage of compounds of Formula I is about 0.25 mg/Kg to about 20 mg/Kg in humans.

[0316] In some embodiments, the unit dosage of compounds of Formula I is about 0.50 mg/Kg to about 19 mg/Kg in humans.

[0317] In some embodiments, the unit dosage of compounds of Formula I is about 0.75 mg/Kg to about 18 mg/Kg in humans.

[0318] In some embodiments, the unit dosage of compounds of Formula I is about 1.0 mg/Kg to about 17 mg/Kg in humans.

[0319] In some embodiments, the unit dosage of compounds of Formula I is about 1.25 mg/Kg to about 16 mg/Kg in humans.

[0320] In some embodiments, the unit dosage of compounds of Formula I is about 1.50 mg/Kg to about 15 mg/Kg in humans.

[0321] In some embodiments, the unit dosage of compounds of Formula I is about 1.75 mg/Kg to about 14 mg/Kg in humans.

[0322] In some embodiments, the unit dosage of compounds of Formula I is about 2.0 mg/Kg to about 13 mg/Kg in humans.

[0323] In some embodiments, the unit dosage of compounds of Formula I is about 3.0 mg/Kg to about 12 mg/Kg in humans.

[0324] In some embodiments, the unit dosage of compounds of Formula I is about 4.0 mg/Kg to about 11 mg/Kg in humans.

[0325] In some embodiments, the unit dosage of compounds of Formula I is about 5.0 mg/Kg to about 10 mg/Kg in humans.

[0326] In some embodiments, the compositions are provided in unit dosage forms suitable for single administration.

[0327] In some embodiments, the compositions are provided in unit dosage forms suitable for twice a day administration.

[0328] In some embodiments, the compositions are provided in unit dosage forms suitable for three times a day administration.

[0329] 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.

[0330] In some embodiments, the composition comprises about 0.1-10% of the active agent in solution.

[0331] In some embodiments, the composition comprises about 0.1-5% of the active agent in solution.

[0332] In some embodiments, the composition comprises about 0.1-4% of the active agent in solution.

[0333] In some embodiments, the composition comprises about 0.15-3% of the active agent in solution.

[0334] In some embodiments, the composition comprises about 0.2-2% of the active agent in solution.

[0335] 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.

[0336] 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.

[0337] 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.

[0338] 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.

[0339] 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.

[0340] 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.

[0341] 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.

[0342] 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.

[0343] 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.

[0344] 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.

[0345] 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.

[0346] 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.

[0347] 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.

[0348] 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.

[0349] 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.

[0350] 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.

[0351] 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.

[0352] 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.

[0353] 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).

[0354] If desired, formulations of the disclosure can be incorporated into a gel formulation (e.g., U.S. Pat. Nos. 4,474,752 and 6,911,211).

[0355] 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.

[0356] 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.

[0357] Formulations of the disclosure 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).

[0358] 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.

[0359] 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.

[0360] 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.

[0361] 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.

[0362] 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.

[0363] 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.

[0364] 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.

[0365] 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 glioblastoma, ovarian, breast, pancreatic cancers, acute lymphoblastic leukemia, acute megakaryoblastic leukemia, chronic myeloid leukemia, Alzheimer's disease, amyotrophic lateral sclerosis, CDKL5 deficiency disorder, Down syndrome, frontotemporal dementia with parkinsonism-17 (FTDP-17), Lewy body dementia, Parkinson's disease, Pick's disease, autism, dementia, epilepsy, Huntington's disease, and multiple sclerosis.

Methods of Treatment

[0366] The compounds and compositions provided herein can be used as inhibitors of DYRK1A, and thus can be used to treat a variety of disorders and diseases in which over expression of DYRK1A is implicated, such as cancer and neurological conditions/disorders/diseases. Non-limiting examples of diseases which can be treated with the compounds and compositions provided herein include a variety of cancers, Alzheimer's disease, amyotrophic lateral sclerosis, CDKL5 deficiency disorder, Down Syndrome, frontotemporal dementia with parkinsonism-17 (FTDP-17), Lewy body dementia, Parkinson's disease, Pick's disease, and additional diseases with pronounced neurodegeneration such as autism, dementia, epilepsy, Huntington's disease, multiple sclerosis; diseases and disorders associated with acquired brain injury such as chronic traumatic encephalopathy, traumatic brain injury, tumor, stroke, tauopathies (e.g., Pick's disease, progressive supranuclear palsy, corticobasal degeneration, argyrophilic grain disease, globular glial tauopathies, primary age-related tauopathy, which includes neurofibrillary tangle dementia, chronic traumatic encephalopathy (CTE), frontotemporal lobar degeneration with tau inclusions (FTLD-tau), and aging-related tau astrogliopathy. Clinical symptoms include frontotemporal dementia, corticobasal syndrome, Richardson syndrome, parkinsonism, pure akinesia with gait freezing and, rarely, motor neuron symptoms or cerebellar ataxia, diabetes, psoriasis, knee osteoarthritis, tendinopathy, human immunodeficiency virus type 1 (HIV-1), human cytomegalovirus (HCMV), hepatitis C virus (HCV), and herpes simplex virus 1 (HSV-1).

[0367] The gene encoding DYRK1A is located on chromosome 21, within the Down syndrome critical region (DSCR), the triploidy of which is responsible for most Down syndrome-associated deficiencies (*FEBS Journal* (2011), 278, 246-256). There is considerable genetical and pharmacological evidence showing that the mere 1.5-fold overexpression of DYRK1A is responsible for most cognitive deficits observed in Down syndrome patients (*Pharmacology & Therapeutics* (2019), 194, 199-221 and *Brain Science* (2018), 8(10), 187). Genetical normalization of DYRK1A levels or pharmacological inhibition of its catalytic activity restores cognitive functions. The development of pharmacological inhibitors of DYRK1A is a major avenue for the treatment of cognitive deficits associated with Down syndrome.

[0368] DYRK1A and DYRK1B are utilized during human cytomegalovirus (HCMV) placental replication. Inhibition of DYRKs prevent replication of various viruses, including hepatitis C virus (HCV), human cytomegalovirus (HCMV), human immunodeficiency virus type 1 (HIV-1), and herpes simplex virus 1 (HSV-1) (*Journal of Virology* (2020), 94(6) and *PLoS ONE* (2015), 10, e0144229).

[0369] There is a growing body of evidence showing that DYRK1A/1B inhibitors induce the proliferation of insulin-producing pancreatic β-cells, making DYRK1A/1B kinases attractive therapeutic targets for β-cell regeneration for both type 1 and type 2 diabetes mellitus and gestational diabetes (*Nature Communications* (2015), 6(8372); *Diabetes* (2016), 65(6), 1660-1671; *JCI Insight* (2020), 5(1), e132594; *Science Translational Medicine* (2020), 12(530); *International Journal of Molecular Sciences* (2021), 22(16), 9083; and *Journal of Medicinal Chemistry* (2021), 64(6), 2901-2922). Other forms of diabetes that may be treated with DYRK inhibitors are maturity onset diabetes of the young (MODY, monogenic diabetes), cases of diabetes that are caused by the body's tissue receptors not responding to insulin, double diabetes (when a type 1 diabetic becomes insulin resistant), diabetes associated with excessive secretion of insulin-antagonistic hormones, malnutrition-related diabetes mellitus (ICD-10 code E12), and diabetes caused by any genetic mutations (autosomal or mitochondrial) that leads to defects in beta cell function.

[0370] There is abundant literature linking DYRK1A with solid cancers and leukemias (*Pharmacology & Therapeutics* (2015), 151, 87-98; *Cancers* (2020), 12(8), 2106; and *Cellular and Molecular Life Sciences* (2021), 78, 603-619). The most prominent examples are pancreatic cancer (*Gut* (2019), 68(8), 1465-1476 and *Gene* (2020), 758, 144960), brain tumors, glioblastoma (*Journal of Clinical Investigation* (2013), 123(6), 2475-2487), acute megakaryoblastic leukemia (AMKL) (*Journal of Clinical Investigation* (2012), 122(3), 948-962), and acute lymphoblastic leukemia (ALL) (*Journal of Clinical Investigation* (2021), 131(1), e135937). Other cancers linked to DYRK1A are ovarian (*Frontiers in Oncology* (2021), 11, 637193), head and neck squamous cell carcinoma (*Scientific Reports* (2016), 6, 36132), hepatocellular carcinoma (*Cell Death & Disease* (2021), 12, 125), DYRK1A regulates DNA damage response (*Scientific Reports* (2019), 9, 6014 and *Scientific Reports* (2019), 9, 6539). In some situations, DYRK1A appears to function as a tumor-suppressor protein (*Molecular & Cellular Oncology* (2015), 2(1), e970048 and *Nature* (2016), 529, 172-177).

[0371] Other cancers can also be treated with the compounds and compositions described herein.

[0372] More particularly, cancers that may be treated by the compounds, compositions and methods described herein include, but are not limited to, the following:

[0373] 1) Breast cancers, including, for example ER^+ breast cancer, ER^- breast cancer, her^{2-} breast cancer, her^{2+} 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; chemoresistant breast cancers (TNBC), 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 (her^{2-}). In some embodiments, the breast cancer may have a high risk Oncotype score.

[0374] 2) Cardiac cancers, including, for example sarcoma, e.g., angiosarcoma, fibrosarcoma, rhabdomyosarcoma, and liposarcoma; myxoma; rhabdomyoma; fibroma; lipoma and teratoma.

[0375] 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; chemoresistant small cell lung cancer (SCLC), and mesothelioma.

[0376] 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; colon cancers with APC gene mutations; 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.

[0377] 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.

[0378] 6) Liver cancers, including, for example, hepatoma, e.g., hepatocellular carcinoma; cholangiocarcinoma; hepatoblastoma; angiosarcoma; hepatocellular adenoma; and hemangioma.

[0379] 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.

[0380] 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, oligodendrocytoma, schwannoma, retinoblastoma, and congenital tumors; and cancers of the spinal cord, e.g., neurofibroma, meningioma, glioma, and sarcoma.

[0381] 9) Gynecological cancers, including, for example, cancers of the uterus, e.g., endometrial cancers (e.g., carcinoma, endometrioid adenocarcinoma, serous carcinoma, clear cell carcinoma, mucinous carcinomas, mixed or undifferentiated carcinoma (including mixed Müllerian tumor), endometrial stromal sarcoma, squamous cell carcinoma of the endometrium, urothelial carcinoma, endometrial cancer with CTNNB1 mutations); cancers of the cervix, e.g., cervical carcinoma, and pre tumor cervical dysplasia; cancers of the ovaries, e.g., BRCA-mutant ovarian cancer, surface epithelial-stromal tumors (epithelial ovarian cancer (Type 1 (endometroid, mucinous, clear cell, low grade serous) or Type 2 (poorly differentiated, carcinosarcoma, and high grade serous))), ovarian carcinoma, including serous cystadenocarcinoma, mucinous cystadenocarcinoma, endometrioid tumors, small cell ovarian cancer (small cell ovarian cancer of hypercalcemic type, small cell ovarian cancer of pulmonary type) 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, primary fallopian tube cancer; Primary peritoneal cancer (also known as serous surface papillary carcinoma, primary peritoneal carcinoma, extra-ovarian serous carcinoma, primary serous papillary carcinoma, and psammomacarcinoma).

[0382] 10) Hematologic cancers, including, for example, cancers of the blood, e.g., acute myeloid leukemia, chronic myeloid leukemia, myelodysplastic syndromes (refractory cytopenia with unilineage dysplasia (refractory anemia, refractory neutropenia, and refractory thrombocytopenia), refractory anemia with ring sideroblasts, refractory cytopenia with multilineage dysplasia, refractory anemias with excess blasts I and II, refractory cytopenia of childhood), and myeloproliferative neoplasms, acute lymphoblastic leukemia, chronic lymphocytic leukemia, myeloproliferative diseases, multiple myeloma, myelodysplastic syndrome, myelodysplastic-myeloproliferative diseases, Hodgkin's lymphoma, non-Hodgkin's lymphoma (malignant lymphoma) and Waldenstrom's macroglobulinemia.

[0383] 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.

[0384] 12) Adrenal gland cancers, including, for example, neuroblastoma.

[0385] 13) Soft-tissue sarcomas (STS) such as fibrosarcoma, malignant fibrous histiocytoma, dermatofibrosarcoma, liposarcoma, rhabdomyosarcoma, leiomyosarcoma, hemangiosarcoma, Kaposi's sarcoma, lymphangiosarcoma, synovial sarcoma, malignant peripheral nerve sheath tumors (also called neurofibrosarcomas, malignant schwannomas, and neurogenic sarcomas), neurofibrosarcoma, extraskeletal chondrosarcoma, extraskeletal osteosarcoma, extraskeletal myxoid chondrosarcoma, extraskeletal mesenchymal, embryonal, alveolar soft part sarcoma, and infantile hemangio-pericytoma.

[0386] More particularly, tumors of the central nervous system that may be treated by the compounds, compositions and methods described herein include:

[0387] 1) Astrocytic tumors, e.g., diffuse astrocytoma (fibrillary, protoplasmic, gemistocytic, mixed), anaplastic (malignant) astrocytoma, glioblastoma multiforme (giant cell glioblastoma and gliosarcoma), pilocytic astrocytoma (pilomyxoid astrocytoma), pleomorphic xanthoastrocytoma, subependymal giant cell astrocytoma, and gliomatosis cerebri.

[0388] 2) Oligodendroglial tumors, e.g., oligodendroglioma and anaplastic oligodendroglioma.

[0389] 3) Oligoastrocytic tumors, e.g., oligoastrocytoma and anaplastic oligoastrocytoma.

[0390] 4) Ependymal tumors, e.g., subependymoma, myxopapillary ependymoma, ependymoma, (cellular, papillary, clear cell, tanycytic), and anaplastic (malignant) ependymoma.

[0391] 5) Choroid plexus tumors, e.g., choroid plexus papilloma, atypical choroid plexus papilloma, and choroid plexus carcinoma.

[0392] 6) Neuronal and mixed neuronal-glial tumors, e.g., gangliocytoma, ganglioglioma, dysembryoplastic neuroepithelial tumor (DNET), dysplastic gangliocytoma of the cerebellum (Lhermitte-Duclos), desmoplastic infantile astrocytoma/ganglioglioma, central neurocytoma, anaplastic ganglioglioma, extraventricular neurocytoma, cerebellar liponeurocytoma, Papillary glioneuronal tumor, Rosette-forming glioneuronal tumor of the fourth ventricle, and paraganglioma of the filum terminale.

[0393] 7) Pineal tumors, e.g., pineocytoma, pineoblastoma, papillary tumors of the pineal region, and pineal parenchymal tumor of intermediate differentiation.

[0394] 8) Embryonal tumors, e.g., medulloblastoma (medulloblastoma with extensive nodularity, anaplastic medulloblastoma, desmoplastic, large cell, melanotic, medullomyoblastoma), medulloepithelioma, supratentorial primitive neuroectodermal tumors, and primitive neuroectodermal tumors (PNETs) such as neuroblastoma, ganglioneuroblastoma, ependymoblastoma, and atypical teratoid/rhabdoid tumor.

[0395] 9) Neuroblastic tumors, e.g., olfactory (esthesioneuroblastoma), olfactory neuroepithelioma, and neuroblastomas of the adrenal gland and sympathetic nervous system.

[0396] 10) Glial tumors, e.g., astroblastoma, chordoid glioma of the third ventricle, and angiocentric glioma.

[0397] 11) Tumors of cranial and paraspinal nerves, e.g., schwannoma, neurofibroma Perineurioma, and malignant peripheral nerve sheath tumor.

[0398] 12) Tumors of the meninges such as tumors of meningothelial cells, e.g., meningioma (atypical meningioma and anaplastic meningioma); mesenchymal tumors, e.g., lipoma, angiolipoma, hibernoma, liposarcoma, solitary fibrous tumor, fibrosarcoma, malignant fibrous histiocytoma, leiomyoma, leiomyosarcoma, rhabdomyoma, rhabdomyosarcoma, chondroma, chondrosarcoma, osteoma, osteosarcoma, osteochondroma, haemangioma, epithelioid hemangioendothelioma, haemangiopericytoma, anaplastic haemangiopericytoma, angiosarcoma, Kaposi Sarcoma, and Ewing Sarcoma; primary melanocytic lesions, e.g., diffuse melanocytosis, melanocytoma, malignant melanoma, meningeal melanomatosis; and hemangioblastomas.

[0399] 13) Tumors of the hematopoietic system, e.g., malignant Lymphomas, plasmocytoma, and granulocytic sarcoma.

[0400] 14) Germ cell tumors, e.g., germinoma, embryonal carcinoma, yolk sac tumor, choriocarcinoma, teratoma, and mixed germ cell tumors.

[0401] 15) Tumors of the sellar region, e.g., craniopharyngioma, granular cell tumor, pituicytoma, and spindle cell oncocytoma of the adenohypophysis.

[0402] 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.

[0403] 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.

[0404] There is mounting evidence for a role of DYRK1A in the onset of Alzheimer’s Disease (*Future Medicinal Chemistry* (2016), 8(6), 681-696 and *European Journal of Medicinal Chemistry* (2018), 158, 559-592). DYRK1A phosphorylates key substrates involved in Alzheimer’s Disease and dementia: Tau, septin 4, amyloid precursor protein (APP), presenilin 1, neprilysin, Muncl8-1, α-synuclein, RCAN1, and β-tubulin. By modulating alternative splicing of Tau exon 10, DYRK1A favors the production of the 3R-Tau splice isoform (characteristic for DS/AD/tauopathy) over the 4R-Tau isoform (*Journal of Biological Chemistry* (2015), 290, 15219-15237).

[0405] Genome-wide association studies (GWAS) have revealed that DYRK1A is a risk factor for Parkinson’s Disease (The Lancet Neurology (2019), 18(12), 1091-1102). DYRK1A phosphorylates key factors for Parkinson’s Disease such as parkin, septin 4, and α-synuclein. Upregulation of micro-RNAs specific for Parkinson’s Disease targets DYRK1A expression. There is further evidence that DYRK1A expression is increased in Parkinson’s Disease and in Pick’s disease (*Neurobiology of Disease* (2005), 20(2), 392-400).

[0406] The compounds and compositions provided herein can be used as inhibitors and/or modulators of the enzyme DYRK1A, and thus can be used to treat a variety of disorders and diseases associated with tau protein, including, but not limited to, Alzheimer’s disease, amyotrophic lateral sclerosis (ALS), down syndrome, frontotemporal dementia (FTD) including FTD with parkinsonism-17 (FTDP-17), behavioural variant frontotemporal dementia (bvFTD), FTD in patients with motor neuron disease (MND) (typically amyotrophic lateral sclerosis, also called FTD-ALS), corticobasal degeneration (CBD) (also called corticobasal ganglionic degeneration), progressive supranuclear palsy, primary progressive aphasia (PPA), globular glial tauopathy (GGT), myotonic dystrophy type 1 (DM1) (also called Steinert disease), myotonic dystrophy type 2 (DM2) (also called proximal myotonic myopathy), Guam complex, argyrophilic grain disease, dementia pugilistica, post-encephalitic parkinsonism, Lewy body dementia, Parkinson’s disease, Pick’s disease, and additional diseases with pronounced neurodegeneration such as autism, dementia, epilepsy, Huntington’s disease, multiple sclerosis; diseases and disorders associated with acquired brain injury such as chronic traumatic encephalopathy, traumatic brain injury, tumor, and stroke.

[0407] Non-limiting examples of neurological disorders (e.g., neurological conditions and neurological 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-Barré 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), macrencephaly, 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.

[0408] The compounds and compositions may also be useful in the inhibition of the development of invasive cancer, tumor angiogenesis and metastasis.

[0409] 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.

[0410] In some embodiments, the disorder or disease is cancer.

[0411] In some embodiments, the disorder or disease is metastatic melanoma.

[0412] In some embodiments, the disorder or disease is tendon regeneration.

[0413] In some embodiments, the disorder or disease is diabetes.

[0414] In some embodiments, the disorder or disease is degenerative disc disease.

[0415] In some embodiments, the disorder or disease is osteoarthritis.

[0416] In some embodiments, the disorder or disease is a viral infection.

[0417] In some embodiments, the disorder or disease is a neurological disorder.

[0418] In some embodiments, the disorder or disease is Alzheimer's disease.

[0419] In some embodiments, the disorder or disease is osteoarthritis.

[0420] In some embodiments, the patient is a human.

[0421] 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.

[0422] 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, synovial sarcoma, 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.

[0423] In some embodiments, the cancer is hepatocellular carcinoma; in some embodiments, the cancer is colon cancer; in some embodiments, the cancer is colorectal cancer; in some embodiments, the cancer is breast cancer; in some embodiments, the cancer is pancreatic cancer; in some embodiments, the cancer is chronic myeloid leukemia (CML); in some embodiments, the cancer is chronic myelomonocytic leukemia; in some embodiments, the cancer is chronic lymphocytic leukemia (CLL); in some embodiments, the cancer is acute myeloid leukemia; in some embodiments, the cancer is acute lymphocytic leukemia; in some embodiments, the cancer is Hodgkin lymphoma; in some embodiments, the cancer is lymphoma; in some embodiments, the cancer is sarcoma; in some embodiments, the cancer is ovarian cancer; in some embodiments, the cancer is lung cancer-non-small cell; in some embodiments, the cancer is lung cancer-small cell; in some embodiments, the cancer is multiple myeloma; in some embodiments, the cancer is nasopharyngeal cancer; in some embodiments, the cancer is neuroblastoma; in some embodiments, the cancer is osteosarcoma; in some embodiments, the cancer is penile cancer; in some embodiments, the cancer is pituitary tumors; in some embodiments, the cancer is prostate cancer; in some embodiments, the cancer is retinoblastoma; in some embodiments, the cancer is rhabdomyosarcoma; in some embodiments, the cancer is salivary gland cancer; in some embodiments, the cancer is skin cancer-basal and squamous cell; in some embodiments, the cancer is skin cancer-melanoma; in some embodiments, the cancer is small intestine cancer; in some embodiments, the cancer is stomach (gastric) cancers; in some embodiments, the cancer is testicular cancer; in some embodiments, the cancer is thymus cancer; in some embodiments, the cancer is thyroid cancer; in some embodiments, the cancer is uterine sarcoma; in some embodiments, the cancer is vaginal cancer; in some embodiments, the cancer is vulvar cancer; in some embodiments, the cancer is Wilms tumor; in some embodiments, the cancer is laryngeal or hypopharyngeal cancer; in some embodiments, the cancer is kidney cancer; in some embodiments, the cancer is Kaposi sarcoma; in some embodiments, the cancer is gestational trophoblastic disease; in some embodiments, the cancer is gastrointestinal stromal tumor; in some embodiments, the cancer is gastrointestinal carcinoid tumor; in some embodiments, the cancer is gallbladder cancer; in some embodiments, the cancer is eye cancer (melanoma and lymphoma); in some embodiments, the cancer is Ewing tumor; in some embodiments, the cancer is esophagus cancer; in some embodiments, the cancer is endometrial cancer; in some embodiments, the cancer is colorectal cancer; in some embodiments, the cancer is cervical cancer; in some embodiments, the cancer is brain or spinal cord tumor; in some embodiments, the cancer is bone metastasis; in some embodiments, the cancer is bone cancer; in some embodiments, the cancer is bladder cancer; in some embodiments, the cancer is bile duct cancer; in some embodiments, the cancer is anal cancer; and in some embodiments, the cancer is adrenal cortical cancer.

[0424] In some embodiments, the disorder or disease is a neurological condition, disorder, or disease, wherein the neurological disease is selected from: Alzheimer's disease, frontotemporal dementias, Parkinson's disease, Huntington's disease, progressive supranuclear palsy, corticobasal degeneration, multiple system atrophy, amyotrophic lateral sclerosis (ALS), inclusion body myositis, autism, degenerative myopathies.

[0425] In some embodiments, the disorder or disease is selected from the group consisting of: Alzheimer's disease, amyotrophic lateral sclerosis, Down syndrome, frontotemporal dementia with parkinsonism-17 (FTDP-17), Lewy body dementia, Parkinson's disease, Pick's disease, and additional diseases with pronounced neurodegeneration such as autism, dementia, epilepsy, Huntington's disease, multiple sclerosis; diseases and disorders associated with acquired brain injury such as chronic traumatic encephalopathy, traumatic brain injury, tumor, and stroke.

[0426] In some embodiments, a compound of Formula I inhibits DYRK1A.

[0427] 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.

[0428] In some embodiments, the disease or disorder comprises tumor growth, cell proliferation, or angiogenesis.

[0429] 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.

[0430] 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.

[0431] 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.

[0432] 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.

Evaluation of Biological Activity

[0433] The biological activity of the compounds described herein can be tested using any suitable assay known to those of skill in the art. For example, the activity of a compound may be tested using one or more of the test methods outlined below.

[0434] For example, in vitro assays for DYRK1A biological activity may be used, e.g., regulation of microtubule-associated protein tau (MAPT/Tau) phosphorylation in neuronal cell lines such as the human SH-SY5Y neuroblastoma cell line. Assays for DYRK1A-regulated level of phosphorylation can include monitoring levels of basal pSer396 Tau, which can be measured, for example, by serial dilutions of a candidate inhibitor composition using a ten micromolar top concentration and detected by ELISA or Western Blotting. An exemplary assay for DYRK-1A-regulated phosphorylation uses the SH-SY5Y cells cultured in a 96 well plate format for a period of time sufficient to stabilize microtubules and Tau phosphorylation, usually at least 2 days, then treated with a 1/3 serial dilution of compounds overnight and lysed. The cell lysate is resolved by SDS PAGE, then transferred to nitrocellulose and probed with an antibody specific for pSer396 Tau. The chemiluminescence signal for HRP-linked antibodies used in western blotting is detected using a Carestream Image Station and blot densitometry for pSer396 and beta-actin are analyzed using ImageJ (NIH).

[0435] In a further example, the activity of a candidate compound can be measured by phosphoTau (Thr212) AlphaLISA by adding the lysate mentioned above onto total Tau-coated plates and detected with a specific pThr212Tau antibody. Colorimetric detection of AlphaLISA signal is performed by EnVision Multilabel Plate Reader (Perkin Elmer).

[0436] To further illustrate this disclosure, the following examples are included. The examples should not, of course, be construed as specifically limiting the disclosure. 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 disclosure 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 disclosure without exhaustive examples.

Examples

Compound Preparation

[0437] The starting materials used in preparing the compounds of the disclosure 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.

[0438] 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* 7^{th} Ed., John Wiley & Sons (2013), Carey and Sundberg, *Advanced Organic Chemistry* 5^{th} Ed., Springer (2007), *Comprehensive Organic Transformations: A Guide to Functional Group Transformations,* 2^{nd} Ed., John Wiley & Sons (1999) (incorporated herein by reference in its entirety)and the like.

[0439] 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 P. Wuts *Greene's Protective Groups in Organic Synthesis,* 5th Ed., John Wiley & Sons (2014), incorporated herein by reference in its entirety.

[0440] Trademarks used herein are examples only and reflect illustrative materials used at the time of the disclosure. 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 disclosure.

[0441] (^{1}H) nuclear magnetic resonance spectra (NMR) were measured in the indicated solvents on a Bruker NMR spectrometer (Avance™ 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.

[0442] The following abbreviations have the indicated meanings:

[0443] Ac_2O=acetic anhydride

[0444] Boc=tert-butyloxycarbonyl

[0445] $B(OiPr)_3$=Triisopropyl borate

[0446] BrettPhos=dicyclohexyl(2',4',6'-triisopropyl-3,6-dimethoxy-[1,1'-biphenyl]-2-yl) phosphine

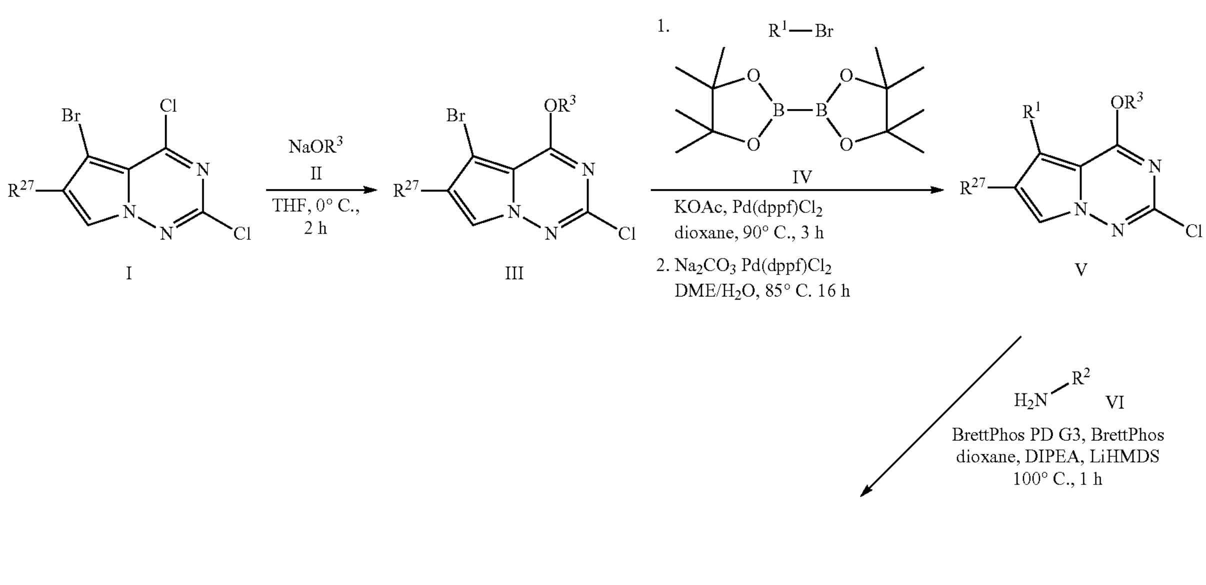
[0447] BrettPhos Pd G3=[(2-di-cyclohexylphosphino-3,6-dimethoxy-2',4',6'-triisopropyl-1,1'-biphenyl)-2-(2'-amino-1,1'-biphenyl)]palladium(II) methanesulfonate methanesulfonate
[0448] brine=saturated aqueous sodium chloride
[0449] nBuLi=n-butyl lithium
[0450] $CDCl_3$=deuterated chloroform
[0451] $(COCl)_2$=oxalyl chloride
[0452] Cs_2CO_3=cesium carbonate
[0453] DCE=1,2-dichloroethane
[0454] DCM=dichloromethane
[0455] DIPEA=N,N-diisopropylethylamine
[0456] DME=1,2-dimethoxyethane, or glyme, or monoglyme
[0457] DMF=N,N-dimethylformamide
[0458] DMPU=N,N'-dimethylpropyleneurea
[0459] DMSO-d_6=deuterated dimethylsulfoxide
[0460] ESIMS=electron spray mass spectrometry
[0461] EtOAc=ethyl acetate
[0462] HATU=1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate
[0463] HCl=hydrochloric acid
[0464] HOAc=acetic acid
[0465] IPA=isopropyl alcohol
[0466] ISCO=Teledyne ISCO, Inc brand CombiFlash® Rf 200
[0467] KOAc=potassium acetate
[0468] LCMS=liquid chromatography-mass spectrometry
[0469] LiHMDS=lithium bis(trimethylsilyl)amide
[0470] MeCN=acetonitrile
[0471] MeOH=methanol
[0472] MeTHF=2-methyltetrahydrofuran
[0473] $MgSO_4$=magnesium sulfate
[0474] MsCl=methanesulfonyl chloride or mesyl chloride
[0475] MTBE=methyl tert-butyl ether
[0476] MW=microwave irradiation
[0477] NaO^{t}Bu=sodium tert-butoxide
[0478] $NaHCO_3$=sodium bicarbonate
[0479] $NaBH(OAc)_3$=Sodium triacetoxyborohydride
[0480] Na_2SO_4=sodium sulfate
[0481] NMR=nuclear magnetic resonance
[0482] ON=overnight
[0483] Pd/C=palladium on carbon
[0484] Pd(dppf)Cl_2=1,1'-bis(diphenylphosphino)ferrocene-palladium(II)dichloride
[0485] $Pd(OH)_2$/C=palladium hydroxide on carbon
[0486] PE=petroleum ether
[0487] PPTS=pyridinium p-toluenesulfonate
[0488] prep-TLC=preparative thin layer chromatography
[0489] QPhos=1,2,3,4,5-pentaphenyl-1'-(di-tert-butylphosphino)ferrocene
[0490] r.t. =room temperature
[0491] TBDMSCl=tert-butyldimethylsilyl chloride
[0492] TEA=triethylamine
[0493] TFA=trifluoroacetic acid
[0494] THF=tetrahydrofuran
[0495] TLC=thin layer chromatography
[0496] TMSOK=potassium trimethylsilanolate
[0497] XPhos=dicyclohexyl[2',4',6'-tris(propan-2-yl)[1,1'-biphenyl]-2-yl]phosphane

[0498] 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 compounds of the disclosure 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.

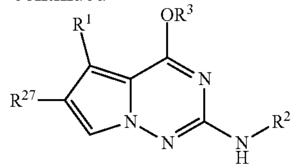
General Procedures

[0499] Compounds of Formula I of the present disclosure can be prepared as depicted in Scheme 1.

Scheme 1



-continued



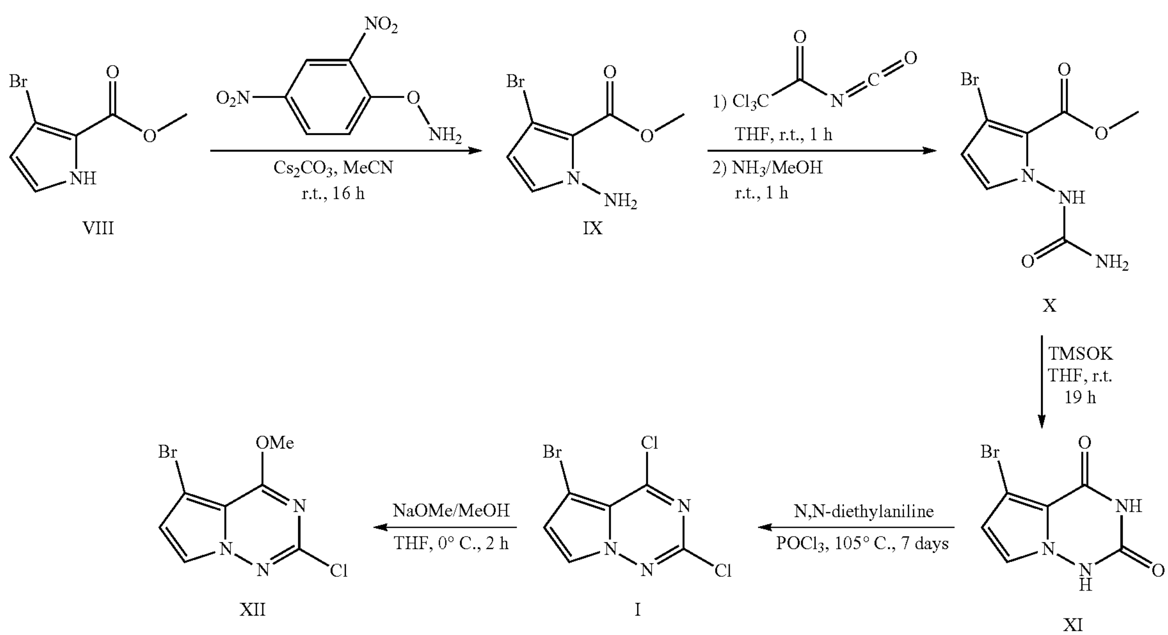
VII

[0500] Scheme 1 describes a method for preparation of 4-alkoxypyrrolo[2,1-f][1,2,4]triazine derivatives (VII) by first displacing the 4-chloride (I) with a variety of alkoxys (II) to produce 2-chloro-5-bromo-4-alkoxypyrrolo[2,1-f][1,2,4]triazine III. Formation of a variety of boronic acid pinacol esters by reacting various bromides (IV) with bis(pinacolato)diboron followed by Suzuki coupling with bromide (III) produces 2-chloro-4-alkoxypyrrolo[2,1-f][1,2,4]triazine (V). The chloro is then displaced with a variety of amines (VI) to produce the final 4-alkoxypyrrolo[2,1-f][1,2,4]triazine (VII).

Illustrative Compound Examples

[0501] Preparation of intermediate 5-bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XII) is depicted below in Scheme 2.

Scheme 2



Step 1

[0502] To a solution of methyl 3-bromo-1H-pyrrole-2-carboxylate (VIII) (100 g, 490.15 mmol, 1 eq.) in MeCN (2 L) was added Cs_2CO_3 (255.52 g, 784.23 mmol, 1.6 eq.) in one portion at 20° C. (no exothermic). The reaction was stirred at room temperature for 5 h. A solution of O-(2,4-dinitrophenyl)hydroxylamine (146.40 g, 735.22 mmol, 1.5 eq.) in MeCN (2 L) was then added dropwise at 0-5° C. under N_2. After addition, the reaction was warmed to room temperature for 16 h. The reaction mixture was filtered, and the filtrate was diluted with MTBE (2 L) and washed with brine (2 L x 3). The above reaction was performed six times.

[0503] The combined organics of five batches were combined, dried over $MgSO_4$, filtered, and concentrated under vacuum to give the crude product. The crude product was purified by column chromatography on silica gel (DCM/PE=0-50%, then EtOAc/PE=20%) to give methyl 1-amino-3-bromo-1H-pyrrole-2-carboxylate (IX) (380 g, 1.62 mol, 55.1% yield, 93.3% purity) as a yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ ppm 3.84 (3 H, s), 6.24 (1H, d, J=2.8 Hz), 6.38 (2 H, br s), 7.12 (1H, d, J=2.8 Hz).

Steps 2-3

[0504] To a solution of methyl 1-amino-3-bromo-1H-pyrrole-2-carboxylate (IX) (190 g, 867.44 mmol, 1 eq.) in THF (1900 mL) was added dropwise 2,2,2-trichloroacetyl isocyanate (179.76 g, 954.18 mmol, 113.06 mL, 1.1 eq.) at 0~5° C., then warmed to room temperature for 1 h. The reaction was then added dropwise to NH_3/MeOH (7 M, 1.24

L, 10 eq) at room temperature, stirred at room temperature for 1 h to give a yellow suspension. The above reaction was performed twice.

[0505] The two reactions were combined and concentrated under vacuum. The residue was triturated with MTBE (4 L) at room temperature for 30 min, filtered. The filter cake was washed with MTBE (500 mL x 3), dried under vacuum to give methyl 3-bromo-1-ureido-1H-pyrrole-2-carboxylate (X) (402 g, 1.53 mol, 88.2% yield, 99.78% purity) as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 3.75 (3 H, s), 6.27 (2 H, br s), 6.28 (1H, d, J=2.8 Hz), 7.10 (1 H, d, J=2.8 Hz), 9.27 (1 H, br s); ESIMS found for $C_7H_8BrN_3O_3$ m/z 262.1 (^{79}BrM+H).

Step 4

[0506] To a solution of methyl 3-bromo-1-ureido-1H-pyrrole-2-carboxylate (X) (67 g, 255.67 mmol, 1 eq.) in THF (4 L) was added TMSOK (65.60 g, 511.33 mmol, 2 eq.) in portions at 0~5° C. under N_2. After stirring for 5 min, the reaction became a thick slurry. The reaction mixture was stirred vigorously at room temperature for 16 h. LCMS showed ~25.8% of starting material remained. An additional portion of TMSOK (16.40 g, 127.83 mmol, 0.5 eq.) was added at room temperature and stirred for 3 h. LCMS showed the reaction was complete. The reaction was concentrated. The residue was diluted with H_2O (1.6 L), cooled with ice-bath, added dropwise HCl (4 M, 160 mL) to pH 2-3, and filtered. The filter cake was washed with H_2O (600 mL×3). The above reaction was performed six times.

[0507] The filter cakes of six reactions were combined, triturated with H_2O (6 L) at room temperature, for 2 h and then filtered. The filter cake was dried in a vacuum drying oven at 60° C. for 24 h to give 5-bromopyrrolo[2,1-f][1,2,4]triazine-2,4(1H,3H)-dione (XI) (320 g, 1.28 mol, 83.4% yield, 91.95% purity) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.49 (1 H, d, J=2.8 Hz), 7.17 (1H, d, J=2.8 Hz), 11.30 (1 H, br s); ESIMS found for $C_6H_4BrN_3O_2$ m/z 232.0 (^{81}BrM+H).

Step 5

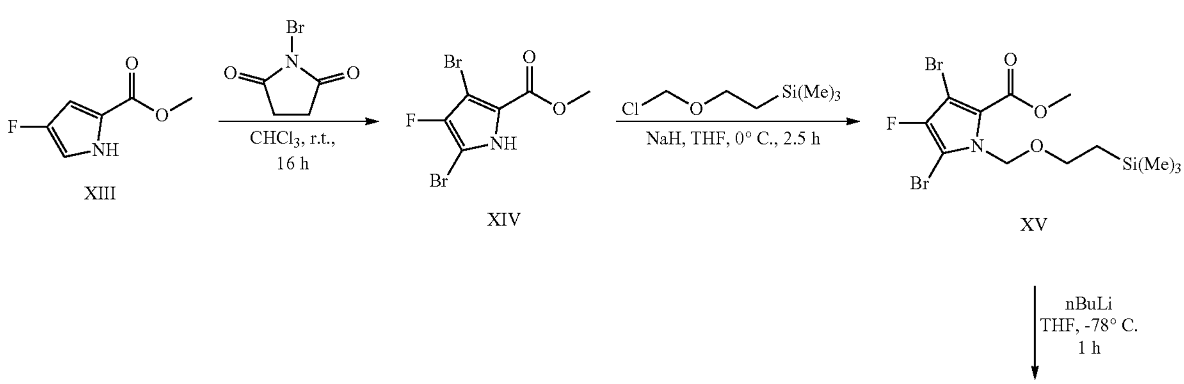
[0508] To a solution of $POCl_3$ (1500 mL) was added 5-bromopyrrolo[2,1-f][1,2,4]triazine-2,4(1H,3H)-dione (XI) (180 g, 782.55 mmol, 1 eq.) in portions at room temperature. N,N-Diethylaniline (291.95 g, 1.96 mol, 312.92 mL, 2.5 eq.) was then added dropwise at room temperature (a little exothermic). After addition, the reaction was heated to 105° C. for 48 h. LCMS showed the starting material was consumed but the intermediate remained, ~4.3% of desired product was formed. The reaction was cooled to 90° C., added an additional $POCl_3$ (500 mL) in one portion, then heated to reflux gently for 24 h. LCMS showed most of intermediate remained, ~11.9% of desired product was formed. The reaction was heated to reflux gently for another 4 days. LCMS showed ~7.4% of intermediate remained, ~55.5% of desired product was formed. The reaction was cooled to 40° C. and distilled under reduced pressure to remove most of $POCl_3$. The residue was diluted with MeTHF (5 L), poured into ice-H_2O (2 L), the added brine (1 L), and separated. The aqueous layer was extracted with MeTHF (1.5 L x 2). The combined organic were washed with brine (1.5 L x 2), dried over $MgSO_4$, filtered, and concentrated under vacuum to give the crude product. The crude product was purified by column chromatography on silica gel (4 kg, 100 ~200 mesh, DCM/PE=0-20%) and triturated with n-heptane (500 mL) at room temperature for 3 h, then filtered to afford 5-bromo-2,4-dichloropyrrolo[2,1-f][1,2,4]triazine (I) (150 g, 556.14 mmol, 71.1% yield, 98.96% purity) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.02 (1 H, d, J=2.4 Hz), 7.79 (1H, d, J=2.4 Hz); ESIMS found for $C_6H_2BrCl_2N_3$ m/z 266.1 (^{79}BrM+H).

Step 6

[0509] To a stirred solution of 5-bromo-2,4-dichloropyrrolo[2,1-f][1,2,4]triazine (I) (8.0 g, 29.97 mmol) in THF (10 mL) was added sodium methoxide (66 mL, 33 mmol) in MeOH dropwise at 0° C. and the mixture was stirred for 2 h. The reaction mixture was quenched with saturated aqueous NH_4Cl, taken into EtOAc, washed with water and brine. The organics were separated, dried over anhydrous Na_2SO_4, concentrated, and dried under high vacuo to obtain 5-bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XII) (6 g, 22.86 mmol, 76.3% yield) as an off-white solid which was used for the next step without purification. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 4.12 (3 H, s), 7.00 (1H, d, J=3.01 Hz), 8.01 (1H, d, J=3.01 Hz); ESIMS found for $C_7H_5BrClN_3O$ m/z 261.1 (^{79}BrM+H).

[0510] Preparation of intermediate 5-bromo-2-chloro-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XXII) is depicted below in Scheme 3.

Scheme 3



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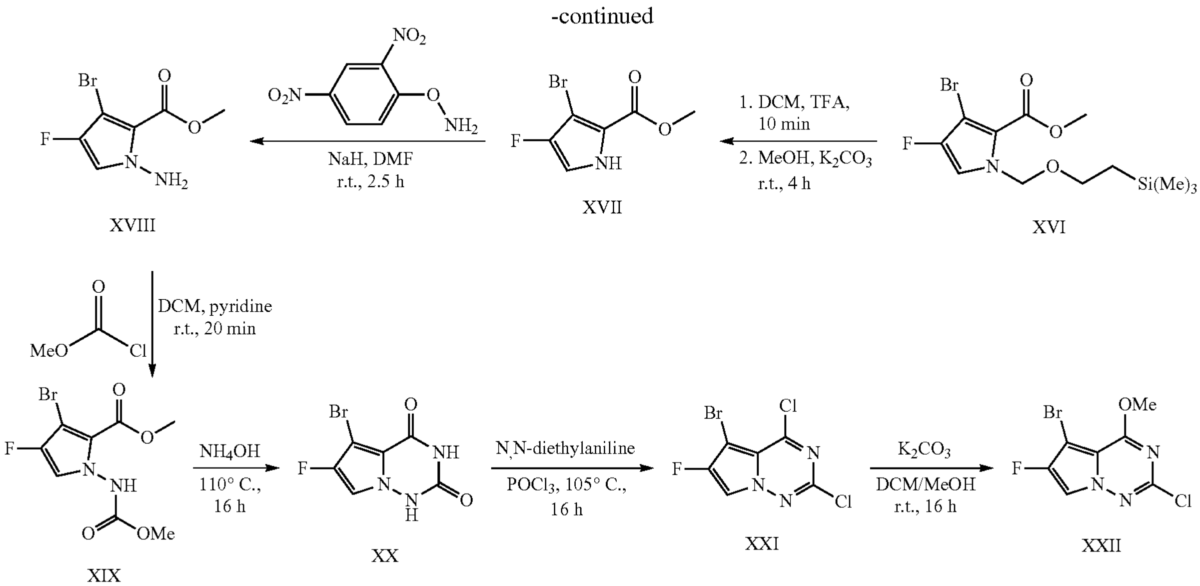


Step 1

[0511] To a solution of methyl 4-fluoro-1H-pyrrole-2-carboxylate (XIII) (commercially available from Pharma-Block (USA), Inc.) (1 g, 6.99 mmol) in $CHCl_3$ (9 mL) at 0° C. was added N-bromosuccinimide (2.64 g, 14.68 mmol). The reaction was stirred at room temperature for 16 h. The reaction mixture was quenched with 10% sodium thiosulfate (50 mL) and extracted with CHC_3 (3×30 mL). The organic layers were combined and washed with aqueous saturated NaCl (50 ml) and evaporated under reduced pressure to produce methyl 3,5-dibromo-4-fluoro-1H-pyrrole-2-carboxylate (XIV) (2.1 g, 6.979 mmol, 99.9% yield) as a beige solid. The product was used as is without further purification. ESIMS found for $C_6H_4Br_2FNO_2$ m/z 299.9 (M+H).

Step 2

[0512] To a solution of methyl 3,5-dibromo-4-fluoro-1H-pyrrole-2-carboxylate (XIV) (2.1 g, 6.98 mmol) in dry THF (25 mL) at 0° C. under N_2 was added slowly NaH (0.43 g, 10.63 mmol) in small portions. The suspension was stirred at 0° C. for 30 min. To the suspension was added (2-(chloromethoxy)ethyl)trimethylsilane (1.9 mL, 10.74 mmol) at 0° C. under N_2. The reaction mixture was stirred at 0° C. for 2 h before quenching with ice-water (20 mL) and extracted with EtOAc (3×30 mL). The EtOAc layer was evaporated under reduced pressure and purified by silica gel column chromatography (100% hexanes) to produce methyl 3,5-dibromo-4-fluoro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrole-2-carboxylate (XV) (2.76 g, 6.401 mmol, 91.7% yield) as an amber liquid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm -0.07 (9 H, s), 0.81 (2H, t, J=7.80 Hz), 3.50 (2H, t, J=7.80 Hz), 3.82 (3 H, s), 5.69 (2 H, s).

Step 3

[0513] To solution of methyl 3,5-dibromo-4-fluoro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrole-2-carboxylate (XV) (2.76 g, 6.4 mmol) in dry THF (60 mL) at −78° C. under N_2 was added nBuLi (2.4 mL, 6. mmol). The reaction mixture was stirred at -78° C. for 1 h. The mixture was carefully quenched with ice water (20 mL), warmed to room temperature, and extracted with EtOAc (3×20 mL). The organics were dried over anhydrous Na_2SO_4, filtered and evaporated onto Celite® and purified by silica gel column chromatography (0→6% EtOAc/hexanes) to produce methyl 3-bromo-4-fluoro-1-((2-(trimethylsilyl) ethoxy) methyl)-1H-pyrrole-2-carboxylate (XVI) (760 mg, 2.157 mmol, 33.7% yield) as a clear oil. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm -0.06 (9 H, s), 0.80 (2H, t, J=7.96 Hz), 3.41-3.50 (2H, m), 3.80 (3H, s), 5.56 (2H, s), 7.52 (1H, d, J=3.29 Hz).

Step 4

[0514] To a stirred solution of methyl 3-bromo-4-fluoro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrole-2-carboxylate (XVI) (881 mg, 2.5 mmol) in DCM (23 mL) was added TFA (23 mL) and the mixture was stirred at room temperature for 10 min. The solvents were concentrated, the residue taken in a mixture of MeOH (12 mL)/water (6 mL). To this mixture was added K_2CO_3 (1.75 g, 12.66 mmol) and stirred at room temperature for 4 h. Water (10 mL) was added, and the solution was neutralized with 1 H HCl and washed with $CHCl_3$ (3×10 mL). The organic layer was stripped onto Celite® and purified by silica gel column chromatography (0→5% MeOH/$CHCl_3$ (7 N NH_3)) to produce methyl 3-bromo-4-fluoro-1H-pyrrole-2-carboxylate (XVII) (450 mg, 2.027 mmol, 81.0% yield) as an off white solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 3.80 (3 H, s), 7.15 (1H, d, J=3.56 Hz), 12.29 (1 H, br s); ESIMS found for $C_6H_5BrFNO_2$ m/z 222.0 (M+H).

Step 5

[0515] To a solution of methyl 3-bromo-4-fluoro-1H-pyrrole-2-carboxylate (XVII) (500 mg, 2.25 mmol) in dry DMF (7 mL) at 0° C. was slowly added NaH (120 mg, 2.93 mmol). After 30 min, 0-(2,4-dinitrophenyl)hydroxylamine (490 mg, 2.48 mmol)) was added in one portion and the reaction was stirred in the ice bath for 1 h and at room temperature for 1 h. LC/MS showed the reaction was incomplete so addition O-(2,4-dinitrophenyl)hydroxylamine (490 mg, 2.48 mmol) and stirred at room temperature for 15 min. The reaction was diluted with water (100 mL) and extracted with EtOAc (3×75 mL). The combined extracts were stripped onto Celite® and purified by silica gel column chromatography (100% $CHCl_3$) to produce methyl 1-amino-3-bromo-4-fluoro-1H-pyrrole-2-carboxylate (XVIII) (501 mg, 2.114 mmol, 93.9% yield) as an off-white solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 3.80 (3H, s), 6.36 (2H, s), 7.25 (1H, d, J=3.29 Hz); ESIMS found for $C_6H_6BrFN_2O_2$ m/z 237.0 (M+H).

Step 6

[0516] To a solution of methyl 1-amino-3-bromo-4-fluoro-1H-pyrrole-2-carboxylate (XVIII) (500 mg, 2.11 mmol) in DCM (10 mL) was added pyridine (210 μL, 2.6 mmol) and methyl carbonochloridate (180 μL, 2.33 mmol) dropwise. The reaction was stirred at room temperature for 20 min. DCM (100 mL) was added and washed with 1 N HCl (2×50 mL), stripped onto Celite® and purified by silica gel column chromatography (0->100% EtOAc/hexanes) to produce methyl 3-bromo-4-fluoro-1-((methoxycarbonyl) amino)-1H-pyrrole-2-carboxylate (XIX) (560 mg, 1.898 mmol, 89.8% yield) as a clear oil. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 3.69 (3 H, br s), 3.76 (3 H, s), 7.48 (1H, br d, J=1.92 Hz), 10.76 (1 H, br s); ESIMS found for $C_6H_5BrFN_2O_4$ m/z 295.0 (M+H).

Step 7

[0517] To NH_4OH (35 mL, 263.7 mmol) in a sealed tube was added methyl 3-bromo-4-fluoro-1-((methoxycarbonyl) amino)-1H-pyrrole-2-carboxylate (XIX) (560 mg, 1.9 mmol). The reaction was sealed and heated to 110° C. for 16 h. The solvent was removed under vacuum and the residue was dissolved in MeCN. The solvent was stripped (3x to remove water) and placed under high vacuum for 1 h, to produce 5-bromo-6-fluoropyrrolo[2,1-f][1,2,4]triazine-2,4 (1H,3H)-dione (XX) (440 mg, 1.774 mmol, 93.5% yield) as a light brown solid. The product was used as is without further purification. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 7.04 (1H, d, J=3.29 Hz), 7.13 (1 H, br s), 9.58 (1 H, br s); ESIMS found for $C_6H_3BrFN_3O_2$ m/z 247.9 (M+H).

Step 8

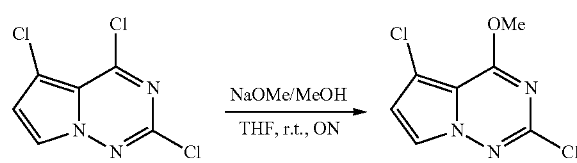
[0518] To a solution of neat $POCl_3$ (3 mL, 32.19 mmol) was added 5-bromo-6-fluoropyrrolo[2,1-f][1,2,4]triazine-2, 4(1H,3H)-dione (XX) (440 mg, 1.77 mmol) in portions at room temperature. N,N-Diethylaniline (0.7 mL, 4.4 mmol) was then added dropwise at room temperature. The reaction was heated at 105° C. for 16 h. The solvent was removed under vacuum before adding water (20 mL) and extracting with EtOAc. The organic layer was stripped onto Celite® and purified by silica gel column chromatography (0->100% EtOAc/hexanes) to produce 5-bromo-2,4-dichloro-6-fluoro-pyrrolo[2,1-f][1,2,4]triazine (XXI) (175 mg, 0.614 mmol, 34.6% yield) as an off-white solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 7.92 (1H, d, J=3.29 Hz); ESIMS found for $C_6HBrCl_2FN_3$ m/z 283.9 (M+H).

Step 9

[0519] To a solution of 5-bromo-2,4-dichloro-6-fluoropyrrolo[2,1-f][1,2,4]triazine (XXI) (175 mg, 0.61 mmol) in MeOH (664 μL) and DCM (2 mL) was added K_2CO_3 (254.1 mg, 1.84 mmol). The flask was capped and the reaction and stirred at room temperature for 16 h. Water (50 mL) was added and extracted with DCM (3×50 mL). The organic layers were separated and washed with water (2×50 mL) and brine (50 mL). The solvent was removed under vacuum to produce 5-bromo-2-chloro-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XXII) (163 mg, 0.581 mmol, 94.6% yield) as a beige solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 4.12 (3 H, s), 8.34 (1H, d, J=3.29 Hz); ESIMS found for $C_7H_4BrClFN_3O$ m/z 279.95 (M+H).

[0520] Preparation of intermediate 2,5-dichloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XXIV) is depicted below in Scheme 4.

Scheme 4



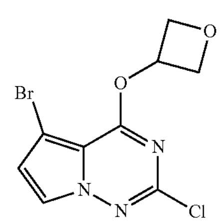
XXIII XXIV

Step 1

[0521] To a stirred solution of 2,4,5-trichloropyrrolo[2,1-f][1,2,4]triazine (XXIII) (commercially available from PharmaBlock Sciences Inc.) (202 mg, 0.910 mmol) in THF (4 mL) was added sodium methoxide (2 mL, 1 mmol) in MeOH dropwise at 0° C. and the mixture was stirred at room temperature overnight. The reaction mixture was quenched with water, taken into EtOAc, and washed with brine. The organics were separated, dried over anhydrous Na_2SO_4, concentrated, and the crude mixture was purified on ISCO (0->100% EtOAc/hexanes). Fractions were collected and concentrated under reduced pressure and dried under high vacuo to obtain 5-bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XXIV) (140 mg, 0.642 mmol, 70.7% yield) as a pale-yellow solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 4.12 (3 H, s), 6.95 (1H, d, J=3.01 Hz), 8.02 (1H, d, J=3.01 Hz).

[0522] The following intermediate was prepared in accordance with the procedure described in the above Scheme 4.

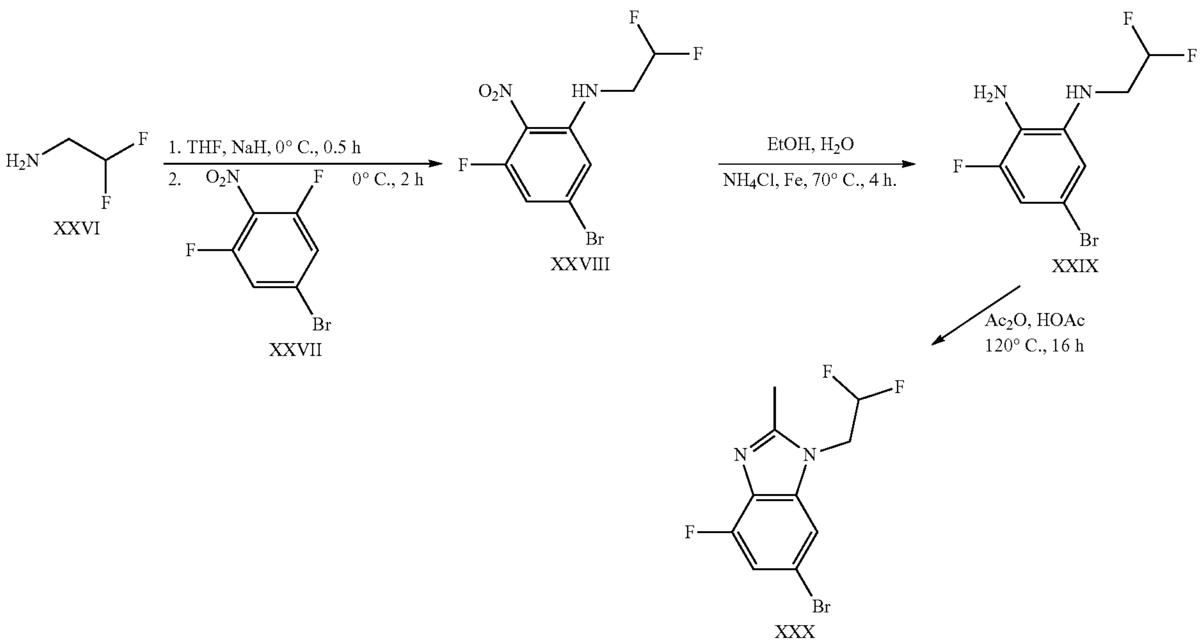
XXV



[0523] 5-Bromo-2-chloro-4-(oxetan-3-yloxy)pyrrolo[2,1-f][1,2,4]triazine (XXV): Off-white solid (558.8 mg, 1.84 mmol, 98.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 4.70 (2H, ddd, J=7.94, 4.65, 1.10 Hz), 4.95 (2H, ddd, J=7.73, 6.37, 0.96 Hz), 5.80 (1 H, tt, J=6.09, 4.86 Hz), 7.05 (1H, d, J=3.01 Hz), 8.05 (1H, d, J=3.01 Hz); ESIMS found $C_9H_7BrClN_3O_2$ m/z 303.95 (M+H).

[0524] Preparation of intermediate 6-bromo-1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazole (XXX) is depicted below in Scheme 5.

Scheme 5



Step 1

[0525] To an ice-cold suspension of sodium hydride (222 mg, 9.2 mmol) in THF (20 mL) was added 2,2-difluoroethylamine (XXVI) (746 mg, 9.32 mmol). The reaction mixture was allowed to stir at 0° C. for 30 min before adding an ice-cold solution of 5-bromo-1,3-difluoro-2-nitrobenzene (XXVII) (2.0 g, 8.4 mmol) in THF (20 mL). Reaction mixture was stirred at 0° C. for 2 h. The reaction was quenched with water. The aqueous layer was extracted with EtOAc, the organics were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified via column chromatography (40 g of silica gel) (0->20% EtOAc/hexanes) to give 5-bromo-N-(2,2-difluoroethyl)-3-fluoro-2-nitroaniline (XXVIII) (500 mg, 0.836 mmol, 19.9% yield) as a yellow solid. ESIMS found for $C_8H_6BrF_3N_2O_2$ m/z 299.0 (^{79}BrM+H).

Step 2

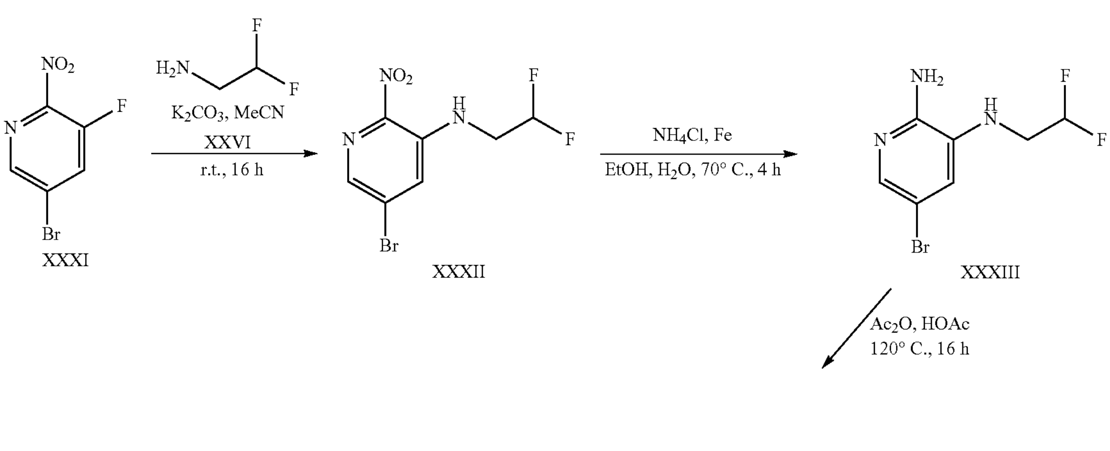
[0526] A mixture of 5-bromo-N-(2,2-difluoroethyl)-3-fluoro-2-nitroaniline (XXVIII) (500 mg, 1.67 mmol), Fe (1.09 g, 16.72 mmol) and NH_4Cl (1.34 g, 25.1 mmol) in a mixture of EtOH (6 mL) and water (2.5 mL) was heated to 70° C. for 4 h. The reaction mixture was cooled and filtered through Celite®. Filtrates were dissolved in EtOAc, washed water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to obtain 5-bromo-N^1-(2,2-difluoroethyl)-3-fluorobenzene-1,2-diamine (XXIX) (420 mg, 1.561 mmol, 93.4% yield) as a brown solid which was used for next reaction without further purification. ESIMS found for $C_8H_8BrF_3N_2$ m/z 269.0 (M+H).

Step 3

[0527] A solution of 5-bromo-N^1-(2,2-difluoroethyl)-3-fluorobenzene-1,2-diamine (XXIX) (420 mg, 1.56 mmol) and Ac_2O(175 μL, 1.85 mmol) in HOAc (8 mL) was heated to 120° C. for 16 h. The reaction mixture was concentrated, the residue partitioned between EtOAc/1 N NaOH, organics separated and washed with water and brine. The organics were dried over anhydrous Na_2SO_4 and concentrated to yield 6-bromo-1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazole (XXX) (380 mg, 1.297 mmol, 83.1% yield) as a light brown solid. ESIMS found for $C_{10}H_{10}BrF_3N_2$ m/z 295.0 (M+H).

[0528] Preparation of intermediate 6-bromo-1-(2,2-difluoroethyl)-2-methyl-1H-imidazo[4,5-b]pyridine (XXXIV) is depicted below in Scheme 6.

Scheme 6



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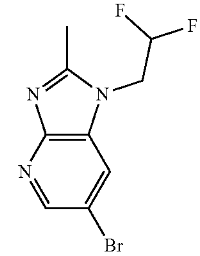


XXXIV

Step 1

[0529] A mixture of 2,2-difluoroethan-1-amine (XXVI) (410 mg, 5.02 mmol), 5-bromo-3-fluoro-2-nitropyridine (XXXI) (commercially available from Ark Pharma Scientific Limited) (1.0 g, 4.53 mmol) and K_2CO_3 (1.38 g, 9.95 mmol) in MeCN (20 mL) was stirred at room temperature for 16 h. The reaction was filtered and concentrated under high vacuum. The residue was taken up in water, stirred for 1 hour and the solids were collected by filtration and dried in vacuo to obtain 5-bromo-N-(2,2-difluoroethyl)-2-nitropyridin-3-amine (XXXII) (1.066 g, 3.780 mmol, 83.5% yield) as a yellow solid which was used for next step without purification. ESIMS found for $C_7H_6BrF_2N_3O_2$ m/z 282.0 (^{79}BrM+H).

Step 2

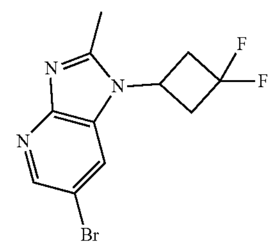
[0530] A mixture of 5-bromo-N-(2,2-difluoroethyl)-2-nitropyridin-3-amine (XXXII) (1.32 g, 4.69 mmol), Fe (3.07 g, 46.95 mmol) and NH_4Cl (3.77 g, 70.48 mmol) was taken in a mixture of EtOH (18 mL), and water (6 mL) and the mixture was heated to 70° C. for 4 h. The reaction mixture was cooled and filtered through Celite®. The filtrates were taken up in EtOAc, washed with water and brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to obtain 5-bromo-N^3-(2,2-difluoroethyl)pyridine-2,3-diamine (XXXIII) (630 mg, 2.499 mmol, 53.2% yield) as a grey solid which was used for next reaction without further purification. ESIMS found for $C_7H_8BrF_2N_3$ m/z 252.0 (^{79}BrM+H).

Step 3

[0531] A solution of 5-bromo-N^3-(2,2-difluoroethyl)pyridine-2,3-diamine (XXXIII) (630 mg, 2.5 mmol) and acetic anhydride (0.28 mL, 2.97 mmol) in HOAc (15 mL) was heated to 120° C. for 16 h. The reaction mixture was concentrated, the residue partitioned between EtOAc/1 N NaOH, organics separated, and washed with water and brine. The organics were dried over anhydrous Na_2SO_4, and solvents were concentrated under high vacuum. The residue was triturated with diethyl ether, sonicated and the solids were collected by filtration and dried under high vacuo to obtain 6-bromo-1-(2,2-difluoroethyl)-2-methylimidazo[4,5-b]pyridine (XXXIV) (325 mg, 1.177 mmol, 47.1% yield) as a grey solid which was used for next step without purification. ESIMS found for $C_9H_8BrF_2N_3$ m/z 276.0 (^{79}BrM+H).

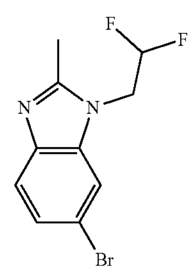
[0532] The following intermediates were prepared in accordance with the procedure described in the above Scheme 6.

XXXV



[0533] 6-Bromo-1-(3,3-difluorocyclobutyl)-2-methyl-1H-imidazo[4,5-b] pyridine (XXXV): Grey solid (1.57 g, 6.178 mmol, 68.3% yield). ESIMS found $C_{11}H_{10}BrF_2N_3$ m/z 302.1 (M+H).

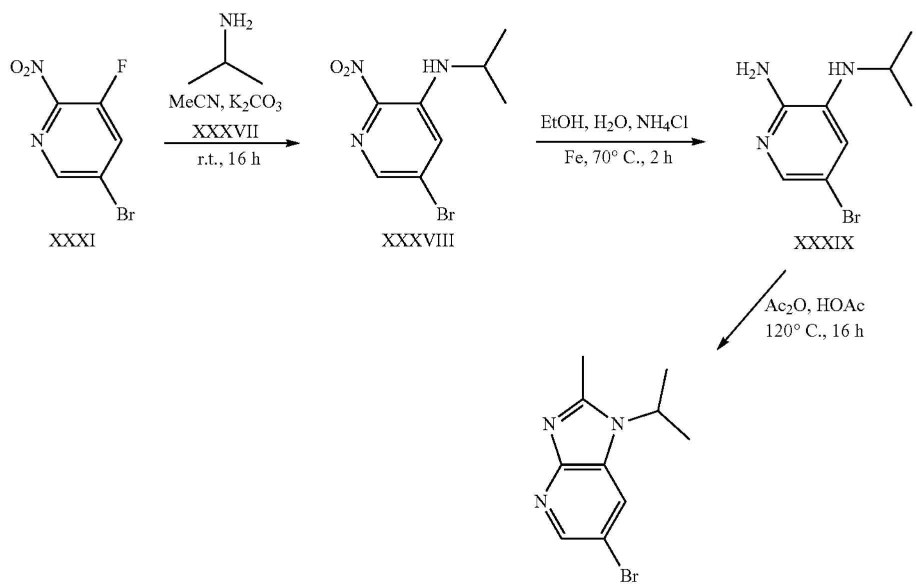
XXXVI



[0534] 6-Bromo-1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazole (XXXVI): Beige solid (970 mg, 3.526 mmol, 79.0% yield). ESIMS found $C_{10}H_9BrF_2N_2$ m/z 275.0 (M+H).

[0535] Preparation of intermediate 6-bromo-1-isopropyl-2-methyl-1H-imidazo[4,5-b]pyridine (XL) is depicted below in Scheme 7.

Scheme 7



Step 1

[0536] A mixture of 2-aminopropane (XXXVII) (0.86 mL, 9.96 mmol), 5-bromo-3-fluoro-2-nitropyridine (XXXI) (2 g, 9.05 mmol) and K_2CO_3 (2.5 g, 18.1 mmol) in MeCN (40 mL) was stirred at room temperature for 16 h. The reaction mixture was added to water (200 mL), stirred for 1 h and the resulting solids were collected by filtration and dried under high vacuo to obtain 5-bromo-N-isopropyl-2-nitropyridin-3-amine (XXXVIII) (2.36 g, 9.074 mmol, 100.3% yield) as a yellow solid which was used for next step without purification. ESIMS found for $C_8H_{10}BrN_3O_2$ m/z 260.0 (M+H).

Step 2

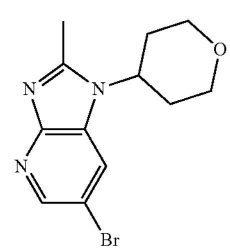
[0537] The mixture of 5-bromo-N-isopropyl-2-nitropyridin-3-amine (XXXVIII) (2.35 g, 9.04 mmol) Fe (5.91 g, 90.35 mmol) and NH_4Cl (7.25 g, 135.53 mmol) was taken in a mixture of EtOH (30 mL), and water (10 mL) and the mixture was heated to 70° C. for 2 h. The reaction mixture was cooled, filtered through Celite®, filtrates were taken into EtOAc, washed with water then brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to obtain 5-bromo-N^3-isopropylpyridine-2,3-diamine (XXXIX) (2.2 g, 9.561 mmol, 105.8% yield) as a dark brown solid which was used for next step without purification. ESIMS found for $C_8H_{12}BrN_3$ m/z 230.05 (M+H).

Step 3

[0538] A solution of 5-bromo-N^3-isopropylpyridine-2,3-diamine (XXXIX) (2.08 g, 9.04 mmol) and Ac_2O (1.05 mL, 10.84 mmol) in HOAc (20 mL) was heated to 120° C. for 16 h. The reaction mixture was concentrated, the residue partitioned between EtOAc/1 N NaOH, organics separated, washed with water and brine. The organics were dried over anhydrous Na_2SO_4, concentrated, and dried under high vacuo to give 6-bromo-1-isopropyl-2-methyl-1H-imidazo[4,5-b]pyridine (XL) (1.57 g, 6.178 mmol, 68.3% yield) as a dark brown solid which was used for next step without purification. ESIMS found for $C_{10}H_{12}BrN_3$ m/z 254.0 (M+H).

[0539] The following intermediate was prepared in accordance with the procedure described in the above Scheme 7.

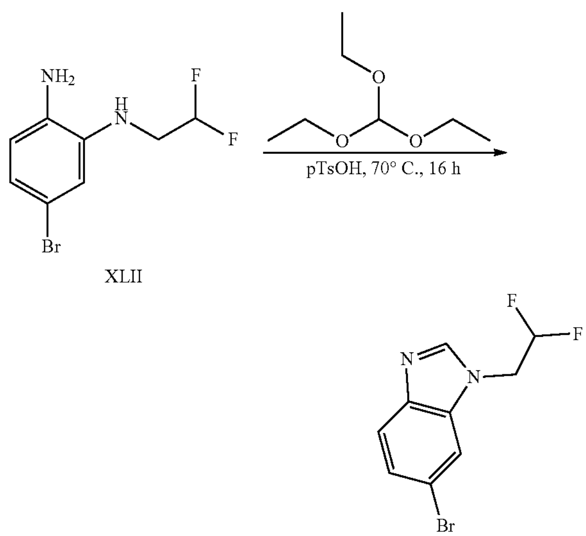
XLI



[0540] 6-Bromo-2-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-imidazo[4,5-b]pyridine (XLI): Grey solid (722 mg, 2.438 mmol, 66.3% yield). ESIMS found $C_{12}H_{14}BrN_3O$ m/z 296.0 (M+H).

[0541] Preparation of intermediate 6-bromo-1-(2,2-difluoroethyl)-1H-benzo[d]imidazole (XLIII) is depicted below in Scheme 8.

Scheme 8



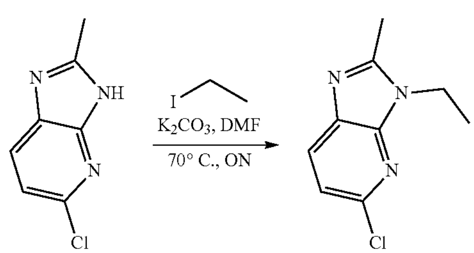
XLIII

Step 1

[0542] To a solution of 5-bromo-N1-(2,2-difluoroethyl) benzene-1,2-diamine (XLII) (3.0 g, 11.95 mmol) in triethoxymethane (60 mL) at room temperature was added p-toluenesulfonic acid (0.23 g, 1.20 mmol). The reaction mixture was stirred at 70° C. for 16 h, then cooled to room temperature. The reaction mixture was concentrated. The reaction mixture was diluted with water (200 mL) and extracted with EtOAc (2×300 mL). The organic layers were concentrated, dried over Na_2SO_4, filtered, and concentrated. The mixture was purified by reverse-phase column chromatography (Regular C18 20-40 um, acetonitrile/0.10% NH_4HCO_3 aqueous solution, gradient: 40%→60% MeCN) to afford 6-bromo-1-(2,2-difluoroethyl)-1H-benzo[d]imidazole (XLIII) (1.5 g, 5.746 mmol, 48.1% yield) as a yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ 8.26 (s 1H), 7.98 (d, J=1.6 Hz, 1H), 7.64 (d, J=8.4 Hz, 1H), 7.38 (dd, J=8.8, 2 Hz, 1H), 6.46 (tt, J=54.3, 3.0 Hz, 1H), 5.36 (td, J=16.4, 3.2 Hz, 2H); ESIMS found for $C_9H_7BrF_2N_2$ m/z 260.9 (M+H).

[0543] Preparation of intermediate 5-chloro-3-ethyl-2-methyl-3H-imidazo[4,5-b]pyridine (XLV) is depicted below in Scheme 9.

Scheme 9



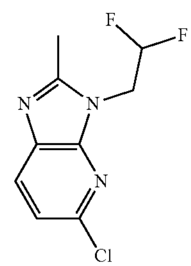
XLIV XLV

Step 1

[0544] A mixture of 5-chloro-2-methyl-3H-imidazo[4,5-b]pyridine (XLIV) (commercially available from eNovation Chemicals, LLC) (0.5 g, 2.98 mmol), iodoethane (0.56 g, 3.58 mmol) and K_2CO_3 (0.83 g, 5.97 mmol) in DMF (10 mL) was heated to 70° C. overnight. The reaction mixture was cooled, solvents concentrated, the residue partitioned between EtOAc/water, the organic layers were separated, washed with brine, dried over anhydrous $MgSO_4$ and the solvents were concentrated under vacuo and dried to obtain 5-chloro-3-ethyl-2-methylimidazo[4,5-b]pyridine (XLV) (466 mg, 2.382 mmol, 79.8% yield) as a dark brown solid which was used for next step without purification. ESIMS found for $C_9H_{10}ClN_3$ m/z 196.05 (M+H).

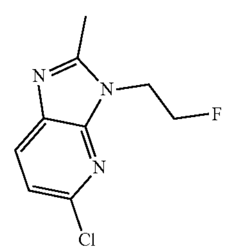
[0545] The following intermediates were prepared in accordance with the procedure described in the above Scheme 9.

XLVI



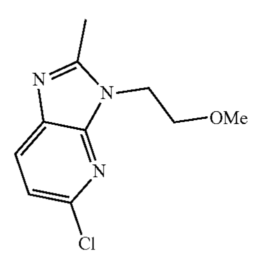
[0546] 5-Chloro-3-(2,2-difluoroethyl)-2-methyl-3H-imidazo[4,5-b]pyridine (XLVI): Beige solid (830 mg, 3.583 mmol, 60.1% yield). ESIMS found $C_9H_8ClF_2N_3$ m/z 232.0 (M+H).

XLVII



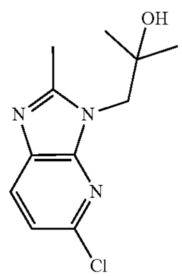
[0547] 5-Chloro-3-(2-fluoroethyl)-2-methyl-3H-imidazo [4,5-b]pyridine (XLVII): Beige solid (220 mg, 1.030 mmol, 57.5% yield). ESIMS found $C_9H_9ClFN_3$ m/z 214.05 (M+H).

XLVIII



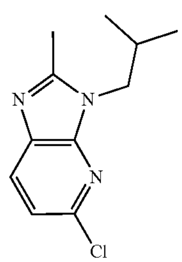
[0548] 5-Chloro-3-(2-methoxyethyl)-2-methyl-3H-imidazo[4,5-b]pyridine (XLVIII): Beige solid (195 mg,0.864 mmol, 48.3% yield). ESIMS found $C_{10}H_{12}C_1N_3O$ m/z 226.1 (M+H).

XLIX



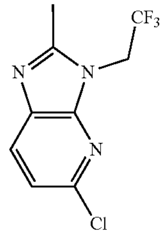
[0549] 1-(5-Chloro-2-methyl-3H-imidazo[4,5-b]pyridin-3-yl)-2-methylpropan-2-ol (XLIX): White solid (229.9 mg, 0.959 mmol, 39.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.13 (6H, s), 2.63 (3H, s), 4.11 (2H, s), 4.80 (1H, s), 7.25 (1H, d, J=8.21 Hz), 7.96 (1H, d, J=8.21 Hz); ESIMS found $C_{11}H_{14}ClN_3O$ m/z 240.1 (M+H).

L



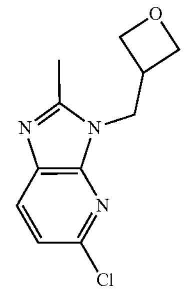
[0550] 5-Chloro-3-isobutyl-2-methyl-3H-imidazo[4,5-b]pyridine (L): White solid (206.8 mg, 0.925 mmol, 38.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.87 (6H, d, J=6.57 Hz), 2.22 (1 H, dquin, J=13.89, 7.07, 7.07, 7.07, 7.07 Hz), 2.58 (3 H, s), 4.01 (2H, d, J=7.67 Hz), 7.26 (1H, d, J=8.21 Hz), 7.98 (1 H, d J=8.21 Hz); ESIMS found $C_{11}H_{14}ClN_3$ m/z 224.1 (M+H).

LI



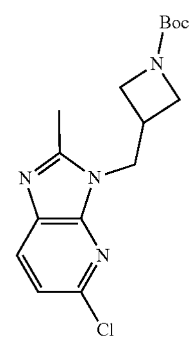
[0551] 5-Chloro-2-methyl-3-(2,2,2-trifluoroethyl)-3H-imidazo[4,5-b]pyridine (LI): Beige solid (372 mg, 1.490 mmol, 50.0% yield). ESIMS found $C_9H_7ClF_3N_3$ m/z 250.0 (M+H).

LII



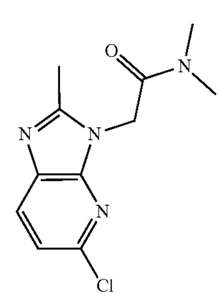
[0552] 5-Chloro-2-methyl-3-(oxetan-3-ylmethyl)-3H-imidazo[4,5-b]pyridine (LII): Light brown solid (289.7 mg, 1.219 mmol, 40.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.59 (3 H, s), 3.43-3.56 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.52 (2H, d, J=7.67 Hz), 4.62 (2H, dd, J=7.67, 6.02 Hz), 7.27 (1H, d, J=8.21 Hz), 7.98 (1H, d, J=8.21 Hz); ESIMS found $C_{11}H_{12}ClN_3O$ m/z 238.1 (M+H).

LIII



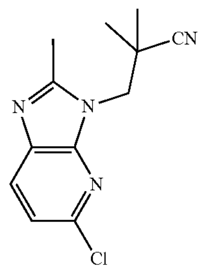
[0553] tert-Butyl 3-((5-chloro-2-methyl-3H-imidazo[4,5-b]pyridin-3-yl)methyl) azetidine-1-carboxylate (LIII): Off-white amorphous solid (532.6 mg, 1.581 mmol, 52.1% yield). ESIMS found $C_{16}H_{21}ClN_4O_2$ m/z 337.1 (M+H).

LIV



[0554] 2-(5-Chloro-2-methyl-3H-imidazo[4,5-b]pyridin-3-yl)-N,N-dimethylacetamide (LIV): Off-white solid (474.4 mg, 1.877 mmol, 62.6% yield). ESIMS found $C_{12}H_{13}ClN_4O$ m/z 253.1 (M+H).

LV



[0555] 3-(5-Chloro-2-methyl-3H-imidazo[4,5-b]pyridin-3-yl)-2,2-dimethylpropanenitrile (LV): Off-white amorphous solid (59.1 mg, 0.238 mmol, 7.9% yield). ESIMS found $C_{12}H_{13}C_1N_4$ m/z 249.1 (M+H).

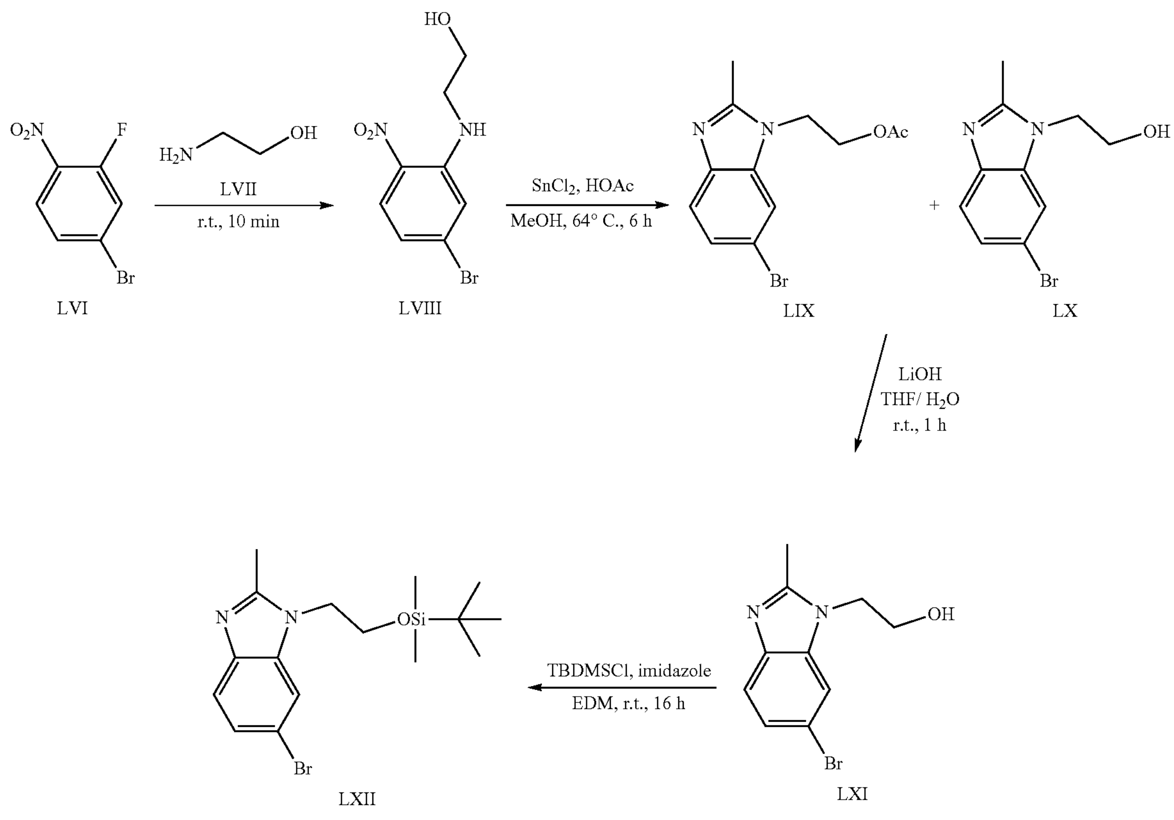
[0556] Preparation of intermediate 6-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-methyl-1H-benzo[d]imidazole (LXII) is depicted below in Scheme 10.

(LVIII) (2.349 g, 8.998 mmol, 99.0% yield) as a yellow solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 3.41 (2 H, q, J=5.48 Hz), 3.63 (2 H, q, J=5.48 Hz), 5.00 (1H, t, J=5.34 Hz), 6.83 (1H, dd, J=9.17, 2.05 Hz), 7.30 (1H, d, J=1.92 Hz), 7.98 (1H, d, J=9.03 Hz), 8.29 (1 H, br t, J=5.06 Hz); ESIMS found for $C_8H_9BrN_2O_3$ m/z 260.96 (M+H).

Step 2

[0558] To a solution of 2-((5-bromo-2-nitrophenyl)amino)ethan-1-ol (LVIII) (1.31 g, 5.02 mmol) in MeOH (50 mL) was added tin(II) chloride (0.96 mL, 20.09 mmol) at room temperature. The reaction mixture was heated to 64° C. for 6 h, then cooled to room temperature. The solvent was removed under vacuum, and the residue was dissolved in water and basified by addition of Na_2CO_3 to pH=9. The mixture was extracted with DCM, and the combined organic phase was washed with water, brine, and dried over anhydrous Na_2SO_4. The solvent was removed under vacuum before adding HOAc (15.6 mL, 271.49 mmol). The solution

Scheme 10



Step 1

[0557] A solution of 4-bromo-2-fluoro-1-nitrobenzene (LVI) (2.0 g, 9.09 mmol) dissolved in 2-aminoethanol (LVII) (2.8 mL, 46.39 mmol) was stirred at room temperature for 10 min. Water (50 mL) was added and extracted with EtOAc and dried onto Celite®. The residue was purified by silica gel column chromatography (0->100% EtOAc/hexanes) to produce 2-((5-bromo-2-nitrophenyl)amino)ethan-1-ol

was heated to reflux for 30 min. The acetic acid was removed under reduced pressure and the residue was purified using silica gel column chromatography (0->50% 7 N NH_3 in MeOH/$CHCl_3$) to produce 2-(6-bromo-2-methyl-1H-benzo[d]imidazol-1-yl)ethyl acetate (LIX) and 2-(6-bromo-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol (LX) (1.45 g, 4.880 mmol, 97.2% yield), as an 80/20 mixture as an off-white solid. ESIMS found for $C_{12}H_{13}BrN_2O_2$ m/z 297.0 (M+H).

Step 3

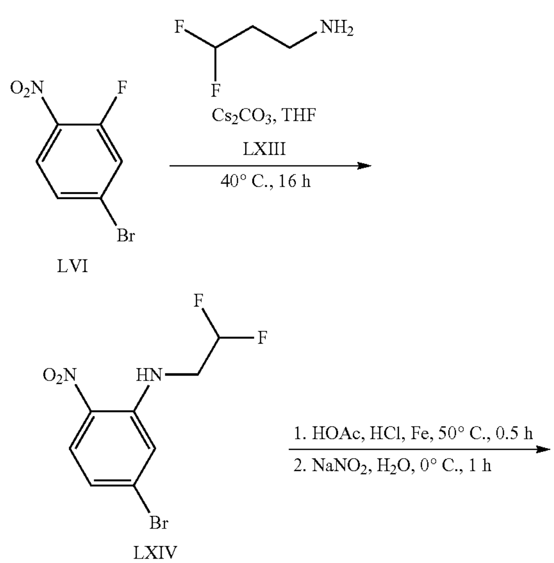
[0559] To a solution of LiOH (3.2 mL, 9.6 mmol) in THF (27 mL)/water (6 mL) was added a mixture of 2-(6-bromo-2-methyl-1H-benzo[d]imidazol-1-yl)ethyl acetate (LIX) and 2-(6-bromo-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol (LX) (1.45 g, 4.88 mmol). The reaction was stirred at room temperature for 1 h. The solution was neutralized with 1 N HCl and stripped onto Celite®, then purified using silica gel column chromatography (0→10% 7 N NH_3 in MeOH/$CHCl_3$) to produce 2-(6-bromo-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol (LXI) (1.02 g, 3.998 mmol, 81.9% yield) as a white solid. ESIMS found for $C_{10}H_{11}BrN_2O$ m/z 255.0 (M+H).

Step 4

[0560] 2-(6-Bromo-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol (LXI) (1.02 g, 4. mmol) was dissolved in DCM (8 mL) under a N_2 atmosphere. Imidazole (0.55 g, 8.1 mmol) and TBDMSCl (0.9 mL, 4.84 mmol) were then added. The reaction mixture was stirred at room temperature for 16 h. The solution was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$ (400 mL). The aqueous layer was back-extracted twice with EtOAc, the organic layer was stripped onto Celite®, then purified using silica gel column chromatography (0→5% MeOH/$CHCl_3$) to produce 6-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-methyl-1H-benzo[d]imidazole (LXII) (1.44 g, 3.899 mmol, 97.5% yield) as a white solid. ESIMS found for $C_{16}H_{25}BrN_2OSi$ m/z 369.1 (M+H).

[0561] Preparation of intermediate 6-bromo-1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazole (LXV) is depicted below in Scheme 11.

Scheme 11



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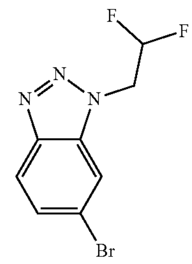


[0562] Step 1

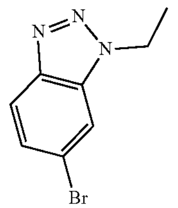
[0563] A solution of 4-bromo-2-fluoro-1-nitrobenzene (LVI) (20.0 g, 98.03 mmol) in THF (500.0 mL) was cooled to 0° C. Cs_2CO_3 (63.9 g, 196.06 mmol) was added, 2,2-difluoroethan-1-amine (LXIII) (36.6 g, 183.81 mmol) was added at 0° C. The reaction was warmed to 40° C. for 16 h. The reaction mixture was extracted with EtOAc (500 L x 3). The combined organics were washed with brine (500 mL×3). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give the crude product. The crude was purified by column chromatography on silica gel (10% EtOAc/PE →20% EtOAc/PE) to give 5-bromo-N-(2,2-difluoroethyl)-2-nitroaniline (LXIV) (23 g, 81.83 mmol, 83.5% yield) as a yellow solid. ^1H NMR (400 MHz, DMSO-d_6) δ 3.99 (tdd, J=15.6, 6.6, 3.8 Hz, 2H), 6.29 (tt, J=55.4, 3.7 Hz, 1H), 6.96 (dd, J=9.2, 2.0 Hz, 1H), 7.51 (d, J=1.6 Hz, 1H), 8.05 (d, J=9.2 Hz, 1H), 8.33 (t, J=6.4 Hz, 1H); ESIMS found for $C_8H_7BrF_2N_2O_2$ m/z 280.9 (M+H).

Step 2

[0564] To a solution of 5-bromo-N-(2,2-difluoroethyl)-2-nitroaniline (LXIV) (12.0 g, 42.86 mmol) in HOAc/HCl (500/50 mL) was added Fe (30.0 g, 428.62 mmol). The reaction mixture was stirred at 50° C. for 30 minutes, then cooled to room temperature and filtered. $NaNO_2$ (3.0 g, 53.58 mmol) in water (20 mL) was then added dropwise into the above acid solution at 0° C. The reaction solution was stirred for 1 h at 0° C. The reaction mixture was concentrated to dryness, the reaction mixture was poured into EtOAc (300 mL) and H_2O (300 mL). The pH was adjusted >7 with $NaHCO_3$. The reaction mixture was extracted with EtOAc (500 mL×3). The combined organics were washed with brine (500 mL×3). The organic layers was concentrated, dried over Na_2SO_4, filtered, and concentrated to give the crude. The crude was purified by column chromatography on silica gel (10% EtOAc/PE->50% EtOAc/PE) to give 6-bromo-1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazole (LXV) (5 g, 19.08 mmol, 44.5%) as a brown solid. ^1H NMR (400 MHz, DMSO-d_6) δ 5.41-5.29 (m, 2H), 6.61 (tt, J=54.2, 3.2 Hz, 1H), 7.60 (dd, J=8.8, 1.7 Hz, 1H), 8.08 (d, J=8.8 Hz, 1H), 8.31 (d, J=1.0 Hz, 1H); ESIMS found for $C_8H_6BrF_2N_3$ m/z 261.9 (M+H).

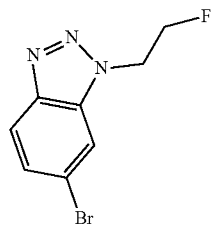
[0565] The following intermediates were prepared in accordance with the procedure described in the above Scheme 11.

LXVI



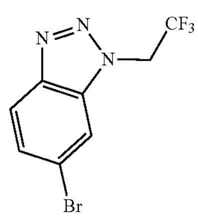
[0566] 6-Bromo-1-ethyl-1H-benzo[d][1,2,3]triazole (LXVI): White solid (4.112 g, 18.188 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.30 (d, J=1.6 Hz, 1H), 8.00 (dd, J=8.8, 3.2 Hz, 1H), 7.54 (dd, J=8.8, 3.2 Hz, 1H), 4.74 (q, J=7.2 Hz, 2H), 1.51 (t, J=7.2 Hz, 3H); ESIMS found for $C_8H_8BrN_3$ m/z 225.9 (M+H).

LXVII



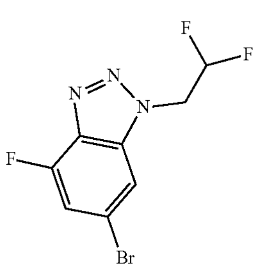
[0567] 6-Bromo-1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazole (LXVII): White solid (4.163 g, 17.057 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (s 1H), 8.05 (d, J=8.4 Hz, 1H), 7.57 (dd, J=8.4, 1.6 Hz, 1H), 5.11 (dt, J=28, 4 Hz, 2H), 4.92 (dt, J=48, 4 Hz, 2H); ESIMS found for $C_8H_7BrFN_3$ m/z 244.0 (M+H).

LXVIII



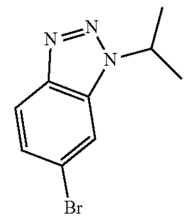
[0568] 6-Bromo-1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazole (LXVIII): White solid (5.05 g, 18.032 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (s 1H), 8.11 (d, J=8.8 Hz, 1H), 7.63 (dd, J=8.4, 1.6 Hz, 1H), 5.90 (q, J=9.2 Hz, 2H); ESIMS found for $C_8H_5BrF_3N_3$ m/z 280.0 (M+H).

LXIX



[0569] 6-Bromo-1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazole (LXIX): White solid (4.112 g, 14.683 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.19 (s 1H), 7.61 (d, J=10.0 Hz, 1H), 6.60 (tt, J=54.3, 3.0 Hz, 1H), 5.36 (td, J=15.81, 2.87 Hz, 2H); ESIMS found for $C_8H_5BrF_3N_3$ m/z 280.0 (M+H).

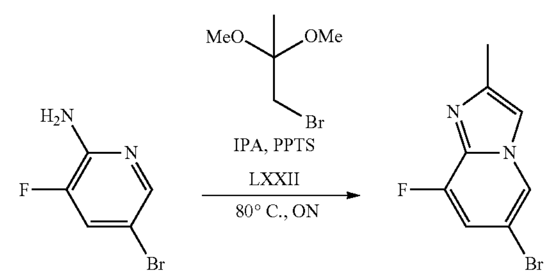
LXX



[0570] 6-Bromo-1-isopropyl-1H-benzo[d][1,2,3]triazole (LXX): White solid (10.58 g, 44.065 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.32 (d, J=1.2 Hz, 1H), 8.03 (d, J=9.2 Hz, 1H), 7.54 (dd, J=8.4, 1.6 Hz, 1H), 5.26 (sep, J=6.8 Hz, 1H), 5.26 (d, J=6.8 Hz, 6H); ESIMS found for $C_9H_{10}BrN_3$ m/z 240.1 (M+H).

[0571] Preparation of intermediate 6-bromo-8-fluoro-2-methylimidazo[1,2-a]pyridine (LXXIII) is depicted below in Scheme 12.

Scheme 12



LXXI

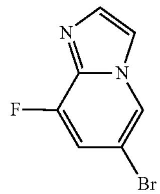
LXXIII

Step 1

[0572] A mixture of 5-bromo-3-fluoropyridin-2-amine (LXXI) (2 g, 10.47 mmol), 1-bromo-2,2-dimethoxypropane (LXXII) (2.11 g, 11.53 mmol) and PPTS (260 mg, 1.05 mmol) in IPA (25 mL) was heated to 80° C. overnight. The reaction mixture was cooled to room temperature, added to water (200 mL) and stirred for 1 h. The resulting solids were collected and dried under high vacuo to obtain 6-bromo-8-fluoro-2-methylimidazo[1,2-a]pyridine (LXXIII) (2.61 g, 11.40 mmol, 108.8% yield) as beige solid which was used for the next step without further purification. ESIMS found for $C_8H_6BrFN_2$ m/z 229.0 (M+H).

[0573] The following intermediate was prepared in accordance with the procedure described in the above Scheme 12.

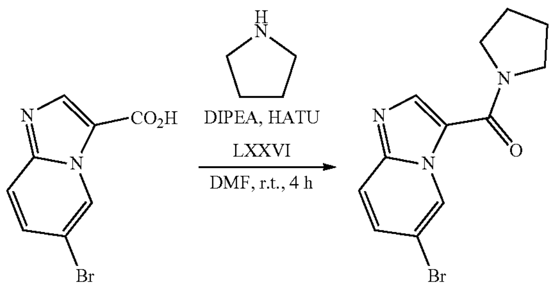
LXXIV



[0574] 6-Bromo-8-fluoroimidazo[1,2-a]pyridine (LXXIV): Beige solid (909.0 mg, 4.228 mmol, 80.7% yield). ESIMS found for $C_7H4BrFN_2$ m/z 214.9 (M+H).

[0575] Preparation of intermediate (6-bromoimidazo[1,2-a]pyridin-3-yl)(pyrrolidin-1-yl)methanone (LXXVII) is depicted below in Scheme 13.

Scheme 13



LXXV

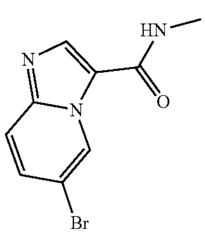
LXXVII

Step 1

[0576] A mixture of 6-bromoimidazo[1,2-a]pyridine-3-carboxylic acid (LXXV) (0.5 g, 2.07 mmol), DIPEA (0.9 mL, 5.17 mmol) and HATU (0.79 g, 2.07 mmol) in DMF (4 mL) was stirred for 5 min. Pyrrolidine (LXXVI) (0.32 mL, 3.18 mmol) was then added, and the reaction mixture was continued to stir at room temperature for 4 h. The solvent were concentrated, the residue partitioned between EtOAc and saturated aqueous $NaHCO_3$, the organic layer was separated, washed with water and brine. The organic layer was dried over anhydrous Na_2SO_4, concentrated and dried under high vacuo to obtain (6-bromoimidazo[1,2-a]pyridin-3-yl)-pyrrolidin-1-ylmethanone (LXXVII) (577 mg, 1.962 mmol, 94.6% yield) as a beige solid. ESIMS found for $C_{12}H_{12}BrN_3O$ m/z 294.0 (M+H).

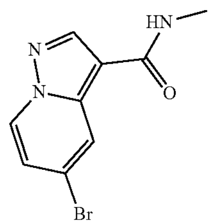
[0577] The following intermediates were prepared in accordance with the procedure described in the above Scheme 13.

LXXVIII



[0578] 6-Bromo-N-methylimidazo[1,2-a]pyridine-3-carboxamide (LXXVIII): Off-white solid (530 mg, 2.086 mmol, 83.8% yield). ESIMS found for C_9HsBrN_3O m/z 254.0 (M+H).

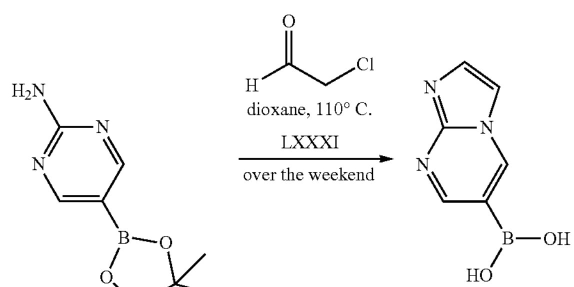
LXXIX



[0579] 5-Bromo-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide (LXXIX): Off-white solid (290 mg, 1.141 mmol, 91.7% yield). ESIMS found for C_9HsBrN_3O m/z 253.95 (M+H).

[0580] Preparation of intermediate imidazo[1,2-a]pyrimidin-6-ylboronic acid (LXXXII) is depicted below in Scheme 14.

Scheme 14



LXXXII

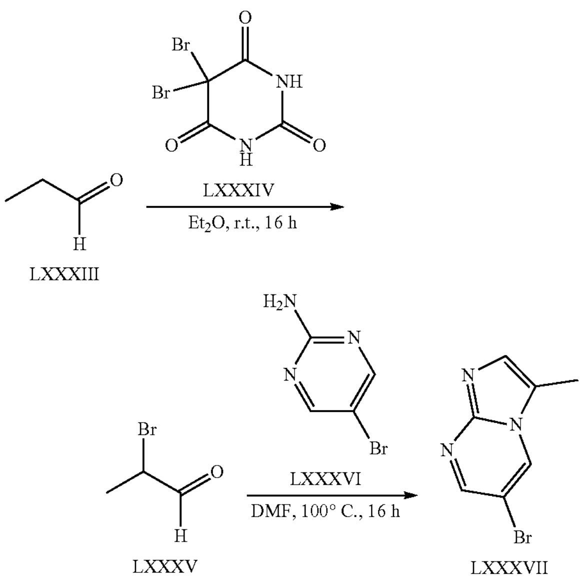
LXXX

Step 1

[0581] A mixture of 5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyrimidin-2-amine (LXXX) (1 g, 4.52 mmol) and chloroacetaldehyde (LXXXI) (0.92 mL, 5.39 mmol) was dissolved in 1,4-dioxane (20 mL) and heated to 110° C. over the weekend. The reaction mixture was cooled, and the solids were collected by filtration and dried under high vacuo to obtain imidazo[1,2-a]pyrimidin-6-ylboronic acid (LXXXII) (650 mg, 3.989 mmol, 88.2% yield) as a brown solid which was used for next step without purification. ESIMS found for $C_6H_6BN_3O_2$ m/z 164.1 (M+H).

[0582] Preparation of intermediate 6-bromo-3-methylimidazo[1,2-a]pyrimidine (LXXXVII) is depicted below in Scheme 15.

Scheme 15



Step 1

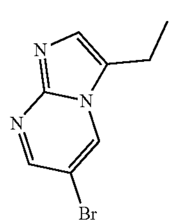
[0583] To a mixture of propionaldehyde (LXXXIII) (5 g, 70 mmol) in Et_2O (150 mL) was added 5,5-dibromopyrimidine-2,4,6(1H,3H,5H)-trione (LXXXIV) (9.91 g, 35 mmol) and the resulting mixture was stirred at room temperature for 16 h. After completion, the mixture was washed by petroleum ether (80 mL×2). The organic layer was filtered and concentrated to give 2-bromopropanal (LXXXV) (2.0 g, 14.6 mmol, 20.9% yield) as a yellow oil.

Step 2

[0584] To a solution of 2-bromopropanal (LXXXV) (0.7 g, 5.11 mol) in DMF (20 mL) was added 5-bromopyrimidin-2-amine (LXXXVI) (0.97 g, 5.56 mmol) at room temperature under Ar. The mixture was stirred at 100° C. for 16 h. After completion, the mixture was diluted with EtOAc and washed with brine (20 mL×3). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue was purified by silica gel column chromatography (0%→20% EtOAc/petroleum ether) to give 6-bromo-3-methylimidazo[1,2-a]pyrimidine (LXXXVII) (80 mg, 0.377 mmol, 7.4% yield) as a white solid. ESIMS found for $C_7H_6BrN_3$ m/z 212.1 (M+H).

[0585] The following intermediate was prepared in accordance with the procedure described in the above Scheme 15.

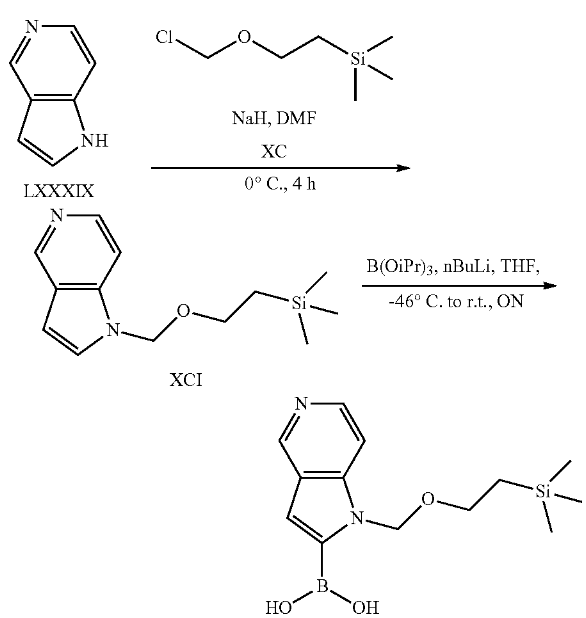
LXXXVIII



[0586] 6-Bromo-3-ethylimidazo[1,2-a]pyrimidine (LXXXVIII): White solid (200 mg, 0.885 mmol, 19.1% yield). ESIMS found $C_8H_8BrN_3$ m/z 226.0 (M+H).

[0587] Preparation of intermediate (1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-c]pyridin-2-yl)boronic acid (XCII) is depicted below in Scheme 16.

Scheme 16



XCII

Step 1

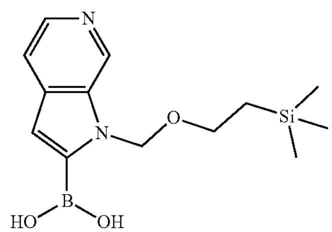
[0588] To a solution of 5-azaindole (LXXXIX) (commercially available from Combi-Blocks Inc.) (2.0 g, 16.93 mmol) in DMF (20 mL) under N_2 was added NaH (0.81 g, 20.18 mmol). The mixture was stirred at 0° C. for 1 h. (2-(Chloromethoxy)ethyl)trimethylsilane (XC) (commercially available from Combi-Blocks Inc.) (3.6 mL, 20.34 mmol) was then added and the mixture was stirred at 0° C. for 4 h. After concentrating in vacuo to remove DMF, ice cold saturated aqueous NH_3Cl was added, and the mixture was extracted with EtOAc. The organic layer was washed with water, brine, and the solvent was concentrated onto Celite® under vacuum. The crude product was purified using column chromatography (0→100% EtOAc/hexanes) to produce 1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-c]pyridine (XCI) (2.32 g, 9.340 mmol, 55.2% yield) as an amber liquid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm -0.11 (9 H, s), 0.75-0.84 (2H, m), 3.40-3.48 (2H, m), 5.58 (2 H, s), 6.64 (1H, dd, J=3.29, 0.82 Hz), 7.55-7.60 (2H, m), 8.23 (1H, d, J=5.75 Hz), 8.84 (1H, d, J=0.82 Hz); ESIMS found for $Cl_3H_{20}N_2OSi$ m/z 249.1 (M+H).

Step 2

[0589] A hexane solution of n-butyllithium (1.21 mL, 3.02 mmol) was added slowly to a solution of 1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-c]pyridine (XCI) (0.5 g, 2.01 mmol) in dry THF (4.0 mL) at −78° C. under N_2. The mixture was stirred at −46° C. for 2 h. Triisopropyl borate (0.93 mL, 4.03 mmol) was added, and the mixture was stirred overnight warming to room temperature. The reaction mixture was quenched with 1 M aqueous HCl and neutralized to pH 8 with 4 N NaOH. The solvent was evaporated onto Celite® and purified by reverse phase (C18) silica gel column chromatography (0→40% MeCN/water (0.1% formic acid as modifier)). LC/MS shows a mixture (40/60) of starting material and [1-(2-trimethylsilylethoxymethyl)pyrrolo[3,2-c]pyridin-2-yl]boronic acid (XCII) (200 mg, 0.684 mmol, 34.0% yield) as an off-white solid. The mixture was used as is without further purification. ESIMS found for $C_{13}H_{21}BN_2O_3Si$ m/z 293.1 (M+H).

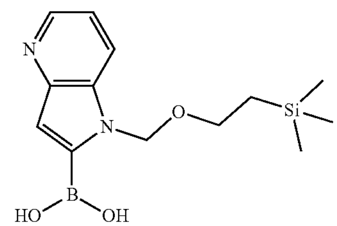
[0590] The following intermediates were prepared in accordance with the procedure described in the above Scheme 16.

XCIII



[0591] (1-((2-(Trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[2,3-c]pyridin-2-yl)boronic acid (XCIII): Tan solid (796 mg, 2.861 mmol, 71.1% yield). ESIMS found $C_{13}H_{21}BN_2O_3Si$ m/z 293.15 (M+H).

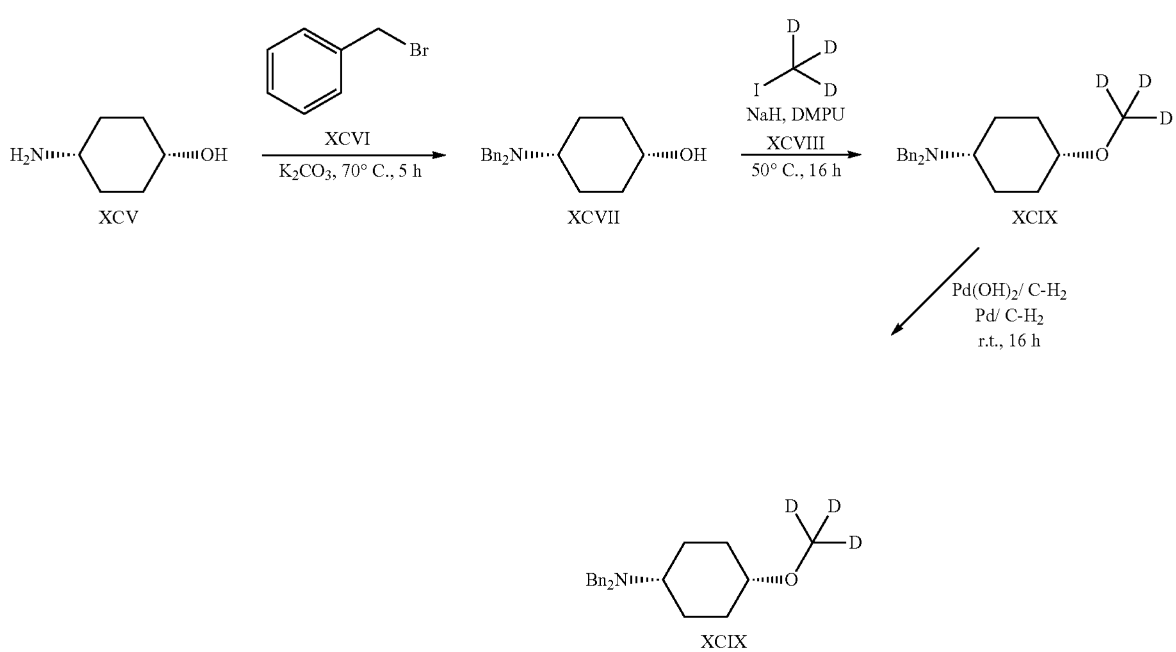
XCIV



[0592] (1-((2-(Trimethylsilyl)ethoxy)methyl)-1H-pyrrolo[3,2-b]pyridin-2-yl)boronic acid (XCIV): Tan solid (831 mg, 2.844 mmol, 70.6% yield). ESIMS found $C_{13}H_{21}BN_2O_3Si$ m/z 293.1 (M+H).

[0593] Preparation of intermediate cis-4-(methoxy-d_3)cyclohexan-1-amine (C) is depicted below in Scheme 17.

Scheme 17



Step 1

[0594] To a solution of cis-4-aminocyclohexan-1-ol (XCV) (5 g, 32.9 mmol), (bromomethyl)benzene (XCVI) (11.25 g, 65.8 mmol) in MeCN (80 mL) was added K_2CO_3 (13.64 g, 98.7 mmol). The mixture was stirred at 70° C. for 5 h. The reaction mixture was concentrated under reduced pressure to remove MeCN. The mixture was diluted with EtOAc and then extracted with EtOAc (100 mL×3) and H_2O. The combined organic layers were concentrated, and the crude residue was purified by silica gel column chromatography (0%→30% EtOAc/PE) to give the cis-4-(dibenzylamino)cyclohexan-1-ol (XCVII) (8.0 g, 27.08 mmol, 82.3% yield) as a white solid. ESIMS found for $C_{20}H_{25}NO$ m/z 296.4 (M+H).

Step 2

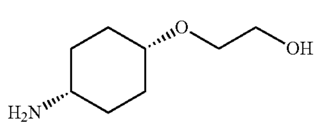
[0595] To a solution of cis-4-(dibenzylamino)cyclohexan-1-ol (XCVII) (8.0 g, 27.08 mmol) in DMPU (80 mL) was added slowly NaH (5.98 g, 149.7 mmol) under nitrogen atmosphere with continuous stirring. The reaction mixture was stirred at room temperature for 1 h. Then iodomethane-d_3 (XCVIII) (10.85 g, 74.86 mmol) was added at room temperature over a period of 10 min. After complete addition, the reaction mixture was stirred for 16 h at 50° C. The reaction mixture was then quenched with saturated aqueous NH_4Cl (300 mL) and stirred for 10 min. The mixture was diluted with EtOAc and then extracted with EtOAc (300 mL×3) and H_2O. The crude residue was purified by silica gel column chromatography (0%->20% EtOAc/PE) to yield cis-N,N-dibenzyl-4-(methoxy-d_3)cyclohexan-1-amine (XCIX) (6 g, 19.202 mmol, 70.9% yield) as a colorless oil. ESIMS found for $C_{21}H_{24}D_3NO$ m/z 313.0 (M+H).

Step 3

[0596] To a solution of cis-N,N-dibenzyl-4-(methoxy-d_3)cyclohexan-1-amine (XCIX) (200 mg, 0.64 mmol) in EtOH (5 mL) was added $Pd(OH)_2/C$ (50 mg) and Pd/C (50 mg). The mixture was stirred at room temperature for 16 h. The mixture was filtered through Celite® and washed with EtOH. The reaction mixture was concentrated under reduced pressure to give the cis-4-(methoxy-d_3)cyclohexan-1-amine (C) (76.4 mg, 0.578 mmol, 90.3% yield) as a colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.51-1.40 (m, 4H), 1.67-1.56 (m, 4H), 1.86 (td, J=9.8, 4.6 Hz, 2H), 2.71 (tt, J=10.8, 5.4 Hz, 1H), 3.34 (td, J=4.8, 2.4 Hz, 1H); ESIMS found for $C_7H_{12}D_3NO$ m/z 133.0 (M+H).

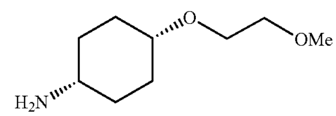
[0597] The following intermediates were prepared in accordance with the procedure described in the above Scheme 17.

CI



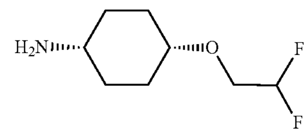
[0598] 2-((cis-4-Aminocyclohexyl)oxy)ethan-1-ol (CI): Colorless oil (0.5 g, 3.14 mmol, 67.4% yield). ESIMS found for $C_8H_{17}NO_2$ m/z 160. (M+H).

CII



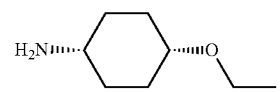
[0599] cis-4-(2-Methoxyethoxy)cyclohexan-1-amine (CII): Colorless oil (1.5 g, 8.65 mmol, 76.6% yield). ESIMS found for $C_9H_{19}NO_2$ m/z 174.1 (M+H).

CIII



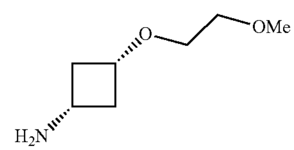
[0600] cis-4-(2,2-Difluoroethoxy)cyclohexan-1-amine (CIII): White solid (1.352 g, 7.54 mmol, 90.3% yield). ESIMS found for $C_8H_{15}F_2NO$ m/z 180.1 (M+H).

CIV



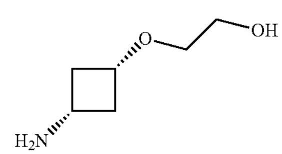
[0601] cis-4-Ethoxycyclohexan-1-amine (CIV): Colorless oil (2 g, 13.96 mmol, 64.4% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, J=7.0 Hz, 3H), 1.49-1.44 (m, 6H), 1.62-1.55 (m, 2H), 1.86-1.79 (m, 2H), 2.4-2.723 (m, 1H), 3.49-3.41 (m, 3H).

CV



[0602] cis-3-(2-Methoxyethoxy)cyclobutan-1-amine (CV): Colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.51 (dd, J=13.4, 5.2 Hz, 2H), 2.49-2.40 (m, 2H), 2.89-2.75 (m, 1H), 3.23 (s, 3H), 3.37-3.35 (m, 3H), 3.47 (s, 2H), 3.54-3.48 (m, 1H).

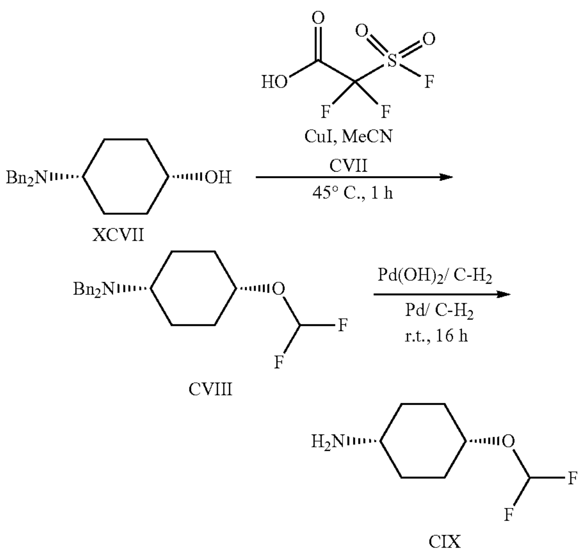
CVI



[0603] 2-(cis-3-Aminocyclobutoxy)ethan-1-ol (CVI): Colorless oil. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.79-1.72 (m, 2H), 2.50-2.45 (m, 2H), 3.08-2.97 (m, 1H), 3.29 (t, J=5.4 Hz, 2H), 3.46 (t, J=5.4 Hz, 2H), 3.73-3.57 (m, 1H).

[0604] Preparation of intermediate cis-4-(difluoromethoxy)cyclohexan-1-amine (CIX) is depicted below in Scheme 18.

Scheme 18



Step 1

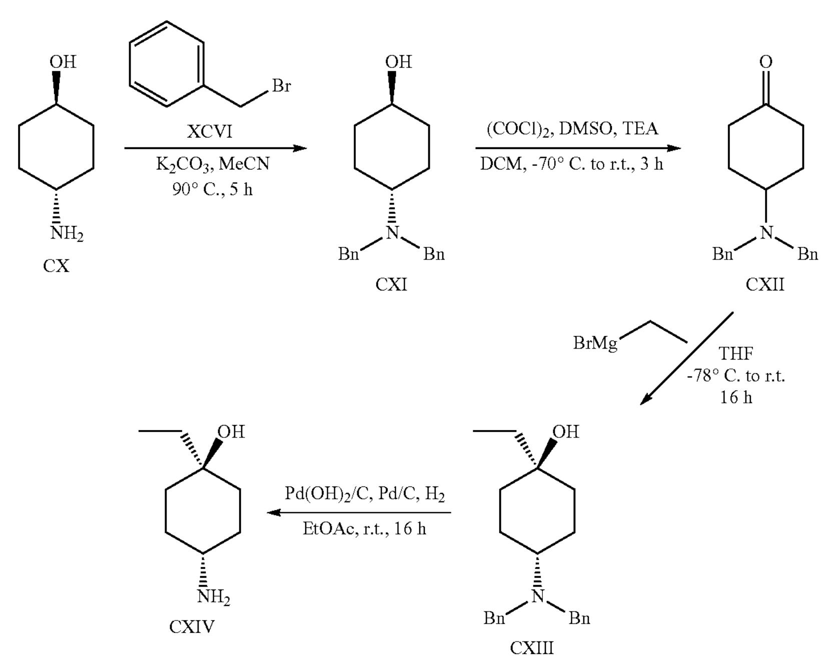
[0605] A solution of cis-4-(dibenzylamino)cyclohexan-1-ol (XCVII) (50 mg, 0.170 mmol), CuI (6.5 mg, 0.034 mmol) in MeCN (5 mL) was heated to 45° C. under nitrogen atmosphere for 5 min. To this mixture was added a solution of 2,2-difluoro-2-(fluorosulfonyl)acetic acid (CVII) (60 mg, 0.339 mmol) in (2 mL) MeCN over 10 min. Then the mixture was stirred at 45° C. for 1 h. Volatile components were then removed via evaporation and the residue was diluted with EtOAc (100 mL) and 100 mL of a 1:1 mixture of water and saturated aqueous $NaHCO_3$. The resulting biphasic mixture containing solids was filtered through a sintered glass Buchner funnel. The filtrate layers were separated, and the aqueous layer was extracted with EtOAc (50 mL). The combined EtOAc layers were washed with 50 mL of a 1:1 mixture of brine and water, dried over anhydrous $MgSO_4$, filtered, and concentrated to an oil. The crude oil was purified by silica gel chromatography (100% hexanes →30% EtOAc/hexanes). Product containing fractions were combined and concentrated to afford the cis-N,N-dibenzyl-4-(difluoromethoxy)cyclohexan-1-amine (CVIII) (25 mg, 0.072 mmol, 42.3% yield) as an oil that solidified to an off-white solid. ESIMS found for $C_{21}H_{25}F_2NO$ m/z 346.1 (M+H).

[0606] Step 2

[0607] To a solution of cis-N,N-dibenzyl-4-(difluoromethoxy)cyclohexan-1-amine (CVIII) (2.8 g, 8.11 mmol) in THF (60 mL) was added Pd $(OH)_2$/C(1.4 g) and Pd/C (1.4 g). The mixture was stirred at room temperature for 16 h. The mixture was filtered through Celite® and washed with THF. The reaction mixture was concentrated under reduced pressure to afford cis-4-(difluoromethoxy)cyclohexan-1-amine (CIX) (1.05 g, 6.36 mmol, 78.4% yield) as a colorless oil. ESIMS found for $C_7H_{13}F_2NO$ m/z 166.1 (M+H).

[0608] Preparation of intermediate trans-4-amino-1-ethylcyclohexan-1-ol (CXIV) is depicted below in Scheme 19.

Scheme 19



Step 1

[0609] To a solution of trans-4-aminocyclohexan-1-ol (CX) (25 g, 0.217 mmol) and benzyl bromide (XCVI) (74.2 g, 0.434 mmol) in MeCN (500 mL) was added K_2CO_3 (90 g, 0.6512 mmol). The mixture was stirred at 90° C. for 5 h. The reaction mixture was concentrated under reduced pressure to remove MeCN. The mixture was diluted with EtOAc and then extracted with EtOAc (100 mL×3) and H_2O. The organic layers were dried over anhydrous Na_2SO_4 and evaporated under high vacuum to produce trans-4-(dibenzylamino)cyclohexan-1-ol (CXI) (32 g, 108.3 mmol, 49.9% yield) as a white solid. The product was directly used in the next step without further purification. ESIMS found for $C_{20}H_{25}NO$ m/z 296.3 (M+H).

Step 2

[0610] To a solution of $(COCl)_2$ (12.89 g, 101.55 mmol) in DCM (150 mL) at −70° C. under N_2 was slowly added DMSO (10.6 g, 135.4 mmol) in DCM (50 mL). trans-4-(dibenzylamino)cyclohexan-1-ol (CXI) (20.0 g, 67.7 mmol) in DMF (50 mL) was added at −70° C. under N_2 and stirred for 30 min. TEA (21.92 g, 216.64 mmol) was then added and the mixture was stirred at −70° C. warming to room temperature over 3 h. The reaction mixture was diluted with H_2O (800 mL) and extracted with DCM (800 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated to give a residue. The residue was purified by column chromatography on silica gel (9->25% EtOAc/PE) to afford 4-(dibenzylamino)cyclohexan-1-one (CXII) (18.0 g, 61.3 mmol, 90.6% yield) as a white solid. ESIMS found for $C_{20}H_{23}NO$ m/z 294.2 (M+H).

Step 3

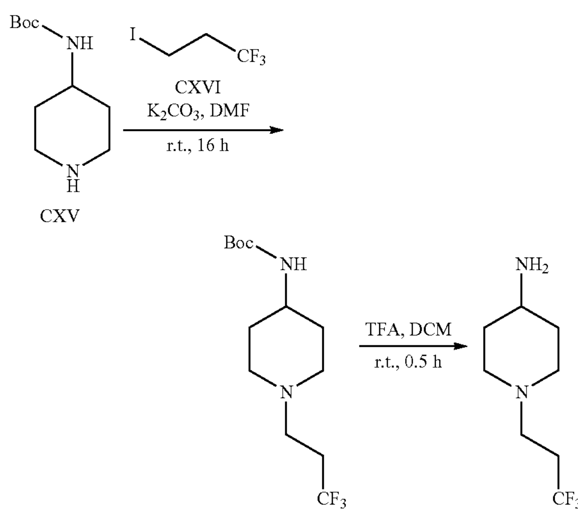
[0611] 4-(Dibenzylamino)cyclohexan-1-one (CXII) (5.0 g, 17.04 mmol) was added to THF (50 mL) at −78° C. under N_2 and stirred for 1 h. Ethylmagnesium bromide (17 mL, 34.08 mmol,) was added and the reaction was stirred at −78° C. warming to room temperature over 16 h. The reaction mixture was diluted with NH_4Cl (100 mL), filtered, and extracted with EtOAc (200 mL×3 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under high vacuum to give a residue. LC/MS showed two products. The residue was purified by column chromatography on silica gel (2->3% EtOAc/PE) to afford only the trans-4-(dibenzylamino)-1-ethylcyclohexan-1-ol (CXIII) (1.5 g, 4.637 mmol, 27.2% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.80 (t, J=7.4 Hz, 3H), 1.17-1.10 (m, 2H), 1.47-1.37 (m, 4H), 1.65 (t, J=11.4 Hz, 4H), 2.41 (s, 1H), 3.57 (s, 4H), 3.91 (s, 1H), 7.21-7.17 (m, 2H), 7.34-7.27 (m, 8H); ESIMS found for $C_{22}H_{29}NO$ m/z 324.2 (M+H).

Step 4

[0612] To a solution of trans-4-(dibenzylamino)-1-ethylcyclohexan-1-ol (CXIII) (1.5 g, 4.6 mmol) in EtOAc (50.0 mL), 10% Pd/C (0.4 g), 20% $Pd(OH)_2$/C (0.4 g) was purged with H_2. The mixture was stirred under a H_2 atm at room temperature for 16 h. The reaction mixture was filter through Celite® and concentrated under high vacuum to give trans-4-amino-1-ethylcyclohexan-1-ol (CXIV) (390 mg, 2.723 mmol, 58.7% yield) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.80 (t, J=7.4 Hz, 3H), 1.14-1.03 (m, 2H), 1.29-1.20 (m, 2H), 1.40 (q, J=7.4 Hz, 2H), 1.59-1.49 (m, 2H), 1.67-1.61 (m, 2H), 2.70-2.61 (m, 1H), 3.84 (br s, 1H); ESIMS found for $C_8H_{17}NO$ m/z 144.1 (M+H).

[0613] Preparation of intermediate 1-(3,3,3-trifluoropropyl)piperidin-4-amine (CXVIII) is depicted below in Scheme 20.

Scheme 20



Step 1

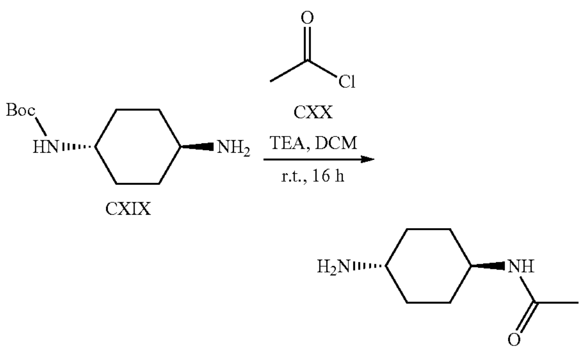
[0614] tert-Butyl piperidin-4-ylcarbamate (CXV) (Commercially available from Combi-Blocks Inc.) (1 g, 4.99 mmol) and K_2CO_3 (1.73 g, 12.52 mmol) were dissolved in DMF (15 mL) and 1-iodo-3,3,3-trifluoropropane (CXVI) (878 μL, 7.49 mmol) was added and the reaction was stirred at room temperature for 16 h. The reaction mixture was poured in EtOAc, and the aqueous layer was separated. The aqueous layer was extracted with EtOAc (×3) and then the combined organic layers were acidified to pH 4.5 with 1 M citric acid. The organic layer was washed three times with small volumes of water to remove unreacted SM. Sufficient amounts of the product remained in the organic layer which was dried using anhydrous $MgSO_4$ and reduced in vacuo to give the product tert-butyl N-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]carbamate (CXVII) (861 mg, 2.906 mmol, 58.2% yield) as a white solid. ESIMS found for $Cl_3H_{23}F_3N_2O_2$ m/z 297.2 (M+H).

Step 2

[0615] tert-Butyl N-[1-(3,3,3-trifluoropropyl)piperidin-4-yl]carbamate (CXVII) (200 mg, 0.670 mmol) was dissolved in DCE (3.2 mL) and TFA (800 μL, 10.38 mmol) was added and the reaction was stirred at room temperature for 30 m. The reaction mixture was blown dry and excess TFA removed by high vacuum to give the crude intermediate 1-(3,3,3-trifluoropropyl)piperidin-4-amine (CXVIII) (209 mg, 0.674 mmol, 99.8% yield) as a white semi-solid which was used without further purification. ESIMS found for $C_8H_{15}F_3N_2$ m/z 197.1 (M+H).

[0616] Preparation of intermediate N-(trans-4-aminocyclohexyl)acetamide (CXXI) is depicted below in Scheme 21.

Scheme 21



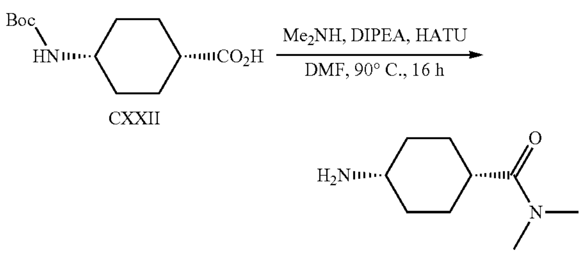
CXXI

Step 1

[0617] To a stirring solution of tert-butyl N-(4-aminocyclohexyl)carbamate (CXIX) (Commercially available from Combi-Blocks Inc.) (0.6 g, 2.8 mmol) in DCM (6 mL) was added TEA (1.2 mL, 8.61 mmol). Acetyl chloride (CXX) (0.22 mL, 3.09 mmol) was then slowly and the reaction mixture was stirred at room temperature for 16 h. The solvent was removed, and the crude material was dissolved in EtOAc, washed with 1 M NaOH, brine, and dried over anhydrous $MgSO_4$ and finally concentrated. The product was dissolved in EtOH (2 mL) and 4 M HCl (1 mL). The solution was stirred at room temperature for 2 h before evaporating to dryness to give the HCl salt of N-(4-aminocyclohexyl)acetamide (CXXI) (480 mg, 2.49 mmol, 89.0% yield) as a white solid. ESIMS found for $C_8H_{16}N_{20}$ m/z 157.05 (M+H).

[0618] Preparation of intermediate cis-4-amino-N,N-dimethylcyclohexane-1-carboxamide (CXXIII) is depicted below in Scheme 22.

Scheme 22



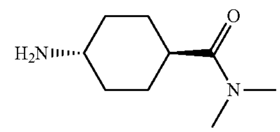
CXXIII

Step 1

[0619] To a stirring solution of 4-(tert-butoxycarbonylamino)cyclohexanecarboxylic acid (CXXII) (Commercially available from Combi-Blocks Inc.) (0.3 g, 1.23 mmol) in DMF (6 mL) was added DIPEA (0.65 mL, 3.73 mmol) and HATU (0.7 g, 1.85 mmol). Reaction was stirred for 5 min at room temperature. Dimethylamine (0.92 mL, 1.84 mmol) was added, and the reaction was heated to 90° C. for 16 h. The reaction was concentrated and dissolved in EtOH (2 mL) and 4 M HCl in dioxane (1 mL). The mixture was stirred for 2 h at room temperature, concentrated under vacuum to yield the HCl salt of 4-amino-N,N-dimethylcyclohexane-1-carboxamide (CXXIII) (280 mg, 1.355 mmol, 109.9% yield) as a light brown viscous solid. ESIMS found for $C_9H_{18}N_2O$ m/z 171.15 (M+H).

[0620] The following intermediate was prepared in accordance with the procedure described in the above Scheme 22.

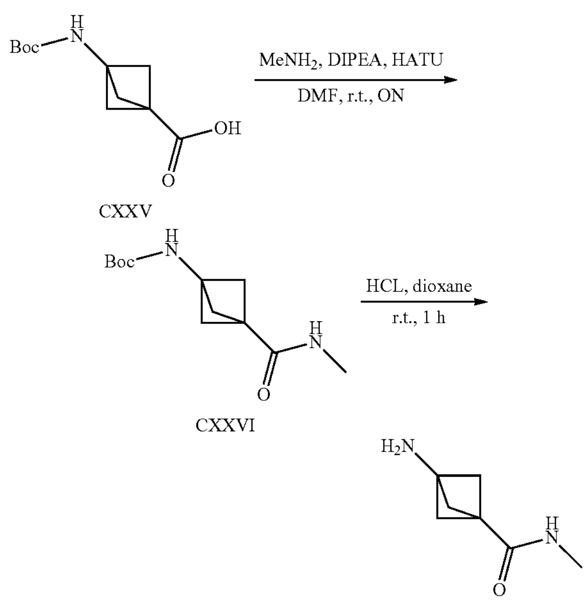
CXXIV



[0621] trans-4-Amino-N,N-dimethylcyclohexane-1-carboxamide (CXXIV): Light brown viscous solid (290 mg, 1.403 mmol, 113.8% yield). ESIMS found for $C_9H_{18}N_2O$ m/z 171.1 (M+H).

[0622] Preparation of intermediate 3-amino-N-methylbicyclo[1.1.1]pentane-1-carboxamide (CXXVII) is depicted below in Scheme 23.

Scheme 23



CXXVII

Step 1

[0623] To a solution of 3-((tert-butoxycarbonyl)amino) bicyclo[1.1.1]pentane-1-carboxylic acid (CXXV) (commercially available from AmBeed, Inc.) (0.5 g, 2.2 mmol) and HATU (0.8 g, 2.09 mmol) in DMF was added DIPEA (0.8 mL, 4.59 mmol) and the mixture was stirred for 5 min. Methanamine HCL (1.49 g, 22.07 mmol) was then added at

−78° C. followed by additional DIPEA (4 mL). The reaction mixture was left stirred at room temperature overnight. The solvents were concentrated, the residue dissolved in EtOAc, washed with saturated aqueous $NaHCO_3$, water and brine. The organics were dried over anhydrous Na_2SO_4, concentrated, and the residue was dried under high vacuum to obtain tert-butyl (3-(methylcarbamoyl)bicyclo[1.1.1]pentan-1-yl)carbamate (CXXVI) (244 mg, 1.015 mmol, 46.2% yield) as off-white solids. ESIMS found for $C_{12}H_{20}N_2O_3$ m/z 241.1 (M+H).

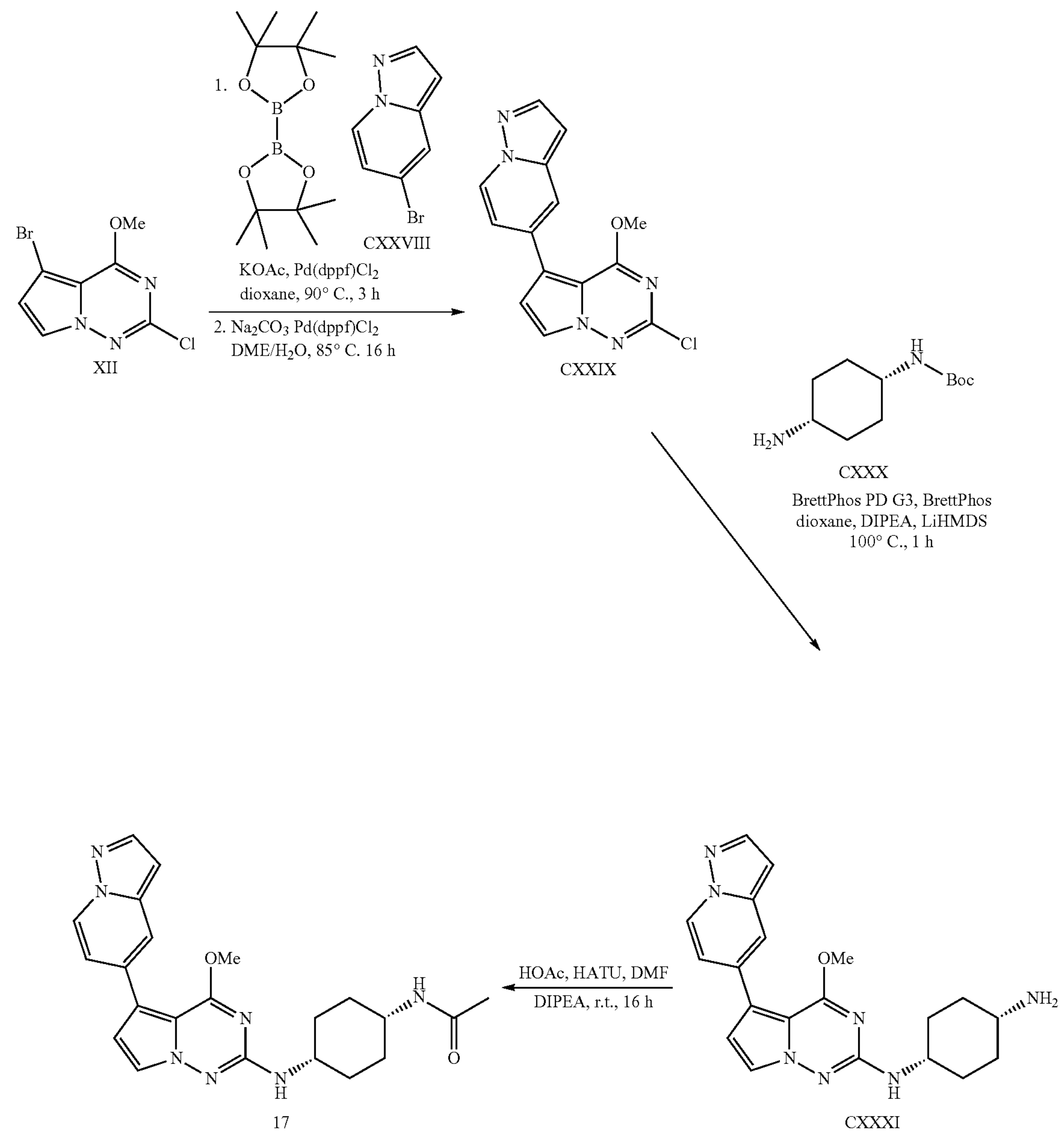
Step 2

[0624] A solution of tert-butyl (3-(methylcarbamoyl)bicyclo[1.1.1]pentan-1-yl)carbamate (CXXVI) (240 mg, 1.0 mmol) in 4 M HCl in dioxane (1.25 mL, 5.0 mmol) was stirred at room temperature for 1 h. The solvents were concentrated and dried under high vacuum overnight to obtain 3-amino-N-methylbicyclo[1.1.1]pentane-1-carboxamide HCL (CXXVII) (177 mg, 1.002 mmol, 100.3% yield) which was used for next step without purification. ESIMS found for $C_7H_{12}N_2O$ m/z 141.15 (M+H).

Example 1

[0625] Preparation of N-(cis-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide (17) is depicted below in Scheme 24.

Scheme 24



Steps 1-2

[0626] A mixture of 5-bromopyrazolo[1,5-a]pyridine (CXXVIII) (1.8 g, 9.14 mmol), Pd(dppf)Cl_2 (311 mg, 0.380 mmol), bis(pinacolato)diboron (2.9 g, 11.42 mmol), and KOAc (2.24 g, 22.82 mmol) in 1,4-dioxane (15 mL) in a sealed tube, it was degassed with N_2 and heated to 90° C. for 3 h. This reaction was cooled to room temperature to which was added 5-bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XII) (2 g, 7.62 mmol), Pd(dppf)Cl_2(311 mg, 0.380 mmol), Na_2CO_3 (15 mL, 15 mmol) and DME (15 mL). The reaction was then degassed with N_2 and heated to 85° C. for 16 h. Water (100 mL) was added and extracted with EtOAc (100 mL×3). The organic layer was evaporated onto Celite® and purified by silica gel column (0→100% EtOAc/hexanes). The tubes which contained pure sample were collected and the solvent removed under vacuum. The impure fractions were combined and re-purified by silica gel column (0→100% EtOAc/hexanes). The tubes which contained pure sample were collected and the solvent removed under vacuum, the impure fractions were combined and re-purified by silica gel column (0→100% EtOAc/hexanes). The three pure fractions were combined and placed under high vacuum to produce 2-chloro-4-methoxy-5-pyrazolo[1,5-a]pyridin-5-ylpyrrolo[2,1-f][1,2,4]triazine (CXXIX) (660 mg, 2.202 mmol, 28.9% yield) as a beige solid. ESIMS found for $C_{14}H_{10}ClN_5O$ m/z 300.1 (M+H).

Step 3

[0627] To a stirred solution of 2-chloro-4-methoxy-5-pyrazolo[1,5-a]pyridin-5-ylpyrrolo[2,1-f][1,2,4]triazine (CXXIX) (100 mg, 0.330 mmol) in 1,4-dioxane (2 mL) were added BrettPhos (19 mg, 0.040 mmol), BrettPhos PD G3 (25 mg, 0.030 mmol), DIPEA (0.13 mL, 0.720 mmol), tert-butyl N-(4-aminocyclohexyl)carbamate (CXXX) (commercially available from Combi-Blocks Inc.) (90 mg, 0.420 mmol) and LiHMDS (1 mL, 1 mmol) at room temperature. The mixture was purged with N_2 and stirred at 100° C. for 1 h. The reaction mixture was concentrated and purified by ISCO (0->6% 7 N NH_3 MeOH/$CHCl_3$). The pure fractions were collected, concentrated under reduced pressure, and dried under high vacuo to obtain cis-N[1]-(4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)cyclohexane-1,4-diamine (CXXXI) (70 mg, 0.186 mmol, 55.6% yield) as an off-white gummy solid. ESIMS found for $C_{20}H_{23}N_7O$ m/z 378.2 (M+H).

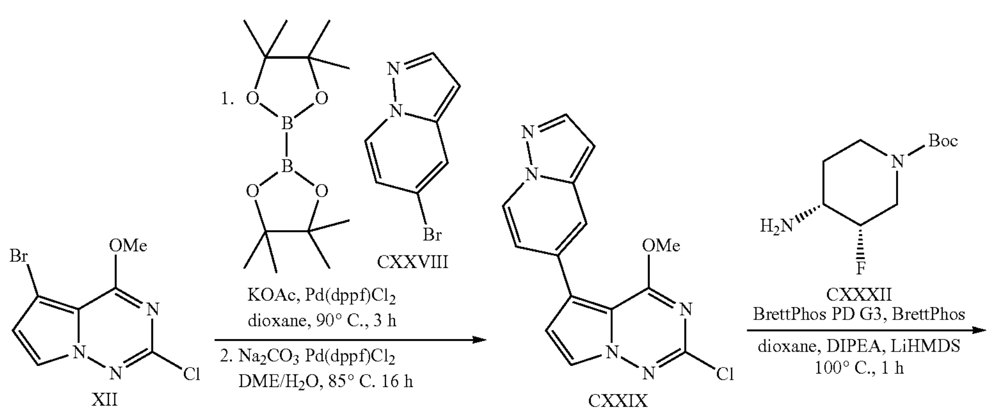
Step 4

[0628] To a solution of HOAc (11 μL, 0.190 mmol), HATU (79 mg, 0.210 mmol) in DMF (0.2 mL) was added DIPEA (85 μL, 0.490 mmol) and the mixture was stirred for 5 min. cis-N[1]-(4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)cyclohexane-1,4-diamine (CXXXI) (60 mg, 0.160 mmol) in DMF (0.3 mL) was then added and the reaction mixture was stirred at room temperature for 16 h. Water (10 mL) was added, and the solution was extracted with EtOAc. The organics were separated, concentrated, absorbed on silica gel, and purified by preparative TLC (4% MeOH/$CHCl_3$) to give N-(cis-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino) cyclohexyl)acetamide (17) (22 mg, 0.052 mmol, 33.0% yield) as a yellow solid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.50-1.59 (2H, m), 1.60-1.72 (4 H, m), 1.74-1.81 (2H, m), 1.81 (3 H, s), 3.64-3.71 (2H, m), 3.99 (3 H, s), 6.47 (1H, d, J=6.30 Hz), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.26, 1.78 Hz), 7.63 (1 H, d, J=2.74 Hz), 7.70 (1H, br d, J=6.84 Hz), 7.81 (1 H, s), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

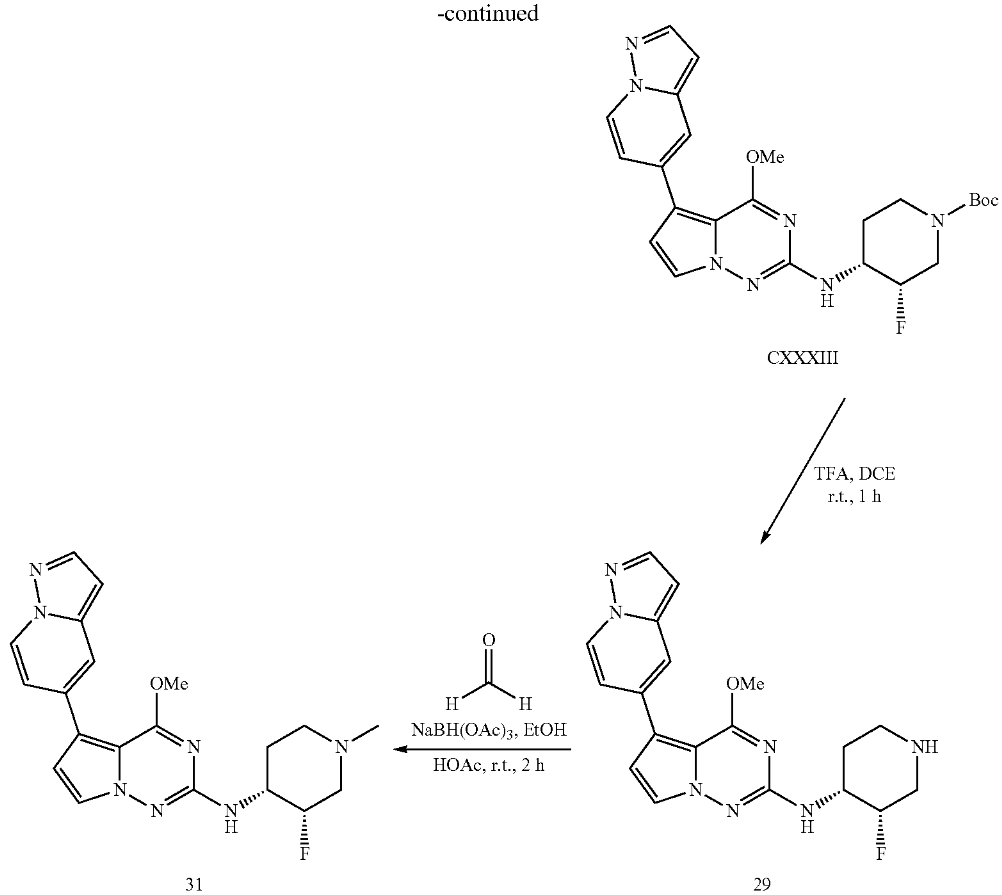
Example 2

[0629] Preparation of 4-methoxy-5-pyrazolo[1,5-a]pyridin-5-yl-N-(3R,4S)-3-fluoropiperidin-4-yl]pyrrolo[2,1-f][1,2,4]triazin-2-amine (29) and N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine (31) are depicted below in Scheme 25.

Scheme 25



-continued



Steps 1-2

[0630] A mixture of 5-bromopyrazolo[1,5-a]pyridine (CXXVIII) (1.8 g, 9.14 mmol), Pd(dppf)Cl_2(311 mg, 0.380 mmol), bis(pinacolato)diboron (2.9 g, 11.42 mmol), and KOAc (2.24 g, 22.82 mmol) in 1,4-dioxane (15 mL) in a sealed tube, it was degassed with N_2 and heated to 90° C. for 3 h. This reaction was cooled to room temperature to which was added 5-bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XII) (2 g, 7.62 mmol), Pd(dppf)Cl_2 (311 mg, 0.380 mmol), Na_2CO_3 (15 mL, 15 mmol) and DME (15 mL). The reaction was then degassed with N_2 and heated to 85° C. for 16 h. Water (100 mL) was added and extracted with EtOAc (100 mL×3). The organic layer was evaporated onto Celite® and purified by silica gel column (0→100% EtOAc/hexanes). The tubes which contained pure sample were collected and the solvent removed under vacuum. The impure fractions were combined and re-purified by silica gel column (0→100% EtOAc/hexanes). The tubes which contained pure sample were collected and the solvent removed under vacuum, the impure fractions were combined and re-purified by silica gel column (0→100% EtOAc/hexanes). The three pure fractions were combined and placed under high vacuum to produce 2-chloro-4-methoxy-5-pyrazolo[1,5-a]pyridin-5-ylpyrrolo[2,1-f][1,2,4]triazine (CXXIX) (660 mg, 2.202 mmol, 28.9% yield) as a beige solid. ESIMS found for $C_{14}H_{10}ClN_5O$ m/z 300.1 (M+H).

Step 3

[0631] To a stirred solution of 2-chloro-4-methoxy-5-pyrazolo[1,5-a]pyridin-5-ylpyrrolo[2,1-f][1,2,4]triazine (CXXIX) (100 mg, 0.330 mmol) in 1,4-dioxane (3 mL) were added BrettPhos (19 mg, 0.040 mmol), BrettPhos PD G3 (25 mg, 0.030 mmol), DIPEA (0.13 mL, 0.720 mmol), 2-methyl-2-propanyl (3S,4R)-4-amino-3-fluoro-1-piperidinecarboxylate (CXXXII) (100 mg, 0.460 mmol) and LiHMDS (1 mL, 1 mmol) at room temperature. The mixture was purged with N_2 and stirred at 100° C. for 1 h. The reaction mixture was concentrated and purified by ISCO (0->100% EtOAc/hexanes). The pure fractions were collected, concentrated under reduced pressure, and dried under high vacuum to obtain tert-butyl (3R,4S)-3-fluoro-4-[(4-methoxy-5-pyrazolo1[1,5-a]pyridin-5-ylpyrrolo[2,1-f][1,2,4]triazin-2-yl)amino]piperidine-1-carboxylate (CXXXIII) (65 mg, 0.135 mmol, 40.5% yield) as a white solid. ESIMS found for $C_{24}H_{28}FN_7O_3$ m/z 482.25 (M+H).

Step 4

[0632] To a stirred solution of tert-butyl (3R,4S)-3-fluoro-4-[(4-methoxy-5-pyrazolo1[1,5-a]pyridin-5-ylpyrrolo[2,1-f][11,2,4]triazin-2-yl)amino]piperidine-1-carboxylate (CXXXIII) (65 mg, 0.130 mmol) in DCM (1 mL) was added TFA (0.5 mL, 6.49 mmol) and stirred at room temperature for 1 h. The reaction mixture was concentrated, treated with 7 N NH_3/MeOH, absorbed on silica gel and purified by ISCO (0->100% $CHCl_3$/MeOH). The pure fractions were collected, concentrated under reduced pressure, and dried under high vacuo to give 4-methoxy-5-pyrazolo1[1,5-a]pyridin-5-yl-N-(3R,4S)-3-fluoropiperidin-4-yl]pyrrolo[2,1-f][1,2,4]triazin-2-amine (29) (45 mg, 0.118 mmol, 87.4% yield) as an off-white solid. ^1H NMR (499 MHz, DMSO-d_6)

δ ppm 1.58-1.65 (1H, m), 1.73 (1 H, qd, J=12.37, 4.24 Hz), 2.56 (1 H, br t, J=12.46 Hz), 2.70 (1H, dd, J=38.70, 14.30 Hz), 2.96 (1H, br d, J=13.14 Hz), 3.13 (1 H, br t, J=11.50 Hz), 3.78-3.93 (1H, m), 4.00 (3 H, s), 4.80 (1H, d, J=50.75 Hz), 6.59 (1H, d, J=1.64 Hz), 6.64 (1H, d, J=7.94 Hz), 6.78 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.39, 1.92 Hz), 7.63 (1H, d, J=2.46 Hz), 7.81 (1H, d, J=1.10 Hz), 7.97 (1H, d, J=2.19 Hz), 8.63 (1H, d, J=7.12 Hz); ESIMS found for $C_{19}H_{20}FN_7O$ m/z 382.2 (M+H).

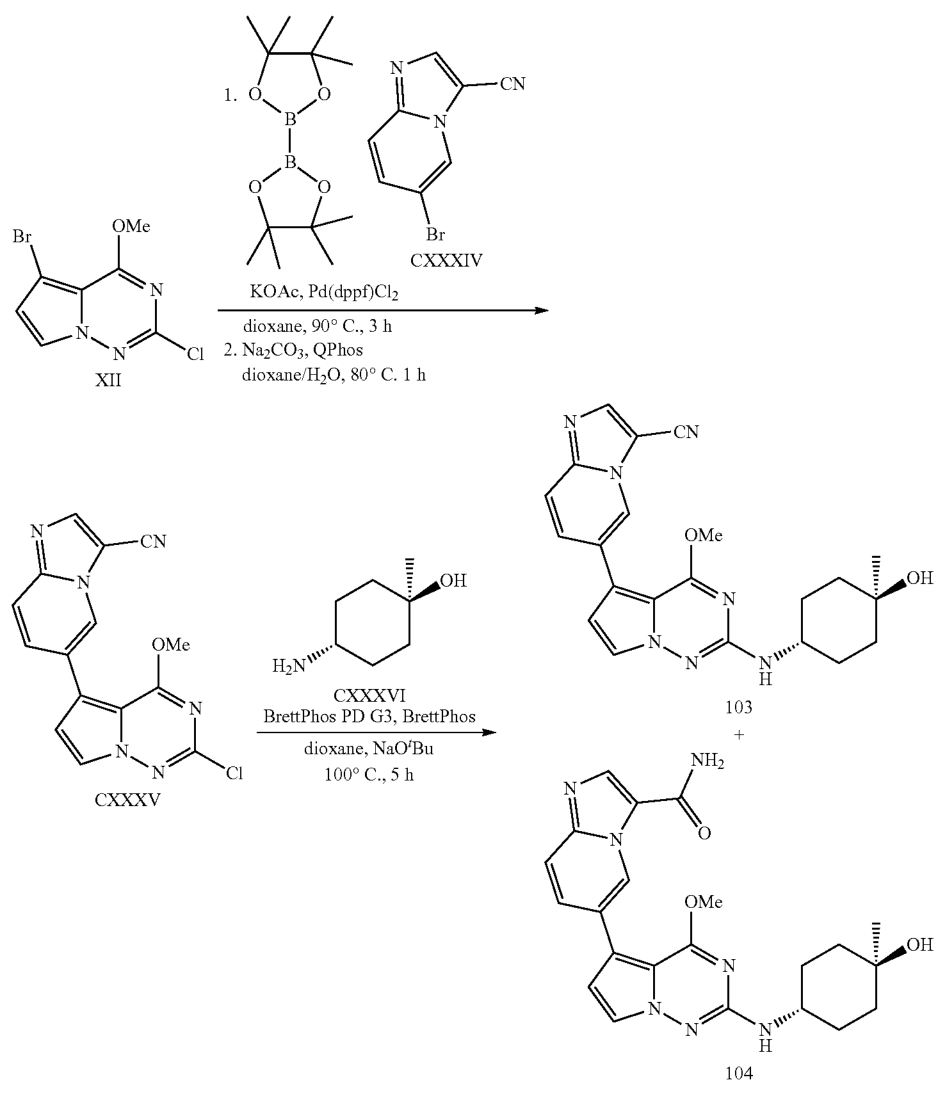
Step 5

[0633] 4-Methoxy-5-pyrazolo[1,5-a]pyridin-5-yl-N-(3R, 4S)-3-fluoropiperidin-4-yl]pyrrolo[2,1-f][1,2,4]triazin-2-amine (29) (40 mg, 0.100 mmol) was dissolved in EtOH (1 mL) and HOAc (15 μL, 0.260 mmol) and formaldehyde (18 μL, 0.320 mmol) were added and the reaction was stirred at room temperature for 20 min. $NaBH(OAc)_3$ (56 mg, 0.260 mmol) was added and the reaction was stirred for 2 h. TLC showed completion of the starting material. The reaction mixture was absorbed on silica gel and purified by ISCO (0->8% 7N NH_3 MeOH/$CHCl_3$). The pure fractions were concentrated, and the residue was dried under high vacuo to yield N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo [2,1-f][1,2,4]triazin-2-amine (31) (30 mg, 0.076 mmol, 72.3% yield) as an off-white solid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.68 (1 H, br dd, J=12.59, 3.01 Hz), 1.92 (1 H, qd, J=12.23, 3.56 Hz), 2.01-2.09 (1H, m), 2.17 (1H, dd, J=37.55, 13.20 Hz), 2.19 (3 H, s), 2.79 (1H, br d, J=11.23 Hz), 3.00-3.09 (1H, m), 3.67-3.83 (1H, m), 4.00 (3 H, s), 4.91 (1H, d, J=50.20 Hz), 6.59 (1H, d, J=1.64 Hz), 6.64 (1H, d, J=7.67 Hz), 6.78 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.12, 1.92 Hz), 7.63 (1H, d, J=2.74 Hz), 7.81 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.63 (1H, d, J=7.39 Hz); ESIMS found for $C_{20}H_{22}FN_7O$ m/z 396.2 (M+1).

Example 3

[0634] Preparation of 6-(2-((trans-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a]pyridine-3-carboxamide (104) and 6-(2-((trans-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a] pyridine-3-carbonitrile (103) are depicted below in Scheme 26.

Scheme 26



Steps 1-2

[0635] A mixture of 6-bromoimidazo[1,2-a]pyridine-3-carbonitrile (CXXXIV) (commercially available from Combi-Blocks Inc) (888 mg, 4.0 mmol), bis(pinacolato) diboron (1.016 g, 4.0 mmol), KOAc (1.18 g, 12.02 mmol) and Pd(dppf)Cl_2(123 mg, 0.15 mmol) were dissolved in 1,4-dioxane (12 mL) and the reaction mixture was purged with N_2 gas for 5 min. The vial was sealed and heated at 95° C. for 3 h. To the above reaction mixture was added 5-bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4] triazine (XII) (525 mg, 2.0 mmol), QPhos (143 mg, 0.2 mmol), and a solution of Na_2CO_3 (1.27 g, 12. mmol) in water (3 mL). The reaction mixture was purged with N_2 gas for 5 min, the vial was sealed and heated for 80° C. for 1 h. The organic layer was separated, absorbed on silica, and purified on ISCO (0->20% MeOH/$CHCl_3$) to obtain 6-(2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a] pyridine-3-carbonitrile (CXXXV) (116 mg, 0.357 mmol, 17.9% yield) as a beige solid. ESIMS found for $C_{15}H_9ClN_6O$ m/z 325.1 (M+H).

Step 3

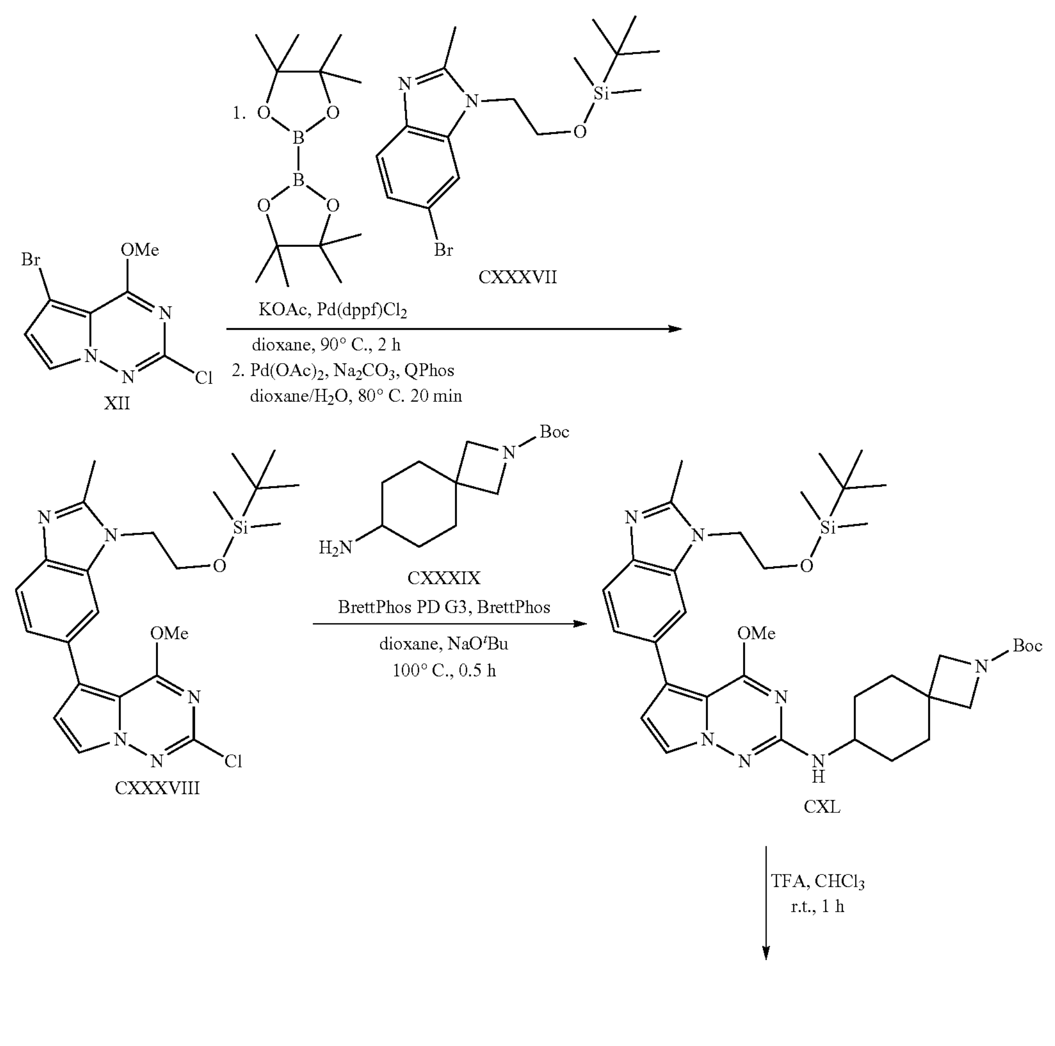
[0636] To a stirred solution of 6-(2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a]pyridine-3-carbonitrile (CXXXV) (116.mg, 0.36 mmol), trans-4-amino-1-methylcyclohexan-1-ol (CXXXVI) (commercially available from PharmaBlock (USA), Inc.) (56.mg, 0.43 mmol), BrettPhos Pd G3 (24.mg, 0.03 mmol) and BrettPhos (19.mg, 0.04 mmol) in 1,4-dioxane (3 mL) was added NaO^{t}Bu (110 mg, 1.14 mmol) at room temperature. The reaction mixture was purged for 5 min with N_2 then heated to 100° C. for 5 h. The reaction mixture concentrated and purified by ISCO (0->20% 7 N NH_3 in MeOH/$CHCl_3$) to obtain two products, 6-(2-((trans-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a] pyridine-3-carbonitrile (103) (12 mg, 0.029 mmol, 8.0% yield) as a beige solid.

[0637] ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.38-1.53 (4H, m), 1.56-1.66 (3H, m), 1.83-1.93 (2H, m), 3.60-3.71 (1H, m), 4.01 (3H, s), 4.23 (1H, s), 6.56 (1H, d, J=7.94 Hz), 6.89 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.74 Hz), 7.81-7.92 (2H, m), 8.44 (1 H, s), 8.77-8.86 (1H, m); ESIMS found for $C_{22}H_{23}N_7O_2$ m/z 418.2 (M+1) and 6-(2-((trans-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a]pyridine-3-carboxamide (104) (2.2 mg, 0.005 mmol, 1.4% yield) as a beige solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.39-1.48 (4H, m), 1.57-1.63 (2H, m), 1.85-1.91 (2H, m), 3.60-3.72 (1H, m), 3.99 (3H, s), 4.23 (1H, s), 6.49 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.46 Hz), 7.34 (1 H, br s), 7.65 (1H, d, J=2.74 Hz), 7.69 (2 H, s), 7.95 (1 H, br s), 8.33 (1 H, s), 9.84 (1 H, s); ESIMS found for $C_{22}H_{25}N_7O_3$ m/z 436.25 (M+1).

Example 4

[0638] Preparation of 1-(7-((5-(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl) ethan-1-one (173) is depicted below in Scheme 27.

Scheme 27



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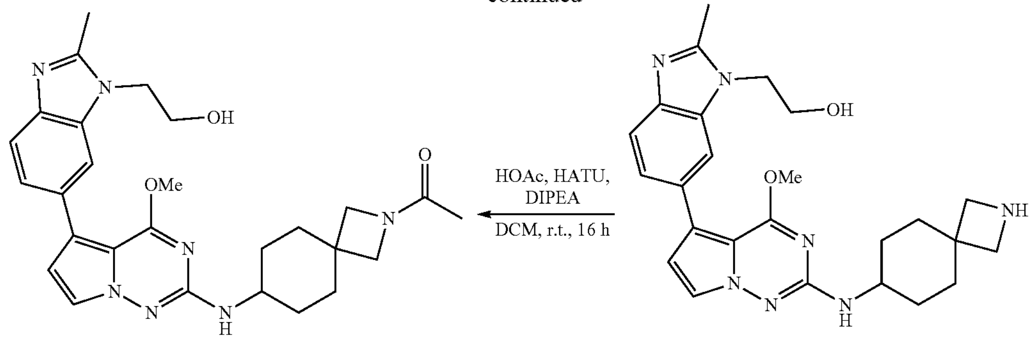


173

CXLI

Steps 1-2

[0639] A mixture of 6-bromo-1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-methyl-1H-benzo[d]imidazole (CXXXVII) (950 mg, 2.57 mmol), Pd(dppf)Cl_2(99 mg, 0.12 mmol), bis(pinacolato)diboron (960 mg, 3.78 mmol) and KOAc (748 mg, 7.62 mmol)in 1,4-dioxane (10 mL) in a sealed tube, it was purged with N_2, sealed, and then heated to 90° C. for 2 h. The LCMS shows a mixture of the boronic acid and the boronic ester.

[0640] This reaction was cooled to room temperature then to this mixture was added 5-bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XII) (660 mg, 2.51 mmol), QPhos (178 mg, 0.25 mmol), Pd$(OAc)_2$ (28 mg, 0.12 mmol), and an aqueous solution of Na_2CO_3 (5 mL, 5.0 mmol). The reaction was purged with N_2, sealed, and then heated to 80° C. for 20 min. Water (100 mL) was added and extracted with EtOAc (3×100 mL). The solvent was reduced onto Celite® and purified by silica gel column chromatography (0→100% EtOAc/hexanes) to produce 5-(1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (CXXXVIII) (460 mg, 0.975 mmol, 38.8% yield) as an off-white solid. ESIMS found for $C_{23}H_{30}ClN_5O_2Si$ m/z 472.2 (M+H).

Step 3

[0641] To a stirred solution of tert-butyl 7-amino-2-azaspiro[3.5]nonane-2-carboxylate HCl (CXXXIX) (commercially available from J&W Pharmlab, LLC) (70 mg, 0.25 mmol), 5-(1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (CXXXVIII) (100 mg, 0.21 mmol), BrettPhos (12 mg, 0.02 mmol), and BrettPhos PD G3 (10 mg, 0.01 mmol) in dioxane (1.6 mL) was added NaO^{t}Bu (62 mg, 0.65 mmol). The solution was purged with N_2, sealed and then heated at 100° C. for 30 min. The solvent reaction was reduced onto Celite® and purified by silica bel column chromatography (0->30% 7 N NH_3 in MeOH/$CHCl_3$) to produce tert-butyl 7-((5-(1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonane-2-carboxylate (CXL) (17 mg, 0.025 mmol, 11.9% yield) as an off-white solid. ESIMS found for $C_{36}H_{53}N_7O_4Si$ m/z 676.4 (M+H).

Step 4

[0642] To a solution of tert-butyl 7-((5-(1-(2-((tert-butyldimethylsilyl)oxy)ethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonane-2-carboxylate (CXL) (17. mg, 0.03 mmol) in $CHCl_3$ (3 mL) was added TFA (1 mL). The reaction was stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the residue was purified by silica gel column chromatography (0->15% 7 N NH_3 in MeOH/$CHCl_3$) to produce 2-(6-(2-((2-azaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol (CXLI) (11 mg, 0.024 mmol, 94.8% yield) as an amber glass. ESIMS found for $C_{25}H_{31}N_7O_2$ m/z 462.3 (M+H).

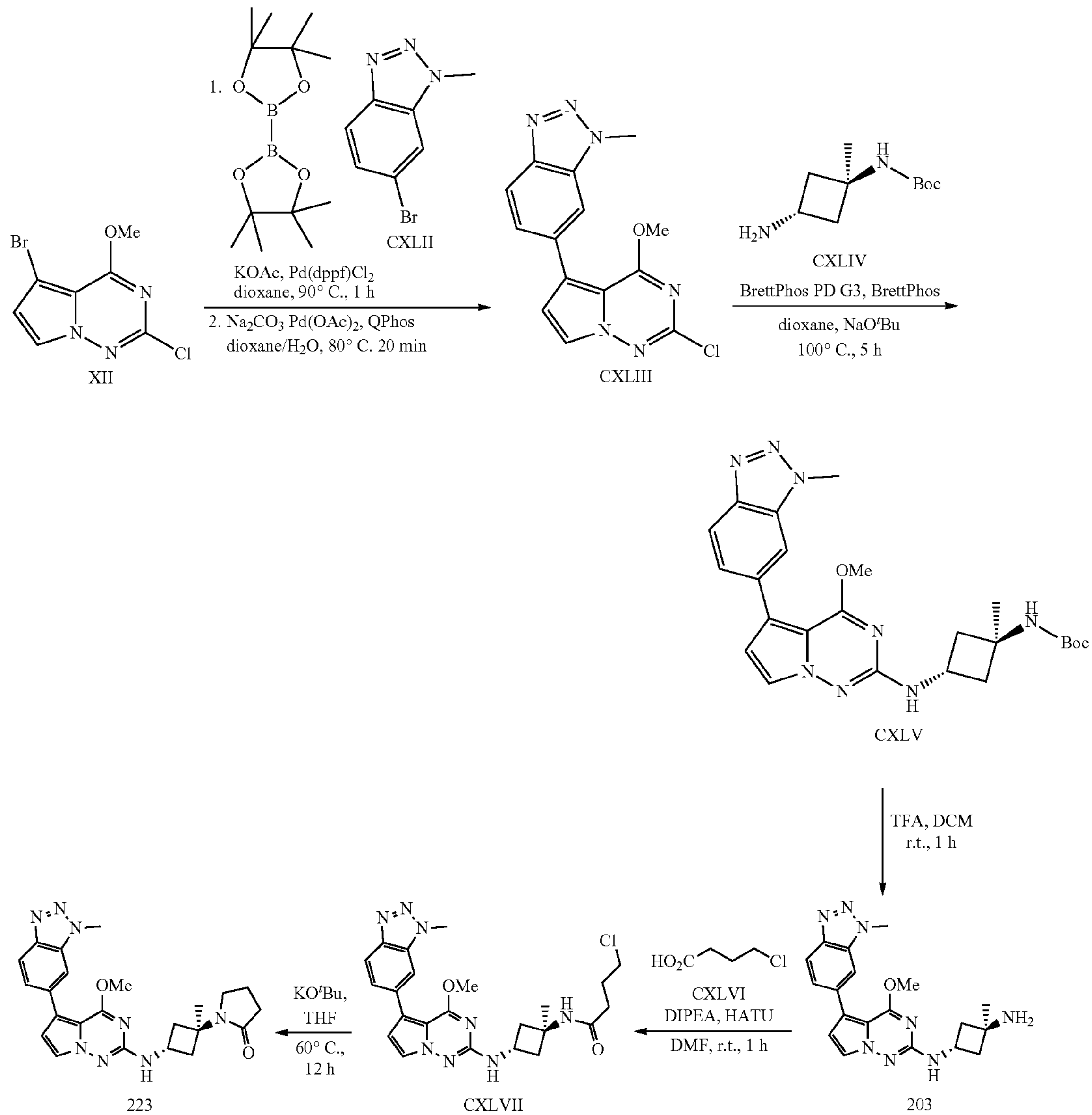
Step 5

[0643] A solution of HATU (10 mg, 0.03 mmol), HOAc (1.5 μL, 0.03 mmol) and DIPEA (12 μL, 0.07 mmol) in DCM (2 mL) was stirred at room temperature for 30 min, then 2-(6-(2-((2-azaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol (CXLI) (11 mg, 0.024 mmol) was added and the solution was stirred at room temperature for 16 h. The solvent was reduced onto Celite® and purified by silica gel column chromatography (0→10% 7 N NH_3 in MeOH/$CHCl_3$) to yield 1-(7-((5-(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo [2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one (173) (6 mg, 0.012 mmol, 50.0% yield) as an off-white solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28-1.39 (2H, m), 1.48-1.60 (2H, m), 1.72-1.79 (3 H, in), 1.83-1.94 (4H, m), 2.60 (3H, s), 3.47 (1H, s), 3.52 (1 H, s), 3.57 (1 H, dt, J=10.20, 6.95 Hz), 3.74 (1 H, s), 3.75-3.79 (2H, m), 3.80 (1 H, s), 3.93 (3H, d, J=1.10 Hz), 4.28 (2 H, br t, J=5.20 Hz), 4.99 (1H, t, J=5.48 Hz), 6.43 (1H, dd, J=16.43, 7.94 Hz), 6.62 (1H, d, J=2.46 Hz), 7.37 (1H, dd, J=8.21, 1.37 Hz), 7.51 (1H, d, J=8.49 Hz), 7.58 (1H, t, J=2.74 Hz), 7.69 (1 H, s); ESIMS found for $C_{27}H_{33}N_7O_3$ m/z 504.3 (M+1).

Example 5

[0644] Preparation of trans-N[1]-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine (203) and 1-(trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)pyrrolidin-2-one (223) are depicted below in Scheme 28.

Scheme 28



Steps 1-2

[0645] A mixture of 6-bromo-1-methyl-1H-benzo[d][1,2,3]triazole (CXLII) (commercially available from Combi-Blocks Inc.) (0.93 g, 4.39 mmol), Pd(dppf)Cl_2(0.17 g, 0.21 mmol), bis(pinacolato)diboron (1.68 g, 6.62 mmol), and KOAc (1.3 g, 13.25 mmol) in 1,4-dioxane (11 mL) in a sealed tube, it was purged with N_2, sealed, and heated to 90° C. for 1 h. The LCMS shows a mixture of the boronic acid and the boronic ester.

[0646] The reaction was cooled to room temperature and then to this mixture was added 5-bromo-2-chloro-4-

methoxypyrrolo[2,1-f][1,2,4]triazine (XII) (1.15 g, 4.38 mmol), $Pd(OAc)_2$ (0.05 g, 0.22 mmol), QPhos (0.32 g, 0.45 mmol), an aqueous solution of Na_2CO_3 (9.2 mL, 9.2 mmol) and 1,4-dioxane (11 mL). The reaction was purged with N_2, sealed, and heated to 80° C. for 20 min. Water (100 mL) was added and extracted with EtOAc (3×100 mL). The solvent was reduced onto Celite® and purified by silica gel column chromatography (0->100% EtOAc/hexanes) to produce 6-(2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-1-methyl-1H-benzo[d][1,2,3]triazole (CXLIII) (0.763 g, 2.424 mmol, 55.3% yield) as an off-white solid. ESIMS found for $C_{14}H_{11}ClN_6O$ m/z 315.1 (M+H).

Step 3

[0647] To a stirred solution of 6-(2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-1-methyl-1H-benzo[d][1,2,3]triazole (CXLIII) (212 mg, 0.67 mmol), tert-butyl (trans-3-amino-1-methylcyclobutyl)carbamate (CXLIV) (commercially available from PharmaBlock (USA), Inc.) (160 mg, 0.8 mmol), BrettPhos PD G3, (46 mg, 0.05 mmol) and BrettPhos (37 mg, 0.07 mmol) in 1,4-dioxane (4 mL) was added NaO^tBu (195 mg, 2.03 mmol). The reaction mixture was purged for 5 min then heated to 100° C. for 30 min. The reaction mixture was concentrated and purified on ISCO (0→10% $MeOH/CHCl_3$) to obtain tert-butyl (trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)carbamate (CXLV) (188 mg, 0.393 mmol, 58.3% yield) as a colorless gum. ESIMS found for $C_{24}H_{30}N_8O_3$ m/z 479.3 (M+H).

Step 4

[0648] To a stirred solution of tert-butyl (trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)carbamate (CXLV) (188 mg, 0.39 mmol) in DCM (2 mL) was added TFA (1.2 mL, 15.58 mmol) and stirred at room temperature for 1 h. The reaction mixture was concentrated, treated with saturated aqueous Na_2CO_3 solution, washed with EtOAc, dried over anhydrous Na_2SO_4, concentrated under vacuum, then absorbed on silica gel, and purified by ISCO (0-20% 7 N NH_3 in $MeOH/CHCl_3$) to give trans-N_1-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine (203) (110 mg, 0.291 mmol, 74.0% yield) as an off-white foam. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.22 (3 H, s), 1.80 (2 H, br s), 1.88-1.98 (2H, m), 2.13-2.22 (2H, m), 3.95 (3 H, s), 4.23-4.33 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 6.90 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.63 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.95-8.00 (1H, m); ESIMS found for $C_{19}H_{22}N_8O$ m/z 379.2 (M+1).

Step 5

[0649] To a solution of 4-chlorobutanoic acid (CXLVI) (16 μL, 0.16 mmol) and HATU (70 mg, 0.18 mmol) in DMF (0.5 mL) was added DIPEA (74 μL, 0.42 mmol) and the mixture was stirred for 10 min. trans-N_1-(4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine (203) (50 mg, 0.13 mmol) in DMF (0.5 mL) was added and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with a saturated aqueous $NaHCO_3$ solution and extracted with EtOAc. The organic layer was separated, concentrated, absorbed on silica gel and purified by ISCO (0->10% $MeOH/CHCl_3$) to obtain 4-chloro-N-(trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)butanamide (CXLVII) (53 mg, 0.110 mmol, 83.1% yield) as an off-white solid. ESIMS found for $C_{23}H_{27}ClN_8O_2$ m/z 483.2 (M+H).

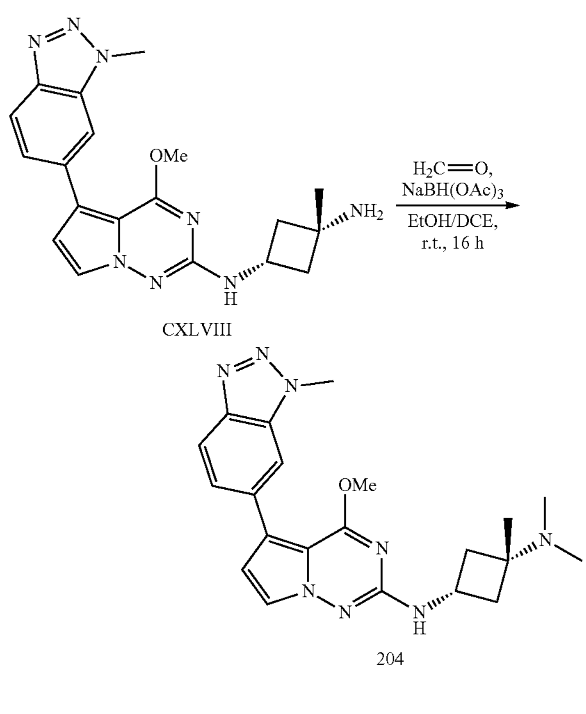
Step 6

[0650] To a solution of 4-chloro-N-(trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)butanamide (CXLVII) (53 mg, 0.11 mmol) in THF (5 mL) was added KO^tBu (37 mg, 0.33 mmol) and the reaction mixture was heated at 60° C. for 12 h. The reaction mixture was quenched with a saturated aqueous $NaHCO_3$ solution and extracted with EtOAc. The organic layer was separated, concentrated, absorbed on silica gel, and purified by ISCO (0->10% $MeOH/CHCl_3$) to yield 1-(trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)pyrrolidin-2-one (223) (23 mg, 0.052 mmol, 46.9% yield) as an off-white solid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3 H, s), 1.92 (2 H, quin, J=7.53 Hz), 2.00-2.08 (2H, m), 2.23 (2H, t, J=8.08 Hz), 2.82-2.92 (2H, m), 3.40 (2H, t, J=6.84 Hz), 3.96 (3 H, s), 4.04-4.12 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 7.06 (1H, d, J=6.30 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.46 Hz), 7.94 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{23}H_{26}N_8O_2$ m/z 447.3 (M+1).

Example 6

[0651] Preparation of cis-N^3-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-N^1,N^1,1-trimethylcyclobutane-1,3-diamine (204) is depicted below in Scheme 29.

Scheme 29



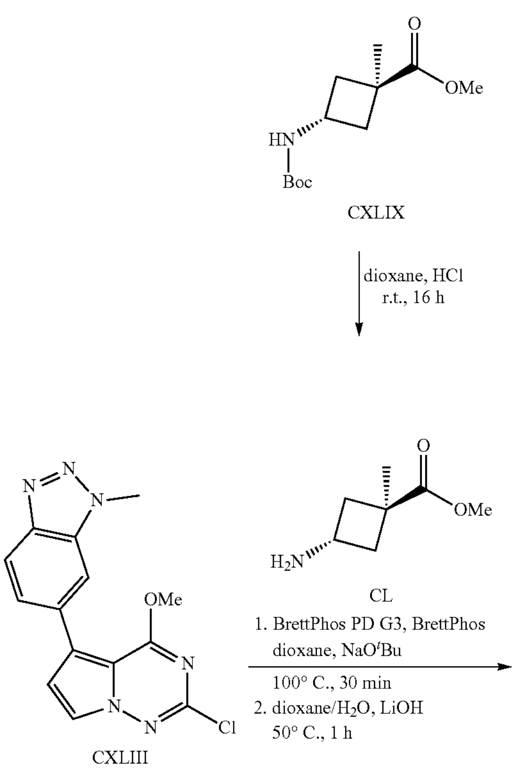
Step 1

[0652] To a stirred solution of (cis-N_1-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine (CXLVIII) (prepared by the method shown in Example 5, steps 1-4) (25 mg, 0.07 mmol) in EtOH (1 mL) and DCE (4 mL) were added formaldehyde (13 μL, 0.17 mmol). The reaction was stirred at room temperature for 30 min before adding NaBH$(OAc)_3$ (70 mg, 0.33 mmol). The reaction was further stirred at room temperature for 16 h. A saturated aqueous Na_2CO_3 solution was added and extracted with DCM. The organic layer was separated and dried over anhydrous Na_2SO_4. The solvent under reduced pressure and the residue purified by ISCO silica gel column chromatography (0->20% 7 N NH_3 in MeOH/$CHCl_3$) to obtain cis-N^3-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-N^1,N^1,1-trimethylcyclobutane-1,3-diamine (204) (18 mg, 0.044 mmol, 67.0% yield) as a white solid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.06 (3 H, s), 1.82-1.92 (2H, m), 2.03 (6 H, s), 2.19 (2 H, td, J=8.15, 2.60 Hz), 3.91-4.01 (1H, m), 3.95 (3H, s), 4.31 (3H, s), 6.74 (1H, d, J=2.46 Hz), 6.95 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{21}H_{26}N_8O$ m/z 407.3 (M+1).

Example 7

[0653] Preparation of (trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)(pyrrolidin-1-yl)methanone (222) is depicted below in Scheme 30.

Scheme 30



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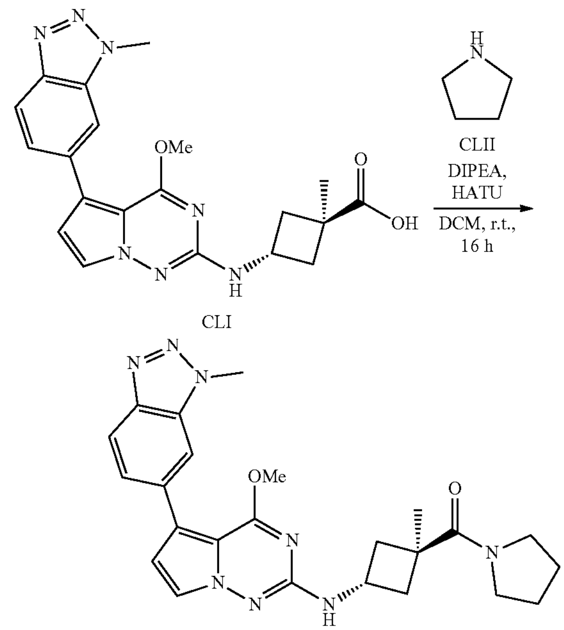


222

Steps 1-3

[0654] To a microwave vial was added methyl trans-3-{[(tert-butoxy)carbonyl]amino}-1-methylcyclobutane-1-carboxylate (CXLIX) (255.1 mg, 1.05 mmol), MeOH (5 mL) and a 4 M solution of HCl in dioxane (0.5 mL, 2. mmol). The vial was sealed, and the solution was stirred at room temperature for 16 h. The solvent was blown off with stream of N_2 while heating to 50° C. The residue was dissolved in MeCN (5 mL), and the solvent was blown off with stream of N_2 while heating to 50° C. This was repeated 2 more times to produce methyl trans-3-amino-1-methylcyclobutane-1-carboxylate (CL) as a white solid,

[0655] To the white residue was added 6-(2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-1-methyl-1H-benzo[d][1,2,3]triazole (CXLIII) (300 mg, 0.95 mmol), 1,4-dioxane (4.8 mL), BrettPhos (50 mg, 0.09 mmol), NaO^{t}Bu (366.4 mg, 3.81 mmol), BrettPhos PD G3 (44 mg, 0.05 mmol). The reaction mixture was purged with N_2, the vial sealed and heated to 100° C. for 30 min. The LC/MS showed a mixture of the methyl ester and the acid.

[0656] To the above solution was added water (2 mL) followed by a 2 M aqueous solution of LiOH (0.48 mL, 0.96 mmol). The reaction was heated at 50° C. for 1 h. The reaction was poured into water (5 mL), neutralized with 1 N HCl and extracted with DCM (3×50 mL). The DCM layer was reduced onto Celite® and purified by silica gel column chromatography (0→50% EtOAc/hexanes) to produce 3-[[4-methoxy-5-(3-methylbenzotriazol-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl]amino]-1-methylcyclobutane-1-carboxylic acid (CLI) (104 mg, 0.2553 mmol, 26.779% yield) as an off white solid. ESIMS found for $C_{20}H_{21}N_7O_3$ m/z 408.2 (M+H).

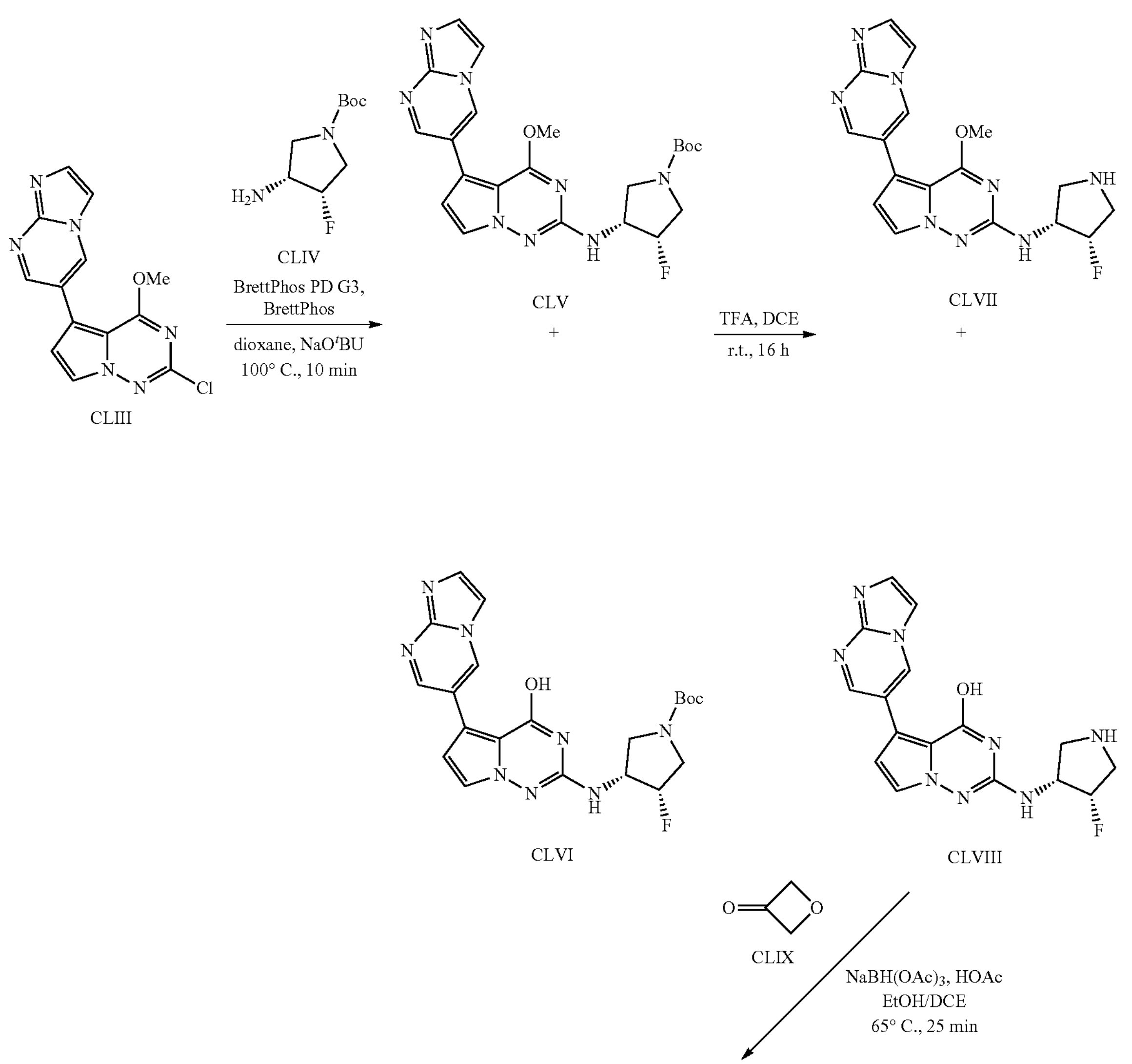
Step 4

[0657] A solution of HATU (34.5 mg, 0.09 mmol), trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxylic acid (CLI) (34.mg, 0.08 mmol) and DIPEA (30.9 μL, 0.18 mmol) in DCM (2 mL) was stirred at room temperature for 30 min before adding pyrrolidine (CLII) (10 μL, 0.12 mmol). The reaction was stirred at room temperature for 16 h. The solvent was reduced onto Celite® and purified by silica gel column chromatography (0→10% 7N NH_3 in MeOH/$CHCl_3$) to obtain (trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)(pyrrolidin-1-yl)methanone (222) (36 mg, 0.078 mmol, 93.7% yield) as a white solid. ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3 H, s), 1.73-1.80 (2H, m), 1.81-1.87 (2H, m), 1.91-1.99 (2H, m), 2.86-2.93 (2H, m), 3.30-3.34 (4H, m), 3.87-3.94 (1 H, m), 3.96 (3H, s), 4.31 (3H, s), 6.74 (1H, d, J=2.46 Hz), 7.07 (1H, d, J=6.57 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{24}H_{28}N_8O_2$ m/z 461.3 (M+1).

Example 8

[0658] Preparation of 2-(((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol (265) is depicted below in Scheme 31.

Scheme 31



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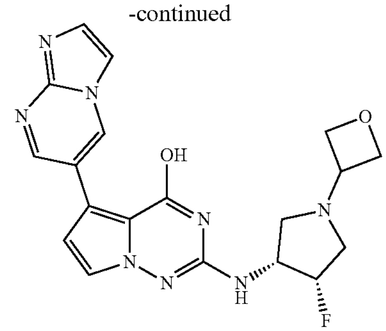


265

Step 1

[0659] 2-Chloro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazine (CLIII) (prepared by the method presented in Example 3, steps 1-2) (200 mg, 0.67 mmol), tert-butyl (3R,4S)-3-amino-4-fluoropyrrolidine-1-carboxylate (CLIV) (commercially available from Pharma-Block (USA), Inc.) (177 mg, 0.87 mmol), BrettPhos Pd G3 (51 mg, 0.06 mmol), BrettPhos (31 mg, 0.06 mmol) and NaO^{t}Bu (192 mg, 2.0 mmol) were suspended in dry 1,4-dioxane (4 mL). The mixture is purged with Ar for 5 min, followed by heating at 100° C. for 10 min. The reaction mixture was added to a saturated aqueous NH_4Cl solution and DCM, and the organic layer was separated. The aqueous layer was extracted with DCM (×2) and the combined organic layers were dried (anhydrous $MgSO_4$) and reduced in vacuo to give a mixture of products tert-butyl (3S,4R)-3-fluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidine-1-carboxylate (CLV) (220 mg, 0.470 mmol, 70.6% yield) and tert-butyl (3S,4R)-3-fluoro-4-((4-hydroxy-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino) pyrrolidine-1-carboxylate (CLVI) (91 mg, 0.200 mmol, 30.1% yield) as an orange fluffy solid which was used without purification. Amounts and yields calculated by LCMS. ESIMS found for $C_{22}H_{25}FN_8O_3$ m/z 469.3 (M+H) and $C_{21}H_{23}FN_8O_3$ m/z 455.2 (M+H).

Step 2

[0660] The mixture of tert-butyl (3S,4R)-3-fluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidine-1-carboxylate (CLV) (220 mg, 0.470 mmol) and tert-butyl (3S,4R)-3-fluoro-4-((4-hydroxy-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidine-1-carboxylate (CLVI) (91 mg, 0.200 mmol) was dissolved in DCE (9 mL) at 0° C. TFA (1 mL) was added and the reaction was stirred at room temperature for 16 h. The reaction mixture was evaporated and excess TFA was removed via high vacuum. The crude product was purified by column chromatography (0->8% 7.0 NH_3 in MeOH/$CHCl_3$) followed by (8->20% 7.0 NH_3 in MeOH/$CHCl_3$) to separate the two compounds, N-((3R,4S)-4-fluoropyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (CLVII) (100 mg, 0.272 mmol, 57.8% yield) was collected as a pale-yellow semi-solid. ESIMS found for $C_{17}H_{17}FN_8O$ m/z 369.2 (M+H). The product 2-(((3R,4S)-4-fluoropyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol (CLVIII) (171 mg, 0.483 mmol, 102.8% yield) was collected as a yellow solid. ESIMS found for $C_{16}H_{15}FN_8O$ m/z 355.2 (M+H). Additional demethylation accorded during TFA Boc deprotection.

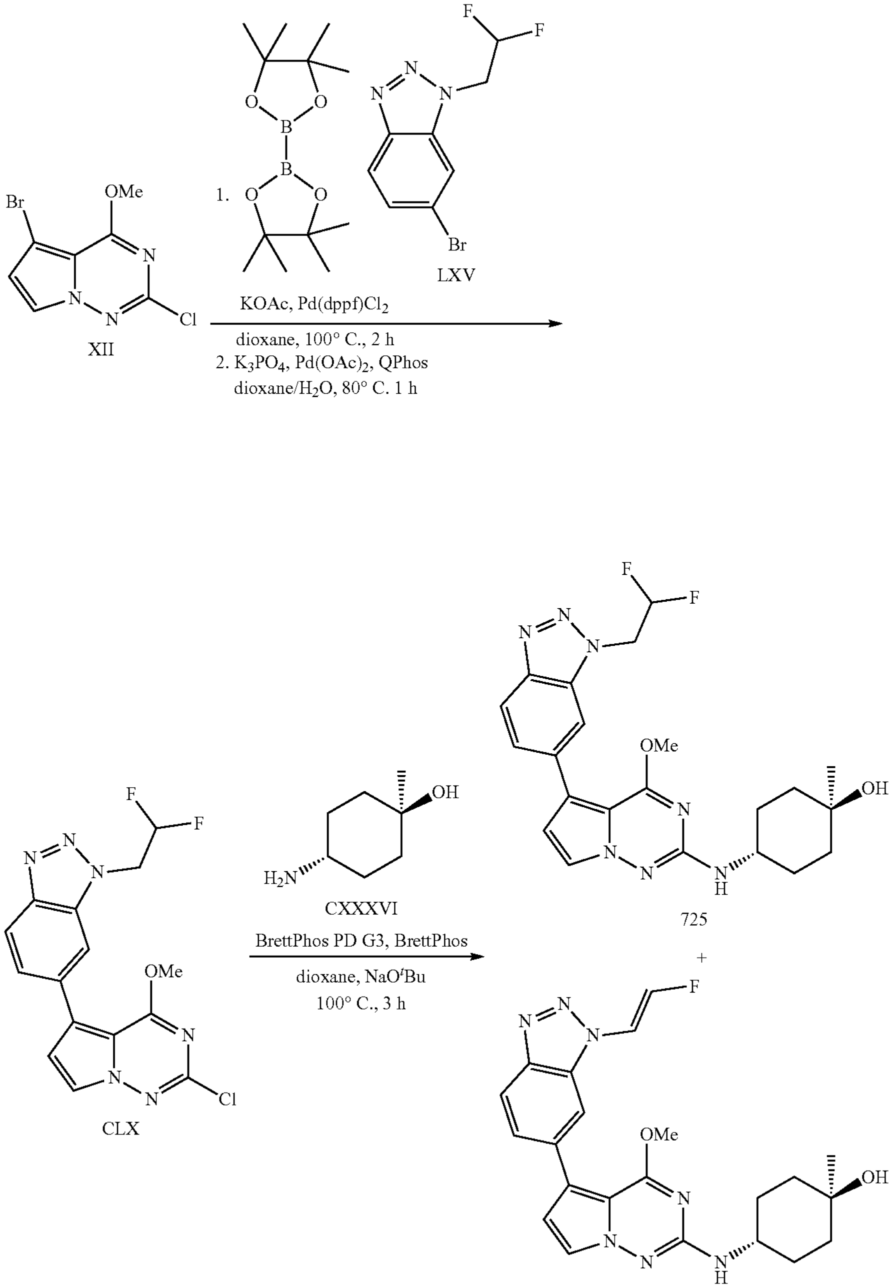
Step 3

[0661] 2-(((3R,4S)-4-Fluoropyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol (CLVIII) (40 mg, 0.11 mmol) was suspended in EtOH (1 mL) and DCE (1 mL). HOAc (19 μL, 0.33 mmol) and oxetan-3-one (CLIX) (33 μL, 0.56 mmol) were then added and the reaction was stirred at 65° C. for 15 min. NaBH$(OAc)_3$ (48 mg, 0.23 mmol) was added and the reaction was stirred for another 10 min. LC/MS showed unreacted starting material therefore additional oxetan-3-one (23 μL, 0.36 mmol) was added and stirred for 10 min at 65° C. followed by additional NaBH$(OAc)_3$ (48 mg, 0.23 mmol). The reaction was stirred for 10 min at 65° C. LC/MS showed minor starting material and the reaction was stopped. The reaction mixture was loaded onto Celite® and purified by silica column chromatography (0→9% 7.0 M NH_3 in MeOH/$CHCl_3$). The product was further purified by HPLC (0→15% MeCN/H_2O (0.1% formic acid)) to produce 2-(((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol (265) (4 mg, 0.010 mmol, 8.6% yield) as an off-white solid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 2.56 (1H, t, J=8.49 Hz), 2.79-2.91 (1H, m), 2.96-3.09 (1H, m), 2.98-3.03 (1H, m), 3.76 (1 H, quin, J=6.09 Hz), 4.22-4.37 (1H, m), 4.46 (2H, t, J=6.02 Hz), 4.58 (2H, t, J=6.57 Hz), 5.25 (1 H, dtd, J=55.95, 4.65, 4.65, 1.00 Hz), 6.29 (1 H, br d, J=6.30 Hz), 6.81 (1H, d, J=2.74 Hz), 7.48 (1H, d, J=2.74 Hz), 7.71 (1H, d, J=1.10 Hz), 7.93 (1H, d, J=1.09 Hz), 8.90 (1H, d, J=2.46 Hz), 9.41 (1H, d, J=2.19 Hz), 10.78 (1 H, br s); ESIMS found for $C_{19}H_{19}FN_8O_2$ m/z 411.2 (M+1).

Example 9

[0662] Preparation of (1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol (725) and (1r,4r)-4-((5-(1-((E)-2-fluorovinyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol (672) are depicted below in Scheme 32.

Scheme 32



672

Steps 1-2

[0663] 6-Bromo-1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazole (LXV) (500 mg, 1.91 mmol), bis(pinacolato) diboron (650 mg, 2.56 mmol), Pd(dppf)Cl_2(75 mg, 0.09 mmol) and KOAc (500 mg, 5.09 mmol) were suspended in dry 1,4-dioxane (12 mL). The reaction was sonicated and degassed for 5 min before heating at 100° C. for 2 h. The reaction mixture was cooled to room temperature and a 2 M aqueous solution of K_3PO_4 (2.52 mL, 5.04 mmol) was added and the reaction was stirred for 5 min. 5-Bromo-2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XII) (443 mg, 1.69 mmol), $Pd(OAc)_2$ (19 mg, 0.08 mmol) and QPhos (84 mg, 0.12 mmol) were added and the reaction was purged with Ar for 5 min. The reaction was heated to 80° C. for 1 h. The reaction mixture was reduced in vacuo and the crude product was purified by column chromatography (100% $CHCl_3$). The product was further purified by column chromatography (0→50% EtOAc/hexanes hold followed by 50→100% EtOAc/hexanes) to give a solid which was triturated with MeOH and filtered washing with MeOH to give 6-(2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazole (CLX) (295 mg, 0.809 mmol, 47.9% yield) as a beige solid. ESIMS found for $C_{15}H_{11}ClF_2N_6O$ m/z 365.1 (M+H).

Step 3

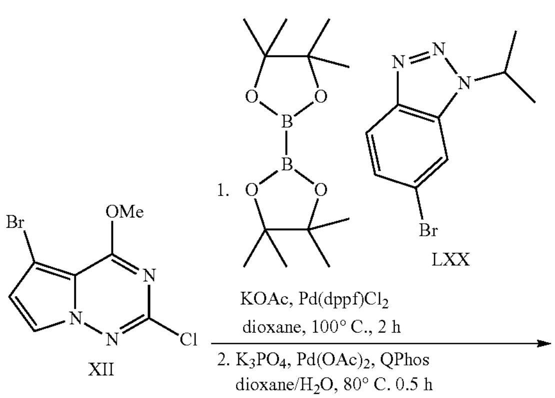
[0664] 6-(2-Chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazole (CLX) (25 mg, 0.07 mmol), trans-4-amino-1-methylcyclohexan-1-ol (CXXXVI) (commercially available from PharmaBlock (USA), Inc.) (9 mg, 0.07 mmol), BrettPhos PD G3 (5.mg, 0.01 mmol), BrettPhos (4.mg, 0.01 mmol) and NaO^tBu (21.mg, 0.22 mmol) were dissolved in dry 1,4-dioxane (0.7 mL) in a microwave vial. The suspension was purged with Ar for 5 min and then the reaction was heated to 100° C. for 3 h. The reaction was reduced in vacuo and loaded onto Celite® and purified by column chromatography (0→90% EtOAc/hexanes). The isolated product was further purified by HPLC (0→35% hold followed by 5% stepwise increases to 80% MeOH/H_2O in 0.1% formic acid). Appropriate fractions were collected and neutralized with saturated aqueous $NaHCO_3$ and extracted with DCM (×2). The combined organic layers were dried over anhydrous $MgSO_4$ and reduced in vacuo to give (1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol (725) as a yellow solid (3 mg, 0.007 mmol, 9.6% yield). ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.40-1.50 (4H, m), 1.57-1.65 (2H, m), 1.84-1.92 (2H, m), 3.60-3.69 (1H, m), 3.94 (3H, s), 4.23 (1H, s), 5.30 (2 H, td, J=15.81, 2.87 Hz), 6.50 (1H, d, J=7.94 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.72 (1H, d, J=2.46 Hz), 7.62-7.65 (1H, m), 7.65 (1H, d, J=2.74 Hz), 8.00-8.05 (2H, m); ESIMS found for $C_{22}H_{25}F_2N_7O_2$ m/z 458.2 (M+1). The elimination side-product, (1r,4r)-4-((5-(1-((E)-2-fluorovinyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol (672) (7 mg, 0.016 mmol, 23.3% yield) was also obtained as a yellow solid.

[0665] ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.51 (4H, m), 1.57-1.66 (2H, m), 1.82-1.93 (2H, m), 3.59-3.71 (1H, m), 3.94 (3H, s), 4.23 (1H, s), 6.51 (1H, d, J=7.94 Hz), 6.74 (1H, d, J=2.74 Hz), 7.34 (1H, dd, J=60.90, 4.10 Hz), 7.45 (1H, dd, J=18.62, 3.83 Hz), 7.65 (1H, d, J=2.46 Hz), 7.69 (1H, d, J=9.03 Hz), 7.92 (1 H, s), 8.08 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{24}FN_7O_2$ m/z 438.2 (M+1).

Example 10

[0666] Preparation of N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (688) and 3-((3R,4S)-3-fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile (690) are depicted below in Scheme 33.

Scheme 33



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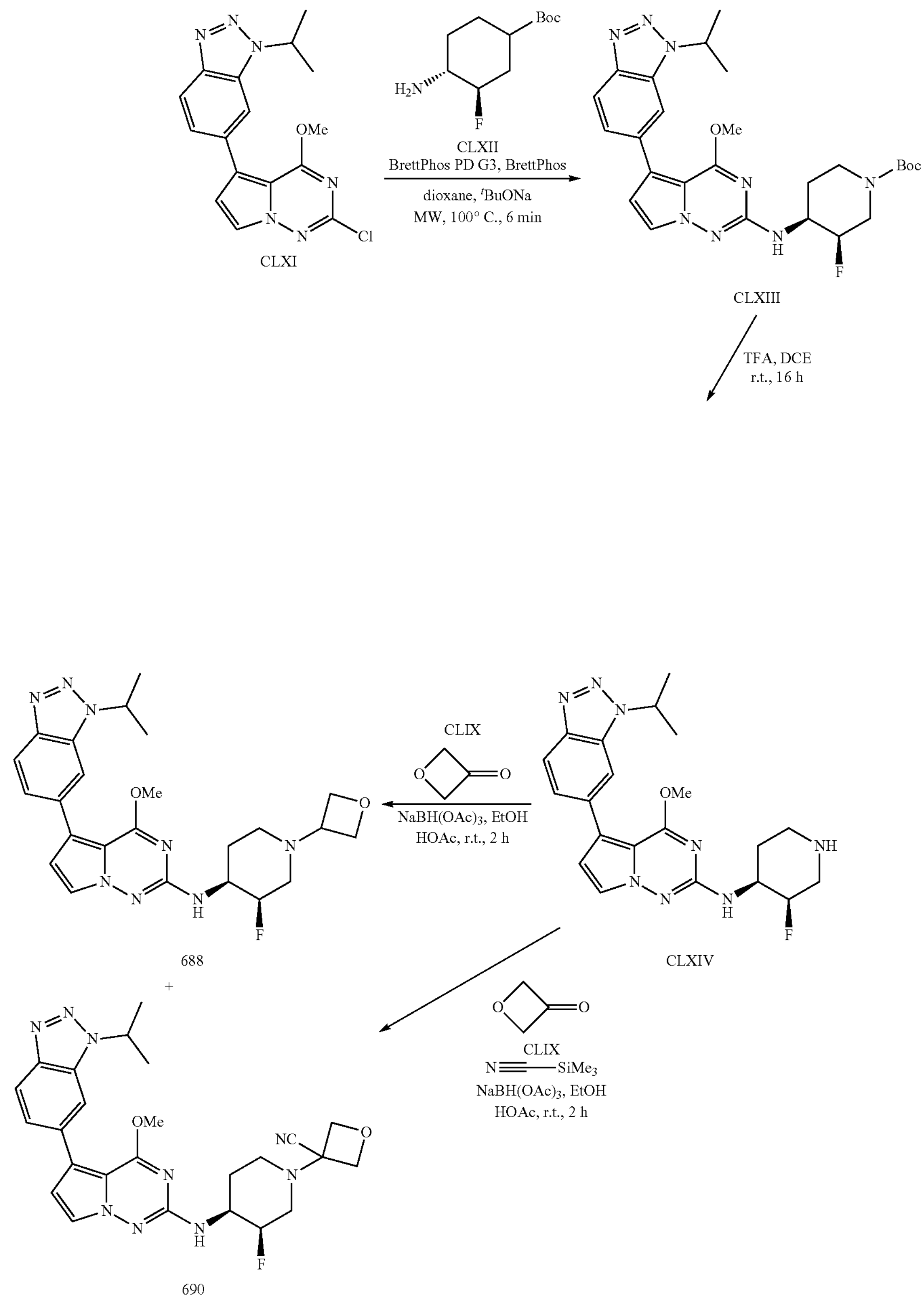
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CLXII
BrettPhos PD G3, BrettPhos
dioxane, ^{t}BuONa
MW, 100° C., 6 min
CLXIII
TFA, DCE
r.t., 16 h
CLXIV
CLIX
NaBH(OAc)$_3$, EtOH
HOAc, r.t., 2 h
688
+
CLIX
N≡—SiMe$_3$
NaBH(OAc)$_3$, EtOH
HOAc, r.t., 2 h
690

Steps 1-2

[0667] Used procedure described in Example 9, Scheme 32, steps 1-2 to produce 6-(2-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-1-isopropyl-1H-benzo[d][1,2,3]triazole (CLXI) (1.022 g, 2.982 mmol, 97.8% yield) as a fluffy red solid. ESIMS found for $C_{16}H_{15}ClN_6O$ m/z 343.1 (M+H).

Step 3

[0668] Used procedure described in Example 9, Scheme 32, step 3 to produce tert-butyl (3R,4S)-3-fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4] triazin-2-yl)amino)piperidine-1-carboxylate (CLXIII) (184 mg, 0.351 mmol, 100.19% yield) as a brown semi-solid. ESIMS found for $C_{26}H_{33}FN_8O_3$ m/z 525.15 (M+H).

Step 4

[0669] Used procedure described in Example 8, Scheme 31, step 2 to produce N-((3R,4S)-3-fluoropiperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (CLXIV) (148 mg, 0.349 mmol, 99.4% yield) as a brown solid. ESIMS found for $C_{21}H_{25}FN_8O$ m/z 425.2 (M+H).

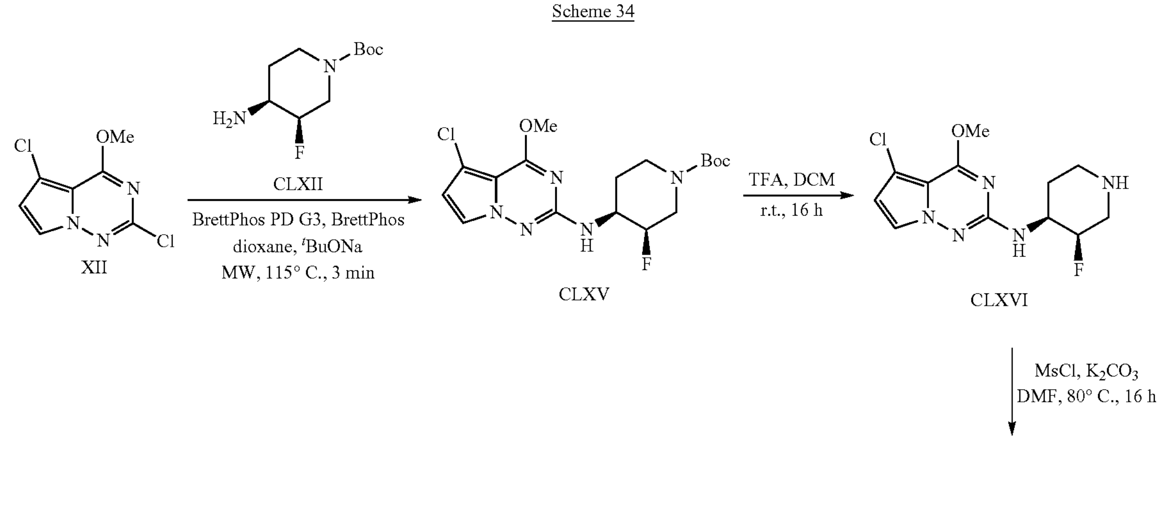
Step 5a and 5b

[0670] N-((3R,4S)-3-Fluoropiperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (CLXIV) (40 mg, 0.09 mmol) was suspended in dry DCE (0.9 mL) followed by EtOH (0.1 mL) to aid dissolution. Acetic acid (16 μL, 0.28 mmol), oxetan-3-one (CLIX) (17 μL, 0.29 mmol), and 3A MS (5 beads) were added before the reaction was heated to 65° C. for 1 h. The reaction was cooled to room temperature and 400 μL of the reaction mixture was removed (leaving 600 μL behind) and was added to a separate vial and both were heated to 65° C. To the first vial was added $NaBH(OAc)_3$ (41 mg, 0.19 mmol) and the reaction was stirred for 10 minutes. To the second vial was added trimethylsilyl cyanide (24 μL, 0.19 mmol) and the reaction was stirred for 10 minutes. Both reactions were loaded onto Celite® separately and were purified by column chromatography (0→2% MeOH/$CHCl_3$). Compound 688 was further purified by HPLC (0→50% MeCN/H_2O with 0.1% formic acid). Compound 690 was further purified by HPLC (0→80% MeCN/H_2O with 0.1% formic acid). N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo [2,1-f][1,2,4]triazin-2-amine (688) (11 mg, 0.023 mmol, 24.3% yield) as a fluffy white solid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.67 (6H, d, J=6.57 Hz), 1.70-1.77 (1H, m), 1.88-1.97 (1H, m), 1.99-2.06 (1H, m), 2.16 (1H, dd, J=37.00, 12.59 Hz), 2.71-2.80 (1H, m), 2.95-3.04 (1H, m), 3.49 (1 H, quin, J=6.37 Hz), 3.74-3.90 (1 H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.43, 3.01 Hz), 4.94 (1H, d, J=49.90 Hz), 5.24 (1 H, spt, J=6.75 Hz), 6.69 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.74 Hz), 7.59 (1H, dd, J=8.76, 1.37 Hz), 7.64 (1H, d, J=2.46 Hz), 7.99 (1H, d, J=8.76 Hz), 8.02 (1 H, s); ESIMS found for $C_{24}H_{29}FN_8O_2$ m/z 481.25 (M+1) and 3-((3R,4S)-3-Fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile (690) (10 mg, 0.020 mmol, 21.0% yield) as a fluffy white solid. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.67 (6H, d, J=6.84 Hz), 1.82 (1 H, br dd, J=12.32, 3.01 Hz), 2.00 (1 H, qd, J=12.37, 3.70 Hz), 2.09-2.18 (1H, m), 2.26 (1H, dd, J=36.20, 12.32 Hz), 2.78-2.86 (1H, m), 3.00-3.11 (1H, m), 3.79-3.95 (1 H, in), 3.97(3 H, s), 4.52 (1H, d, J=6.84 Hz), 4.65 (1H, d, J=7.12 Hz), 4.76 (2H, t, J=6.84 Hz), 5.04 (1H, d, J=49.35 Hz), 5.24 (1 H, spt, J=6.75 Hz), 6.78 (1H, d, J=2.46 Hz), 6.81 (1H, d, J=7.67 Hz), 7.59 (1H, dd, J=8.76, 1.37 Hz), 7.66 (1H, d, J=2.46 Hz), 7.99 (1H, d, J=8.49 Hz), 8.02 (1 H, s); ESIMS found for $C_{25}H_{28}FN_9O_2$ m/z 506.2 (M+1).

Example 11

[0671] Preparation of 5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(methylsulfonyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (1145) is depicted below in Scheme 34.

Scheme 34



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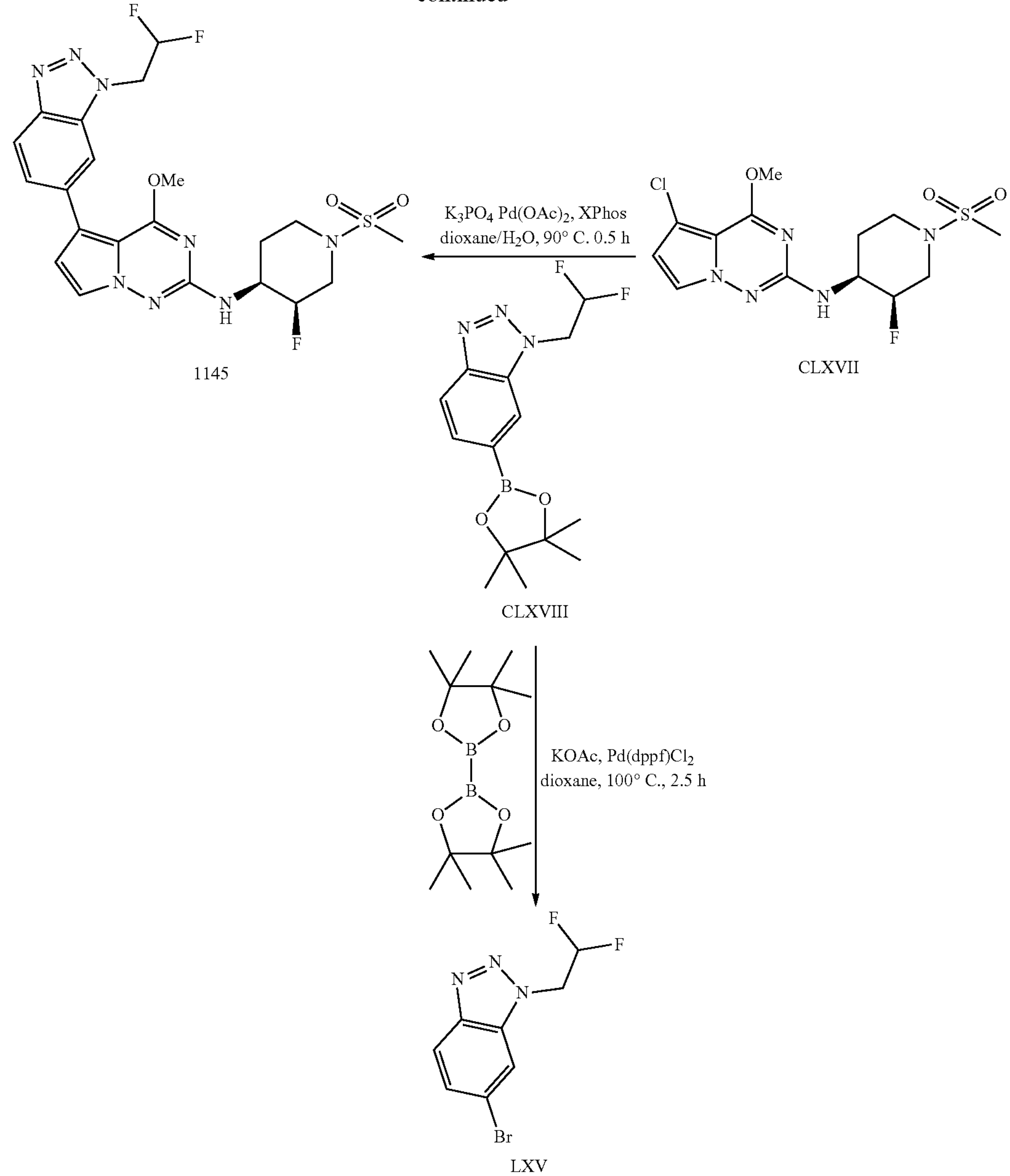


Step 1

[0672] 2,5-Dichloro-4-methoxypyrrolo[2,1-f][1,2,4]triazine (XII) (700 mg, 3.21 mmol), tert-butyl (3R,4S)-4-amino-3-fluoropiperidine-1-carboxylate (CLXII) (commercially available from Advanced ChemBlocks Inc.) (771 mg, 3.53 mmol), BrettPhos Pd G3 (146 mg, 0.16 mmol), BrettPhos (86 mg, 0.16 mmol) and ^{t}BuONa (770 mg, 8.01 mmol) were charged in a microwave vial and dry 1,4-dioxane (20 mL) was added. 3A MS (8 beads) were added and the reaction was stirred for 1 h at room temperature. The sieves were removed quickly, and the reaction was sealed and purged with Ar for 5 min followed by microwave irradiation to 115° C. for 3 min. The reaction mixture poured into DCM and water and the organic layer was separated. The aqueous layer was extracted with DCM (×2) and the combined organic layers were dried ($MgSO_4$) and reduced in vacuo to give the crude product tert-butyl (3R,4S)-4-((5-chloro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidine-1-carboxylate (CLXV) (1,284 g, 3.211 mmol, 100.0% yield), assuming quantitative yield, as a brown semi-solid which was used without further purification. ESIMS found for $C_{17}H_{23}ClFN_5O_3$ m/z 344.10 (M+H-^{t}Bu).

Step 2

[0673] Used procedure described in Example 8, Scheme 31, step 2 to produce 5-chloro-N-((3R,4S)-3-fluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (CLXVI) (381 mg, 1.271 mmol, 39.6% yield) as a pale-yellow solid. ESIMS found for $C_{12}H_{15}ClFN_5O$ m/z 300.1 (M+H).

Step 3

[0674] K_2CO_3 (115 mg, 0.83 mmol) and MsCl (45 mg, 0.39 mmol) were suspended in DMF (1 mL) and 5-chloro-N-((3R,4S)-3-fluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (CLXVI) (50 mg, 0.17 mmol) was added, and the reaction was heated to 80° C. for 16 h. The reaction was loaded onto Celite® and purified by column chromatography (0→45% EtOAc/hexanes) to give 5-chloro-N-((3R,4S)-3-fluoro-1-(methylsulfonyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (CLXVII) (13 mg, 0.034 mmol, 20.6% yield) as a pearlescent white solid. ESIMS found for $C_{13}H_{17}ClFN_5O_3S$ m/z 378.1 (M+H).

Step 4

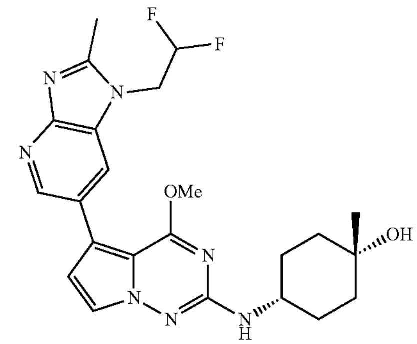
[0675] 6-Bromo-1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazole (LXV) (5.16 g, 19.69 mmol), bis(pinacolato) diboron (7.51 g, 29.57 mmol), $Pd(dppf)Cl_2$(803 mg, 0.98 mmol) and KOAc (5.8 g, 59.1 mmol) were suspended in dry 1,4-dioxane (100 mL). The reaction was sonicated and degassed for 5 minutes before heating at 100° C. for 2.5 h. The reaction mixture was loaded onto Celite® and purified by column chromatography (0→50% EtOAc/hexanes) to produce 1-(2,2-difluoroethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-benzo[d][1,2,3]triazole (CLXVIII) (5.654 g, 18.291 mmol, 92.9% yield) as a fluffy pale-orange solid. ESIMS found for $C_{14}H_{18}BF_2N_3O_2$ m/z 310.15 (M+H).

Step 5

[0676] 5-Chloro-N-((3R,4S)-3-fluoro-1-(methylsulfonyl) piperidin-4-yl)-4-methoxypyrrolo [2,1-f][1,2,4]triazin-2-amine (CLXVII) (13 mg, 0.03 mmol), 1-(2,2-difluoroethyl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-benzo [d][1,2,3]triazole (CLXVIII) (17 mg, 0.05 mmol), $Pd(OAc)_2$ (2 mg, 0.01 mmol), and XPhos (3 mg, 0.01 mmol) were suspended in dry 1,4-dioxane (0.5 mL). K_2PO_4 (52 μL, 0.1 mmol) was added and the reaction was sonicated and bubbled with Ar for 5 min. The reaction was then heated to 90° C. for 30 min. The reaction mixture was loaded onto Celite® and purified by column chromatography (0→1.5% MeOH/$CHCl_3$). The product was further purified by HPLC (0→35% MeCN/H_2O with 0.1% formic acid) to yield 5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(methylsulfonyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine (1145) (6 mg, 0.011 mmol, 33.2% yield) as a fluffy white solid after lyophilization. ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.77-1.88 (1H, m), 1.96 (1 H, qd, J=12.50, 4.38 Hz), 2.93 (3 H, s), 3.02 (1 H, td, J=12.25, 2.60 Hz), 3.20 (1H, dd, J=37.55, 12.59 Hz), 3.61-3.70 (1H, m), 3.80-3.89 (1H, m), 3.90-4.04 (1H, m), 3.96 (3 H, s), 5.05 (1H, d, J=49.10 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.88 (1H, d, J=7.94 Hz), 7.63 (1H, d, J=2.46 Hz), 7.64-7.66 (1H, m), 8.02-8.05 (2H, m); ESIMS found for $C_{21}H_{23}F_3N_8O_3S$ m/z 525.15 (M+1).

[0677] The following compounds were prepared in accordance with the procedures described in the above Schemes 1-34.

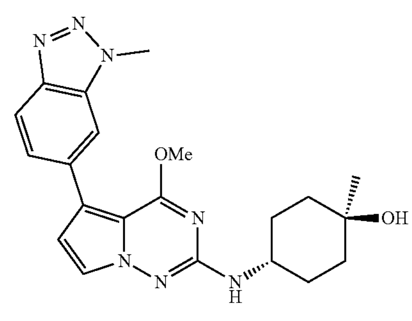
1



[0678] cis-4-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-imidazo[4,5-b]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 1.

[0679] Beige solid (2.8 mg, 0.005 mmol, 2.5% yield). ^1H NMR (499 MHz, CHLOROFORM-d) δ ppm 1.29 (3 H, s), 1.58-1.68 (4H, m), 1.75 (2H, br d, J=10.68 Hz), 1.99-2.06 (2H, m), 2.72 (3 H, s), 3.66-3.74 (1H, m), 3.95 (3 H, s), 4.50 (2 H, td, J=14.80, 2.50 Hz), 6.12 (1 H, tt, J=54.60, 3.00 Hz), 6.60 (1H, d, J=2.46 Hz), 7.47 (1H, d, J=2.19 Hz), 7.81 (1 H, br s), 8.73 (1 H, br s); ESIMS found for $C_{23}H_{27}F_2N_7O_2$ m/z 472.2 (M+1).

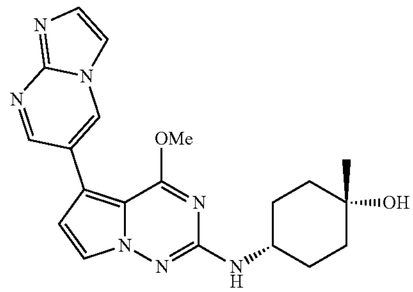
3



[0680] trans-4-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 3.

[0681] Beige solid (10 mg, 0.025 mmol, 10.0% yield). ^1H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.53 (4H, m), 1.56-1.65 (2H, m), 1.84-1.93 (2H, m), 3.59-3.71 (1H, m), 3.95 (3H, s), 4.24 (1H, s), 4.31 (3 H, s), 6.48 (1H, d, J=7.94 Hz), 6.73 (1H, d, J=2.74 Hz), 7.61 (1H, dd, J=8.49, 1.37 Hz), 7.64 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{21}H_{25}N_7O_2$ m/z 408.25 (M+1).

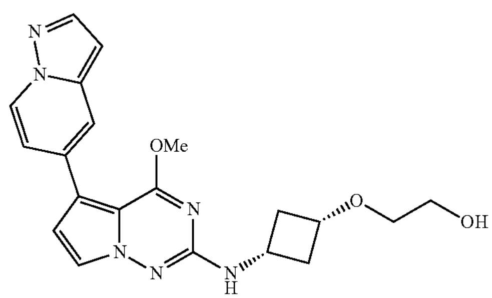
4



[0682] cis-4-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 4.

[0683] Off-white solid (15 mg, 0.038 mmol, 22.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.36 (2 H, td, J=13.00, 4.11 Hz), 1.58 (2H, br d, J=12.32 Hz), 1.61-1.75 (4H, m), 3.45-3.60 (1H, m), 3.97 (3H, s), 4.00 (1H, s), 6.57 (1H, d, J=7.94 Hz), 6.76 (1 H, d, J=2.46 Hz), 7.64 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

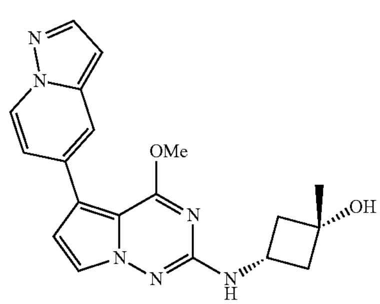
6



[0684] 2-(cis-3-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol6.

[0685] White solid (28 mg, 0.071 mmol, 35.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.82-1.93 (2H, m), 2.60-2.69 (2H, m), 3.30-3.33 (2H, m), 3.48 (2 H, q, J=5.48 Hz), 3.68-3.74 (1H, m), 3.74-3.81 (1H, m), 3.98 (3 H, s), 4.60 (1H, t, J=5.61 Hz), 6.58 (1H, d, J=1.92 Hz), 6.77 (1H, d, J=2.46 Hz), 7.04 (1H, d, J=7.39 Hz), 7.10 (1H, dd, J=7.26, 1.78 Hz), 7.60 (1H, d, J=2.46 Hz), 7.80 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{20}H_{22}N_6O_3$ m/z 395.2 (M+1).

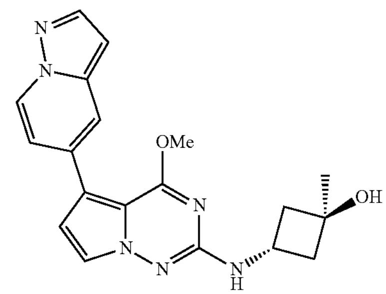
7



[0686] cis-3-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol7.

[0687] Off-white solid (53 mg, 0.145 mmol, 54.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 2.02 (2 H, td, J=8.90, 2.19 Hz), 2.31-2.41 (2H, m), 3.72 (1 H, dq, J=15.16, 7.72 Hz), 3.98 (3H, s), 4.92 (1H, s), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 6.95 (1H, d, J=6.57 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.63 (1H, d, J=2.74 Hz), 7.80 (1 H, d, J=1.10 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{19}H_{20}N_6O_2$ m/z 365.2 (M+1).

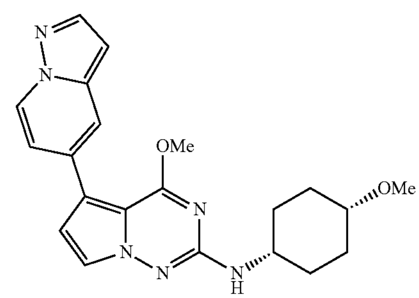
8



[0688] trans-3-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 8.

[0689] White solid (16 mg, 0.044 mmol, 16.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28 (3 H, s), 1.93-2.05 (2H, m), 2.27-2.35 (2H, m), 3.98 (3 H, s), 4.25 (1 H, sxt, J=7.34 Hz), 4.79 (1 H, s), 6.58 (1H, d, J=1.92 Hz), 6.76 (1H, d, J=2.74 Hz), 6.95 (1H, d, J=6.57 Hz), 7.10 (1H, dd, J=7.12, 1.92 Hz), 7.62 (1H, d, J=2.46 Hz), 7.80 (1H, d, J=0.82 Hz), 7.97 (1 H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{19}H_{20}N_6O_2$ m/z 365.2 (M+1).

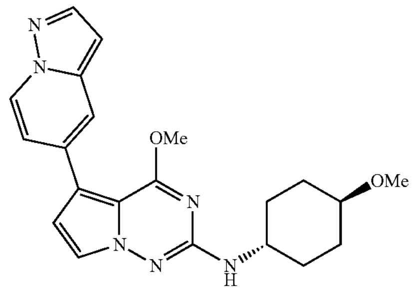
9



[0690] 4-Methoxy-N-(cis-4-methoxycyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 9.

[0691] Off-white solid (25 mg, 0.064 mmol, 31.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.54 (2H, m), 1.55-1.65 (2H, m), 1.65-1.73 (2H, m), 1.80-1.88 (2H, m), 3.22 (3 H, s), 3.34 (1H, br d, J=2.19 Hz), 3.59-3.70 (1H, m), 3.98 (3 H, s), 6.56-6.58 (1H, m), 6.58 (1 H, s), 6.75 (1H, d, J=2.46 Hz), 7.10 (1H, dd, J=7.26, 2.05 Hz), 7.61 (1H, d, J=2.74 Hz), 7.80 (1H, d, J=1.09 Hz), 7.96 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

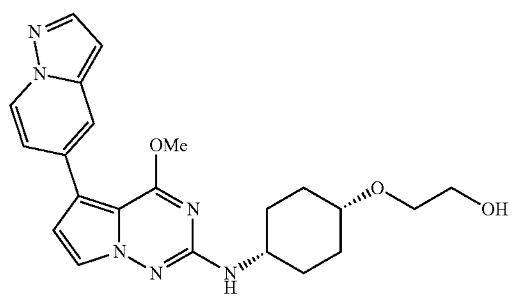
10



[0692] 4-Methoxy-N-(trans-4-methoxycyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 10.

[0693] Off-white solid (40 mg, 0.102 mmol, 50.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14-1.26 (2H, m), 1.27-1.40 (2H, m), 2.01 (4 H, br t, J=10.81 Hz), 3.12 (1 H, tt, J=10.23, 3.73 Hz), 3.24 (3 H, s), 3.51-3.63 (1H, m), 3.98 (3 H, s), 6.57 (1H, d, J=7.94 Hz), 6.58 (1H, d, J=1.64 Hz), 6.75 (1H, d, J=2.46 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.63 (1H, d, J=2.74 Hz), 7.80 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

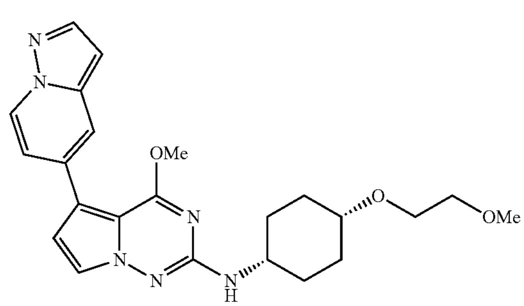
13



[0694] 2-((cis-4-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol 13.

[0695] Off-white semi-solid. (10 mg, 0.024 mmol, 14.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.55 (2H, m), 1.60-1.73 (4H, m), 1.78-1.88 (2H, m), 3.38-3.42 (2H, m), 3.47 (1 H, br s), 3.50 (2 H, q, J=5.48 Hz), 3.57-3.69 (1H, m), 3.98 (3 H, s), 4.51 (1H, t, J=5.48 Hz), 6.55 (1H, d, J=7.67 Hz), 6.58 (1H, d, J=1.37 Hz), 6.75 (1H, d, J=2.46 Hz), 7.10 (1 H, dd, J=7.39, 1.64 Hz), 7.61 (1H, d, J=2.74 Hz), 7.80 (1 H, s), 7.97 (1H, d, J=1.92 Hz), 8.62 (1 H, d, J=7.39 Hz); ESIMS found for $C_{22}H_{26}N_6O_3$ m/z 423.3 (M+1).

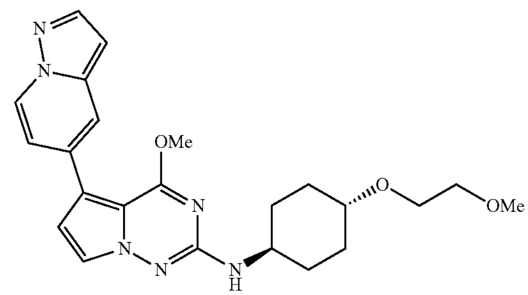
15



[0696] 4-Methoxy-N-(cis-4-(2-methoxyethoxy)cyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 15.

[0697] Fluffy off-white solid (33 mg, 0.0756 mmol, 45.3% yield). ^{1}HNMR(499 MHz, DMSO-d_6) δ ppm 1.45-1.55 (2H, m), 1.59-1.73 (4H, m), 1.78-1.88 (2H, m), 3.27 (3 H, s), 3.43-3.46 (2H, m), 3.46-3.48 (1H, m), 3.48-3.52 (2H, m), 3.57-3.69 (1H, m), 3.98 (3 H, s), 6.58 (1H, d, J=2.19 Hz), 6.59 (1H, d, J=7.85 Hz), 6.75 (1H, d, J=2.46 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.61 (1H, d, J=2.74 Hz), 7.80 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{23}H_{28}N_6O_3$ m/z 437.25 (M+1).

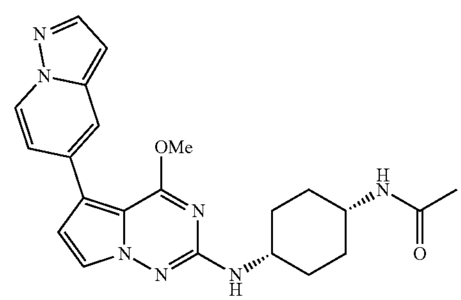
16



[0698] 4-Methoxy-N-(trans-4-(2-methoxyethoxy)cyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 16.

[0699] White solid (31 mg, 0.071 mmol, 35.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.18-1.37 (4H, m), 2.00 (4H, br d, J=10.95 Hz), 3.20-3.27 (1H, m), 3.25 (3 H, s), 3.40-3.45 (2H, m), 3.53 (2H, t, J=4.93 Hz), 3.54-3.60 (1H, m), 3.97 (3 H, s), 6.56 (1H, d, J=8.21 Hz), 6.58 (1H, d, J=1.64 Hz), 6.75 (1H, d, J=2.46 Hz), 7.10 (1H, dd, J=7.39, 1.64 Hz), 7.63 (1H, d, J=2.74 Hz), 7.80 (1 H, s), 7.96 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{23}H_{28}N_6O_3$ m/z 437.2 (M+1).

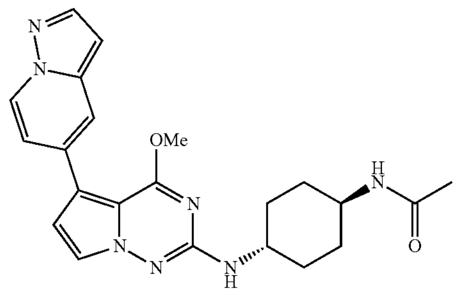
17



[0700] N-(cis-4-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide 17.

[0701] White solid (22 mg, 0.052 mmol, 33.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.50-1.59 (2H, m), 1.60-1.72 (4H, m), 1.74-1.81 (2H, m), 1.81 (3 H, s), 3.64-3.71 (2H, m), 3.99 (3 H, s), 6.47 (1H, d, J=6.30 Hz), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.26, 1.78 Hz), 7.63 (1H, d, J=2.74 Hz), 7.70 (1H, br d, J=6.84 Hz), 7.81 (1 H, s), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

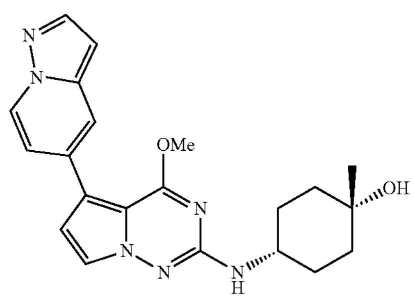
18



[0702] N-(trans-4-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide 18.

[0703] White solid (2 mg, 0.005 mmol, 2.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.19-1.29 (2H, m), 1.30-1.40 (2H, m), 1.78 (3 H, s), 1.81 (2H, br d, J=11.50 Hz), 1.99 (2H, br d, J=10.13 Hz), 3.45-3.51 (1H, m), 3.52-3.59 (1H, m), 3.97 (3 H, s), 6.56 (1H, d, J=8.21 Hz), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 7.10 (1H, dd, J=7.26, 2.05 Hz), 7.63 (1H, d, J=2.46 Hz), 7.74 (1H, d, J=7.67 Hz), 7.80 (1H, d, J=1.09 Hz), 7.97 (1H, d, J=2.46 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

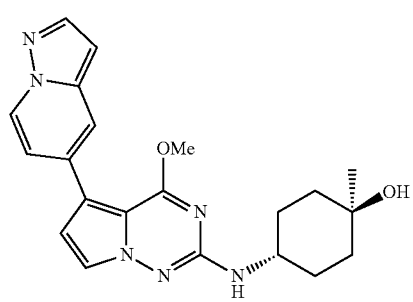
19



[0704] cis-4-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 19.

[0705] Off-white solid (20 mg, 0.051 mmol, 42.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.36 (2 H, td, J=13.00, 4.38 Hz), 1.58 (2H, br d, J=12.05 Hz), 1.61-1.68 (2H, m), 1.69-1.75 (2H, m), 3.45-3.59 (1H, m), 3.98 (3H, s), 3.99 (1H, s), 6.52 (1H, d, J=7.94 Hz), 6.58 (1H, d, J=1.64 Hz), 6.74 (1H, d, J=2.74 Hz), 7.10 (1H, dd, J=7.12, 1.92 Hz), 7.60 (1H, d, J=2.74 Hz), 7.80 (1H, d, J=1.09 Hz), 7.96 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

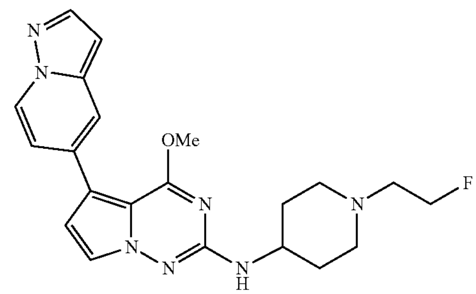
20



[0706] trans-4-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 20.

[0707] Beige solid (5 mg, 0.013 mmol, 8.3% yield). ^{1}H NMR (499 MHz, CHLOROFORM-d) δ ppm 1.32 (3 H, s), 1.47-1.58 (2H, m), 1.60-1.68 (2H, m), 1.71-1.79 (2 H, m), 2.09-2.18 (2H, m), 3.86 (1H, br d, J=3.83 Hz), 4.01 (3H, s), 4.12 (1H, s), 6.53 (1 H, br s), 6.64 (1H, d, J=2.46 Hz), 7.04 (1H, br d, J=5.75 Hz), 7.47 (1H, d, J=2.46 Hz), 7.71 (1 H, br s), 7.96 (1 H, br s), 8.50 (1H, br d, J=6.57 Hz); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

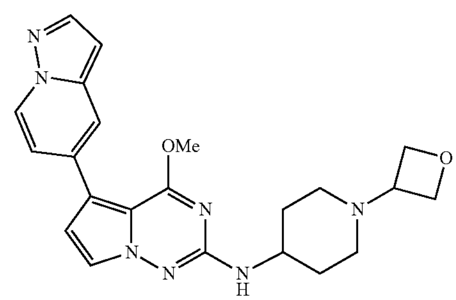
24



[0708] N-(1-(2-Fluoroethyl)piperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 24.

[0709] Off-white solid (17 mg, 0.042 mmol, 20.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.46-1.60 (2H, m), 1.85-1.96 (2H, m), 2.11 (2 H, br t, J=11.09 Hz), 2.61 (2 H, dt, J=28.25, 4.95 Hz), 2.84-2.93 (2H, m), 3.53-3.66 (1H, m), 3.98 (3 H, s), 4.53 (2 H, dt, J=47.70, 4.95 Hz), 6.58 (1H, d, J=1.64 Hz), 6.62 (1H, d, J=7.94 Hz), 6.76 (1H, d, J=2.74 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.62 (1H, d, J=2.46 Hz), 7.81 (1H, d, J=1.10 Hz), 7.97 (1H, d, J=2.46 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{21}H_{24}FN_7O$ m/z 410.2 (M+1).

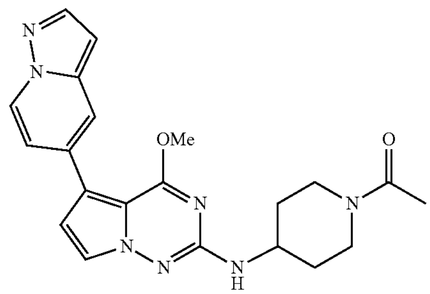
26



[0710] 4-Methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 26.

[0711] Off-white solid (2 mg, 0.005 mmol, 1.2% yield). ^{1}H NMR (499 MHz, METHANOL-d_4) δ ppm 1.57-1.70 (2H, m), 2.06 (2 H, br t, J=11.77 Hz), 2.09-2.15 (2H, m), 2.80 (2H, br d, J=11.77 Hz), 3.53 (1 H, quin, J=6.43 Hz), 3.67-3.77 (1H, m), 4.03 (3 H, s), 4.62 (2H, t, J=6.30 Hz), 4.69-4.75 (2H, m), 6.54-6.61 (1H, m), 6.70 (1H, d, J=2.46 Hz), 7.14 (1H, dd, J=7.39, 1.92 Hz), 7.47 (1H, d, J=2.46 Hz), 7.79 (1H, d, J=1.10 Hz), 7.92 (1H, d, J=2.19 Hz), 8.46 (1H, d, J=7.12 Hz); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

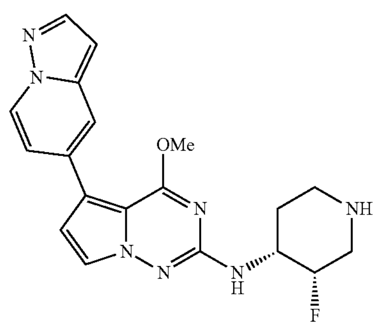
27



[0712] 1-(4-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 27.

[0713] Beige solid (11 mg, 0.027 mmol, 13.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27-1.39(1 H,m), 1.40-1.52 (1H, m), 1.87-1.94 (1H, m), 1.94-2.00 (1H, m), 2.01 (3 H, s), 2.70-2.81 (1H, m), 3.12-3.19 (1H, m), 3.78-3.87 (2H, m), 3.99 (3 H, s), 4.24-4.34 (1H, m), 6.59 (1H, dd, J=2.19, 0.82 Hz), 6.73 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.12, 1.92 Hz), 7.63 (1H, d, J=2.74 Hz), 7.81 (1H, d, J=1.10 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.2 (M+1).

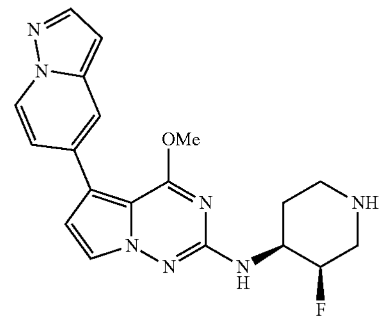
29



[0714] N-((3S,4R)-3-Fluoropiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 29.

[0715] Off-white solid (45 mg, 0.118 mmol, 87.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.57-1.65 (1H, m), 1.73 (1 H, qd, J=12.37, 4.24 Hz), 2.56 (1 H, br t, J=12.46 Hz), 2.71 (1H, dd, J=39.25, 14.30 Hz), 2.96 (1H, br d, J=13.14 Hz), 3.13 (1 H, br t, J=11.50 Hz), 3.77-3.94 (1H, m), 4.00 (3 H, s), 4.80 (1H, d, J=50.75 Hz), 6.59 (1H, d, J=1.64 Hz), 6.64 (1H, d, J=7.94 Hz), 6.78 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.39, 1.92 Hz), 7.63 (1H, d, J=2.46 Hz), 7.81 (1H, d, J=1.10 Hz), 7.97 (1H, d, J=2.19 Hz), 8.63 (1H, d, J=7.12 Hz); ESIMS found for $C_{19}H_{20}FN_7O$ m/z 382.2 (M+1).

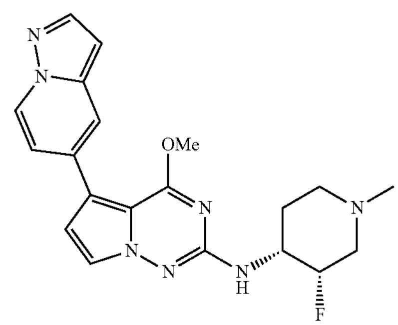
30



[0716] N-((3R,4S)-3-Fluoropiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 30.

[0717] Brown solid (109 mg, 0.286 mmol, 99.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.89-1.96 (1H, m), 2.07 (1 H, qd, J=13.23, 4.11 Hz), 2.75 (1 H, s), 3.11-3.18 (1H, m), 3.27-3.38 (1H, m), 3.58-3.66 (1H, m), 4.01 (3 H, s), 4.05-4.18 (1H, m), 5.20 (1H, d, J=47.45 Hz), 6.60 (1H, d, J=1.92 Hz), 6.81 (1H, d, J=2.46 Hz), 7.06 (1H, d, J=7.39 Hz), 7.11 (1 H, dd, J=7.12, 1.92 Hz), 7.59 (1H, d, J=2.74 Hz), 7.82 (1H, d, J=1.37 Hz), 7.98 (1H, d, J=2.19 Hz), 8.64 (1H, br d, J=7.39 Hz); ESIMS found for $C_{19}H_{20}FN_7O$ m/z 382.2 (M+1).

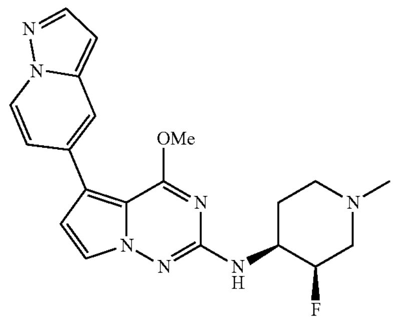
31



[0718] N-((3S,4R)-3-Fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 31.

[0719] Off-white solid (30 mg, 0.076 mmol, 72.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68 (1 H, br dd, J=12.59, 3.01 Hz), 1.92 (1 H, qd, J=12.23, 3.56 Hz), 2.01-2.09 (1H, m), 2.17 (1H, dd, J=37.55, 13.20 Hz), 2.19 (3 H, s), 2.79 (1H, br d, J=11.23 Hz), 3.00-3.09 (1H, m), 3.67-3.83 (1H, m), 4.00 (3 H, s), 4.91 (1H, d, J=50.20 Hz), 6.59 (1H, d, J=1.64 Hz), 6.64 (1H, d, J=7.67 Hz), 6.78 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.12, 1.92 Hz), 7.63 (1H, d, J=2.74 Hz), 7.81 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.63 (1H, d, J=7.39 Hz); ESIMS found for $C_{20}H_{22}FN_7O$ m/z 396.2 (M+1).

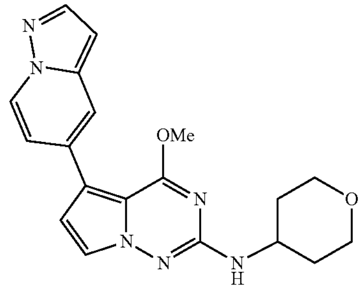
34



[0720] N-((3R,4S)-3-Fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 34.

[0721] Off-white solid (43 mg, 0.109 mmol, 38.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.65-1.72 (1H, m), 1.92 (1 H, qd, J=12.27, 3.70 Hz), 2.01-2.09 (1H, m), 2.17 (1H, dd, J=37.55, 13.20 Hz), 2.19 (3 H, s), 2.80 (1H, br d, J=11.77 Hz), 3.01-3.07 (1H, m), 3.67-3.83 (1H, m), 4.00 (3 H, s), 4.91 (1H, d, J=49.90 Hz), 6.59 (1H, d, J=1.37 Hz), 6.65 (1H, d, J=7.67 Hz), 6.78 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.26, 2.05 Hz), 7.63 (1H, d, J=2.74 Hz), 7.81 (1H, d, J=1.10 Hz), 7.97 (1H, d, J=2.19 Hz), 8.63 (1H, d, J=7.12 Hz); ESIMS found for $C_{20}H_{22}FN_7O$ m/z 396.3 (M+1).

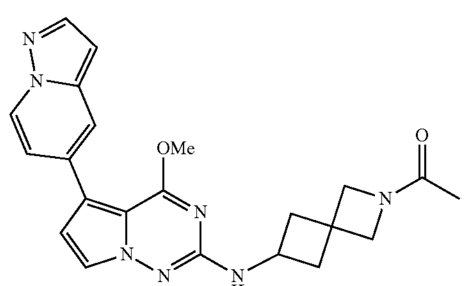
36



[0722] 4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(tetrahydro-2H-pyran-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 36.

[0723] Off-white solid (8 mg, 0.022 mmol, 6.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.47-1.60 (2H, m), 1.89 (2 H, br dd, J=12.46, 2.05 Hz), 3.36-3.45 (2H, m), 3.73-3.85 (1H, m), 3.85-3.92 (2 H,m), 3.99 (3 H,s), 6.58 (1H, d, J=1.92 Hz), 6.71 (1H, d, J=7.94 Hz), 6.76 (1H, d, J=2.46 Hz), 7.10 (1H, dd, J=7.26, 1.78 Hz), 7.63 (1H, d, J=2.74 Hz), 7.81 (1 H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{19}H_{20}N_6O_2$ m/z 365.2 (M+1).

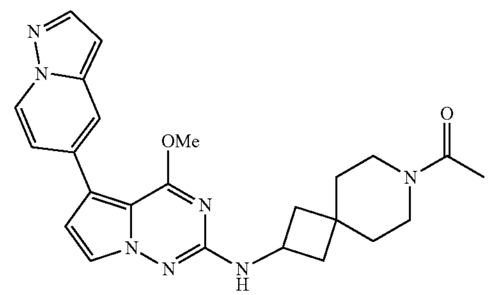
37



[0724] 1-(6-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.3]heptan-2-yl)ethan-1-one 37.

[0725] White solid (28 mg, 0.067 mmol, 38.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.69-1.76 (3H, m), 2.13-2.25 (2H, m), 2.52-2.60 (2H, m), 3.77 (1H, s), 3.89 (1H, s), 3.98 (3 H, s), 4.04-4.11 (1H, m), 4.05 (1H, s), 4.17 (1H, s), 6.58 (1H, d, J=1.92 Hz), 6.77 (1 H, d, J=2.46 Hz), 7.03 (1H, t, J=6.98 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.62 (1H, dd, J=4.79, 2.60 Hz), 7.80 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{22}H_{23}N_7O_2$ m/z 418.2 (M+1).

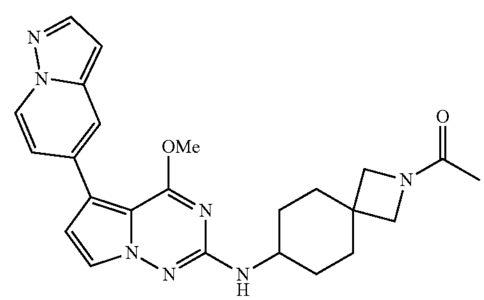
39



[0726] 1-(2-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-7-azaspiro[3.5]nonan-7-yl)ethan-1-one 39.

[0727] Off-white solid (50 mg, 0.112 mmol, 79.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.40-1.46 (1H, m), 1.49-1.56 (2H, m), 1.57-1.64 (1H, m), 1.74-1.84 (2H, m), 1.95-2.01 (3H, m), 2.26 (2 H, br dd, J=9.86, 8.21 Hz), 3.26-3.30 (1H, m), 3.30-3.32 (1H, m), 3.35-3.39 (1H, m), 3.39-3.44 (1H, m), 3.98 (3 H, s), 4.14-4.25 (1H, m), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 7.02 (1H, t, J=7.12 Hz), 7.10 (1H, dd, J=7.12, 1.92 Hz), 7.59-7.66 (1H, m), 7.80 (1H, d, J=1.09 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{24}H_{27}N_7O_2$ m/z 446.2 (M+1).

40



[0728] 1-(7-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one 40.

[0729] Off-white solid (75 mg, 0.168 mmol, 95.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.26-1.39 (2H, m), 1.48-1.60 (2H, m), 1.73-1.78 (3H, m), 1.83-1.93 (4H, m), 3.47(1 H, s), 3.52(1 H, s), 3.57(1 H,brdd,J=7.53, 3.15 Hz), 3.74(1 H, s), 3.80(1 H, s), 3.98 (3H, d, J=1.10 Hz), 6.54 (1H, dd, J=16.15, 7.94 Hz), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.62 (1H, t, J=2.87 Hz), 7.80 (1H, d, J=1.09 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{24}H_{27}N_7O_2$ m/z 446.2 (M+1).

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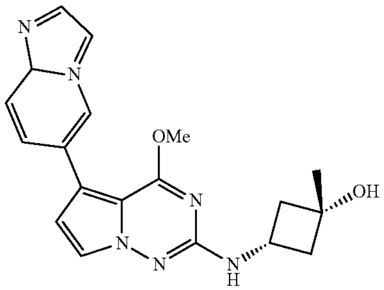
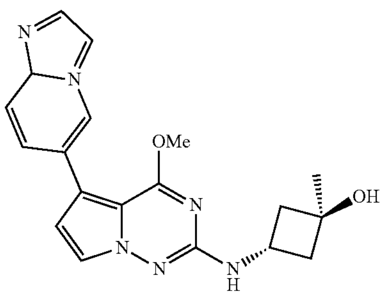


[0730] cis-3-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxy-pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 43.

[0731] White solid (19 mg, 0.052 mmol, 31.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 1.96-2.07 (2H, m), 2.31-2.41 (2H, m), 3.71 (1 H, dq, J=15.16, 7.72 Hz), 3.96 (3H, s), 4.91 (1H, s), 6.67 (1H, d, J=2.74 Hz), 6.92 (1H, d, J=6.84 Hz), 7.43 (1H, dd, J=9.31, 1.64 Hz), 7.54 (1H, d, J=9.31 Hz), 7.56 (1H, d, J=0.82 Hz), 7.62 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{19}H_{20}N_6O_2$ m/z 365.2 (M+1).

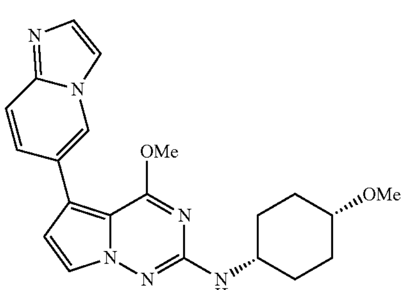
44



[0732] trans-3-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 44.

[0733] Off-white semi-solid (10 mg, 0.027 mmol, 16.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28 (3 H, s), 1.94-2.03 (2H, m), 2.28-2.35 (2H, m), 3.96 (3 H, s), 4.25 (1 H, sxt, J=7.39 Hz), 4.78 (1 H, br s), 6.68 (1H, d, J=2.74 Hz), 6.93 (1H, d, J=6.84 Hz), 7.43 (1H, dd, J=9.31, 1.64 Hz), 7.54 (1H, d, J=9.58 Hz), 7.56 (1 H, s), 7.61 (1H, d, J=2.74 Hz), 7.95 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{19}H_{20}N_6O_2$ m/z 365.2 (M+1).

45



[0734] 5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(cis-4-methoxycyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 45.

[0735] Off-white solid (2.6 mg, 0.007 mmol, 4.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.54 (2H, m), 1.55-1.65 (2H, m), 1.69 (2 H, dt, J=8.35, 4.04 Hz), 1.80-1.88 (2H, m), 3.22 (3 H, s), 3.29-3.37 (1H, m), 3.56-3.71 (1H, m), 3.96 (3 H, s), 6.54 (1H, d, J=7.67 Hz), 6.67 (1H, d, J=2.46 Hz), 7.43 (1H, dd, J=9.31, 1.37 Hz), 7.54 (1H, d, J=9.31 Hz), 7.56 (1 H, s), 7.61 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

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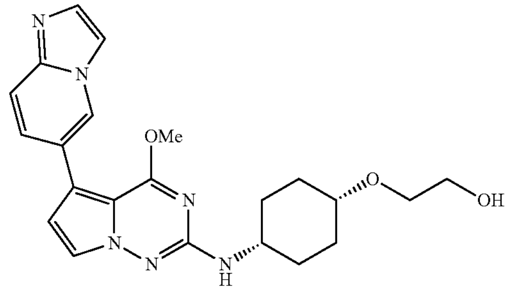
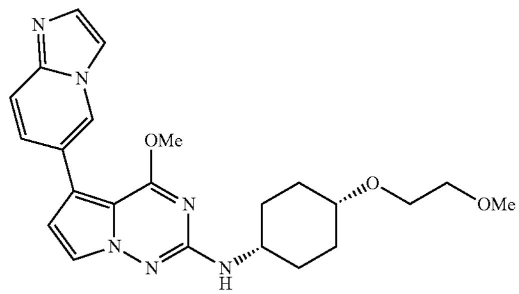


[0736] 2-((cis-4-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol 49.

[0737] Orange semi-solid. (6 mg, 0.014 mmol, 6.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.56 (2H, m), 1.60-1.74 (4H, m), 1.78-1.88 (2H, m), 3.38-3.42 (2H, m), 3.47 (1 H, br s), 3.50 (2 H, q, J=5.20 Hz), 3.58-3.70 (1H, m), 3.96 (3 H, s), 4.51 (1 H, br t, J=5.34 Hz), 6.52 (1H, d, J=7.67 Hz), 6.67 (1H, d, J=2.46 Hz), 7.47 (1H, br d, J=9.03 Hz), 7.56 (1H, br d, J=9.03 Hz), 7.58-7.60 (1H, m), 7.61 (1H, d, J=2.46 Hz), 7.98 (1 H, br s), 8.70 (1 H, br s); ESIMS found for $C_{22}H_{26}N_6O_3$ m/z 423.25 (M+1).

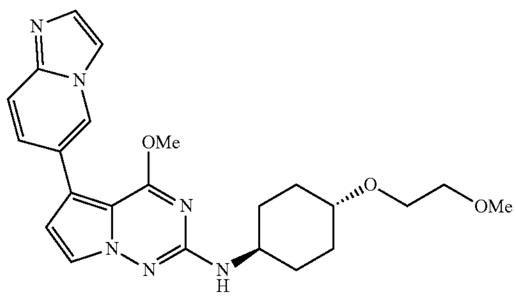
51



[0738] 5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(cis-4-(2-methoxyethoxy) cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 51.

[0739] White solid (3 mg, 0.007 mmol, 4.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.44-1.56 (2H, m), 1.58-1.74 (4H, m), 1.77-1.88 (2H, m), 3.27 (3 H, s), 3.43-3.46 (2 H, m), 3.47 (1 H, br s), 3.48-3.52 (2H, m), 3.62 (1 H, ddt, J=12.53, 8.56, 4.52, 4.52 Hz), 3.96 (3 H, s), 6.56 (1H, d, J=7.67 Hz), 6.67 (1H, d, J=2.46 Hz), 7.43 (1H, dd, J=9.45, 1.78 Hz), 7.54 (1 H, d, J=9.31 Hz), 7.56 (1H, d, J=1.09 Hz), 7.61 (1H, d, J=2.74 Hz), 7.95 (1 H, s), 8.68 (1H, d, J=1.64 Hz); ESIMS found for $C_{23}H_{28}N_6O_3$ m/z 437.2 (M+1).

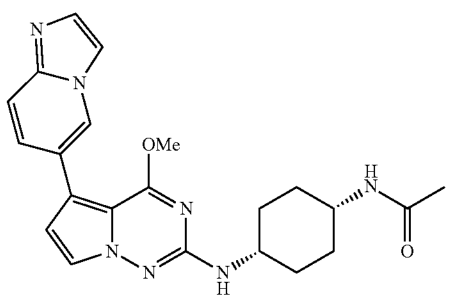
52



[0740] 5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(trans-4-(2-methoxyethoxy) cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 52.

[0741] White solid (5 mg, 0.012 mmol, 5.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.18-1.26 (2H, m), 1.27-1.36 (2H, m), 2.00 (4H, br d, J=10.95 Hz), 3.20-3.26 (1H, m), 3.25 (3 H, s), 3.42 (2H, dd, J=5.75, 3.83 Hz), 3.53 (2H, dd, J=5.75, 3.83 Hz), 3.55-3.60 (1 H, m), 3.95 (3 H, s), 6.52 (1H, d, J=7.94 Hz), 6.67 (1H, d, J=2.46 Hz), 7.43 (1H, dd, J=9.45, 1.78 Hz), 7.54 (1H, d, J=9.31 Hz), 7.56 (1H, d, J=1.09 Hz), 7.63 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 8.64-8.70 (1H, m); ESIMS found for $C_{23}H_{28}N_6O_3$ m/z 437.2 (M+1).

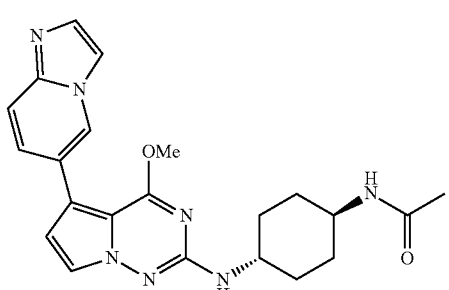
53



[0742] N-(cis-4-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide 53.

[0743] Off-white solid (8 mg, 0.019 mmol, 37.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.50-1.59 (2H, m), 1.60-1.71 (4H, m), 1.73-1.81 (2H, m), 1.81 (3 H, s), 3.67 (2H, br d, J=3.56 Hz), 3.97 (3 H, s), 6.43 (1H, d, J=6.30 Hz), 6.68 (1H, d, J=2.74 Hz), 7.44 (1H, dd, J=9.31, 1.64 Hz), 7.54 (1H, d, J=9.31 Hz), 7.57 (1 H, s), 7.62 (1H, d, J=2.46 Hz), 7.70 (1H, br d, J=7.12 Hz), 7.95 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

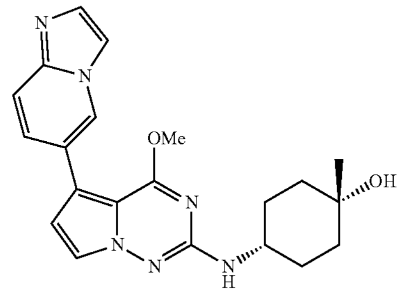
54



[0744] N-(trans-4-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide 54.

[0745] Off-white solid (17 mg, 0.041 mmol, 24.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.19-1.29 (2H, m), 1.29-1.39 (2H, m), 1.78 (3 H, s), 1.79-1.85 (2H, m), 1.99 (2H, br d, J=10.95 Hz), 3.44-3.59 (2H, m), 3.95 (3 H, s), 6.53 (1H, d, J=8.21 Hz), 6.67 (1 H, d, J=2.46 Hz), 7.43 (1H, dd, J=9.45, 1.51 Hz), 7.54 (1H, d, J=9.31 Hz), 7.56 (1 H, s), 7.63 (1 H, d, J=2.46 Hz), 7.74 (1H, d, J=7.67 Hz), 7.95 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

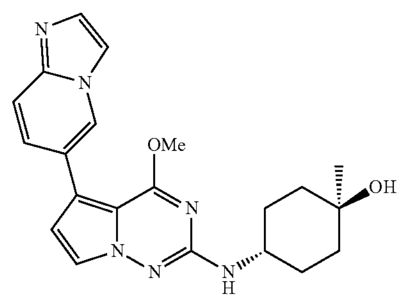
55



[0746] cis-4-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 55.

[0747] Off-white solid (7.9 mg, 0.020 mmol, 14.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.36 (2 H, td, J=13.00, 4.11 Hz), 1.58 (2H, br d, J=12.32 Hz), 1.60-1.68 (2H, m), 1.68-1.74 (2H, m), 3.45-3.57 (1H, m), 3.96 (3H, s), 4.00 (1H, s), 6.49 (1H, d, J=7.94 Hz), 6.66 (1H, d, J=2.46 Hz), 7.43 (1H, dd, J=9.58, 1.64 Hz), 7.54 (1H, d, J=9.31 Hz), 7.56 (1H, d, J=0.82 Hz), 7.60 (1H, d, J=2.74 Hz), 7.95 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

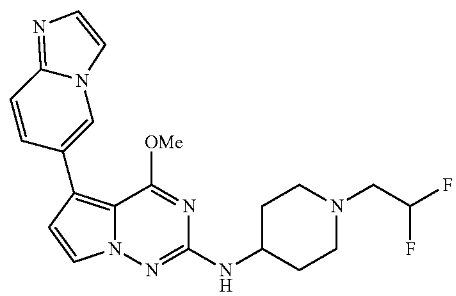
56



[0748] trans-4-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 56.

[0749] Beige solid (16 mg, 0.041 mmol, 20.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.37-1.52 (4H, m), 1.56-1.64 (2H, m), 1.81-1.93 (2H, m), 3.57-3.70 (1H, m), 3.96 (3H, s), 4.24 (1H, s), 6.47 (1H, d, J=7.94 Hz), 6.67 (1H, d, J=2.46 Hz), 7.43 (1H, dd, J=9.31, 1.64 Hz), 7.54 (1H, d, J=9.31 Hz), 7.56 (1 H, s), 7.62 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

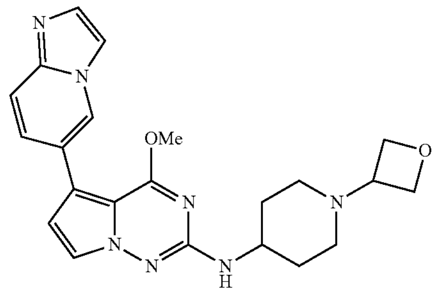
61



[0750] N-(1-(2,2-Difluoroethyl)piperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 61.

[0751] White solid (5 mg, 0.012 mmol, 5.8% yield). H NMR (499 MHz, DMSO-d_6) δ ppm 1.48-1.62 (2H, m), 1.89 (2H, br d, J=10.95 Hz), 2.22-2.31 (2H, m), 2.72 (2 H, td, J=15.74, 4.38 Hz), 2.90 (2H, br d, J=11.77 Hz), 3.53-3.65 (1H, m), 3.96 (3 H, s), 6.13 (1 H, tt, J=55.95, 4.40 Hz), 6.59 (1H, d, J=7.94 Hz), 6.68 (1H, d, J=2.74 Hz), 7.43 (1H, dd, J=9.45, 1.78 Hz), 7.54 (1H, d, J=9.58 Hz), 7.56 (1H, d, J=0.82 Hz), 7.62 (1H, d, J=2.74 Hz), 7.95 (1 H, s), 8.65-8.70 (1H, m); ESIMS found for $C_{21}H_{23}F_2N_7O$ m/z 428.2 (M+1).

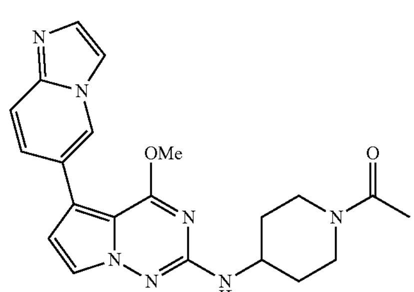
62



[0752] 5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 62.

[0753] Colorless semi-solid. (10 mg, 0.024 mmol, 14.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.48-1.61 (2H, m), 1.84-1.98 (4H, m), 2.71 (2H, br d, J=11.22 Hz), 3.41 (1 H, br s), 3.54-3.65 (1H, m), 3.96 (3 H, s), 4.43 (2H, t, J=6.16 Hz), 4.54 (2H, t, J=6.57 Hz), 6.63 (1H, d, J=7.94 Hz), 6.68 (1H, d, J=2.46 Hz), 7.44 (1H, dd, J=9.31, 1.37 Hz), 7.55 (1H, br d, J=9.31 Hz), 7.57 (1 H, br s), 7.62 (1H, d, J=2.46 Hz), 7.96 (1 H, s), 8.68 (1 H, s); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

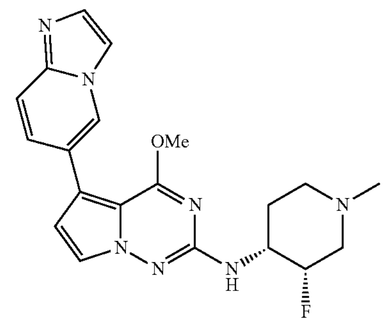
63



[0754] 1-(4-((5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 63.

[0755] Beige solid (9 mg, 0.022 mmol, 13.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.29-1.38 (1H, m), 1.39-1.50 (1H, m), 1.88-1.95 (1H, m), 1.97 (1H, br d, J=13.14 Hz), 2.01 (3 H, s), 2.69-2.82 (1H, m), 3.11-3.20 (1H, m), 3.77-3.87 (2H, m), 3.97(3 H, s), 4.28(1 H, br d, J=12.59 Hz), 6.68-6.72 (2H, m), 7.47 (1H, d, J=9.31 Hz), 7.56 (1H, d, J=9.31 Hz), 7.59 (1 H, s), 7.63 (1H, d, J=2.46 Hz), 7.97 (1 H, s), 8.70 (1 H, s); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.2 (M+1).

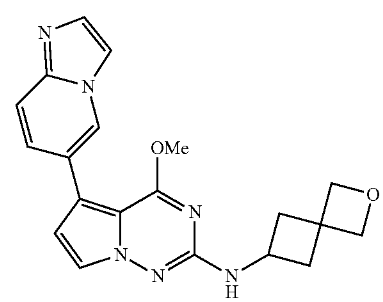
67



[0756] N-((3S,4R)-3-Fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 67.

[0757] White solid (5.5 mg, 0.014 mmol, 10.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.63-1.74 (1H, m), 1.92 (1 H, qd, J=12.27, 3.70 Hz), 2.06 (1 H, br t, J=11.09 Hz), 2.11-2.24 (1H, m), 2.19 (3 H, s), 2.80 (1H, br d, J=10.95 Hz), 3.00-3.07 (1H, m), 3.66-3.83 (1H, m), 3.98 (3 H, s), 4.91 (1H, d, J=49.90 Hz), 6.61 (1H, d, J=7.94 Hz), 6.70 (1H, d, J=2.74 Hz), 7.44 (1H, dd, J=9.45, 1.78 Hz), 7.55 (1H, d, J=9.31 Hz), 7.57 (1 H, s), 7.62 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 8.69 (1 H, s); ESIMS found for $C_{20}H_{22}FN_7O$ m/z 396.2 (M+1).

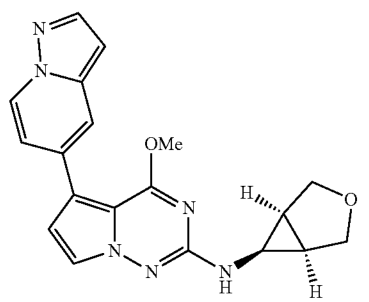
74



[0758] 5-(Imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(2-oxaspiro[3.3]heptan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 74.

[0759] White solid (4.0 mg, 0.011 mmol, 4.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.12-2.23 (2H, m), 2.61 (2H, ddd, J=9.86, 7.53, 2.87 Hz), 3.95-4.04 (1H, m), 3.97 (3H, s), 4.51 (2H, s), 4.63 (2 H, s), 6.58 (1H, d, J=1.92 Hz), 6.76 (1H, d, J=2.46 Hz), 7.00 (1H, d, J=7.12 Hz), 7.10 (1H, dd, J=7.26, 1.78 Hz), 7.61 (1H, d, J=2.74 Hz), 7.80 (1 H, s), 7.97 (1H, d, J=1.92 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{20}H_{20}N_6O_2$ m/z 377.2 (M+1).

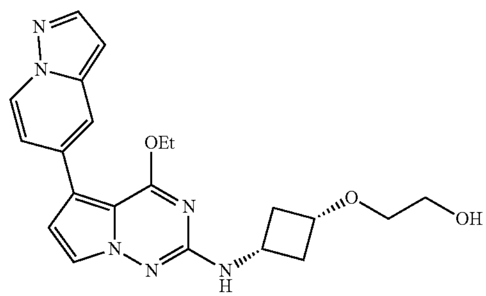
80



[0760] N-((1R,5S,6s)-3-Oxabicyclo[3.1.0]hexan-6-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 80.

[0761] Off-white solid (16 mg, 0.044 mmol, 13.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.95-2.04 (2H, m), 2.86 (1 H, td, J=6.78, 3.15 Hz), 3.81-3.88 (4H, m), 4.00 (3 H, s), 6.39 (1H, d, J=3.01 Hz), 6.59 (1H, d, J=1.64 Hz), 6.78 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=7.39, 1.92 Hz), 7.65 (1H, d, J=2.46 Hz), 7.82 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{1-9}H_{18}N_6O_2$ m/z 363.2 (M+1).

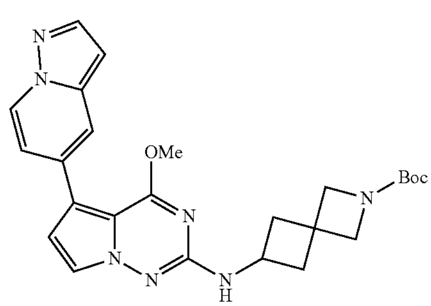
91



[0762] 2-(cis-3-((4-Ethoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol 91.

[0763] Off-white solid (4 mg, 0.010 mmol, 4.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.33 (3H, t, J=7.12 Hz), 1.87 (2 H, qd, J=8.53, 2.87 Hz), 2.58-2.68 (2H, m), 3.30-3.33 (2H, m), 3.48 (2 H, q, J=5.20 Hz), 3.68-3.73 (1H, m), 3.74-3.81 (1H, m), 4.47 (2 H, q, J=7.12 Hz), 4.60 (1H, t, J=5.48 Hz), 6.57 (1H, d, J=1.37 Hz), 6.78 (1H, d, J=2.46 Hz), 6.98 (1 H, d, J=7.39 Hz), 7.13 (1H, dd, J=7.26, 1.78 Hz), 7.59 (1H, d, J=2.46 Hz), 7.86 (1 H, s), 7.96 (1 H, d, J=2.19 Hz), 8.63 (1H, d, J=7.39 Hz); ESIMS found for $C_{21}H_{24}N_6O_3$ m/z 409.2 (M+1).

92



[0764] tert-Butyl 6-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.3]heptane-2-carboxylate 92.

[0765] Off-white solid (103 mg, 0.217 mmol, 64.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.37 (9 H, s), 2.11-2.21 (2H, m), 2.51-2.57 (2H, m), 3.79 (2 H, br s), 3.91 (2 H, br s), 3.97 (3 H, s), 4.01-4.09 (1H, m), 6.58 (1H, d, J=1.64 Hz), 6.77 (1H, d, J=2.74 Hz), 7.01 (1H, d, J=7.12 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.62 (1H, d, J=2.74 Hz), 7.80 (1H, d, J=1.10 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{25}H_{29}N_7O_3$ m/z 476.2 (M+1).

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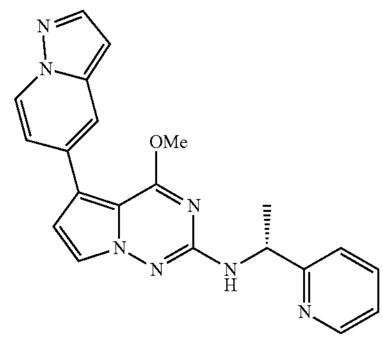
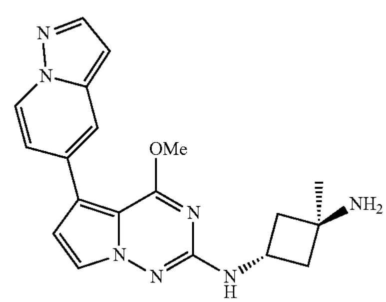


[0766] (R)-4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(1-(pyridin-2-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 93.

[0767] Beige solid (18 mg, 0.047 mmol, 17.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.49 (3H, d, J=7.12 Hz), 3.98 (3 H, s), 5.00 (1 H, quin, J=7.19 Hz), 6.58 (1H, d, J=2.19 Hz), 6.74 (1H, d, J=2.74 Hz), 7.09 (1H, dd, J=7.12, 1.92 Hz), 7.19 (1H, d, J=7.94 Hz), 7.23 (1 H, ddd, J=7.46, 4.86, 0.82 Hz), 7.46 (1H, d, J=7.94 Hz), 7.55 (1H, d, J=2.74 Hz), 7.74 (1 H, td, J=7.67, 1.64 Hz), 7.79 (1H, d, J=1.10 Hz), 7.96 (1H, d, J=2.19 Hz), 8.48-8.56 (1H, m), 8.61 (1 H, d, J=7.12 Hz); ESIMS found for $C_{21}H_{19}N_7O$ m/z 386.2 (M+1).

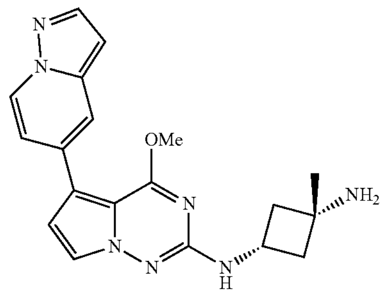
94



[0768] trans-N_1-(4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine 94.

[0769] Off-white solid (67 mg, 0.184 mmol, 85.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.22 (3 H, s), 1.82 (2 H, br s), 1.89-1.97 (2H, m), 2.12-2.22 (2H, m), 3.98 (3 H, s), 4.27 (1 H, sxt, J=7.56 Hz), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 6.92 (1H, d, J=7.12 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.61 (1H, d, J=2.74 Hz), 7.80 (1H, d, J=1.09 Hz), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{1-9}H_{21}N_7O$ m/z 364.2 (M+1).

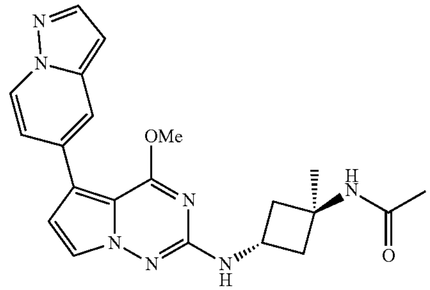
95



[0770] cis-N_1-(4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine 95.

[0771] Off-white foam (157 mg, 0.432 mmol, 69.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.19 (3 H, s), 1.76 (2 H, br s), 1.86 (2 H, td, J=8.90, 2.46 Hz), 2.33 (2H, ddd, J=9.03, 7.53, 2.60 Hz), 3.85 (1 H, dq, J=15.50, 7.79 Hz), 3.97 (3 H, s), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.46 Hz), 6.81 (1H, d, J=7.12 Hz), 7.10 (1H, dd, J=7.12, 1.92 Hz), 7.63 (1H, d, J=2.74 Hz), 7.80 (1H, d, J=1.10 Hz), 7.96 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{19}H_{21}N_7O$ m/z 364.2 (M+1).

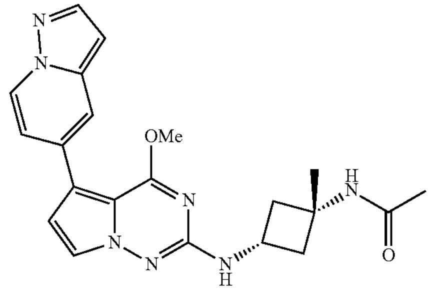
96



[0772] N-(trans-3-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 96.

[0773] Off-white solid (34 mg, 0.084 mmol, 45.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.81 (3H, s), 1.92-1.98 (2H, m), 2.63 (2H, ddd, J=10.27, 7.80, 2.74 Hz), 3.98 (3 H, s), 4.19 (1 H, sxt, J=7.78 Hz), 6.58 (1H, d, J=1.64 Hz), 6.76 (1H, d, J=2.74 Hz), 7.01 (1H, d, J=7.12 Hz), 7.10 (1H, dd, J=7.26, 2.05 Hz), 7.61 (1H, d, J=2.74 Hz), 7.80 (1 H, d, J=1.10 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.2 (M+1).

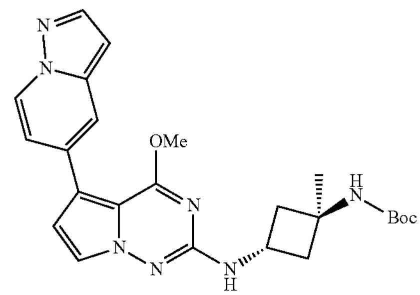
97



[0774] N-(cis-3-((4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 97.

[0775] Off-white solid (27 mg, 0.067 mmol, 96.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.10-2.21 (2H, m), 2.42 (2H, ddd, J=9.65, 7.46, 2.60 Hz), 3.98 (3 H, s), 3.99-4.07 (1H, m), 6.58 (1H, d, J=1.92 Hz), 6.76 (1H, d, J=2.74 Hz), 7.00 (1H, d, J=6.84 Hz), 7.10 (1H, dd, J=7.26, 2.05 Hz), 7.63 (1H, d, J=2.46 Hz), 7.80 (1H, d, J=1.09 Hz), 7.97 (1H, d, J=2.19 Hz), 8.02 (1 H, s), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.2 (M+1).

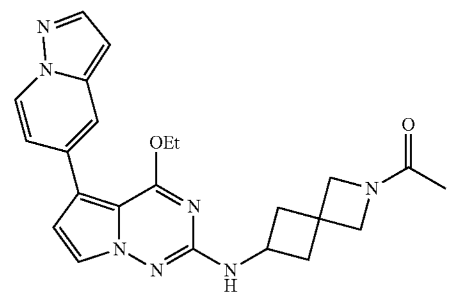
98



[0776] tert-Butyl (trans-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)carbamate 98.

[0777] Off-white solid (107 mg, 0.231 mmol, 46.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.33 (3H, s), 1.41 (9H, s), 1.86-1.96 (2H, m), 2.56-2.67 (2H, m), 3.97 (3 H, s), 4.17 (1 H, sxt, J=7.83 Hz), 6.58 (1H, d, J=1.37 Hz), 6.76 (1H, d, J=2.74 Hz), 7.00 (2H, d, J=7.39 Hz), 7.10 (1H, dd, J=7.39, 1.92 Hz), 7.63 (1H, d, J=2.46 Hz), 7.80 (1H, d, J=1.09 Hz), 7.97 (1H, d, J=2.46 Hz), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{24}H_{29}N_7O_3$ m/z 464.2 (M+1).

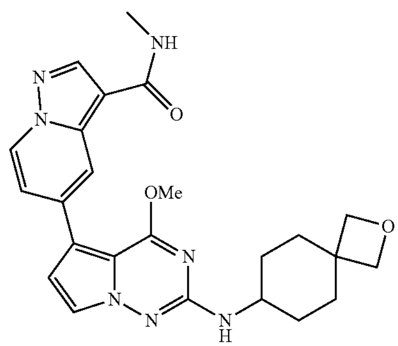
99



[0778] 1-(6-((4-Ethoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.3]heptan-2-yl)ethan-1-one 99.

[0779] White solid (5 mg, 0.012 mmol, 6.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.33 (3H, t, J=7.12 Hz), 1.69-1.77 (3H, m), 2.13-2.25 (2H, m), 2.51-2.60 (2H, m), 3.77 (1H, s), 3.89 (1H, s), 4.05 (1 H, s), 4.05-4.10 (1H, m), 4.17 (1 H, s), 4.46 (2 H, q, J=7.12 Hz), 6.57 (1H, d, J=1.92 Hz), 6.78 (1H, d, J=2.46 Hz), 6.98 (1H, t, J=6.57 Hz), 7.13 (1H, dd, J=7.26, 1.78 Hz), 7.61 (1H, dd, J=4.52, 2.60 Hz), 7.85 (1 H, s), 7.96 (1H, d, J=2.19 Hz), 8.63 (1 H, d, J=7.39 Hz); ESIMS found for $C_{23}H_{25}N_7O_2$ m/z 432.2 (M+1).

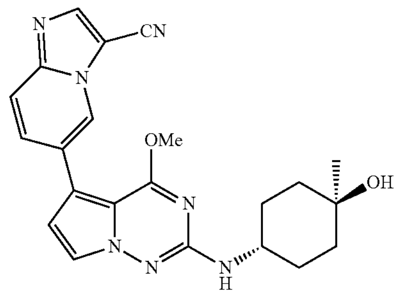
102



[0780] 5-(2-((2-Oxaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide 102.

[0781] Beige solid (30 mg, 0.065 mmol, 42.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.20-1.34 (2H, m), 1.52 (2 H, td, J=12.94, 3.42 Hz), 1.82-1.93 (2H, m), 2.07 (2 H, br d, J=13.14 Hz), 2.79 (3H, d, J=4.65 Hz), 3.49-3.61 (1H, m), 4.01 (3H, s), 4.24 (2H, s), 4.32 (2 H, s), 6.57 (1H, d, J=7.94 Hz), 6.83 (1H, d, J=2.74 Hz), 7.28 (1H, dd, J=7.26, 2.05 Hz), 7.64 (1 H, d, J=2.46 Hz), 8.10 (1 H, q, J=4.56 Hz), 8.45 (1 H, s), 8.52 (1H, dd, J=1.92, 0.82 Hz), 8.64-8.73 (1H, m); ESIMS found for $C_{24}H_{27}N_7O_3$ m/z 462.2 (M+1).

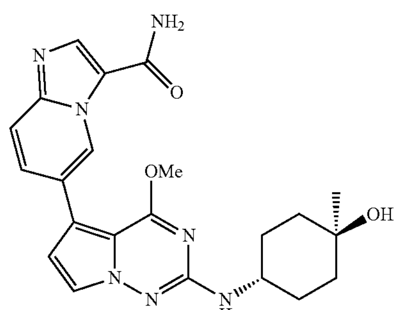
103



[0782] 6-(2-((trans-4-Hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a]pyridine-3-carbonitrile 103.

[0783] Beige solid (12 mg, 0.029 mmol, 8.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.38-1.53 (4H, m), 1.56-1.66 (3H, m), 1.83-1.93 (2H, m), 3.60-3.71 (1 H, m), 4.01 (3H, s), 4.23 (1H, s), 6.56 (1H, d, J=7.94 Hz), 6.89 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.74 Hz), 7.81-7.92 (2H, m), 8.44 (1 H, s), 8.77-8.86 (1H, m); ESIMS found for $C_{22}H_{23}N_7O_2$ m/z 418.2 (M+1).

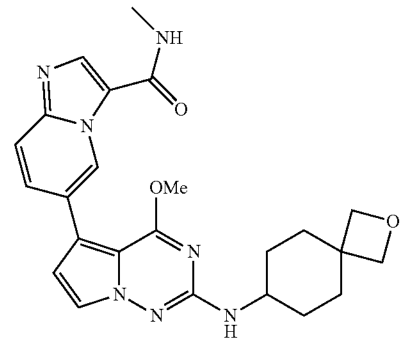
104



[0784] 6-(2-((trans-4-Hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a]pyridine-3-carboxamide 104.

[0785] Beige solid (2.2 mg, 0.005 mmol, 1.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.39-1.48 (4H, m), 1.57-1.63 (2H, m), 1.85-1.91 (2H, m), 3.60-3.72 (1H, m), 3.99 (3H, s), 4.23 (1H, s), 6.49 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.46 Hz), 7.34 (1 H, br s), 7.65 (1H, d, J=2.74 Hz), 7.69 (2 H, s), 7.95 (1 H, br s), 8.33 (1 H, s), 9.84 (1 H, s); ESIMS found for $C_{22}H_{25}N_7O_3$ m/z 436.25 (M+1).

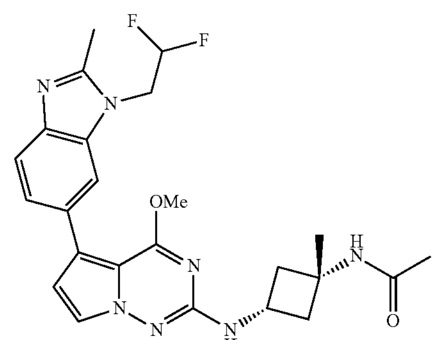
107



[0786] 6-(2-((2-Oxaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide 107.

[0787] Off-white solid (37 mg, 0.080 mmol, 32.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.17-1.37 (2H, m), 1.52 (2 H, td, J=12.87, 3.29 Hz), 1.81-1.91 (2H, m), 2.07 (2H, br d, J=13.14 Hz), 2.82 (3H, d, J=4.65 Hz), 3.48-3.61 (1H, m), 4.00 (3H, s), 4.24 (2H, s), 4.32 (2 H, s), 6.52 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.46 Hz), 7.63 (1H, d, J=2.46 Hz), 7.68 (2 H, d, J=1.37 Hz), 8.26 (1 H, s), 8.43 (1 H, q, J=4.38 Hz), 9.80 (1H, t, J=1.37 Hz); ESIMS found for $C_{24}H_{27}N_7O_3$ m/z 462.2 (M+1).

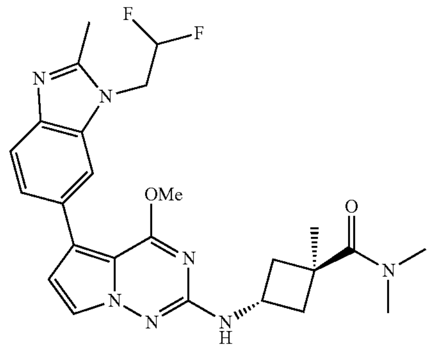
108



[0788] N-(cis-3-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 108.

[0789] White solid (5 mg, 0.0103 mmol, 28.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.10-2.21 (2H, m), 2.42 (2H, ddd, J=9.65, 7.46, 2.60 Hz), 2.56 (3H, s), 3.91 (3H, s), 3.96-4.10 (1H, m), 4.69-4.81 (2H, m), 6.47 (1 H, tt, J=54.40, 3.00 Hz), 6.61 (1H, d, J=2.74 Hz), 6.90 (1H, d, J=7.12 Hz), 7.35 (1H, dd, J=8.21, 1.64 Hz), 7.49 (1 H, d, J=8.21 Hz), 7.59 (1H, d, J=2.74 Hz), 7.69 (1 H, s), 8.02 (1 H, s); ESIMS found for $C_{24}H_{27}F_2N_7O_2$ m/z 484.2 (M+1).

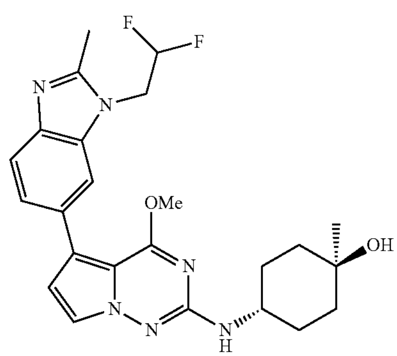
109



[0790] trans-3-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide 109.

[0791] White solid (20 mg, 0.040 mmol, 75.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.39 (3 H, s), 1.94-2.02 (2H, m), 2.56 (3 H, s), 2.81-2.94 (8H, m), 3.85-3.95 (1H, m), 3.92 (3 H, s), 4.68-4.80 (2H, m), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.60 (1H, d, J=2.46 Hz), 6.98 (1H, d, J=6.57 Hz), 7.35 (1H, dd, J=8.35, 1.51 Hz), 7.49 (1H, d, J=8.21 Hz), 7.59 (1H, d, J=2.46 Hz), 7.69 (1 H, s); ESIMS found for $C_{25}H_{29}F_2N_7O_2$ m/z 498.3 (M+1).

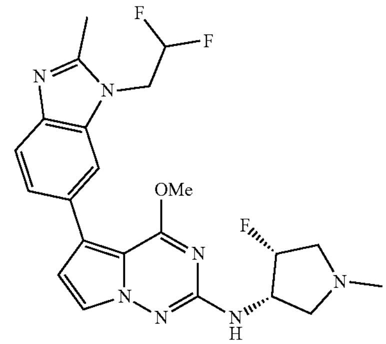
112



[0792] trans-4-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 112.

[0793] White solid (8 mg, 0.020 mmol, 6.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.51 (4H, m), 1.57-1.64 (2H, m), 1.83-1.92 (2H, m), 2.56 (3 H, s), 3.59-3.70 (1H, m), 3.92 (3 H, s), 4.23 (1 H, br s), 4.74 (2 H, td, J=16.02, 2.46 Hz), 6.47 (1 H, tt, J=54.50, 3.00 Hz), 6.38 (1H, d, J=7.94 Hz), 6.60 (1H, d, J=2.46 Hz), 7.35 (1H, dd, J=8.35, 1.51 Hz), 7.49 (1H, d, J=8.49 Hz), 7.59 (1H, d, J=2.74 Hz), 7.69 (1 H, s); ESIMS found for $C_{24}H_{28}F_2N_6O_2$ m/z 471.25 (M+1).

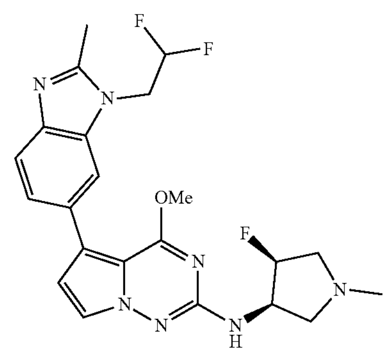
113



[0794] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 113.

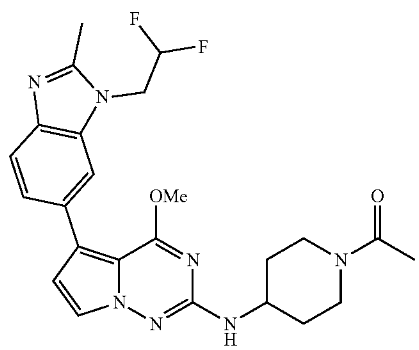
[0795] White fluffy solid (13 mg, 0.028 mmol, 84.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.31 (3 H, s), 2.56(3 H, s), 2.57-2.65 (2H, m), 2.88-2.96 (1H, m), 3.16(1H, ddd, J=29.35, 11.64, 4.79 Hz), 3.94 (3 H, s), 4.19-4.35 (1H, m), 4.74 (2 H, td, J=16.08, 2.60 Hz), 5.21 (1 H, dtd, J=55.95, 5.07, 5.07, 1.92 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.64 (1H, d, J=2.46 Hz), 6.65 (1H, d, J=7.94 Hz), 7.36 (1H, dd, J=8.21, 1.64 Hz), 7.50 (1H, d, J=8.21 Hz), 7.61 (1 H, d, J=2.74 Hz), 7.70 (1 H, s); ESIMS found for $C_{22}H_{24}F_3N_7O$ m/z 460.2 (M+1).

114



[0796] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 114.

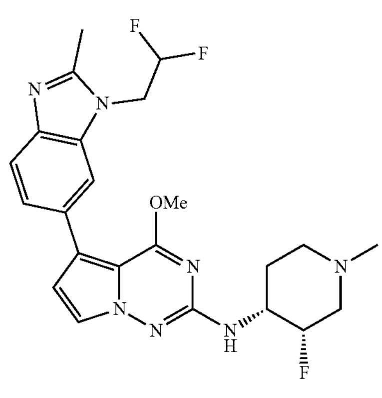
[0797] White fluffy solid (13 mg, 0.028 mmol, 84.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.31 (3 H, s), 2.56(3 H, s), 2.58-2.65 (2H, m), 2.88-2.96 (1H, m), 3.16(1H, ddd, J=29.60, 11.77, 4.93 Hz), 3.94 (3 H, s), 4.20-4.35 (1H, m), 4.75 (2 H, td, J=16.02, 2.46 Hz), 5.21 (1 H, dtd, J=55.95, 5.00, 5.00, 2.05 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.64 (1H, d, J=2.46 Hz), 6.66 (1H, d, J=7.94 Hz), 7.36 (1H, dd, J=8.21, 1.64 Hz), 7.50 (1H, d, J=8.21 Hz), 7.61 (1 H, d, J=2.46 Hz), 7.70 (1 H, s); ESIMS found for $C_{22}H_{24}F_3N_7O$ m/z 460.2 (M+1).



122

[0798] 1-(4-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f]1[1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 122.

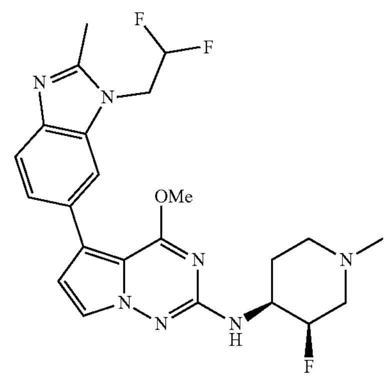
[0799] White solid (5 mg, 0.010 mmol, 3.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28-1.38 (1H, m), 1.39-1.51 (1H, m), 1.89-1.95 (1H, m), 1.95-2.00 (1H, m), 2.01 (3H, s), 2.56 (3H, s), 2.70-2.80 (1H, m), 3.09-3.21 (1H, m), 3.77-3.87 (2H, m), 3.92 (3 H, s), 4.28 (1H, br d, J=14.51 Hz), 4.69-4.81 (2H, m), 6.47 (1 H, tt, J=54.50, 3.00 Hz), 6.60-6.63 (2 H, m), 7.35 (1H, dd, J=8.21, 1.64 Hz), 7.50 (1H, d, J=8.49 Hz), 7.59 (1H, d, J=2.46 Hz), 7.69 (1 H, s); ESIMS found for $C_{24}H_{27}F_2N_7O_2$ m/z 484.25 (M+1).



124

[0800] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 124.

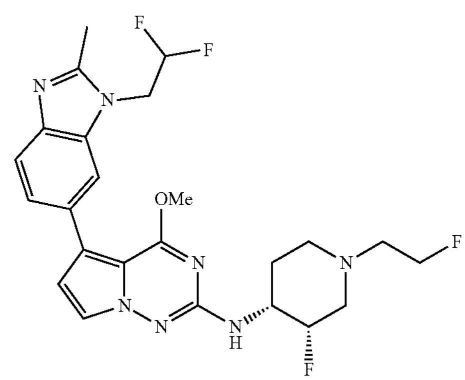
[0801] White solid (17 mg, 0.036 mmol, 33.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.64-1.74 (1H, m), 1.85-1.99 (1H, m), 2.06 (1 H, br t, J=11.36 Hz), 2.18 (1H, dd, J=37.85, 12.60 Hz), 2.19 (3H, s), 2.56 (3H, s), 2.80 (1H, br d, J=10.13 Hz), 3.01-3.11 (1H, m), 3.67-3.84 (1H, m), 3.93 (3 H, s), 4.74 (2 H, td, J=16.08, 2.60 Hz), 4.91 (1H, d, J=50.20 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.51 (1H, d, J=7.94 Hz), 6.63 (1H, d, J=2.46 Hz), 7.36 (1H, dd, J=8.49, 1.64 Hz), 7.50 (1H, d, J=8.49 Hz), 7.59 (1H, d, J=2.46 Hz), 7.70 (1 H, s); ESIMS found for $C_{23}H_{26}F_3N_7O$ m/z 474.3 (M+1).



127

[0802] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 127.

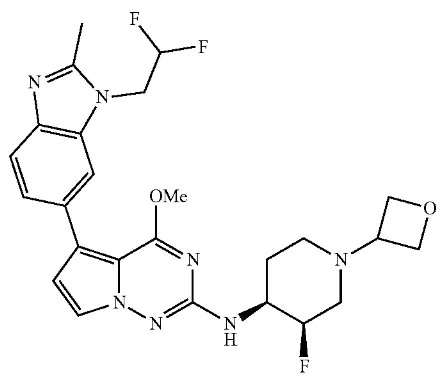
[0803] White solid (6 mg, 0.013 mmol, 38.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.23 (3 H, s), 1.65-1.74 (1H, m), 1.92 (1 H, qd, J=12.23, 4.11 Hz), 2.03-2.12 (1H, m), 2.13-2.29 (1H, m), 2.20(3 H, s), 2.56(3 H, s), 2.81 (1 H, brd, J=9.86 Hz), 3.06(1 H, brt, J=10.40 Hz), 3.68-3.83 (1H, m), 3.93 (3 H, s), 4.74 (2 H, td, J=16.08, 2.60 Hz), 4.92 (1H, d, J=49.65 Hz), 6.47 (1 H, tt, J=54.40, 3.00 Hz), 6.51 (1H, d, J=7.94 Hz), 6.63 (1H, d, J=2.46 Hz), 7.36 (1H, dd, J=8.35, 1.51 Hz), 7.50 (1H, d, J=8.21 Hz), 7.59 (1H, d, J=2.74 Hz), 7.69 (1 H, s); ESIMS found for $C_{23}H_{26}F_3N_7O$ m/z 474.3 (M+1).



129

[0804] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 129.

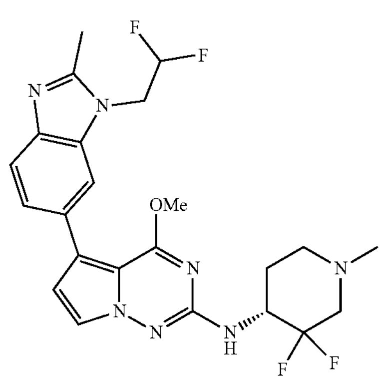
[0805] White fluffy solid (28 mg, 0.055 mmol, 82.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.65-1.75 (1H, m), 1.92 (1 H, qd, J=12.32, 4.11 Hz), 2.25 (1 H, br t, J=11.23 Hz), 2.38 (1H, dd, J=37.60, 12.90 Hz), 2.56 (3 H, s), 2.63-2.74 (2H, m), 2.88-2.97 (1H, m), 3.13-3.21 (1H, m), 3.71-3.87 (1H, m), 3.93 (3 H, s), 4.54 (2 H, dt, J=48.00, 4.95 Hz), 4.74 (2 H, td, J=16.02, 2.19 Hz), 4.92 (1H, d, J=49.40 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.53 (1H, d, J=7.94 Hz), 6.63 (1H, d, J=2.74 Hz), 7.36 (1H, dd, J=8.35, 1.51 Hz), 7.50 (1H, d, J=8.21 Hz), 7.59 (1H, d, J=2.46 Hz), 7.70 (1 H, s); ESIMS found for $C_{24}H_{27}F_4N_7O$ m/z 506.3 (M+1).



137

[0806] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 137.

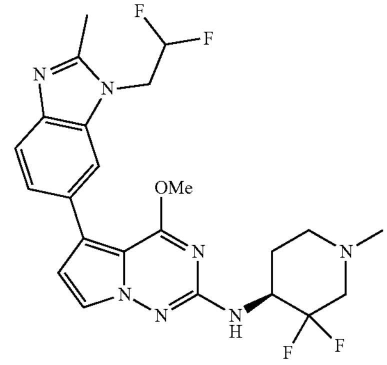
[0807] White solid (27 mg, 0.052 mmol, 48.1% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.69-1.77 (1H, m), 1.91 (1 H, qd, J=12.09, 3.42 Hz), 1.98-2.06 (1H, m), 2.09-2.22 (1H, m), 2.56 (3 H, s), 2.76 (1H, br d, J=10.40 Hz), 2.94-3.04 (1H, m), 3.49 (1 H, quin, J=6.43 Hz), 3.74-3.89 (1H, m), 3.94 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.43, 3.01 Hz), 4.74 (2 H, td, J=16.08, 2.60 Hz), 4.94 (1H, d, J=49.65 Hz), 6.47 (1 H, tt, J=54.60, 3.00 Hz), 6.57 (1H, d, J=7.94 Hz), 6.63 (1H, d, J=2.46 Hz), 7.36 (1H, dd, J=8.49, 1.64 Hz), 7.50 (1H, d, J=8.21 Hz), 7.58 (1H, d, J=2.74 Hz), 7.69 (1 H, s); ESIMS found for $C_{25}H_{28}F_3N_7O_2$ m/z 516.3 (M+1).



138

[0808] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 138.

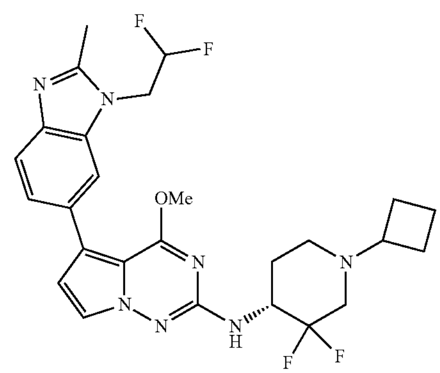
[0809] White fluffy solid (9 mg, 0.018 mmol, 58.3% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.74-1.89 (2H, m), 2.13-2.22 (1H, m), 2.26 (3 H, s), 2.32-2.45 (1H, m), 2.56(3 H, s), 2.78(1 H, brd, J=11.50 Hz), 3.00-3.10 (1H, m), 3.95(3 H, s), 4.16-4.32 (1H, m), 4.74 (2 H, td, J=15.88, 2.46 Hz), 6.47 (1 H, tt, J=54.55, 3.25 Hz), 6.64 (1H, d, J=2.74 Hz), 6.72 (1 H, d, J=9.58 Hz), 7.36 (1H, dd, J=8.35, 1.51 Hz), 7.50 (1H, d, J=8.21 Hz), 7.60 (1H, d, J=2.46 Hz), 7.70 (1 H, s); ESIMS found for $C_{23}H_{25}F_4N_7O$ m/z 492.2 (M+1).



139

[0810] (S)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 139.

[0811] White fluffy solid (8 mg, 0.016 mmol, 45.7% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.74-1.90 (2H, m), 2.13-2.22 (1H, m), 2.26 (3 H, s), 2.32-2.45 (1H, m), 2.56(3 H, s), 2.78(1 H, brd, J=11.50 Hz), 3.00-3.10 (1H, m), 3.95(3 H, s), 4.16-4.32 (1H, m), 4.74 (2 H, td, J=16.02, 2.46 Hz), 6.47 (1 H, tt, J=54.40, 3.25 Hz), 6.64 (1H, d, J=2.46 Hz), 6.72 (1 H, d, J=9.31 Hz), 7.36 (1H, dd, J=8.35, 1.51 Hz), 7.50 (1H, d, J=8.21 Hz), 7.60 (1H, d, J=2.74 Hz), 7.70 (1 H, s); ESIMS found for $C_{23}H_{25}F_4N_7O$ m/z 492.2 (M+1).

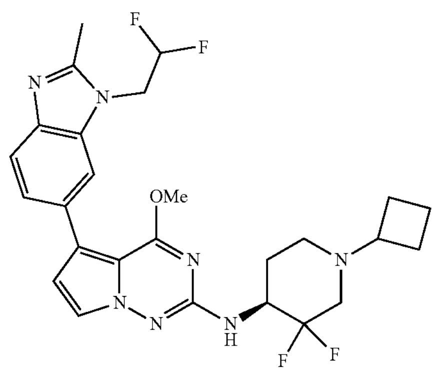


140

[0812] (R)—N-(1-Cyclobutyl-3,3-difluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 140.

[0813] White fluffy solid (10 mg, 0.019 mmol, 56.1% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.56-1.69 (2H, m), 1.71-1.92 (4H, m), 2.00 (3 H, br s), 2.58 (3 H, s), 2.71-2.94 (2H, m), 2.95-3.09 (1H, m), 3.95 (3 H, s), 4.18-4.38 (1H, m), 4.76 (2 H, td, J=15.90, 2.45 Hz), 6.48 (1 H, tt, J=54.40, 3.00 Hz), 6.65 (1H, d, J=2.46 Hz), 6.76 (1 H, br s), 7.38 (1H, dd, J=8.35, 1.51 Hz), 7.52 (1H, d, J=8.21 Hz), 7.60 (1H, d, J=2.46 Hz), 7.72 (1 H, s); ESIMS found for $C_{26}H_{29}F_4N_7O$ m/z 532.3 (M+1).

141



[0814] (S)—N-(1-Cyclobutyl-3,3-difluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 141.

[0815] White fluffy solid (11 mg, 0.021 mmol, 58.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.85 (1H, m), 1.86-1.93 (1H, m), 2.16 (1 H, br t, J=10.27 Hz), 2.33-2.47 (1H, m), 2.58 (3 H, s), 2.76 (1H, br d, J=11.22 Hz), 2.96-3.07 (1H, m), 3.60 (1 H, quin, J=6.30 Hz), 3.95 (3 H, s), 4.23-4.37 (1H, m), 4.44 (2 H, dt, J=15.06, 6.16 Hz), 4.55 (2 H, td, J=6.57, 3.56 Hz), 4.77 (2 H, td, J=15.90, 2.40 Hz), 6.48 (1 H, tt, J=54.40, 3.00 Hz), 6.65 (1H, d, J=2.46 Hz), 6.80 (1H, d, J=9.31 Hz), 7.39 (1H, dd, J=8.35, 1.51 Hz), 7.52 (1H, d, J=8.21 Hz), 7.60 (1H, d, J=2.46 Hz), 7.73 (1 H, s); ESIMS found for $C_{26}H_{29}F_4N_7O$ m/z 532.3 (M+1).

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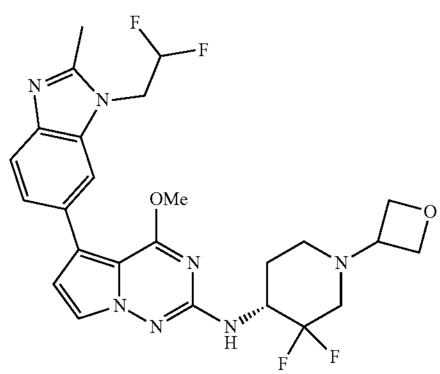
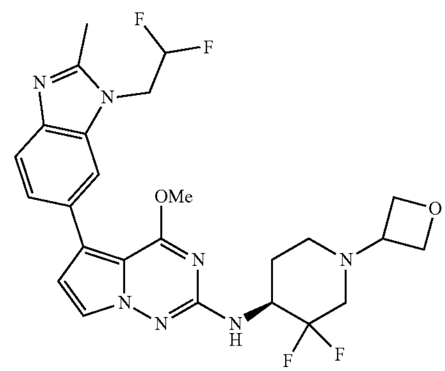


[0816] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 142.

[0817] White fluffy solid (14 mg, 0.026 mmol, 50.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.85 (1H, m), 1.86-1.93 (1H, m), 2.16 (1 H, br t, J=10.27 Hz), 2.33-2.47 (1H, m), 2.58 (3 H, s), 2.76 (1H, br d, J=11.22 Hz), 2.96-3.07 (1H, m), 3.60 (1 H, quin, J=6.30 Hz), 4.23-4.37 (1H, m), 4.44 (2 H, dt, J=15.06, 6.16 Hz), 4.55 (2 H, td, J=6.57, 3.56 Hz), 4.77 (2 H, td, J=15.90, 2.40 Hz), 6.48 (1 H, tt, J=54.40, 3.00 Hz), 6.65 (1H, d, J=2.46 Hz), 6.80 (1 H, d, J=9.31 Hz), 7.39 (1H, dd, J=8.35, 1.51 Hz), 7.52 (1H, d, J=8.21 Hz), 7.60 (1H, d, J=2.46 Hz), 7.73 (1 H, s); ESIMS found for $C_{25}H_{27}F_4N_7O_2$ m/z 534.3 (M+1).

143



[0818] (S)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 143.

[0819] White fluffy solid (11 mg, 0.021 mmol, 39.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.75-1.85 (1H, m), 1.86-1.93 (1H, m), 2.12-2.22 (1H, m), 2.33-2.46 (1H, m), 2.58 (3 H, s), 2.76 (1H, br d, J=11.50 Hz), 2.97-3.07 (1H, m), 3.60 (1 H, quin, J=6.23 Hz), 3.95 (3 H, s), 4.23-4.36 (1H, m), 4.44 (2 H, dt, J=14.92, 6.23 Hz), 4.55 (2 H, td, J=6.57, 3.56 Hz), 4.77 (2 H, td, J=16.00, 2.45 Hz), 6.48 (1 H, tt, J=54.40, 3.00 Hz), 6.65 (1H, d, J=2.74 Hz), 6.80 (1 H, d, J=9.31 Hz), 7.39 (1H, dd, J=8.35, 1.51 Hz), 7.52 (1H, d, J=8.21 Hz), 7.60 (1H, d, J=2.74 Hz), 7.73 (1 H, s); ESIMS found for $C_{25}H_{27}F_4N_7O_2$ m/z 534.3 (M+1).

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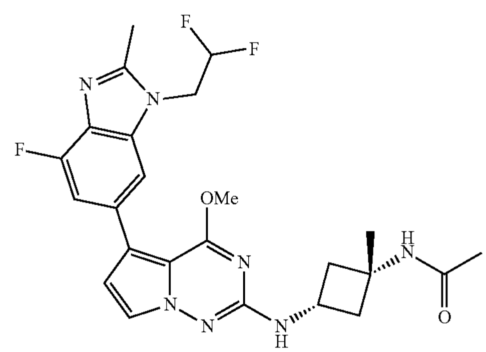

[0820] N-((1s,3s)-3-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 148.

[0821] White solid (15 mg, 0.030 mmol, 24.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.15 (2 H, br dd, J=11.50, 8.76 Hz), 2.37-2.45 (2H, m), 2.57 (3H, s), 3.93 (3H, s), 4.02 (1 H, sxt, J=7.72 Hz), 4.77 (2 H, td, J=16.02, 2.46 Hz), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.66 (1H, d, J=2.74 Hz), 6.94 (1H, d, J=6.84 Hz), 7.19 (1H, dd, J=12.18, 1.23 Hz), 7.57 (1 H, s), 7.60 (1H, d, J=2.74 Hz), 8.02 (1 H, s); ESIMS found for $C_{24}H_{26}F_3N_7O_2$ m/z 502.2 (M+1).

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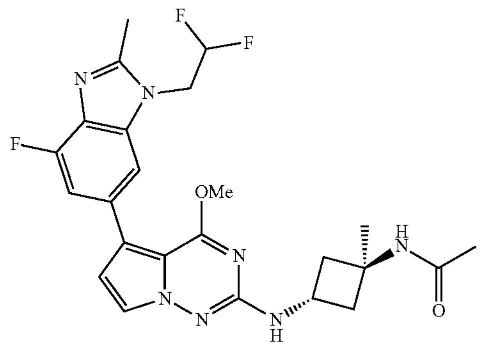
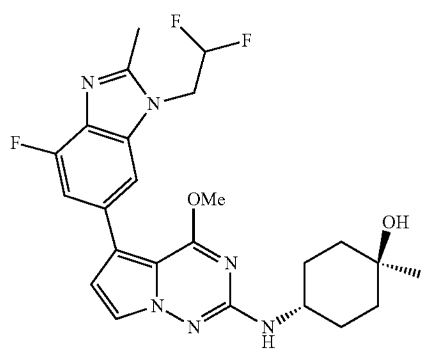


[0822] N-((1r,3r)-3-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 149.

[0823] White solid (15 mg, 0.030 mmol, 22.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.81 (3H, s), 1.90-2.00 (2H, m), 2.58 (3 H, s), 2.60-2.66 (2H, m), 3.93 (3 H, s), 4.18 (1 H, sxt, J=7.72 Hz), 4.77 (2 H, td, J=16.08, 2.33 Hz), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.66 (1H, d, J=2.46 Hz), 6.95 (1H, d, J=7.39 Hz), 7.19 (1H, dd, J=12.18, 1.23 Hz), 7.57 (1 H, s), 7.58 (1H, d, J=2.46 Hz), 7.93 (1 H, s); ESIMS found for $C_{24}H_{26}F_3N_7O_2$ m/z 502.2 (M+1).

151



[0824] trans-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 151.

[0825] White solid (5 mg, 0.010 mmol, 6.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.36-1.53 (4H, m), 1.56-1.65 (2H, m), 1.83-1.92 (2H, m), 2.58 (3 H, s), 3.59-3.70 (1H, m), 3.94 (3H, s), 4.23 (1H, s), 4.70-4.84 (2H, m), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.42 (1H, d, J=7.94 Hz), 6.65 (1H, d, J=2.74 Hz), 7.19 (1H, dd, J=12.18, 1.23 Hz), 7.57 (1 H, s), 7.60 (1H, d, J=2.74 Hz); ESIMS found for $C_{24}H_{27}F_3N_6O_2$ m/z 489.3 (M+1).

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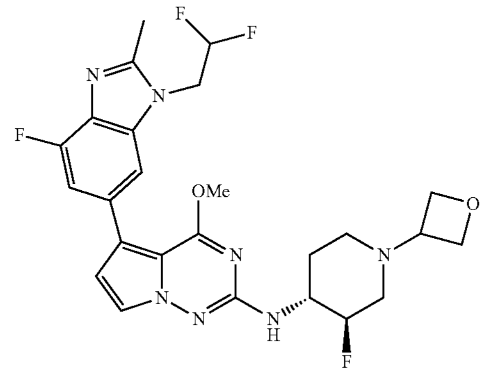

[0826] 5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 159.

[0827] Fluffy white solid (6 mg, 0.011 mmol, 17.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67-1.76 (1H, m), 1.91 (1 H, qd, J=12.05, 3.56 Hz), 1.98-2.06 (1H, m), 2.15 (1H, dd, J=36.75, 12.87 Hz), 2.58 (3 H, s), 2.76 (1H, br d, J=11.77 Hz), 2.98 (1 H, brt, J=10.54 Hz), 3.49 (1 H, quin, J=6.37 Hz), 3.75-3.89 (1H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.77 (2 H, td, J=16.02, 2.74 Hz), 4.93 (1H, d, J=49.10 Hz), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.62 (1H, d, J=7.67 Hz), 6.68 (1H, d, J=2.46 Hz), 7.20 (1H, dd, J=12.32, 1.10 Hz), 7.58 (1 H, s), 7.59 (1H, d, J=2.74 Hz); ESIMS found for $C_{25}H_{27}F_4N_7O_2$ m/z 534.2 (M+1).

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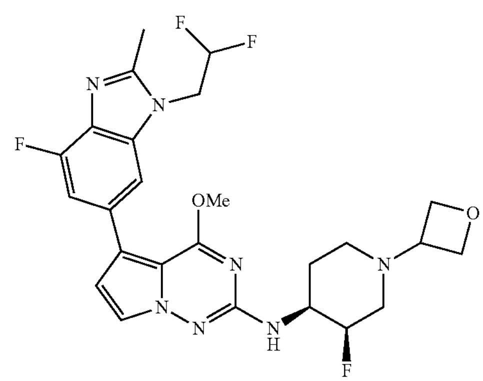

[0828] 5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 161.

[0829] White solid (11 mg, 0.021 mmol, 35.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68-1.77 (1H, m), 1.85-1.97 (1H, m), 1.98-2.06 (1H, m), 2.15 (1H, dd, J=37.05, 12.59 Hz), 2.58 (3 H, s), 2.71-2.81 (1H, m), 2.94-3.04 (1H, m), 3.49 (1 H, quin, J=6.43 Hz), 3.73-3.89 (1H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.78 (2 H, td, J=16.02, 2.46 Hz), 4.93 (1H, d, J=49.90 Hz), 6.49 (1 H, tt, J=54.30, 3.00 Hz), 6.63 (1H, d, J=7.94 Hz), 6.68 (1H, d, J=2.46 Hz), 7.20 (1H, dd, J=12.32, 1.37 Hz), 7.58 (1 H, s), 7.60 (1H, d, J=2.46 Hz); ESIMS found for $C_{25}H_{27}F_4N_7O_2$ m/z 534.2 (M+1).

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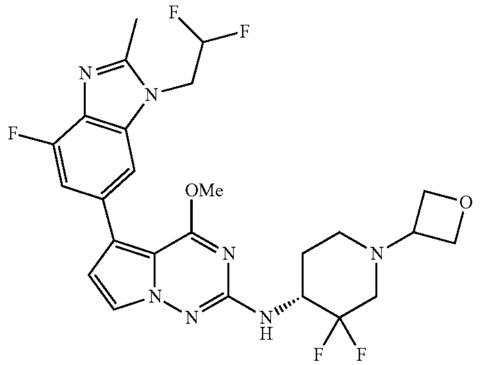
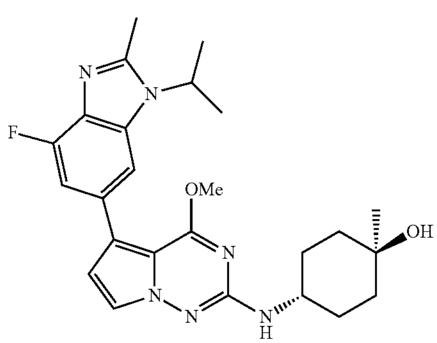


[0830] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 164.

[0831] Yellowish-white solid (8 mg, 0.015 mmol, 14.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.85 (1H, m), 1.86-1.93 (1H, m), 2.13-2.22 (1H, m), 2.40 (1H, dd, J=27.15, 11.38 Hz), 2.58 (3 H, s), 2.76 (1H, br d, J=11.23 Hz), 2.94-3.08 (1H, m), 3.60 (1 H, quin, J=6.23 Hz), 3.93-4.01 (3H, m), 4.23-4.37 (1H, m), 4.44 (2 H, dt, J=15.06, 6.16 Hz), 4.55 (2 H, td, J=6.57, 3.56 Hz), 4.77 (2 H, td, J=16.08, 2.33 Hz), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.70 (1H, d, J=2.46 Hz), 6.83 (1H, d, J=9.58 Hz), 7.17-7.24 (1H, m), 7.58 (1 H, s), 7.60 (1H, d, J=2.74 Hz); ESIMS found for $C_{25}H_{26}F_5N_7O_2$ m/z 552.2 (M+1).

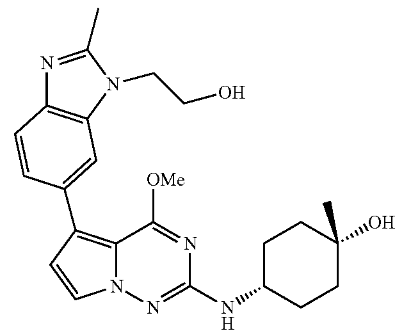
168



[0832] trans-4-((5-(4-Fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 168.

[0833] White solid (20 mg, 0.043 mmol, 16.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.38-1.50 (4H, m), 1.56-1.62 (2H, m), 1.59 (6H, d, J=6.84 Hz), 1.83-1.91 (2H, m), 2.58 (3 H, s), 3.59-3.70 (1H, m), 3.94 (3H, s), 4.23 (1H, s), 4.76 (1 H, spt, J=6.94 Hz), 6.42 (1H, d, J=7.94 Hz), 6.66 (1H, d, J=2.74 Hz), 7.11 (1H, dd, J=12.18, 1.23 Hz), 7.59 (1 H, d, J=2.46 Hz), 7.63 (1H, d, J=1.09 Hz); ESIMS found for $C_{25}H_{31}FN_6O_2$ m/z 467.3 (M+1).

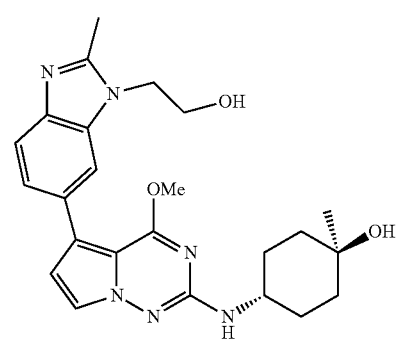
169



[0834] cis-3-((5-(1-(2-Hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 169.

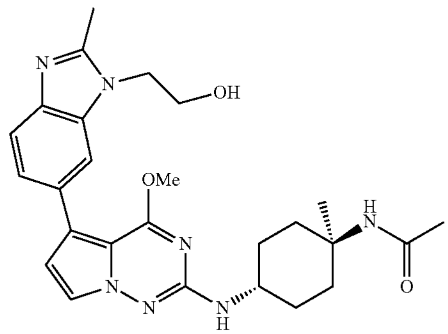
[0835] White solid (7 mg, 0.017 mmol, 49.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 2.01 (2 H, td, J=8.90, 2.19 Hz), 2.35 (2H, ddd, J=8.90, 7.26, 2.74 Hz), 2.55 (3 H, s), 3.67-3.73 (1H, m), 3.75 (2 H, q, J=5.38 Hz), 3.93 (3 H, s), 4.24 (2H, t, J=5.34 Hz), 4.91 (1 H, s), 4.96 (1H, t, J=5.48 Hz), 6.60 (1H, d, J=2.74 Hz), 6.81 (1H, d, J=6.57 Hz), 7.30 (1 H, dd, J=8.35, 1.51 Hz), 7.47 (1H, d, J=8.21 Hz), 7.58 (1H, d, J=2.46 Hz), 7.62 (1H, d, J=1.37 Hz); ESIMS found for $C_{22}H_{26}N_6O_3$ m/z 423.2 (M+1).

170

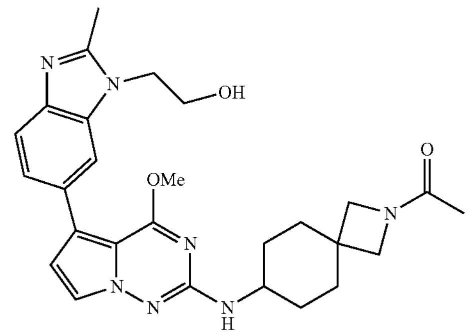


[0836] trans-3-((5-(1-(2-Hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 170.

[0837] White solid (3 mg, 0.007 mmol, 127.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28 (3 H, s), 1.96-2.01 (2H, m), 2.27-2.34 (2H, m), 2.61 (3 H, s), 3.76 (2 H, q, J=5.20 Hz), 3.93 (3 H, s), 4.20-4.27 (1H, m), 4.29 (2 H, br t, J=5.06 Hz), 4.78 (1 H, s), 4.99 (1H, t, J=5.34 Hz), 6.62 (1H, d, J=2.46 Hz), 6.85 (1H, d, J=6.84 Hz), 7.38 (1H, br d, J=8.49 Hz), 7.52 (1H, d, J=8.21 Hz), 7.58 (1H, d, J=2.74 Hz), 7.70 (1 H, s); ESIMS found for $C_{22}H_{26}N_6O_3$ m/z 423.2 (M+1).



171



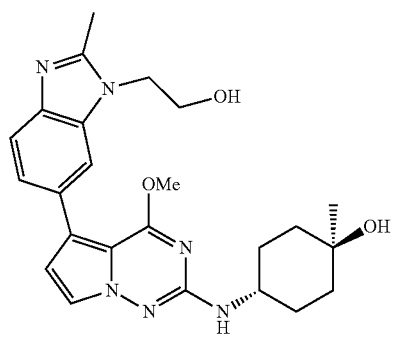
173

[0838] N-(trans-3-((5-(1-(2-Hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 171.

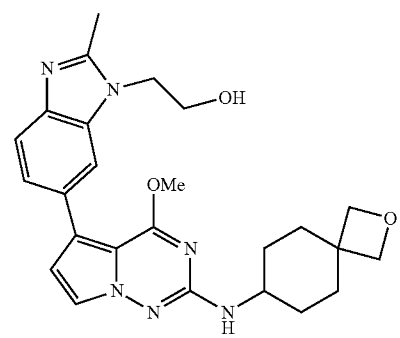
[0839] White solid (6 mg,0.0130 mmol, 62.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.81 (3H, s), 1.91-1.99 (2H, m), 2.55 (3 H, s), 2.59-2.67 (2H, m), 3.75 (2H, br d, J=3.83 Hz), 3.93 (3 H, s), 4.14-4.21 (1H, m), 4.24 (2 H, br t, J=5.34 Hz), 4.96 (1 H, br s), 6.60 (1H, d, J=2.46 Hz), 6.89 (1H, d, J=7.12 Hz), 7.30 (1H, dd, J=8.08, 1.23 Hz), 7.47 (1 H, br d, J=7.94 Hz), 7.56 (1H, d, J=2.46 Hz), 7.61 (1 H, s), 7.93 (1 H, s); ESIMS found for $C_{24}H_{29}N_7O_3$ m/z 464.3 (M+1).

[0842] 1-(7-((5-(1-(2-Hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one 173.

[0843] Off-white solid (6 mg, 0.012 mmol, 50.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28-1.39 (2H, m), 1.48-1.60 (2H, m), 1.72-1.79 (3H, m), 1.83-1.94 (4H, m), 2.60 (3H, s), 3.47 (1H, s), 3.52 (1 H, s), 3.57 (1 H, dt, J=10.20, 6.95 Hz), 3.74 (1 H, s), 3.75-3.79 (2H, m), 3.80 (1 H, s), 3.93 (3H, d, J=1.10 Hz), 4.28 (2 H, br t, J=5.20 Hz), 4.99 (1H, t, J=5.48 Hz), 6.43 (1H, dd, J=16.43, 7.94 Hz), 6.62 (1H, d, J=2.46 Hz), 7.37 (1H, dd, J=8.21, 1.37 Hz), 7.51 (1H, d, J=8.49 Hz), 7.58 (1H, t, J=2.74 Hz), 7.69 (1 H, s); ESIMS found for $C_{27}H_{33}N_7O_3$ m/z 504.3 (M+1).



172



174

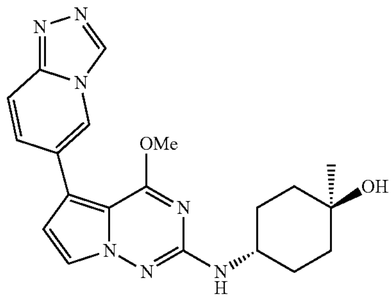
[0840] trans-4-((5-(1-(2-Hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 172.

[0841] White solid (14 mg, 0.031 mmol, 54.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.37-1.51 (4H, m), 1.59 (2H, br d, J=10.95 Hz), 1.83-1.93 (2H, m), 2.55 (3 H, s), 3.60-3.69 (1H, m), 3.75 (2 H, q, J=5.48 Hz), 3.93 (3 H, s), 4.20-4.27 (3H, m), 4.95 (1H, t, J=5.34 Hz), 6.36 (1H, d, J=7.94 Hz), 6.59 (1H, d, J=2.46 Hz), 7.30 (1H, dd, J=8.35, 1.51 Hz), 7.46 (1H, d, J=8.21 Hz), 7.58 (1H, d, J=2.74 Hz), 7.61 (1 H, s); ESIMS found for $C_{24}H_{30}N_6O_3$ m/z 451.3 (M+1).

[0844] 2-(6-(2-((2-Oxaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol 174.

[0845] White solid (6 mg, 0.013 mmol, 57.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.20-1.33 (2H, m), 1.52 (2 H, td, J=12.87, 3.29 Hz), 1.83-1.93 (2H, m), 2.06 (2 H, br d, J=12.87 Hz), 2.55 (3 H, s), 3.48-3.60 (1H, m), 3.74 (2 H, q, J=5.38 Hz), 3.92 (3 H, s), 4.21-4.25 (2H, m), 4.24 (2H, s), 4.32 (2H, s), 4.95 (1H, t, J=5.34 Hz), 6.38 (1H, d, J=7.94 Hz), 6.59 (1H, d, J=2.74 Hz), 7.30 (1H, dd, J=8.21, 1.64 Hz), 7.46 (1H, d, J=8.21 Hz), 7.57 (1H, d, J=2.46 Hz), 7.61 (1H, d, J=1.37 Hz); ESIMS found for $C_{25}H_{30}N_6O_3$ m/z 463.3 (M+1).

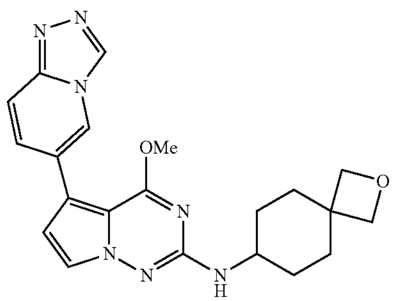
187



[0846] trans-4-((5-([1,2,4]Triazolo[4,3-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 187.

[0847] Off-white solid (9 mg, 0.023 mmol, 13.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.37-1.53 (4H, m), 1.56-1.64 (2H, m), 1.83-1.92 (2H, m), 3.64 (1 H, br dd, J=8.08, 3.70 Hz), 3.97 (3H, s), 4.23 (1H, s), 6.52 (1H, d, J=7.67 Hz), 6.72 (1H, d, J=2.74 Hz), 7.61 (1H, dd, J=9.45, 1.51 Hz), 7.65 (1H, d, J=2.46 Hz), 7.76 (1H, d, J=9.58 Hz), 8.69 (1 H, s), 9.26 (1 H, s); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

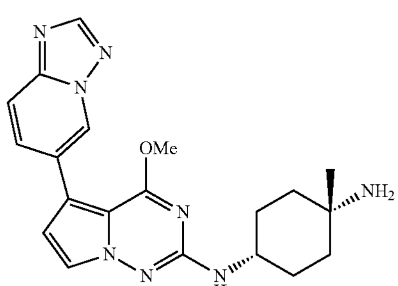
188



[0848] 5-([1,2,4]Triazolo[4,3-a]pyridin-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 188.

[0849] Beige solid (17 mg, 0.042 mmol, 21.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.20-1.32 (2H, m), 1.52 (2 H, td, J=12.94, 3.42 Hz), 1.82-1.92 (2H, m), 2.06 (2 H, br d, J=13.14 Hz), 3.48-3.63 (1H, m), 3.97 (3H, s), 4.23 (2H, s), 4.31 (2 H, s), 6.54 (1H, d, J=7.94 Hz), 6.72 (1H, d, J=2.74 Hz), 7.60 (1H, dd, J=9.58, 1.64 Hz), 7.64 (1H, d, J=2.74 Hz), 7.76 (1 H, d, J=9.58 Hz), 8.69 (1H, t, J=1.23 Hz), 9.26 (1 H, s); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.2 (M+1).

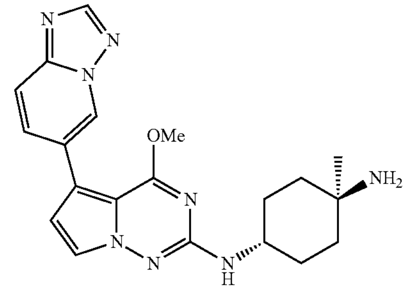
189



[0850] cis-N_1-(5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine 189.

[0851] White foam (108 mg, 0.296 mmol, 62.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.19 (3 H, s), 1.76 (2 H, br s), 1.86 (2 H, td, J=8.76, 2.46 Hz), 2.27-2.38 (2H, m), 3.85 (1 H, sxt, J=7.78 Hz), 3.96 (3 H, s), 6.80 (1H, d, J=2.46 Hz), 6.84 (1H, d, J=7.12 Hz), 7.66 (1H, d, J=2.74 Hz), 7.81-7.86 (1H, m), 7.87-7.92 (1H, m), 8.49 (1 H, s), 9.06 (1H, dd, J=1.64, 0.82 Hz); ESIMS found for $C_{18}H_2O$ N_8O m/z 365.2 (M+1).

190



[0852] trans-N^1-(5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine 190.

[0853] White foam (83 mg, 0.228 mmol, 65.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.22 (3 H, s), 1.74 (2 H, br s), 1.88-1.98 (2H, m), 2.12-2.22 (2H, m), 3.96 (3 H, s), 4.27 (1 H, sxt, J=7.50 Hz), 6.80 (1H, d, J=2.46 Hz), 6.93 (1H, d, J=7.12 Hz), 7.64 (1H, d, J=2.46 Hz), 7.82-7.86 (1H, m), 7.87-7.91 (1H, m), 8.49 (1 H, s), 9.03-9.10 (1H, m); ESIMS found for $C_{18}H_2O$ N_8O m/z 365.2 (M+1).

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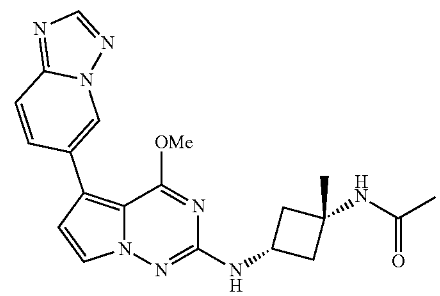
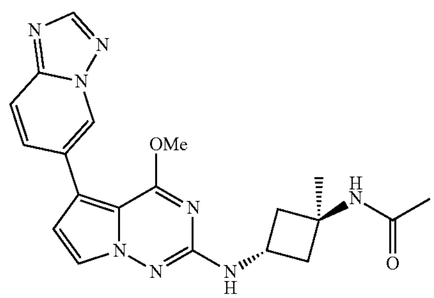


[0854] N-(cis-3-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 191.

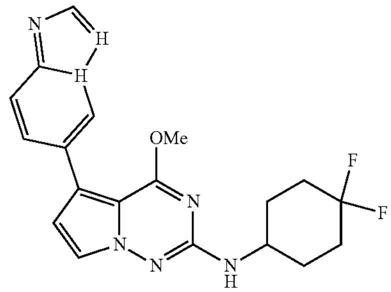
[0855] Off-white solid (27 mg, 0.066 mmol, 96.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.10-2.22 (2H, m), 2.42 (2H, ddd, J=9.65, 7.46, 2.60 Hz), 3.96 (3 H, s), 4.02 (1 H, sxt, J=7.83 Hz), 6.80 (1H, d, J=2.74 Hz), 7.03 (1H, d, J=6.84 Hz), 7.66 (1H, d, J=2.46 Hz), 7.82-7.85 (1H, m), 7.87-7.91 (1H, m), 8.02 (1H, s), 8.49 (1H, s), 9.06 (1H, d, J=1.10 Hz); ESIMS found for $C_{20}H_{22}N_8O_2$ m/z 407.2 (M+1).



192

[0856] N-(trans-3-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 192.

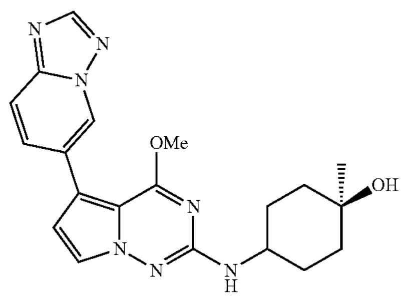
[0857] Off-white solid (27 mg, 0.066 mmol, 96.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.81 (3H, s), 1.89-2.01 (2H, m), 2.64 (2H, ddd, J=10.13, 7.94, 2.74 Hz), 3.96 (3 H, s), 4.13-4.27 (1H, m), 6.80 (1H, d, J=2.74 Hz), 7.03 (1H, d, J=7.12 Hz), 7.64 (1H, d, J=2.74 Hz), 7.81-7.86 (1H, m), 7.87-7.91 (1H, m), 7.93 (1H, s), 8.49 (1H, s), 9.06 (1 H, s); ESIMS found for $C_{20}H_{22}N_8O_2$ m/z 407.2 (M+1).



193

[0858] 5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-N-(4,4-difluorocyclohexyl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 193.

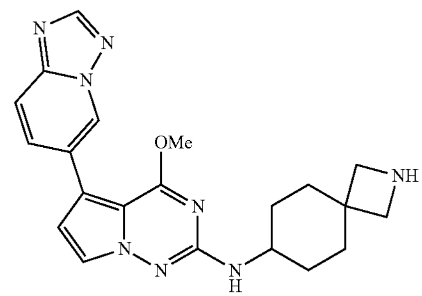
[0859] Off-white solid (15 mg, 0.038 mmol, 18.8% yield). ^{1}H NMR (499 MHz, CHLOROFORM-d) δ ppm 1.62-1.75 (2H, m), 1.88-2.06 (2H, m), 2.11-2.27 (4H, m), 3.87 (1 H, br dd, J=5.07, 1.78 Hz), 4.02 (3 H, s), 6.64 (1H, d, J=2.74 Hz), 7.50 (1H, d, J=2.74 Hz), 7.82 (2 H, s), 8.09 (1H, d, J=7.67 Hz), 8.40 (1 H, s), 8.82 (1 H, s); ESIMS found for $C_{19}H_{19}F_2N_7O$ m/z 400.2 (M+1).



194

[0860] trans-4-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 194.

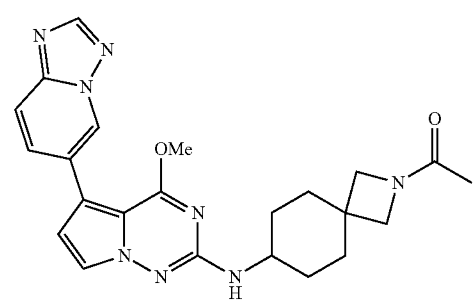
[0861] Off-white solid (41 mg, 0.104 mmol, 44.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.37-1.52 (4H, m), 1.55-1.65 (2H, m), 1.82-1.93 (2H, m), 3.64 (1 H, br dd, J=8.08, 3.70 Hz), 3.96 (3H, s), 4.24 (1H, s), 6.52 (1H, d, J=7.94 Hz), 6.79 (1H, d, J=2.46 Hz), 7.66 (1H, d, J=2.46 Hz), 7.80-7.86 (1H, m), 7.87-7.94 (1H, m), 8.49 (1 H, s), 9.02-9.10 (1H, m); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).



195

[0862] 5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxy-N-(2-azaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 195.

[0863] Off-white foam (55 mg, 0.136 mmol, 71.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.25-1.34 (2H, m), 1.37-1.49 (2H, m), 1.84 (3H, br d, J=10.13 Hz), 1.96 (2 H, br d, J=12.87 Hz), 3.14 (2 H, br s), 3.20 (2 H, br s), 3.46-3.62 (2H, m), 3.95 (3 H, s), 6.51 (1 H, d, J=7.94 Hz), 6.79 (1H, d, J=2.74 Hz), 7.64 (1H, d, J=2.74 Hz), 7.81-7.85 (1H, m), 7.87-7.91 (1H, m), 8.49 (1 H, s), 9.06 (1 H, s); ESIMS found for $C_{21}H_{24}N_8O$ m/z 405.3 (M+1).

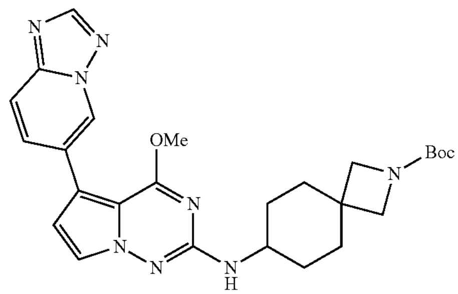


196

[0864] 1-(7-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one 196.

[0865] Off-white solid (46 mg, 0.103 mmol, 83.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.26-1.41 (2H, m), 1.48-1.60 (2H, m), 1.72-1.80 (3H, m), 1.83-1.93 (4H, m), 3.47 (1H, s), 3.52 (1H, s), 3.57 (1 H, br dd, J=6.98, 2.87 Hz), 3.74 (1H, s), 3.80 (1H, s), 3.96 (3H, d, J=1.10 Hz), 6.56 (1H, dd, J=16.02, 7.80 Hz), 6.80 (1H, d, J=2.74 Hz), 7.65 (1H, t, J=2.87 Hz), 7.80-7.86 (1H, m), 7.86-7.93 (1H, m), 8.49 (1 H, s), 9.04-9.10 (1H, m); ESIMS found for $C_{23}H_{26}N_8O_2$ m/z 447.3 (M+1).

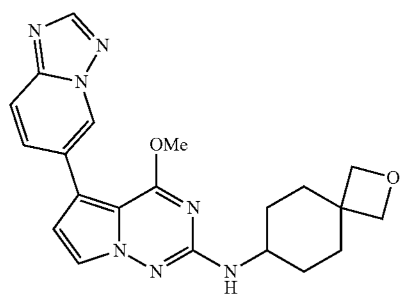
197



[0866] tert-Butyl 7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonane-2-carboxylate 197.

[0867] Off-white foam (98 mg, 0.194 mmol, 58.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27-1.36 (2H, m), 1.38 (9 H, s), 1.46-1.58 (2H, m), 1.86 (4H, br d, J=10.40 Hz), 3.55 (5 H, br s), 3.96 (3 H, s), 6.52 (1H, br d, J=7.39 Hz), 6.80 (1H, d, J=2.46 Hz), 7.64 (1 H, d, J=2.74 Hz), 7.82-7.85 (1H, m), 7.87-7.91 (1H, m), 8.49 (1 H, s), 9.06 (1 H, s); ESIMS found for $C_{26}H_{32}N_8O_3$ m/z 505.3 (M+1).

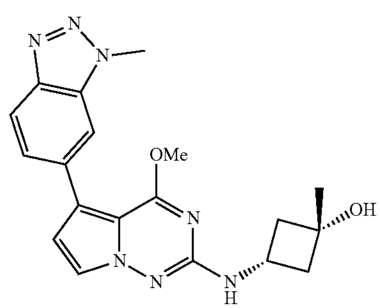
198



[0868] 5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 198.

[0869] Off-white solid (46 mg, 0.114 mmol, 56.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.19-1.31 (2H, m), 1.52 (2 H, td, J=12.87, 3.29 Hz), 1.87 (2 H, brdd, J=13.14, 3.29 Hz), 2.06 (2H, br d, J=13.14 Hz), 3.48-3.60 (1H, m), 3.95 (3H, s), 4.23 (2H, s), 4.32 (2 H, s), 6.54 (1H, d, J=7.94 Hz), 6.79 (1H, d, J=2.74 Hz), 7.64 (1H, d, J=2.74 Hz), 7.80-7.85 (1H, m), 7.87-7.92 (1H, m), 8.49 (1 H, s), 9.06 (1 H, s); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.2 (M+1).

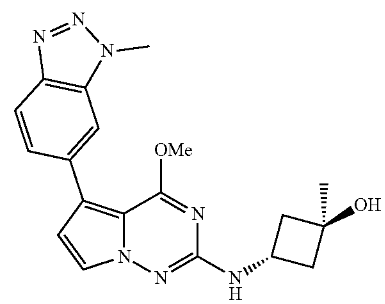
199



[0870] cis-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 199.

[0871] Off-white solid (12 mg, 0.032 mmol, 16.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 2.02 (2 H, td, J=8.83, 2.33 Hz), 2.31-2.40 (2H, m), 3.72 (1 H, dq, J=15.09, 7.75 Hz), 3.95 (3H, s), 4.31 (3H, s), 4.92 (1 H, s), 6.74 (1H, d, J=2.46 Hz), 6.93 (1 H, d, J=6.57 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.64 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.97 (1 H, d, J=8.49 Hz); ESIMS found for $C_{19}H_{21}N_7O_2$ m/z 380.2 (M+1).

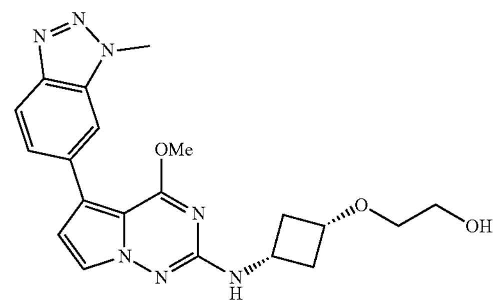
200



[0872] trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 200.

[0873] White solid (5 mg, 0.013 mmol, 8.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28 (3 H, s), 1.95-2.03 (2H, m), 2.28-2.35 (2H, m), 3.95 (3 H, s), 4.21-4.29 (1H, m), 4.31 (3H, s), 4.79 (1H, s), 6.74 (1H, d, J=2.74 Hz), 6.94 (1H, d, J=6.84 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.63 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{1-9}H_{21}N_7O_2$ m/z 380.2 (M+1).

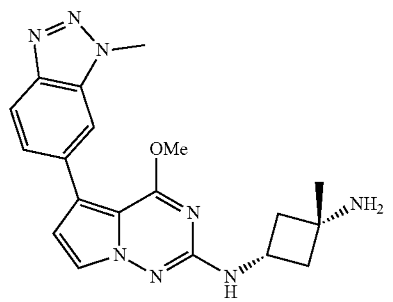
201



[0874] 2-(cis-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol 201.

[0875] Off-white solid (27 mg, 0.066 mmol, 25.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.82-1.94 (2H, m), 2.60-2.71 (2H, m), 3.29-3.34 (2H, m), 3.48 (2 H, q, J=5.48 Hz), 3.68-3.75 (1H, m), 3.75-3.83 (1H, m), 3.95 (3H, s), 4.31 (3H, s), 4.60 (1H, t, J=5.61 Hz), 6.75 (1H, d, J=2.74 Hz), 7.02 (1H, d, J=7.39 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.62 (1H, d, J=2.46 Hz), 7.94 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{20}H_{23}N_7O_3$ m/z 410.2 (M+1).

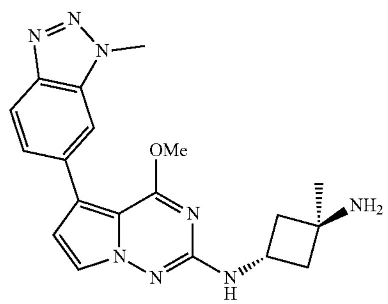
202



[0876] cis-N[1]-(4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine 202.

[0877] Off-white solid (155 mg, 0.410 mmol, 70.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.19 (3 H, s), 1.77 (2 H, br s), 1.86 (2 H, td, J=8.83, 2.33 Hz), 2.33 (2H, ddd, J=8.97, 7.46, 2.74 Hz), 3.86 (1 H, dq, J=15.50, 7.79 Hz), 3.95 (3H, s), 4.31 (3H, s), 6.74 (1H, d, J=2.46 Hz), 6.80 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.76, 1.64 Hz), 7.64 (1H, d, J=2.74 Hz), 7.93 (1H, d, J=1.37 Hz), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{19}H_{22}N_8O$ m/z 379.25 (M+1).

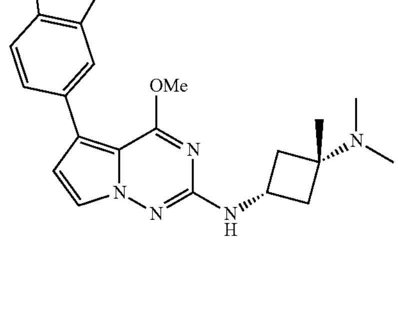
203



[0878] trans-N_1-(4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine 203.

[0879] Off-white foam (110 mg, 0.291 mmol, 74.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.22 (3 H, s), 1.80 (2 H, br s), 1.88-1.98 (2H, m), 2.13-2.22 (2H, m), 3.95 (3 H, s), 4.23-4.33 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 6.90 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.63 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.95-8.00 (1H, m); ESIMS found for $C_{1-9}H_{22}N_8O$ m/z 379.2 (M+1).

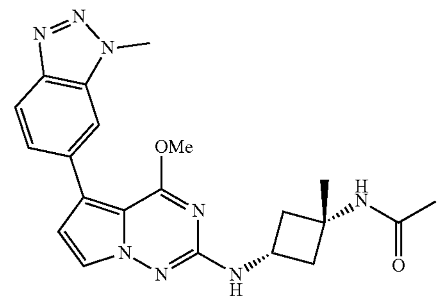
204



[0880] cis-N[3]-(4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-N[1],N[1],1-trimethylcyclobutane-1,3-diamine 204.

[0881] White solid (18 mg, 0.044 mmol, 67.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.06 (3 H, s), 1.82-1.92 (2H, m), 2.03 (6 H, s), 2.19 (2 H, td, J=8.15, 2.60 Hz), 3.91-4.01 (1H, m), 3.95 (3H, s), 4.31 (3H, s), 6.74 (1H, d, J=2.46 Hz), 6.95 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{21}H_{26}N_8O$ m/z 407.3 (M+1).

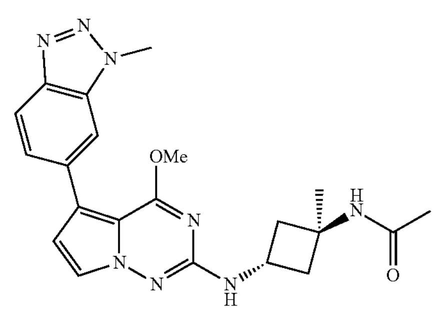
191



[0882] N-(cis-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 205.

[0883] Off-white solid (25 mg, 0.060 mmol, 90.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.11-2.21 (2H, m), 2.42 (2H, ddd, J=9.58, 7.39, 2.46 Hz), 3.95 (3 H, s), 3.99-4.08 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 6.99 (1H, d, J=6.84 Hz), 7.60 (1H, dd, J=8.76, 1.64 Hz), 7.65 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=9.03 Hz), 8.02 (1 H, s); ESIMS found for $C_{21}H_{24}N_8O_2$ m/z 421.2 (M+1).

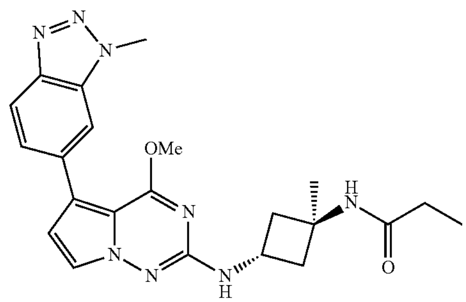
206



[0884] N-(trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 206.

[0885] Off-white solid (84 mg, 0.200 mmol, 92.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.82 (3H, s), 1.90-2.00 (2H, m), 2.64 (2H, ddd, J=10.20, 7.87, 2.46 Hz), 3.95 (3 H, s), 4.19 (1 H, sxt, J=7.78 Hz), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 6.99 (1 H, d, J=7.39 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.62 (1H, d, J=2.74 Hz), 7.93 (2 H, s), 7.97 (1 H, d, J=8.49 Hz); ESIMS found for $C_{21}H_{24}N_8O_2$ m/z 421.2 (M+1).

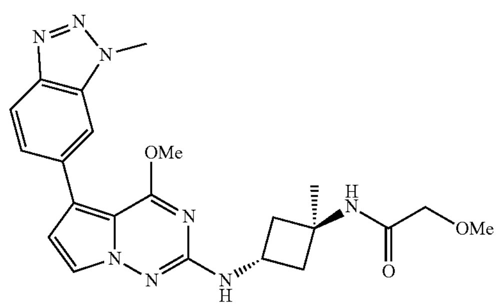
207



[0886] N-(trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)propionamide 207.

[0887] Off-white solid (30 mg, 0.069 mmol, 96.8% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.00 (3H, t, J=7.53 Hz), 1.36 (3 H, s), 1.92-2.00 (2H, m), 2.08 (2 H, q, J=7.57 Hz), 2.64 (2H, ddd, J=10.27, 7.94, 2.60 Hz), 3.95 (3 H, s), 4.19 (1 H, sxt, J=7.78 Hz), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 6.99 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.62 (1H, d, J=2.46 Hz), 7.83 (1H, s), 7.93 (1H, s), 7.97 (1H, d, J=8.76 Hz), 8.31 (1 H, s); ESIMS found for $C_{22}H_{26}N_8O_2$ m/z 435.3 (M+1).

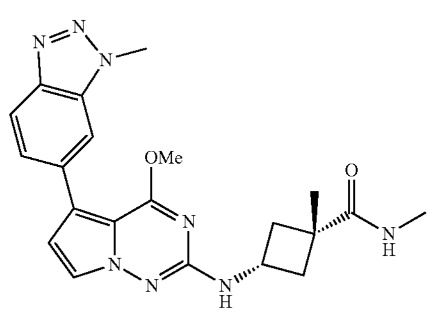
208



[0888] 2-Methoxy-N-(trans-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 208.

[0889] Off-white solid (15 mg, 0.033 mmol, 63.0% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.39 (3 H, s), 1.95-2.05 (2H, m), 2.69-2.78 (2H, m), 3.78 (2H, s), 3.95 (3H, s), 4.13-4.24 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.74 Hz), 7.01 (1H, d, J=7.39 Hz), 7.60 (1 H, dd, J=8.76, 1.37 Hz), 7.63 (1H, d, J=2.74 Hz), 7.72 (1H, s), 7.93 (1H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{26}N_8O_3$ m/z 451.3 (M+1).

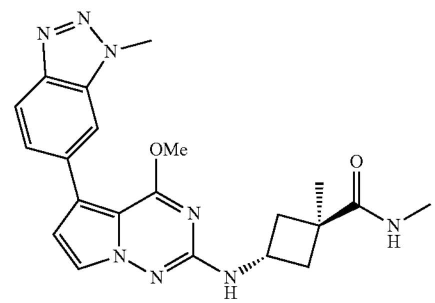
209



[0890] cis-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide 209.

[0891] Off-white solid (7.3 mg, 0.017 mmol, 9.4% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.34 (3 H, s), 2.14-2.22 (2H, m), 2.22-2.31 (2H, m), 2.58 (3H, d, J=4.38 Hz), 3.94 (3 H, s), 4.20 (1 H, sxt, J=7.88 Hz), 4.31 (3 H, s), 6.75 (1H, d, J=2.74 Hz), 6.93 (1H, d, J=7.12 Hz), 7.47 (1 H, q, J=4.29 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.65 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.96-8.00 (1H, m); ESIMS found for $C_{21}H_{24}N_8O_2$ m/z 421.2 (M+1).

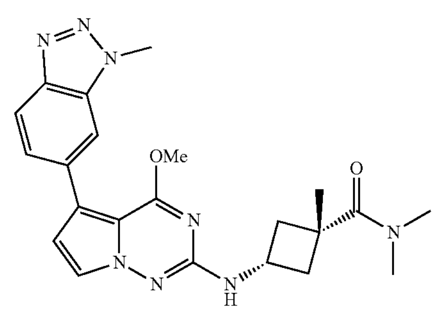
210



[0892] trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide 210.

[0893] White solid (35 mg, 0.083 mmol, 99.7% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.32 (3 H, s), 1.86-1.94 (2H, m), 2.62 (3H, d, J=4.38 Hz), 2.70-2.79 (2H, m), 3.95 (3 H, s), 4.04 (1 H, sxt, J=7.99 Hz), 4.31 (3 H, s), 6.74 (1H, d, J=2.74 Hz), 6.98 (1H, d, J=7.39 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.60-7.64 (1H, m), 7.66 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{21}H_{24}N_8O_2$ m/z 421.2 (M+1).

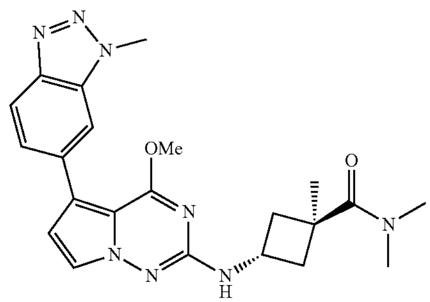
211



[0894] cis-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide 211.

[0895] White solid (4.4 mg, 0.010 mmol, 5.5% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.38 (3 H, s), 2.27-2.40 (4H, m), 2.80 (3H, s), 2.87 (3H, s), 3.94 (3 H, s), 4.18 (1 H, dq, J=15.74, 7.89 Hz), 4.31 (3 H, s), 6.75 (1H, d, J=2.74 Hz), 6.94 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.76, 1.64 Hz), 7.65 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{26}N_8O_2$ m/z 435.3 (M+1).

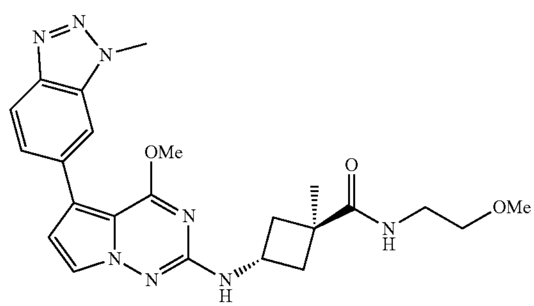
212



[0896] trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide 212.

[0897] White solid (35 mg, 0.081 mmol, 96.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.40 (3 H, s), 1.94-2.03 (2H, m), 2.84 (3 H, br s), 2.89 (3 H, s), 2.89-2.94 (2H, m), 3.86-3.94 (1H, m), 3.96 (3H, s), 4.31 (3H, s), 6.74 (1H, d, J=2.74 Hz), 7.08 (1H, d, J=6.30 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.64 (1H, d, J=2.74 Hz), 7.93 (1H, d, J=1.10 Hz), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{26}N_8O_2$ m/z 435.3 (M+1).

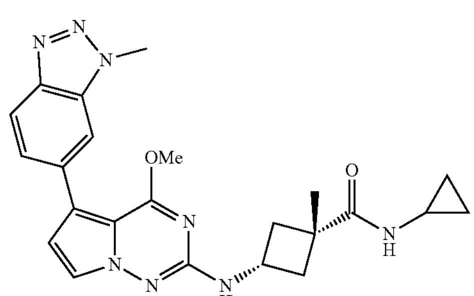
214



[0898] trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N-(2-methoxyethyl)-1-methylcyclobutane-1-carboxamide 214.

[0899] White solid (39 mg, 0.084 mmol, 45.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.32 (3 H, s), 1.84-1.94 (2H, m), 2.70-2.80 (2H, m), 3.22-3.28 (2H, m), 3.26 (3 H, s), 3.35-3.39 (2H, m), 3.95 (3 H, s), 4.03 (1 H, sxt, J=7.94 Hz), 4.31 (3 H, s), 6.74 (1H, d, J=2.74 Hz), 6.98 (1H, d, J=7.39 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.65 (1H, d, J=2.46 Hz), 7.69 (1 H, t, J=5.61 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{23}H_{28}N_8O_3$ m/z 465.3 (M+1).

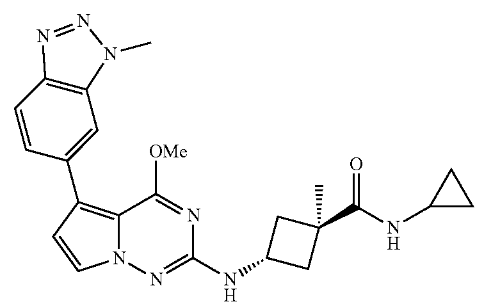
217



[0900] cis-N-Cyclopropyl-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide 217.

[0901] Off-white solid (7 mg, 0.016 mmol, 8.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.39-0.46 (2H, m), 0.56-0.64 (2H, m), 1.32 (3 H, s), 2.13-2.20 (2H, m), 2.20-2.29 (2H, m), 2.58-2.67 (1H, m), 3.94 (3 H, s), 4.17 (1 H, sxt, J=7.88 Hz), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 6.92 (1H, d, J=7.12 Hz), 7.49 (1H, d, J=4.11 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.65 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{23}H_{26}N_8O_2$ m/z 447.2 (M+1).

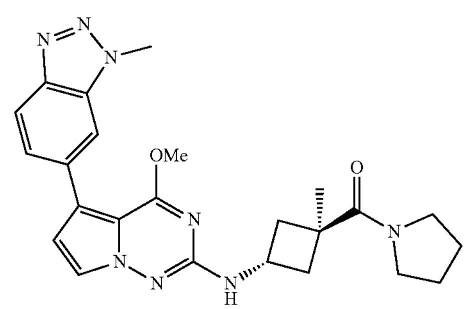
218



[0902] trans-N-Cyclopropyl-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide 218.

[0903] White solid (44 mg, 0.099 mmol, 53.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.42-0.49 (2H, m), 0.58-0.65 (2H, m), 1.30 (3 H, s), 1.82-1.92 (2H, m), 2.67 (1 H, tq, J=7.46, 3.88 Hz), 2.74 (2H, ddd, J=9.92, 7.87, 2.46 Hz), 3.95 (3 H, s), 3.97-4.04 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.74 Hz), 6.98 (1H, d, J=7.39 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.62 (1H, d, J=4.38 Hz), 7.66 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{23}H_{26}N_8O_2$ m/z 447.25 (M+1).

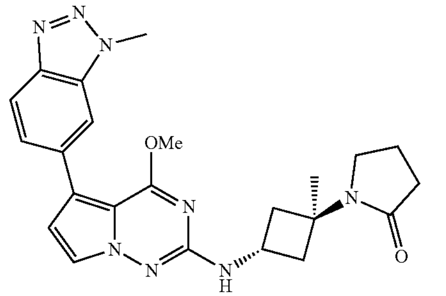
222



[0904] (trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)(pyrrolidin-1-yl)methanone 222.

[0905] White solid (36 mg, 0.078 mmol, 93.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3 H, s), 1.73-1.80 (2H, m), 1.81-1.87 (2H, m), 1.91-1.99 (2H, m), 2.86-2.93 (2H, m), 3.30-3.34 (4H, m), 3.87-3.94 (1H, m), 3.96 (3 H, s), 4.31(3 H, s), 6.74 (1H, d, J=2.46 Hz), 7.07 (1H, d, J=6.57 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{24}H_{28}N_8O_2$ m/z 461.3 (M+1).

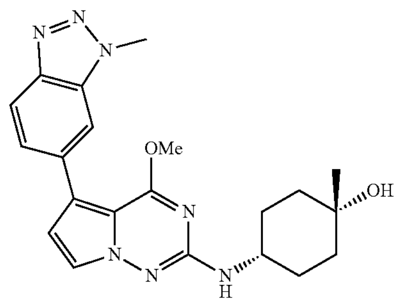
223



[0906] 1-(trans-3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)pyrrolidin-2-one 223.

[0907] Off-white solid (23 mg, 0.052 mmol, 46.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3 H, s), 1.92 (2 H, quin, J=7.53 Hz), 2.00-2.08 (2H, m), 2.23 (2H, t, J=8.08 Hz), 2.82-2.92 (2H, m), 3.40 (2H, t, J=6.84 Hz), 3.96 (3 H, s), 4.04-4.12 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.46 Hz), 7.06 (1H, d, J=6.30 Hz), 7.60 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.46 Hz), 7.94 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{23}H_{26}N_8O_2$ m/z 447.3 (M+1).

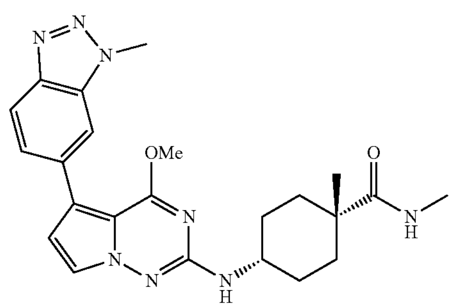
224



[0908] cis-4-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 224.

[0909] Off-white solid (36 mg, 0.088 mmol, 34.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.37 (2 H, td, J=13.00, 4.38 Hz), 1.58 (2H, br d, J=12.32 Hz), 1.61-1.69 (2H, m), 1.69-1.75 (2H, m), 3.47-3.58 (1H, m), 3.95 (3H, s), 4.00 (1H, s), 4.31 (3 H, s), 6.50 (1H, d, J=7.94 Hz), 6.72 (1H, d, J=2.46 Hz), 7.59-7.63 (2H, m), 7.93 (1 H, s), 7.97 (1 H, d, J=8.49 Hz); ESIMS found for $C_{21}H_{25}N_7O_2$ m/z 408.2 (M+1).

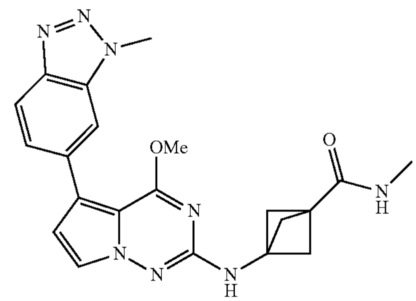
225



[0910] cis-4-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclohexane-1-carboxamide 225.

[0911] Off-white solid (10 mg, 0.022 mmol, 31.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.03 (3 H, s), 1.15-1.27 (2H, m), 1.27-1.37 (2H, m), 1.77-1.87 (2H, m), 2.18 (2H, br d, J=12.32 Hz), 2.61 (3H, d, J=4.38 Hz), 3.49-3.61 (1H, m), 3.93 (3 H, s), 4.31 (3 H, s), 6.51 (1H, d, J=7.94 Hz), 6.73 (1H, d, J=2.46 Hz), 7.53 (1 H, q, J=4.38 Hz), 7.59-7.61 (1 H, m), 7.62 (1H, d, J=2.46 Hz), 7.93 (1H, d, J=0.82 Hz), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{23}H_{28}N_8O_2$ m/z 449.3 (M+1).

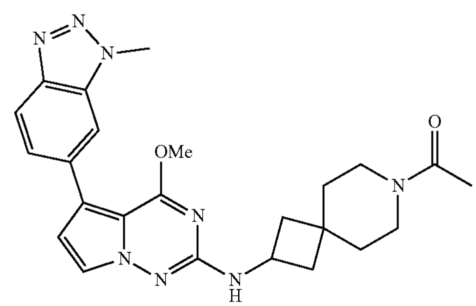
226



[0912] 3-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N-methylbicyclo[1.1.1]pentane-1-carboxamide 226.

[0913] Off-white solid (5 mg, 0.012 mmol, 5.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.23 (6 H, s), 2.55-2.59 (3H, m), 3.96 (3H, s), 4.31 (3H, s), 6.79 (1H, d, J=2.46 Hz), 7.47 (1 H, s), 7.61 (1H, dd, J=8.76, 1.37 Hz), 7.64 (1H, d, J=2.46 Hz), 7.73 (1 H, q, J=4.47 Hz), 7.95 (1 H, s), 7.98 (1H, d, J=8.76 Hz); ESIMS found for $C_{21}H_{22}N_8O_2$ m/z 419.2 (M+1).

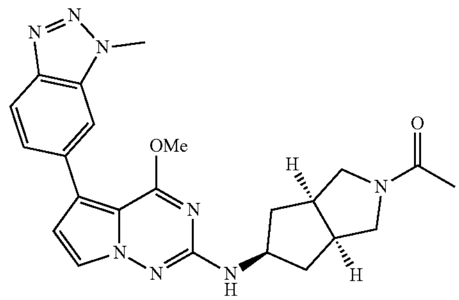
227



[0914] 1-(2-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-7-azaspiro[3.5]nonan-7-yl)ethan-1-one 227.

[0915] Off-white solid (23 mg, 0.050 mmol, 69.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.41-1.46 (1H, m), 1.52 (2 H, br t, J=10.27 Hz), 1.57-1.63 (1H, m), 1.76-1.85 (2H, m), 1.95-2.00 (3H, m), 2.23-2.32 (2H, m), 3.26-3.30 (1H, m), 3.31-3.35 (1H, m), 3.35-3.39 (1H, m), 3.40-3.44 (1H, m), 3.95 (3 H, s), 4.15-4.26 (1H, m), 4.31 (3 H, s), 6.74 (1 H, d, J=2.46 Hz), 7.00 (1H, t, J=7.12 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.63-7.65 (1H, m), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{24}H_{28}N_8O_2$ m/z 461.3 (M+1).

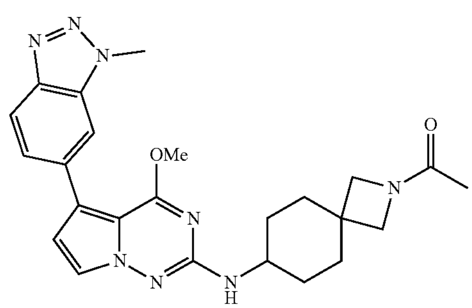
228



[0916] 1-((3aR,5r,6aS)-5-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)hexahydrocyclopenta[c]pyrrol-2(1H)-yl)ethan-1-one 228.

[0917] Off-white solid (74 mg, 0.166 mmol, 89.4% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.34-1.49 (2H, m), 1.94 (3 H, s), 2.24-2.36 (2H, m), 2.57 (1 H, quind, J=8.01, 8.01, 8.01, 8.01, 4.65 Hz), 2.62-2.72 (1H, m), 3.35-3.46 (3H, m), 3.59 (1H, dd, J=10.68, 7.94 Hz), 3.95 (3 H, s), 4.07-4.20 (1H, m), 4.31 (3 H, s), 6.74 (1H, d, J=2.74 Hz), 6.82 (1H, d, J=7.39 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.63 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=9.03 Hz); ESIMS found for $C_{23}H_{26}N_8O_2$ m/z 447.2 (M+1).

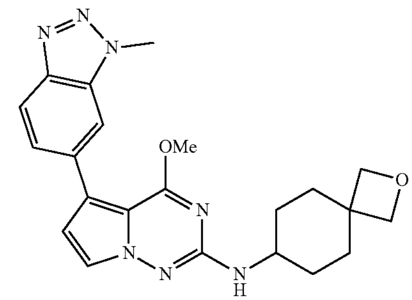
229



[0918] 1-(7-((4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one 229.

[0919] Off-white solid (12 mg, 0.026 mmol, 72.7% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.27-1.39 (2H, m), 1.49-1.61 (2H, m), 1.72-1.78 (3H, m), 1.82-1.94 (4H, m), 3.47 (1 H, s), 3.52(1 H, s), 3.54-3.65 (1H, m), 3.75 (1H, s), 3.80 (1H, s), 3.95 (3H, d, J=1.10 Hz), 4.31(3 H, s), 6.52 (1H, dd, J=16.43, 7.94 Hz), 6.74 (1H, d, J=2.74 Hz), 7.61 (1H, dd, J=8.62, 1.51 Hz), 7.63 (1H, t, J=2.87 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{24}H_{28}N_8O_2$ m/z 461.3 (M+1).

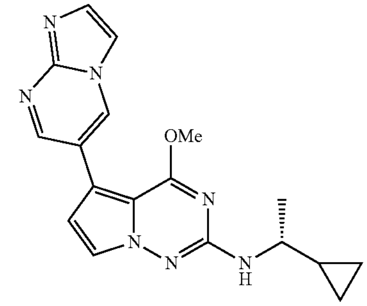
230



[0920] 4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 230.

[0921] Beige solid (28 mg, 0.067 mmol, 35.0% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.21-1.33 (2H, m), 1.53 (2 H, td, J=12.87, 3.29 Hz), 1.82-1.93 (2H, m), 2.07 (2 H, br d, J=13.14 Hz), 3.51-3.61 (1H, m), 3.94 (3H, s), 4.24 (2H, s), 4.31 (3H, s), 4.32 (2H, s), 6.50 (1H, d, J=7.94 Hz), 6.73 (1H, d, J=2.74 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.63 (1H, d, J=2.46 Hz), 7.93 (1 H, s), 7.97 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{25}N_7O_2$ m/z 420.2 (M+1).

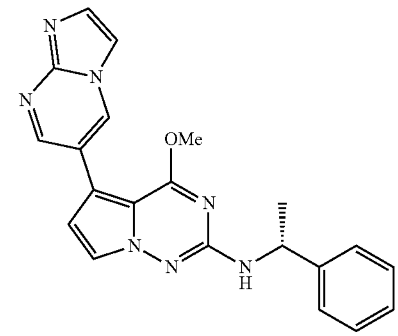
231



[0922] (R)—N-(1-Cyclopropylethyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 231.

[0923] Beige solid (4 mg, 0.011 mmol, 6.9% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 0.16-0.24 (1H, m), 0.33-0.40 (2H, m), 0.47 (1 H, s), 0.97-1.07 (1H, m), 1.23 (3H, d, J=6.57 Hz), 3.33-3.38 (1H, m), 3.97 (3 H, s), 6.66 (1H, d, J=8.49 Hz), 6.76 (1H, d, J=2.46 Hz), 7.63 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O$ m/z 350.2 (M+1).

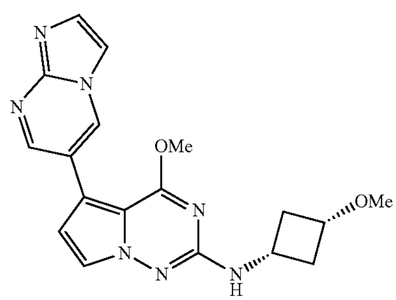
233



[0924] (R)-5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-phenylethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 233.

[0925] Off-white solid (10 mg, 0.026 mmol, 15.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.46 (3H, d, J=7.12 Hz), 3.98 (3 H, s), 4.95 (1 H, quin, J=7.39 Hz), 6.74 (1H, d, J=2.46 Hz), 7.17-7.22 (1H, m), 7.28-7.33 (3H, m), 7.43 (2H, d, J=7.39 Hz), 7.58 (1H, d, J=2.74 Hz), 7.71 (1H, d, J=1.10 Hz), 7.91 (1H, d, J=1.09 Hz), 8.71 (1H, d, J=2.46 Hz), 9.06 (1 H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{19}N_7O$ m/z 386.2 (M+1).

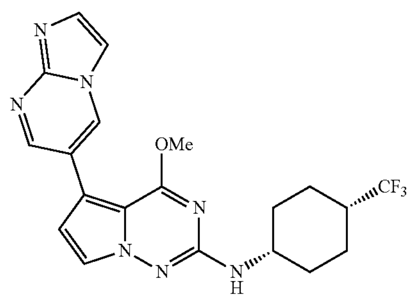
236



[0926] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-3-methoxycyclobutyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 236.

[0927] White solid (65 mg, 0.178 mmol, 53.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.78-1.91 (2H, m), 2.59-2.70 (2H, m), 3.14 (3 H, s), 3.61 (1 H, quin, J=7.12 Hz), 3.73-3.87 (1H, m), 3.97 (3 H, s), 6.78 (1H, d, J=2.46 Hz), 7.07 (1H, d, J=7.39 Hz), 7.65 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.09 Hz), 7.92 (1H, d, J=1.09 Hz), 8.73 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.2 (M+1).

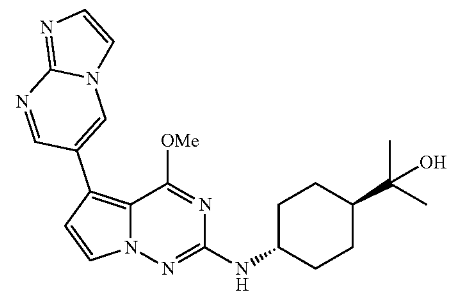
239



[0928] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-(trifluoromethyl)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 239.

[0929] Off-white solid (31 mg, 0.072 mmol, 36.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.59-1.69 (4H, m), 1.69-1.80 (2H, m), 1.95-2.06 (2H, m), 2.23-2.35 (1H, m), 3.87-3.95 (1H, m), 4.00 (3 H, s), 6.78 (1H, d, J=2.46 Hz), 6.80 (1H, d, J=6.30 Hz), 7.66 (1 H, d, J=2.46 Hz), 7.72 (1H, d, J=1.10 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{20}F_3N_7O$ m/z 432.2 (M+1).

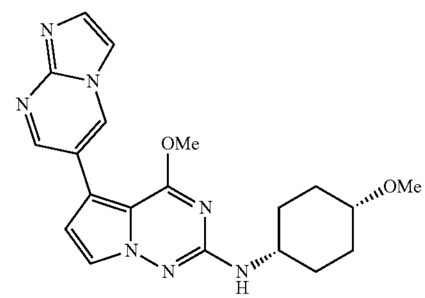
242



[0930] 2-(trans-4-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol 242.

[0931] White solid (1 mg, 0.002 mmol, 1.4% yield). ^{1}H NMR (499 MHz, CHLOROFORM-d) δ ppm 1.22 (6 H, s), 1.24-1.30 (3H, m), 1.31-1.41 (2H, m), 1.95 (2 H, br d, J=12.05 Hz), 2.30 (2H, br d, J=10.95 Hz), 3.66 (1 H, tdt, J=11.21, 11.21, 7.63, 3.87, 3.87 Hz), 4.00 (3 H, s), 4.37 (1H, d, J=7.94 Hz), 6.59 (1H, d, J=2.46 Hz), 7.49 (1H, d, J=2.46 Hz), 7.57 (1 H, br s), 7.85 (1 H, br s), 8.42-8.66 (2H, m), 8.79 (1 H, br s); ESIMS found for $C_{22}H_{27}N_7O_2$ m/z 422.2 (M+1).

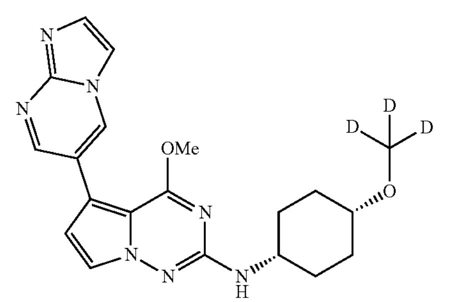
243



[0932] 5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-methoxycyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 243.

[0933] White solid (71 mg, 0.181 mmol, 54.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.54 (2H, m), 1.56-1.65 (2H, m), 1.66-1.73 (2H, m), 1.80-1.89 (2H, m), 3.22 (3 H, s), 3.34-3.37 (1H, m), 3.55-3.70 (1H, m), 3.97 (3 H, s), 6.62 (1H, d, J=7.67 Hz), 6.76 (1 H, d, J=2.46 Hz), 7.65 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.10 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

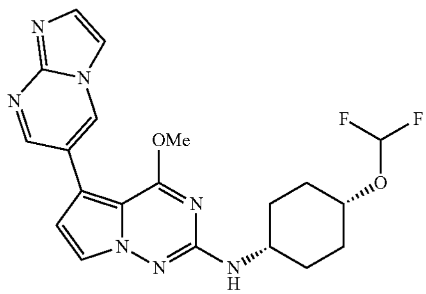
245



[0934] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-(methoxy-d_3)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 245.

[0935] Off-white solid (49 mg, 0.124 mmol, 41.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.44-1.54 (2H, m), 1.55-1.65 (2H, m), 1.65-1.73 (2H, m), 1.80-1.88 (2H, m), 3.33-3.38 (1H, m), 3.58-3.71 (1H, m), 3.97 (3 H, s), 6.62 (1H, d, J=7.67 Hz), 6.76 (1H, d, J=2.46 Hz), 7.65 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1 H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz) ESIMS found for $C_{20}H_{20}[^2H_3]N_7O_2$ m/z 397.2 (M+1).

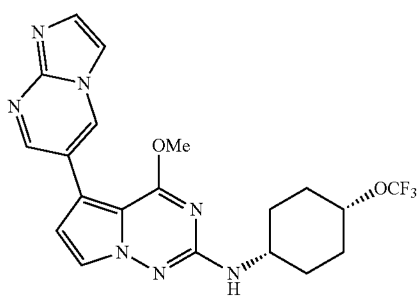
250



[0936] N-(cis-4-(Difluoromethoxy)cyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 250.

[0937] Beige solid (21 mg, 0.049 mmol, 21.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.61-1.72 (4H, m), 1.74-1.82 (2H, m), 1.87 (2 H, dt, J=9.58, 4.79 Hz), 3.68 (1 H, br dd, J=8.08, 3.97 Hz), 3.98 (3 H, s), 4.29 (1 H, br s), 6.72 (1H, t, J=77.05 Hz), 6.73 (1H, d, J=7.67 Hz), 6.77 (1H, d, J=2.46 Hz), 7.65 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{21}F_2N_702$ m/z 430.2 (M+1).

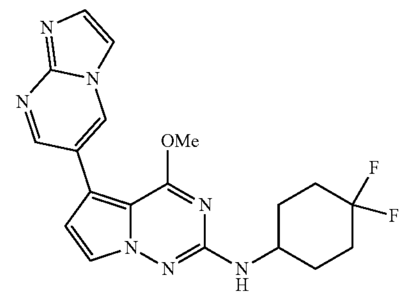
252



[0938] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-(trifluoromethoxy)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 252.

[0939] Off-white solid (31 mg, 0.069 mmol, 34.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.61-1.71 (2H, m), 1.71-1.79 (2H, m), 1.83 (2 H, td, J=8.42, 3.97 Hz), 1.91-1.99 (2H, m), 3.65-3.77 (1H, m), 3.98 (3 H, s), 4.60 (1 H, dt, J=5.00, 2.29 Hz), 6.76 (1H, d, J=7.67 Hz), 6.77 (1H, d, J=2.74 Hz), 7.66 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1 H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.74 Hz); ESIMS found for $C_{20}H_{20}F_3N_7O_2$ m/z 448.2 (M+1).

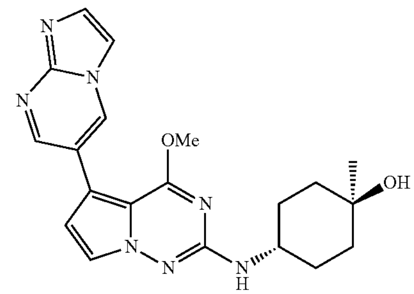
254



[0940] N-(4,4-Difluorocyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 254.

[0941] Off-white solid (68 mg, 0.170 mmol, 56.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.54-1.69 (2H, m), 1.85-2.02 (4H, m), 2.03-2.16 (2H, m), 3.74-3.86 (1H, m), 3.98 (3 H, s), 6.78 (1H, d, J=2.46 Hz), 6.80 (1H, d, J=7.67 Hz), 7.67 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.09 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{19}H_{19}F_2N_7O$ m/z 400.2 (M+1).

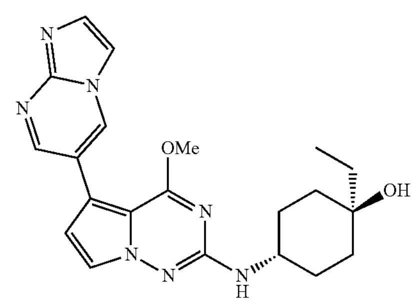
257



[0942] trans-4-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 257.

[0943] Off-white solid (25 mg, 0.064 mmol, 29.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.36-1.52 (4H, m), 1.55-1.68 (2H, m), 1.82-1.93 (2H, m), 3.58-3.72 (1H, m), 3.97 (3H, s), 4.24 (1H, s), 6.54 (1H, d, J=7.94 Hz), 6.76 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.92 (1H, d, J=1.10 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

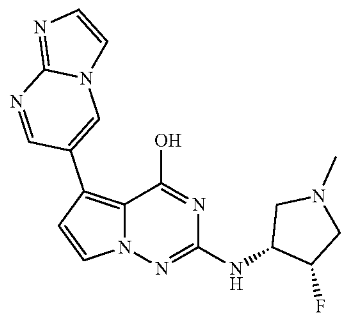
258



[0944] trans-1-Ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol 258.

[0945] Off-white solid (13 mg, 0.032 mmol, 24.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.83 (3H, t, J=7.39 Hz), 1.31-1.39 (2H, m), 1.40-1.49 (4H, m), 1.64 (2 H, br d, J=10.68 Hz), 1.85 (2 H, br dd, J=12.05, 6.30 Hz), 3.68 (1 H, dt, J=8.01, 3.80 Hz), 3.97 (3 H, s), 3.98 (1 H, br s), 6.53 (1H, d, J=7.67 Hz), 6.76 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.46 Hz), 7.72 (1H, s), 7.92 (1H, s), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{25}N_7O_2$ m/z 408.2 (M+1).

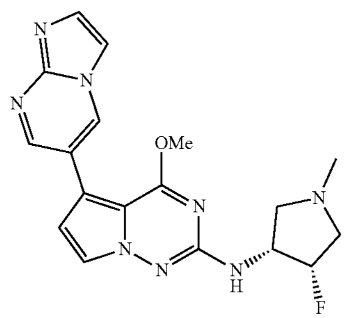
261



[0946] 2-(((3R,4S)-4-Fluoro-1-methylpyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol 261.

[0947] Pale-yellow semi-solid (11 mg, 0.030 mmol, 26.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.29 (3 H, s), 2.47-2.52 (16H, m), 2.71 (1H, ddd, J=30.45, 12.05, 1.10 Hz), 2.88 (1H, dd, J=9.17, 7.26 Hz), 2.96 (1H, ddd, J=31.85, 12.10, 4.70 Hz), 4.19-4.34 (1H, m), 5.22 (1 H, dtd, J=55.95, 5.20, 5.20, 1.35 Hz), 6.17 (1H, br d, J=7.39 Hz), 6.81 (1H, d, J=2.74 Hz), 7.48 (1H, d, J=2.74 Hz), 7.71 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.90 (1H, d, J=2.46 Hz), 9.41 (1H, d, J=2.46 Hz), 10.69 (1 H, br s); ESIMS found for $C_{17}H_{17}FN_8O$ m/z 369.2 (M+1).

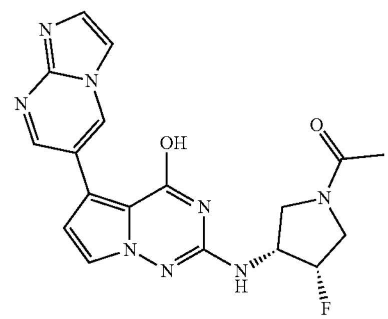
262



[0948] N-((3R,4S)-4-Fluoro-1-methylpyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 262.

[0949] Pale-yellow semi-solid (12 mg, 0.031 mmol, 39.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.31 (3 H, s), 2.55-2.66 (2H, m), 2.92 (1H, t, J=8.08 Hz), 3.17 (1H, ddd, J=29.35, 11.80, 4.95 Hz), 4.00 (3 H, s), 4.20-4.35 (1H, m), 5.21 (1 H, dtd, J=55.95, 5.20, 5.20, 1.95 Hz), 6.81 (1H, d, J=2.46 Hz), 6.84 (1H, d, J=7.67 Hz), 7.69 (1H, d, J=2.74 Hz), 7.73 (1H, d, J=1.09 Hz), 7.93 (1H, d, J=1.09 Hz), 8.74 (1H, d, J=2.46 Hz), 9.10 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}FN_8O$ m/z 383.2 (M+1).

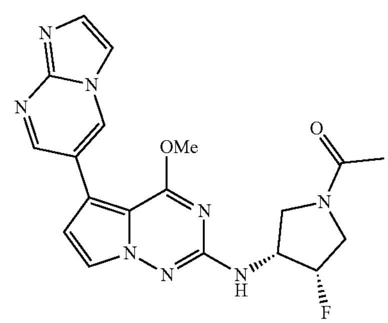
263



[0950] 1-((3S,4R)-3-Fluoro-4-((4-hydroxy-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one 263.

[0951] Pale yellow solid (7 mg, 0.018 mmol, 15.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.91-2.03 (3H, m), 3.48-3.76 (2H, m), 3.79-3.93 (1H, m), 3.99-4.09 (1H, m), 4.28-4.61 (1H, m), 5.22-5.49 (1H, m), 6.30-6.43 (1H, m), 6.83 (1 H, br s), 7.48 (1H, d, J=2.19 Hz), 7.71 (1H, s), 7.94 (1H, s), 8.91 (1H, d, J=1.64 Hz), 9.41 (1 H, s), 10.77 (1 H, br s); ESIMS found for $C_{18}H_{17}FN_8O_2$ m/z 397.2 (M+1).

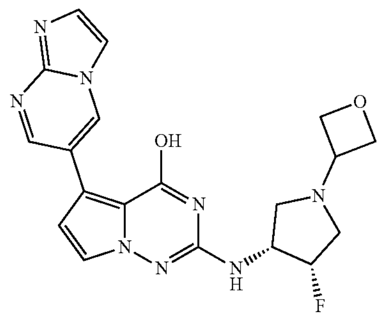
264



[0952] 1-((3S,4R)-3-Fluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one 264.

[0953] Yellow solid (24 mg, 0.059 mmol, 74.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.93-2.01 (3H, m), 3.47-3.57 (1H, m), 3.58-3.76 (1H, m), 3.78-3.97 (2H, m), 4.01 (3H, d, J=1.37 Hz), 4.28-4.59 (1H, m), 5.24-5.50 (1H, m), 6.83 (1H, t, J=2.33 Hz), 7.15 (1H, dd, J=7.12, 4.65 Hz), 7.70 (1H, dd, J=3.83, 2.74 Hz), 7.73 (1 H, s), 7.94 (1H, d, J=0.82 Hz), 8.75 (1H, d, J=2.46 Hz), 9.11 (1H, d, J=2.46 Hz); ESIMS found for $C_{19}H_{19}FN_8O_2$ m/z 411.2 (M+1).

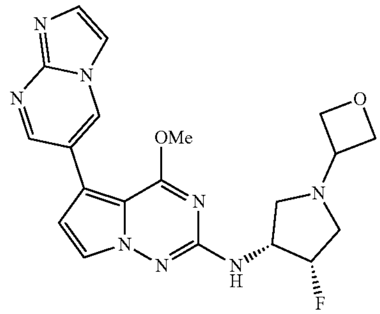
265



[0954] 2-(((3R,4S)-4-Fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol 265.

[0955] Off-white solid (4 mg, 0.010 mmol, 8.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.56 (1H, t, J=8.49 Hz), 2.79-2.91 (1H, m), 2.96-3.09 (1H, m), 2.98-3.03 (1H, m), 3.76 (1 H, quin, J=6.09 Hz), 4.22-4.37 (1H, m), 4.46 (2H, t, J=6.02 Hz), 4.58 (2H, t, J=6.57 Hz), 5.25 (1 H, dtd, J=55.95, 4.65, 4.65, 1.00 Hz), 6.29 (1H, br d, J=6.30 Hz), 6.81 (1H, d, J=2.74 Hz), 7.48 (1H, d, J=2.74 Hz), 7.71 (1H, d, J=1.10 Hz), 7.93 (1H, d, J=1.09 Hz), 8.90 (1H, d, J=2.46 Hz), 9.41 (1H, d, J=2.19 Hz), 10.78 (1 H, br s); ESIMS found for $C_{19}H_{19}FN_8O_2$ m/z 411.2 (M+1).

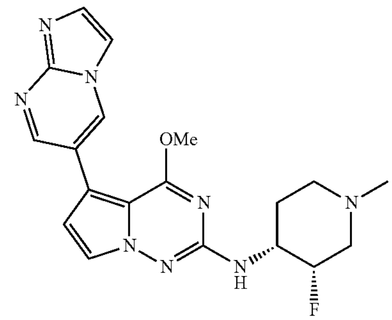
266



[0956] N-((3R,4S)-4-Fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 266.

[0957] Off-white solid (15 mg, 0.035 mmol, 33.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.69 (1H, t, J=9.17 Hz), 2.77 (1H, ddd, J=29.65, 12.10, 1.10 Hz), 3.01 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=32.95, 12.05, 4.40 Hz), 3.74-3.84 (1H, m), 4.00 (3 H, s), 4.23-4.38 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 5.25 (1 H, dtd, J=55.65, 4.65, 4.65, 1.65 Hz), 6.82 (1H, d, J=2.46 Hz), 6.90 (1H, d, J=7.67 Hz), 7.69 (1H, d, J=2.74 Hz), 7.73 (1H, d, J=1.10 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.10 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{21}FN_8O_2$ m/z 425.2 (M+1).

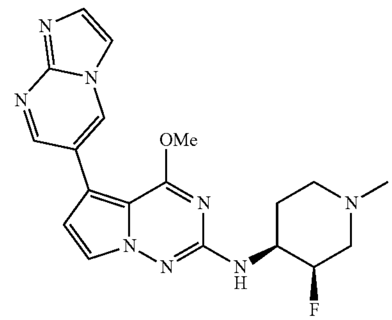
267



[0958] N-((3S,4R)-3-Fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 267.

[0959] White solid (14 mg, 0.035 mmol, 67.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.65-1.72 (1H, m), 1.92 (1 H, qd, J=12.18, 3.70 Hz), 2.02-2.10 (1H, m), 2.11-2.25 (1H, m), 2.19 (3 H, s), 2.80 (1H, br d, J=12.32 Hz), 3.00-3.12 (1H, m), 3.67-3.84 (1H, m), 3.99 (3H, s), 4.55 (4H, s), 4.91 (1H, d, J=50.20 Hz), 6.70 (1H, d, J=7.94 Hz), 6.79 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.74 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{19}H_{21}FN_8O$ m/z 397.2 (M+1).

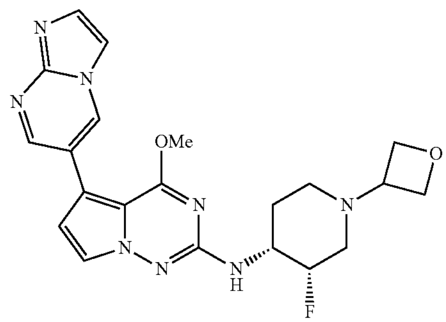
268



[0960] N-((3R,4S)-3-Fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 268.

[0961] White solid (15 mg, 0.038 mmol, 72.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.62-1.74 (1H, m), 1.92 (1 H, qd, J=12.09, 3.70 Hz), 2.01-2.10 (1H, m), 2.11-2.24 (1H, m), 2.18 (3 H, s), 2.79 (1H, br d, J=11.23 Hz), 3.00-3.11 (1H, m), 3.68-3.83 (1H, m), 3.99 (3 H, s), 4.91 (1H, d, J=50.20 Hz), 6.69 (1H, d, J=7.94 Hz), 6.79 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{19}H_{21}FN_8O$ m/z 397.2 (M+1).

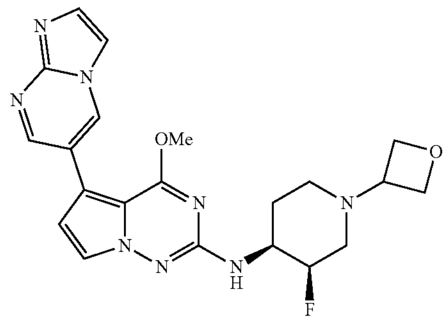
269



[0962] N-((3S,4R)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 269.

[0963] White solid (13 mg, 0.030 mmol, 36.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.66-1.78 (1H, m), 1.92 (1 H, qd, J=12.14, 3.56 Hz), 1.98-2.06 (1H, m), 2.10-2.25 (1H, m), 2.76 (1H, br d, J=10.13 Hz), 2.93-3.06 (1H, m), 3.49 (1 H, quin, J=6.30 Hz), 3.74-3.90 (1H, m), 3.99 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.94 (1H, d, J=49.35 Hz), 6.76 (1H, d, J=7.67 Hz), 6.79 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.74 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{23}FN_8O_2$ m/z 439.2 (M+1).

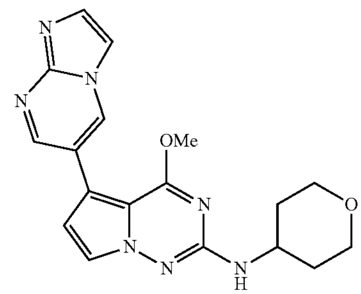
270



[0964] N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 270.

[0965] White solid (23 mg, 0.053 mmol, 37.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.69-1.76 (1H, m), 1.92 (1 H, qd, J=12.14, 3.29 Hz), 1.98-2.06 (1H, m), 2.08-2.24 (1H, m), 2.71-2.80 (1H, m), 2.94-3.05 (1H, m), 3.49 (1 H, quin, J=6.50 Hz), 3.74-3.91 (1H, m), 3.99 (3 H, s), 4.40 (1H, t, J=6.02 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.50, 3.15 Hz), 4.93 (1H, d, J=49.35 Hz), 6.76 (1H, d, J=7.94 Hz), 6.79 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.46 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{23}FN_8O_2$ m/z 439.2 (M+1).

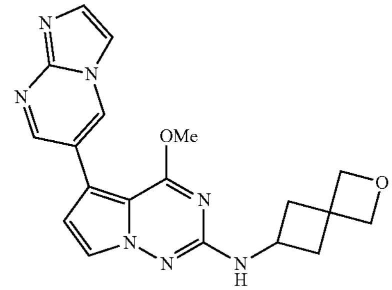
271



[0966] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(tetrahydro-2H-pyran-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 271.

[0967] Beige solid (4 mg, 0.011 mmol, 6.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.48-1.61 (2H, m), 1.90 (2 H, br dd, J=12.59, 2.19 Hz), 3.40 (2 H, td, J=11.64, 1.92 Hz), 3.76-3.84 (1H, m), 3.85-3.91 (2H, m), 3.98 (3 H, s), 6.74 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.09 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1 H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz) ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.2 (M+1).

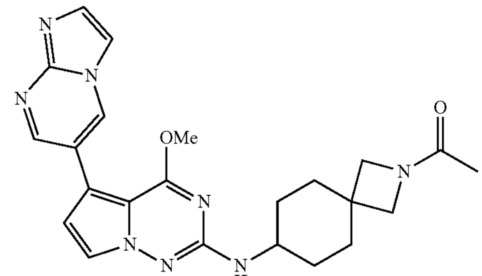
272



[0968] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(2-oxaspiro[3.3]heptan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 272.

[0969] Off-white solid (6 mg, 0.016 mmol, 6.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.12-2.23 (2H, m), 2.61 (2H, ddd, J=9.99, 7.53, 2.74 Hz), 3.92-4.05 (1H, m), 3.96 (3H, s), 4.51 (2H, s), 4.63 (2 H, s), 6.78 (1H, d, J=2.74 Hz), 7.03 (1H, d, J=7.12 Hz), 7.66 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.92 (1H, d, J=1.37 Hz), 8.72 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{19}H_{19}N_7O_2$ m/z 378.2 (M+1).

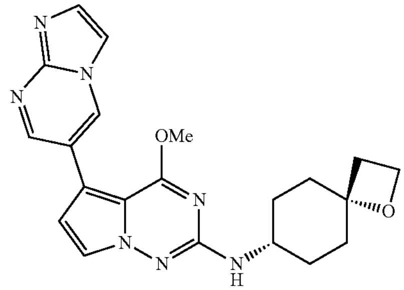
273



[0970] 1-(7-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one 273.

[0971] Colorless gum (10 mg, 0.022 mmol, 21.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.26-1.40 (2H, m), 1.49-1.61 (2H, m), 1.74-1.77 (3H, m), 1.83-1.93 (4H, m), 3.47 (1H, s), 3.52 (1H, s), 3.53-3.63 (1H, m), 3.75 (1H, s), 3.80 (1H, s), 3.97 (3 H, s), 6.59 (1H, dd, J=16.70, 7.94 Hz), 6.77 (1H, d, J=2.74 Hz), 7.67 (1H, t, J=2.87 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{23}H_{26}N_8O_2$ m/z 447.3 (M+1).

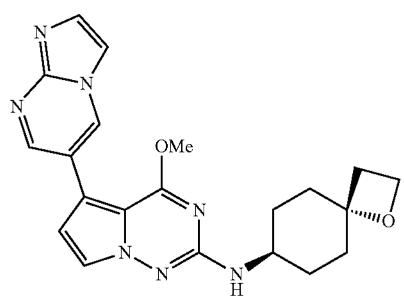
274



[0972] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((4s,7s)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 274.

[0973] White solid (4.2 mg, 0.0104 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.28-1.41 (2H, m), 1.52 (2 H, td, J=12.38, 3.38 Hz), 1.85-1.98 (2H, m), 2.05 (2H, br d, J=12.88 Hz), 2.34 (2H, t, J=7.69 Hz), 3.50-3.64 (1H, m), 3.97 (3 H, s), 4.37 (2H, t, J=7.69 Hz), 6.58 (1 H, d, J=7.75 Hz), 6.76 (1H, d, J=2.63 Hz), 7.67 (1H, d, J=2.63 Hz), 7.72 (1 H, s), 7.92 (1H, d, J=1.00 Hz), 8.73 (1H, d, J=2.38 Hz), 9.08 (1H, d, J=2.38 Hz); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.0 (M+1).

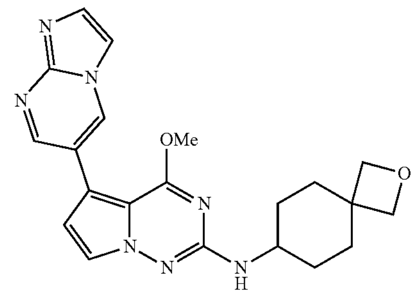
275



[0974] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((4r,7r)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 275.

[0975] White solid (4.20 mg, 0.010 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.29-1.43 (2H, m), 1.47-1.60 (2H, m), 1.86-1.97 (2H, m), 2.05 (2H, br d, J=12.88 Hz), 2.34 (2H, t, J=7.69 Hz), 3.51-3.63 (1H, m), 3.97 (3 H, s), 4.37 (2H, t, J=7.69 Hz), 6.58 (1H, d, J=7.75 Hz), 6.76 (1H, d, J=2.63 Hz), 7.67 (1H, d, J=2.63 Hz), 7.72 (1 H, s), 7.92 (1H, d, J=1.00 Hz), 8.73 (1H, d, J=2.38 Hz), 9.08 (1H, d, J=2.38 Hz); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.0 (M+1).

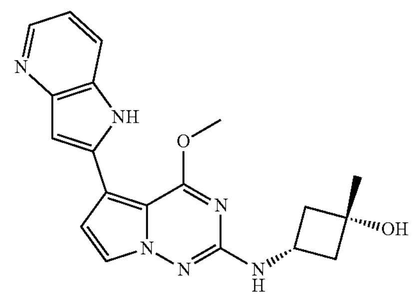
276



[0976] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 276.

[0977] Beige solid (32 mg, 0.079 mmol, 29.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.20-1.32 (2H, m), 1.52 (2 H, td, J=12.87, 3.29 Hz), 1.87 (2 H, br dd, J=13.14, 3.29 Hz), 2.07 (2H, br d, J=13.14 Hz), 3.48-3.62 (1H, m), 3.96 (3H, s), 4.24 (2H, s), 4.32 (2 H, s), 6.55 (1H, d, J=7.94 Hz), 6.76 (1H, d, J=2.46 Hz), 7.66 (1H, d, J=2.46 Hz), 7.73 (1 H, s), 7.93 (1 H, s), 8.73 (1H, d, J=2.19 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{23}N_7O_2$ m/z 406.2 (M+1).

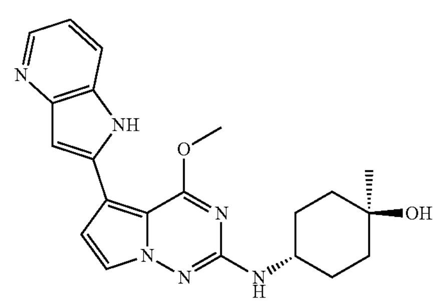
277



[0978] cis-3-((4-Methoxy-5-(1H-pyrrolo[3,2-b]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 277.

[0979] Beige solid (39 mg, 0.107 mmol, 46.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 1.99-2.07 (2H, m), 2.31-2.40 (2H, m), 3.72 (1 H, dq, J=15.09, 7.75 Hz), 4.11 (3H, s), 4.92 (1H, s), 6.94 (1H, dd, J=2.19, 0.82 Hz), 6.99 (1H, d, J=2.74 Hz), 7.00 (1 H, d, J=6.57 Hz), 7.03 (1H, dd, J=7.95, 4.65 Hz), 7.65 (1H, d, J=2.74 Hz), 7.70 (1 H, dt, J=8.01, 1.20 Hz), 8.25 (1H, dd, J=4.65, 1.37 Hz), 11.18 (1H, d, J=1.92 Hz); ESIMS found for $C_{1-9}H_2O$ N_6O_2 m/z 365.2 (M+1).

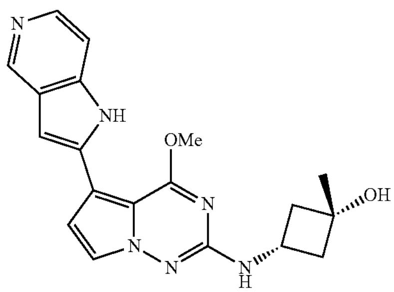
280



[0980] trans-4-((4-Methoxy-5-(1H-pyrrolo[3,2-b]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 280.

[0981] Yellow solid (37 mg, 0.094 mmol, 39.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.33-1.52 (4H, m), 1.54-1.63 (2H, m), 1.82-1.91 (2H, m), 3.64 (1 H, dt, J=8.08, 4.18 Hz), 4.12 (3H, s), 4.23 (1H, s), 6.55 (1H, d, J=7.94 Hz), 6.93 (1H, d, J=1.37 Hz), 6.98 (1H, d, J=2.74 Hz), 7.03 (1H, dd, J=7.95, 4.65 Hz), 7.65 (1H, d, J=2.74 Hz), 7.69-7.72 (1H, m), 8.25 (1H, dd, J=4.65, 1.37 Hz), 11.18 (1H, d, J=1.92 Hz); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

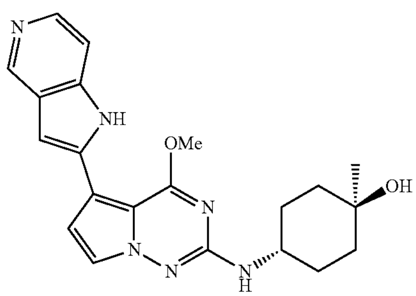
281



[0982] cis-3-((4-Methoxy-5-(1H-pyrrolo[3,2-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 281.

[0983] Off-white solid (2 mg, 0.006 mmol, 9.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 1.97-2.07 (2H, m), 2.30-2.41 (2H, m), 3.71 (1 H, dq, J=15.09, 7.65 Hz), 4.10 (3H, s), 4.93 (1H, s), 6.93 (1H, d, J=1.10 Hz), 6.95 (1H, d, J=2.74 Hz), 6.98 (1H, d, J=6.57 Hz), 7.34 (1H, d, J=5.48 Hz), 7.64 (1H, d, J=2.74 Hz), 8.11 (1H, d, J=5.48 Hz), 8.76 (1 H, s), 11.41 (1 H, s); ESIMS found for $C_{1\text{-}9}H_2O$ N_6O_2 m/z 365.2 (M+1).

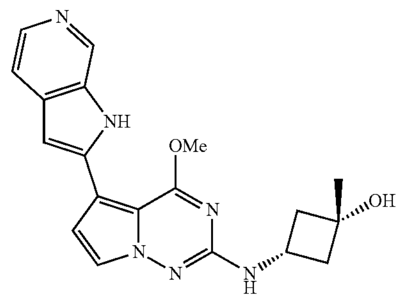
282



[0984] trans-4-((4-Methoxy-5-(1H-pyrrolo[3,2-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 282.

[0985] White solid (7 mg, 0.018 mmol, 31.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.36-1.52 (4H, m), 1.57-1.65 (2H, m), 1.83-1.92 (2H, m), 3.63 (1 H, br dd, J=7.80, 3.70 Hz), 4.11 (3H, s), 4.24 (1H, s), 6.53 (1H, d, J=7.94 Hz), 6.93 (1H, d, J=1.10 Hz), 6.95 (1H, d, J=2.74 Hz), 7.34 (1H, d, J=5.75 Hz), 7.64 (1H, d, J=2.46 Hz), 8.12 (1H, br d, J=5.48 Hz), 8.76 (1 H, s), 11.41 (1H, d, J=0.82 Hz); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

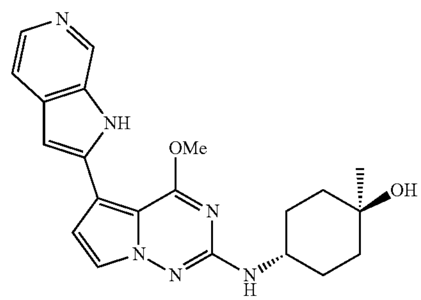
283



[0986] cis-3-((4-Methoxy-5-(1H-pyrrolo[2,3-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 283.

[0987] Tan solid (6 mg, 0.017 mmol, 40.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 1.96-2.07 (2H, m), 2.30-2.41 (2H, m), 3.66-3.78 (1H, m), 4.11 (3H, s), 4.93 (1H, s), 6.86 (1H, d, J=1.64 Hz), 6.99 (1H, d, J=2.74 Hz), 7.02 (1H, d, J=6.57 Hz), 7.45 (1 H, br d, J=5.20 Hz), 7.65 (1H, d, J=2.74 Hz), 8.04 (1H, br d, J=4.93 Hz), 8.70 (1 H, br s), 11.42 (1 H, s); ESIMS found for $C_{19}H_{20}N_6O_2$ m/z 365.2 (M+1).

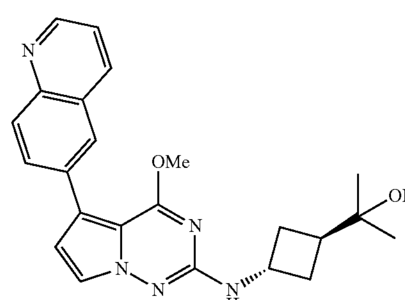
284



[0988] trans-4-((4-Methoxy-5-(1H-pyrrolo[2,3-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 284.

[0989] Beige solid (12 mg, 0.031 mmol, 66.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.30-1.53 (4H, m), 1.54-1.63 (2H, m), 1.63-1.77 (2H, m), 3.47-3.70 (1H, m), 4.11 (3H, d, J=1.64 Hz), 6.58 (1H, dd, J=14.51, 7.94 Hz), 6.86 (1H, d, J=1.64 Hz), 6.98 (1H, t, J=2.87 Hz), 7.45 (1H, br d, J=5.48 Hz), 7.64 (1H, dd, J=14.78, 2.46 Hz), 8.04 (1H, br d, J=4.93 Hz), 8.70 (1 H, s), 11.41 (1 H, br s); ESIMS found for $C_{21}H_{24}N_6O_2$ m/z 393.2 (M+1).

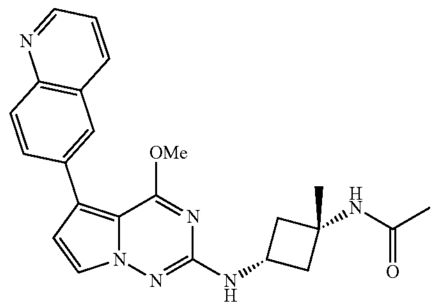
287



[0990] 2-(trans-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutyl)propan-2-ol 287.

[0991] Yellow solid (36 mg, 0.089 mmol, 46.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.05 (6 H, s), 1.98 (2H, ddd, J=12.39, 9.65, 5.89 Hz), 2.16-2.27 (1H, m), 2.27-2.36 (2H, m), 3.96 (3 H, s), 4.09 (1 H, dq, J=13.62, 6.96 Hz), 4.19 (1 H, s), 6.76 (1H, d, J=2.74 Hz), 6.96 (1H, d, J=6.84 Hz), 7.52 (1H, dd, J=8.21, 4.11 Hz), 7.64 (1H, d, J=2.46 Hz), 7.94-8.01 (2 H, m), 8.10 (1 H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{23}H_{25}N_5O_2$ m/z 404.2 (M+1).

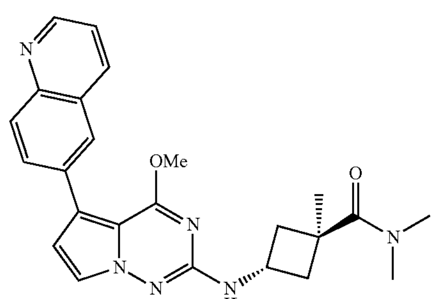
288



[0992] N-(cis-3-((4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 288.

[0993] Off-white solid (39 mg, 0.094 mmol, 97.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.10-2.21 (2H, m), 2.43 (2H, ddd, J=9.58, 7.39, 2.46 Hz), 3.96 (3 H, s), 4.04 (1 H, sxt, J=7.72 Hz), 6.77 (1H, d, J=2.46 Hz), 7.00 (1H, d, J=6.84 Hz), 7.52 (1H, dd, J=8.35, 4.24 Hz), 7.66 (1H, d, J=2.74 Hz), 7.95-8.01 (2H, m), 8.03 (1H, s), 8.11 (1H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{23}H_{24}N_6O_2$ m/z 417.2 (M+1).

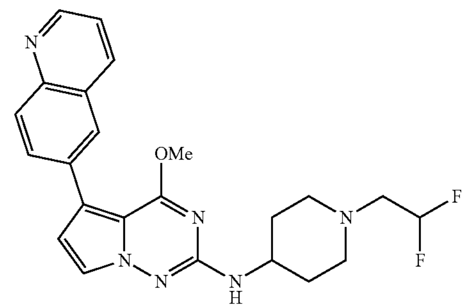
290



[0994] trans-3-((4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide 290.

[0995] Light yellow solid (32 mg, 0.074 mmol, 60.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.40 (3 H, s), 1.95-2.05 (2H, m), 2.80-2.95 (8H, m), 3.91 (1 H, dq, J=14.78, 7.30 Hz), 3.97 (3 H, s), 6.78 (1H, d, J=2.74 Hz), 7.08 (1H, d, J=6.57 Hz), 7.56 (1H, dd, J=8.35, 4.24 Hz), 7.66 (1H, d, J=2.46 Hz), 8.00 (2H, s), 8.13 (1H, s), 8.40 (1H, d, J=7.39 Hz), 8.88 (1 H, br d, J=3.01 Hz); ESIMS found for $C_{24}H_{26}N_6O_2$ m/z 431.2 (M+1).

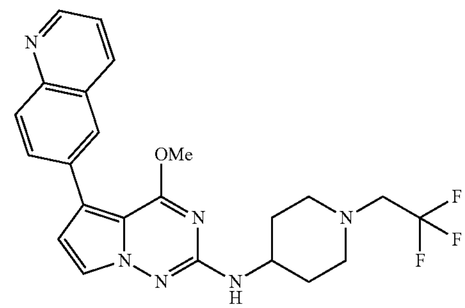
304



[0996] N-(1-(2,2-Difluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 304.

[0997] Yellow solid (42 mg, 0.096 mmol, 37.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.47-1.62 (2H, m), 1.85-1.95 (2H, m), 2.21-2.32 (2H, m), 2.72 (2 H, td, J=15.61, 4.38 Hz), 2.91 (2H, br d, J=11.77 Hz), 3.54-3.66 (1H, m), 3.96 (3 H, s), 6.14 (1 H, tt, J=55.95, 4.38 Hz), 6.61 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.46 Hz), 7.47-7.57 (1H, m), 7.65 (1H, d, J=2.74 Hz), 7.94-8.03 (2H, m), 8.11 (1 H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{23}H_{24}F_2N_6O$ m/z 439.2 (M+1).

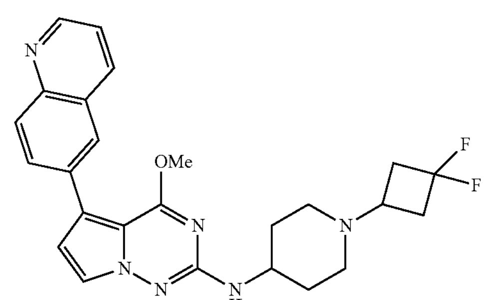
305



[0998] 4-Methoxy-5-(quinolin-6-yl)-N-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 305.

[0999] Off-white solid (30 mg, 0.066 mmol, 26.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.49-1.61 (2H, m), 1.91 (2H, br d, J=9.86 Hz), 2.39-2.48 (2H, m), 2.93 (2 H, br d, J=11.77 Hz), 3.17 (2 H, q, J=10.40 Hz), 3.55-3.66 (1H, m), 3.96 (3 H, s), 6.62 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.46 Hz), 7.52 (1H, dd, J=8.21, 4.11 Hz), 7.65 (1H, d, J=2.74 Hz), 7.94-8.03 (2H, m), 8.11 (1 H, s), 8.36 (1H, dd, J=8.49, 1.64 Hz), 8.86 (1H, dd, J=4.38, 1.64 Hz); ESIMS found for $C_{23}H_{23}F_3N_6O$ m/z 457.2 (M+1).

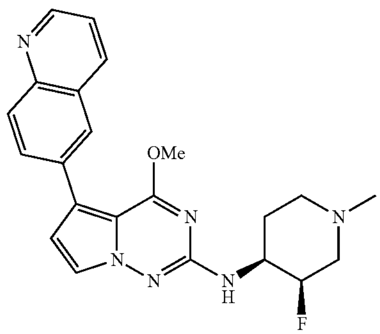
306



[1000] N-(1-(3,3-Difluorocyclobutyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 306.

[1001] White solid (4 mg, 0.009 mmol, 4.6% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.45-1.59 (2H, m), 1.86-1.97 (4H, m), 2.32-2.46 (2H, m), 2.59-2.73 (3H, m), 2.80(2 H, br d, J=11.50 Hz), 3.56-3.66 (1H, m), 3.96 (3 H, s), 6.63 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.46 Hz), 7.52 (1H, dd, J=8.35, 4.24 Hz), 7.65 (1H, d, J=2.74 Hz), 7.94-8.03 (2H, m), 8.11 (1 H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{25}H_{26}F_2N_6O$ m/z 465.2 (M+1).

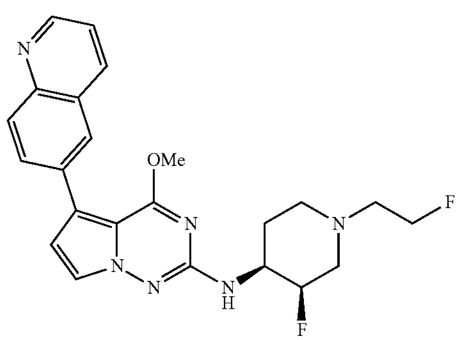
310



[1002] N-((3R,4S)-3-Fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 310.

[1003] Off-white solid (11 mg, 0.027 mmol, 88.5% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.69 (1 H, br dd, J=13.00, 3.42 Hz), 1.93 (1 H, qd, J=12.18, 3.70 Hz), 2.06 (1 H, brt, J=10.95 Hz), 2.12-2.25 (1H, m), 2.19(3 H, s), 2.74-2.86 (1H, m), 3.00-3.11 (1H, m), 3.69-3.85 (1H, m), 3.98 (3 H, s), 4.92 (1H, d, J=49.90 Hz), 6.63 (1H, d, J=7.67 Hz), 6.79 (1H, d, J=2.46 Hz), 7.53 (1H, dd, J=8.21, 4.38 Hz), 7.65 (1H, d, J=2.46 Hz), 7.95-8.04 (2H, m), 8.12 (1 H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{22}H_{23}FN_6O$ m/z 407.2 (M+1).

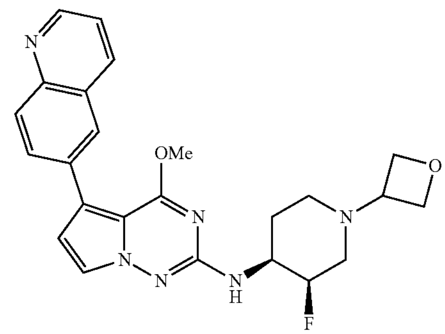
314



[1004] N-((3R,4S)-3-Fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 314.

[1005] Off-white fluffy solid (16 mg, 0.037 mmol, 47.7% yield). ^{1}H NMR (500 MHz, DMSO-d$_6$) δ ppm 1.66-1.77 (1H, m), 1.93 (1 H, qd, J=12.21, 3.43 Hz), 2.26 (1 H, br t, J=11.25 Hz), 2.39 (1H, dd, J=37.60, 12.90 Hz), 2.68 (2 H, dt, J=28.60, 5.25 Hz), 2.93 (1H, br d, J=10.70 Hz), 3.13-3.22 (1H, m), 3.73-3.89 (1H, m), 3.98 (3 H, s), 4.55 (2 H, dt, J=47.75, 4.95 Hz), 4.93 (1H, d, J=49.70 Hz), 6.64 (1H, d, J=7.68 Hz), 6.79 (1H, d, J=2.47 Hz), 7.53 (1H, dd, J=8.23, 4.39 Hz), 7.65 (1H, d, J=2.47 Hz), 7.94-8.04 (2H, m), 8.12 (1 H, s), 8.36 (1H, dd, J=8.23, 1.37 Hz), 8.86 (1H, dd, J=4.12, 1.37 Hz); ESIMS found for $C_{23}H_{24}F_2N_6O$ m/z 439.2 (M+1).

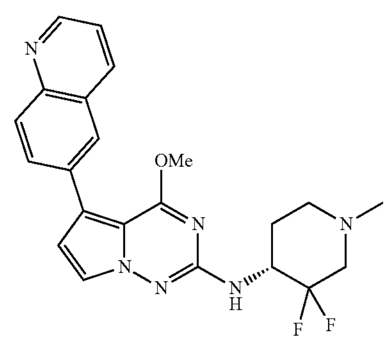
318



[1006] N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 318.

[1007] Beige solid (15 mg, 0.033 mmol, 72.9% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.68-1.79 (1H, m), 1.93 (1 H, qd, J=12.18, 3.15 Hz), 1.98-2.08 (1H, m), 2.16 (1H, dd, J=37.00, 12.60 Hz), 2.76 (1H, br d, J=11.23 Hz), 2.95-3.05 (1H, m), 3.50 (1 H, quin, J=6.43 Hz), 3.75-3.92 (1H, m), 3.98 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.95 (1H, d, J=49.65 Hz), 6.69 (1H, d, J=7.94 Hz), 6.79 (1H, d, J=2.74 Hz), 7.49-7.57 (1H, m), 7.65 (1H, d, J=2.74 Hz), 7.95-8.04 (2H, m), 8.12 (1 H, s), 8.36 (1H, dd, J=8.21, 1.64 Hz), 8.86 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{24}H_{25}FN_6O_2$ m/z 449.3 (M+1).

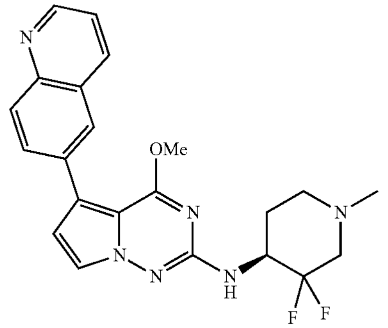
319



[1008] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 319.

[1009] Off-white solid (17 mg, 0.040 mmol, 74.7% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.76-1.91 (2H, m), 2.12-2.23 (1H, m), 2.26 (3 H, s), 2.33-2.46 (1H, m), 2.79(1 H,brd,J=11.77 Hz),2.99-3.11 (1 H,m),3.99(3 H,s),4.18-4.33(1 H,m), 6.81 (1H, d, J=2.46 Hz), 6.83 (1H, d, J=9.31 Hz), 7.53 (1H, dd, J=8.21, 4.11 Hz), 7.67 (1H, d, J=2.46 Hz), 7.99 (2H, s), 8.12 (1H, s), 8.33-8.40 (1H, m), 8.86 (1H, dd, J=4.24, 1.51 Hz); ESIMS found for $C_{22}H_{22}F_2N_6O$ m/z 425.2 (M+1).

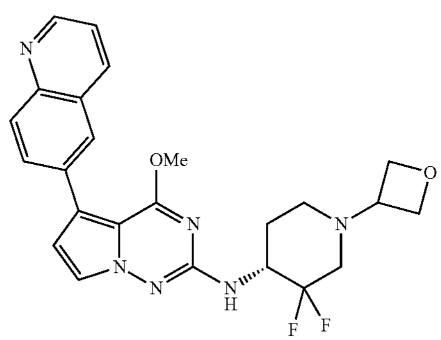
320



[1010] (S)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 320.

[1011] Yellow solid (11 mg, 0.026 mmol, 88.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.77-1.92 (2H, m), 2.13-2.22 (1H, m), 2.26 (3 H, s), 2.34-2.45 (1H, m), 2.79 (1H, br d, J=11.23 Hz), 2.99-3.12 (1H, m), 3.99 (3 H, s), 4.17-4.33 (1H, m), 6.81 (1H, d, J=2.46 Hz), 6.83 (1H, d, J=9.31 Hz), 7.53 (1H, dd, J=8.21, 4.11 Hz), 7.67 (1H, d, J=2.46 Hz), 7.99 (2H, s), 8.12 (1H, s), 8.36 (1H, d, J=8.21 Hz), 8.86 (1H, d, J=4.11 Hz); ESIMS found for $C_{22}H_{22}F_2N_6O$ m/z 425.2 (M+1).

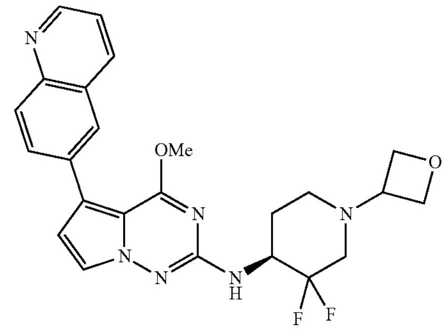
321



[1012] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 321.

[1013] Off-white solid (15 mg, 0.033 mmol, 72.9% yield). ^{1}H NMR (499 MHz, CHLOROFORM-d) δ ppm 1.77-1.87 (1H, m), 2.19-2.30 (2H, m), 2.31-2.45 (1H, m), 2.82-2.90 (1H, m), 3.05-3.15 (1H, m), 3.70 (1 H, quin, J=6.43 Hz), 4.01 (3 H, s), 4.25-4.41 (1H, m), 4.63-4.67 (1H, m), 4.68 (1H, d, J=6.30 Hz), 4.69-4.71 (2H, m), 4.71-4.73 (1H, m), 6.70 (1 H, d, J=2.46 Hz), 7.41 (1H, dd, J=8.35, 4.24 Hz), 7.48 (1H, d, J=2.74 Hz), 7.94-7.99 (2H, m), 8.10 (1H, d, J=8.49 Hz), 8.18 (1H, d, J=7.39 Hz), 8.90 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{24}H_{24}F_2N_6O_2$ m/z 467.2 (M+1).

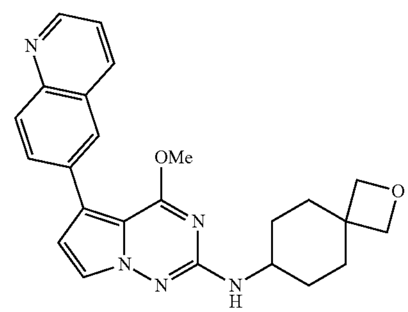
322



[1014] (S)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 322.

[1015] Off-white solid (15 mg, 0.033 mmol, 72.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.77-1.86 (1H, m), 1.87-1.94 (1H, m), 2.13-2.20 (1H, m), 2.37-2.46 (1H, m), 2.76 (1H, br d, J=11.50 Hz), 2.97-3.07 (1H, m), 3.61 (1 H, quin, J=6.37 Hz), 4.00 (3 H, s), 4.24-4.39 (1H, m), 4.44 (2 H, dt, J=15.06, 6.16 Hz), 4.55 (2 H, td, J=6.57, 3.83 Hz), 6.81 (1H, d, J=2.74 Hz), 6.89 (1H, d, J=9.58 Hz), 7.53 (1H, dd, J=8.21, 4.11 Hz), 7.66 (1H, d, J=2.74 Hz), 7.96-8.04 (2H, m), 8.12 (1 H, s), 8.36 (1H, dd, J=8.49, 1.64 Hz), 8.86 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{24}H_{24}F_2N_6O_2$ m/z 467.3 (M+1).

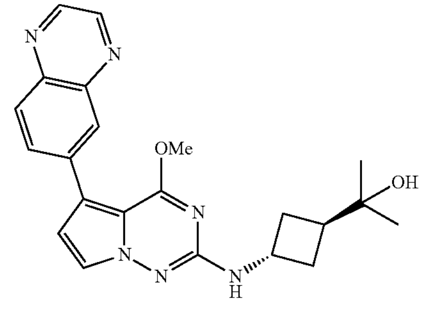
326



[1016] 4-Methoxy-5-(quinolin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 326.

[1017] Off-white solid (61 mg, 0.147 mmol, 53.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.21-1.34 (2H, m), 1.53 (2 H, td, J=12.87, 3.29 Hz), 1.82-1.94 (2H, m), 2.07 (2H, br d, J=13.42 Hz), 3.49-3.61 (1H, m), 3.95 (3H, s), 4.24 (2H, s), 4.32 (2 H, s), 6.50 (1H, d, J=7.94 Hz), 6.76 (1H, d, J=2.74 Hz), 7.52 (1H, dd, J=8.21, 4.11 Hz), 7.64 (1H, d, J=2.74 Hz), 7.94-8.03 (2H, m), 8.10 (1H, d, J=1.37 Hz), 8.35 (1H, dd, J=8.49, 1.64 Hz), 8.86 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{24}H_{25}N_5O_2$ m/z 416.2 (M+1).

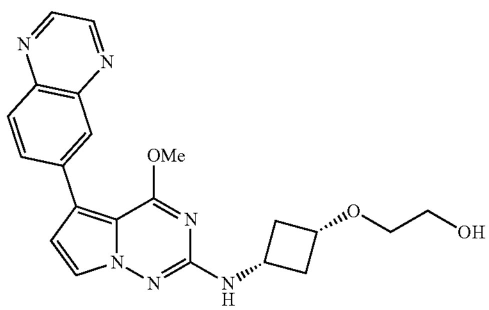
328



[1018] 2-(trans-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutyl)propan-2-ol 328.

[1019] Yellow solid (36 mg, 0.089 mmol, 46.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.05 (6 H, s), 1.93-2.04 (2H, m), 2.16-2.26 (1H, m), 2.28-2.36 (2H, m), 3.97 (3 H, s), 4.05-4.15 (1H, m), 4.19 (1 H, s), 6.86 (1H, d, J=2.74 Hz), 7.01 (1H, d, J=6.84 Hz), 7.66 (1 H, d, J=2.46 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{24}N_6O_2$ m/z 405.2 (M+1).

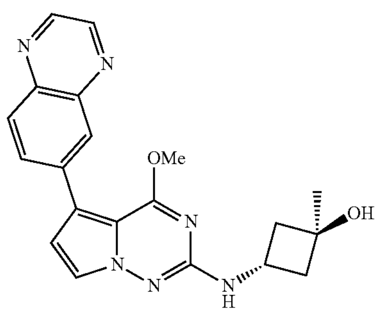
329



[1020] 2-(cis-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol 329.

[1021] Yellow solid (25 mg, 0.062 mmol, 24.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.82-1.95 (2H, m), 2.58-2.72 (2H, m), 3.31-3.34 (2H, m), 3.49 (2 H, q, J=5.48 Hz), 3.69-3.76 (1H, m), 3.76-3.84 (1H, m), 3.97 (3 H, s), 4.60 (1H, t, J=5.48 Hz), 6.88 (1H, d, J=2.74 Hz), 7.07 (1H, d, J=7.39 Hz), 7.66 (1H, d, J=2.74 Hz), 8.05-8.08 (1H, m), 8.09-8.13 (1 H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{21}H_{22}N_6O_3$ m/z 407.2 (M+1).

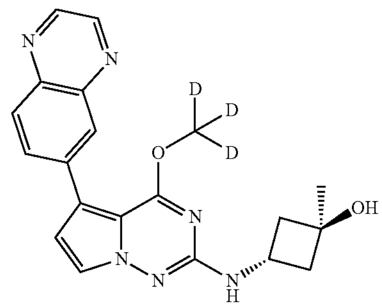
330



[1022] trans-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 330.

[1023] Light yellow solid (5 mg, 0.013 mmol, 6.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28 (3 H, s), 1.95-2.05 (2H, m), 2.27-2.37 (2H, m), 3.97 (3 H, s), 4.27 (1 H, dq, J=14.78, 7.39 Hz), 4.80 (1 H, s), 6.87 (1H, d, J=2.74 Hz), 6.99 (1H, d, J=6.84 Hz), 7.67 (1H, d, J=2.46 Hz), 8.05-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{20}H_{20}N_6O_2$ m/z 377.2 (M+1).

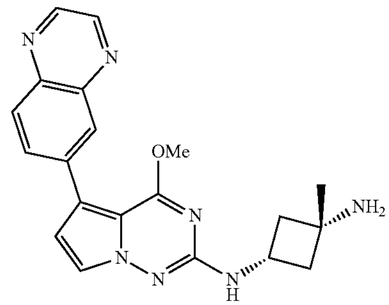
331



[1024] trans-3-((4-(Methoxy-d_3)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 331.

[1025] Yellow solid (5 mg, 0.013 mmol, 5.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.28 (3 H, s), 1.95-2.06 (2H, m), 2.28-2.38 (2H, m), 4.27 (1 H, dq, J=14.54, 7.29 Hz), 4.80 (1 H, s), 6.87 (1H, d, J=2.46 Hz), 6.99 (1H, d, J=6.84 Hz), 7.67 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{20}H_{17}[^2H_3]N_6O_2$ m/z 380.2 (M+1).

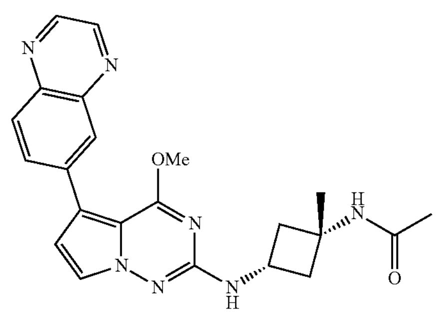
332



[1026] cis-N_1-(4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine 332.

[1027] Yellow solid (64 mg, 0.171 mmol, 70.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.20 (3 H, s), 1.77 (2 H, br s), 1.87 (2 H, br dd, J=11.23, 8.76 Hz), 2.29-2.39 (2H, m), 3.87 (1 H, dq, J=15.50, 7.79 Hz), 3.97 (3 H, s), 6.85 (1H, d, J=7.12 Hz), 6.86 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.12 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{20}H_{21}N_7O$ m/z 376.3 (M+1).

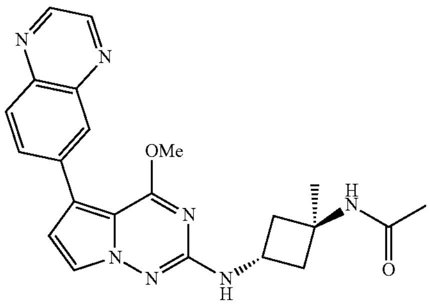
333



[1028] N-(cis-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 333.

[1029] Yellow solid (24 mg, 0.058 mmol, 98.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.12-2.22 (2H, m), 2.43 (2H, ddd, J=9.58, 7.39, 2.74 Hz), 3.97 (3 H, s), 4.04 (1 H, dq, J=15.40, 7.83 Hz), 6.87 (1H, d, J=2.46 Hz), 7.05 (1H, d, J=7.12 Hz), 7.69 (1H, d, J=2.46 Hz), 8.03 (1 H, s), 8.04-8.08 (1H, m), 8.09-8.12 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{22}H_{23}N_7O_2$ m/z 418.2 (M+1).

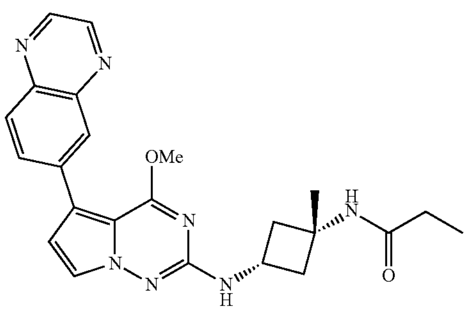
334



[1030] N-(trans-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 334.

[1031] Yellow solid (96 mg, 0.230 mmol, 90.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.82 (3H, s), 1.90-2.03 (2H, m), 2.58-2.71 (2H, m), 3.97 (3 H, s), 4.20 (1 H, sxt, J=7.83 Hz), 6.87 (1H, d, J=2.74 Hz), 7.05 (1H, d, J=7.39 Hz), 7.66 (1H, d, J=2.74 Hz), 7.94 (1 H, s), 8.04-8.08 (1H, m), 8.08-8.13 (1H, m), 8.23 (1H, d, J=1.64 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{23}N_7O_2$ m/z 418.2 (M+1).

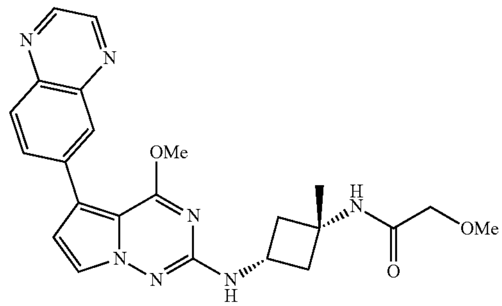
335



[1032] N-(cis-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)propionamide 335.

[1033] Yellow solid (27 mg, 0.063 mmol, 83.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.98 (3H, t, J=7.67 Hz), 1.38 (3 H, s), 2.02 (2 H, q, J=7.57 Hz), 2.13-2.23 (2H, m), 2.43 (2H, ddd, J=9.65, 7.46, 2.60 Hz), 3.97 (3 H, s), 4.04 (1 H, dq, J=15.30, 7.77 Hz), 6.87 (1H, d, J=2.46 Hz), 7.04 (1H, d, J=6.84 Hz), 7.69 (1H, d, J=2.74 Hz), 7.93 (1 H, s), 8.05-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{25}N_7O_2$ m/z 432.2 (M+1).

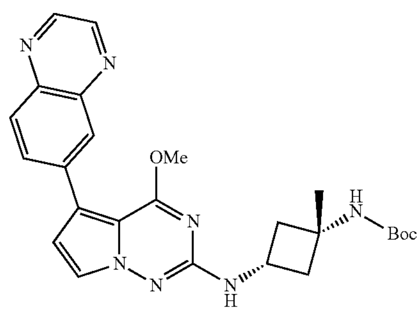
336



[1034] 2-Methoxy-N-(cis-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 336.

[1035] Yellow solid (27 mg, 0.060 mmol, 75.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.41 (3 H, s), 2.14-2.26 (2H, m), 2.44-2.49 (2H, m), 3.31 (3H, s), 3.73 (2H, s), 3.97 (3 H, s), 4.05 (1 H, dq, J=15.33, 7.85 Hz), 6.88 (1H, d, J=2.46 Hz), 7.06 (1H, d, J=7.12 Hz), 7.69 (1H, d, J=2.74 Hz), 7.87 (1 H, s), 8.05-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{25}N_7O_3$ m/z 448.2 (M+1).

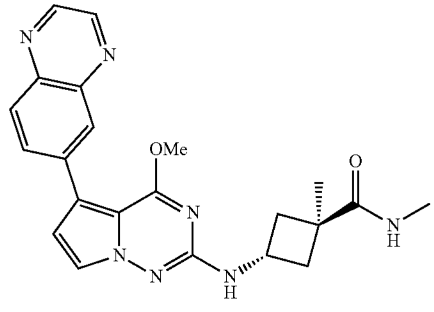
337



[1036] tert-Butyl (cis-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)carbamate 337.

[1037] Amber solid (118 mg, 0.248 mmol, 51.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.35 (3H, s), 1.38 (9H, s), 2.17 (2 H, br s), 2.32-2.42 (2H, m), 3.97 (3 H, s), 3.98-4.05 (1H, m), 6.87 (1H, d, J=2.46 Hz), 6.98-7.09 (2H, m), 7.68 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{25}H_{29}N_7O_3$ m/z 476.3 (M+1).

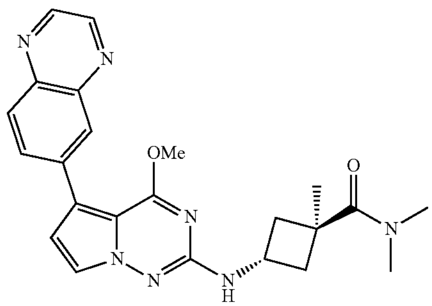
338



[1038] trans-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide 338.

[1039] Yellow solid (27 mg, 0.065 mmol, 81.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.32 (3 H, s), 1.85-1.96 (2H, m), 2.63 (3H, d, J=4.65 Hz), 2.71-2.81 (2H, m), 3.97 (3 H, s), 4.05 (1 H, sxt, J=7.99 Hz), 6.87 (1H, d, J=2.74 Hz), 7.04 (1H, d, J=7.39 Hz), 7.62 (1 H, q, J=4.29 Hz), 7.69 (1H, d, J=2.46 Hz), 8.04-8.08 (1H, m), 8.08-8.12 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{22}H_{23}N_7O_2$ m/z 418.2 (M+1).

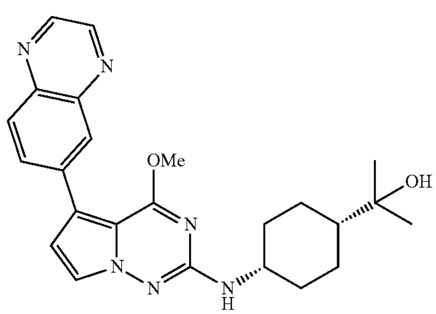
339



[1040] trans-3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide 339.

[1041] Beige solid (24 mg, 0.056 mmol, 70.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.40 (3 H, s), 1.93-2.05 (2H, m), 2.84 (3 H, br s), 2.89 (3 H, br s), 2.90-2.94 (2H, m), 3.86-3.95 (1H, m), 3.97 (3 H, s), 6.87 (1H, d, J=2.46 Hz), 7.13 (1H, d, J=6.57 Hz), 7.68 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.08-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{25}N_7O_2$ m/z 432.2 (M+1).

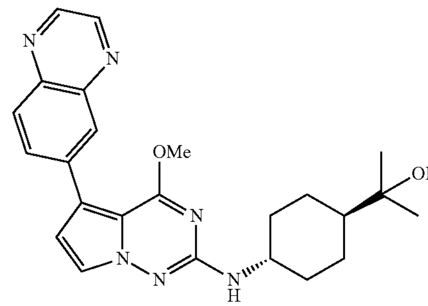
341



[1042] 2-(cis-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol341.

[1043] Yellow solid (30 mg, 0.069 mmol, 36.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.06 (6 H, s), 1.18-1.23 (1H, m), 1.33-1.43 (2H, m), 1.43-1.52 (2H, m), 1.57 (2H, br d, J=10.40 Hz), 1.96-2.07 (2H, m), 3.92-3.97 (1H, m), 4.00 (1H, s), 4.00 (3H, s), 6.48 (1 H, d, J=6.30 Hz), 6.87 (1H, d, J=2.46 Hz), 7.66 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.14 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{24}H_{28}N_6O_2$ m/z 433.2 (M+1).

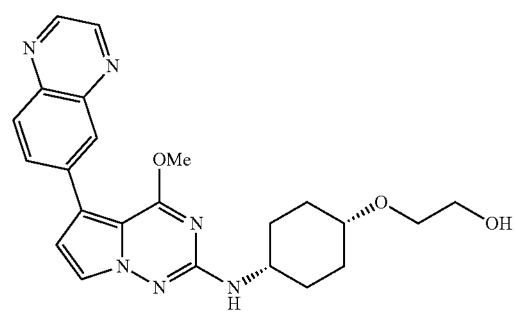
342



[1044] 2-(trans-4-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol 342.

[1045] Yellow solid (16 mg, 0.037 mmol, 19.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.05 (6 H, s), 1.07-1.15 (2H, m), 1.16-1.30 (3H, m), 1.83 (2H, br d, J=12.05 Hz), 2.04 (2H, br d, J=9.86 Hz), 3.47-3.59 (1H, m), 3.97 (3H, s), 4.03 (1H, s), 6.55 (1H, d, J=8.21 Hz), 6.86 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.74 Hz), 8.05-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{24}H_{28}N_6O_2$ m/z 433.3 (M+1).

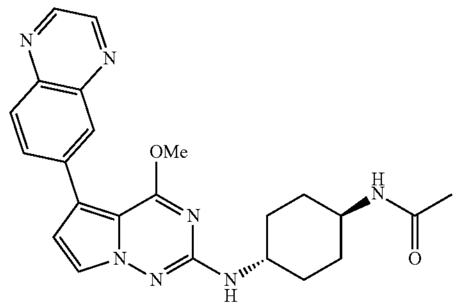
343



[1046] 2-((cis-4-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol 343.

[1047] White solid (8.0 mg, 0.018 mmol, 7.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.57 (2H, m), 1.60-1.75 (4H, m), 1.80-1.89 (2H, m), 3.40 (2H, t, J=5.47 Hz), 3.48 (1H, br d, J=2.19 Hz), 3.51 (2 H, q, J=5.57 Hz), 3.65 (1 H, tt, J=8.25, 4.21 Hz), 3.97 (3 H, s), 4.52 (1H, t, J=5.61 Hz), 6.59 (1H, d, J=7.67 Hz), 6.86 (1H, d, J=2.46 Hz), 7.66 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{23}H_{26}N_6O_3$ m/z 435.2 (M+1).

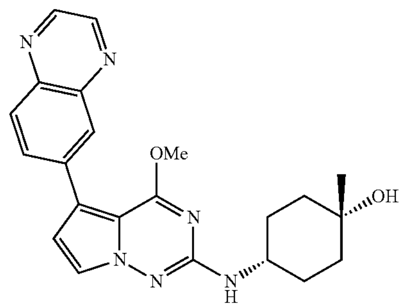
344



[1048] N-(trans-4-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide 344.

[1049] Yellow solid (5 mg, 0.012 mmol, 4.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.20-1.30 (2H, m), 1.31-1.41 (2H, m), 1.79 (3 H, s), 1.82 (2H, br d, J=10.40 Hz), 2.01 (2H, br d, J=10.13 Hz), 3.45-3.53 (1H, m), 3.53-3.61 (1H, m), 3.97 (3 H, s), 6.60 (1H, d, J=8.21 Hz), 6.86 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=2.46 Hz), 7.75 (1H, d, J=7.67 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{25}N_7O_2$ m/z 432.2 (M+1).

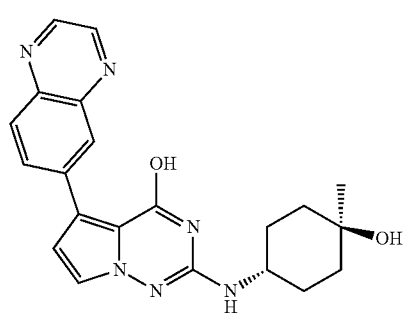
345



[1050] cis-4-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol345.

[1051] Yellow solid (16 mg, 0.040 mmol, 15.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.13 (3 H, s), 1.37 (2 H, td, J=13.07, 4.24 Hz), 1.58 (2H, br d, J=12.05 Hz), 1.61-1.69 (2H, m), 1.70-1.75 (2H, m), 3.47-3.60 (1H, m), 3.97 (3H, s), 4.01 (1H, s), 6.56 (1H, d, J=7.94 Hz), 6.85 (1H, d, J=2.46 Hz), 7.65 (1H, d, J=2.46 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{24}N_6O_2$ m/z 405.2 (M+1).

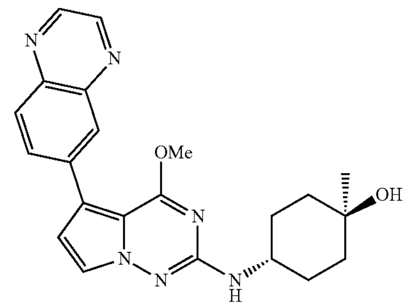
346



[1052] 2-((trans-4-Hydroxy-4-methylcyclohexyl)amino)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][11,2,4]triazin-4-ol 346.

[1053] Yellow solid (10 mg, 0.026 mmol, 10.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.40-1.48 (4H, m), 1.49-1.56 (2H, m), 1.85-1.96 (2H, m), 3.63-3.74 (1H, m), 4.23 (1 H, s), 5.92 (1 H, br s), 6.85 (1H, d, J=2.74 Hz), 7.47 (1H, d, J=2.74 Hz), 8.03 (1 H, d, J=9.31 Hz), 8.34 (1H, dd, J=9.03, 1.92 Hz), 8.59 (1H, d, J=1.64 Hz), 8.87 (1H, d, J=2.19 Hz), 8.91 (1H, d, J=2.19 Hz); ESIMS found for $C_{21}H_{22}N_6O_2$ m/z 391.2 (M+1).

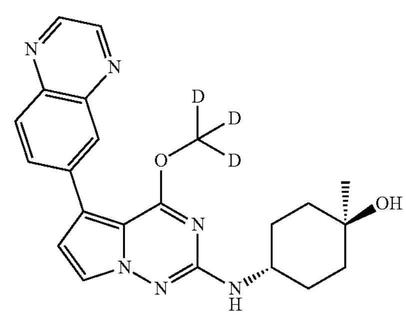
347



[1054] trans-4-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol347.

[1055] Yellow solid (26 mg, 0.064 mmol, 40.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.54 (4H, m), 1.56-1.65 (2H, m), 1.85-1.93 (2H, m), 3.65 (1 H, br dd, J=7.94, 3.56 Hz), 3.97 (3H, s), 4.24 (1H, s), 6.54 (1H, d, J=7.94 Hz), 6.86 (1H, d, J=2.46 Hz), 7.68 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{22}H_{24}N_6O_2$ m/z 405.2 (M+1).

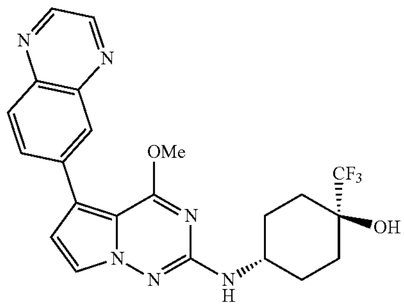
348



[1056] trans-4-((4-(Methoxy-d_3)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 348.

[1057] Yellow solid (38 mg, 0.093 mmol, 36.7% yield). ^{1}HNMR(499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.37-1.53 (4H, m), 1.55-1.65 (2H, m), 1.84-1.92 (2H, m), 3.66 (1 H, br dd, J=8.21, 3.83 Hz), 4.24 (1 H, s), 6.53 (1H, d, J=7.94 Hz), 6.86 (1H, d, J=2.74 Hz), 7.68 (1 H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{21}[^2H_3]N_6O_2$ m/z 408.2 (M+1).

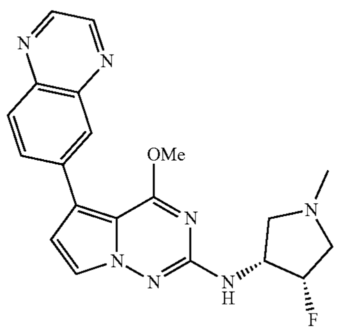
349



[1058] trans-4-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-(trifluoromethyl)cyclohexan-1-ol 349.

[1059] Off-white solid (18 mg, 0.039 mmol, 16.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.53 (2H, br d, J=12.59 Hz), 1.82-1.90 (4H, m), 1.90-1.99 (2H, m), 3.87-3.94 (1H, m), 4.00 (3H, s), 5.70 (1H, s), 6.83 (1H, d, J=5.75 Hz), 6.87 (1H, d, J=2.46 Hz), 7.68 (1H, d, J=2.46 Hz), 8.05-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{21}F_3N_6O_2$ m/z 459.2 (M+1).

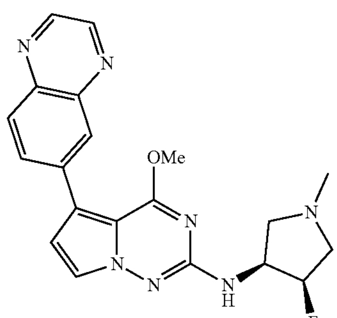
350



[1060] N-((3R,4S)-4-Fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 350.

[1061] Yellow solid (33 mg, 0.084 mmol, 86.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.31 (3 H, s), 2.55-2.66 (1H, m), 2.61-2.64 (1H, m), 2.92 (1H, t, J=8.08 Hz), 3.17(1 H, ddd, J=29.85, 11.50, 4.65 Hz), 3.99 (3 H, s), 4.21-4.36 (1H, m), 5.22 (1 H, dtd, J=55.95, 4.95, 4.95, 1.90 Hz), 6.82 (1H, d, J=7.67 Hz), 6.91 (1H, d, J=2.74 Hz), 7.70 (1H, d, J=2.74 Hz), 8.05-8.09 (1H, m), 8.10-8.14 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.64 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{20}H_{20}FN_7O$ m/z 394.2 (M+1).

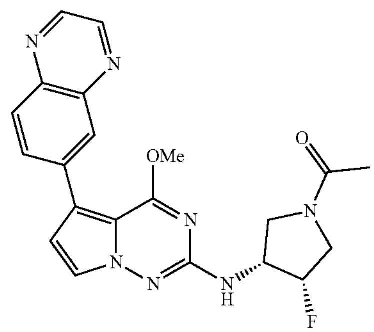
351



[1062] N-((3S,4R)-4-Fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 351.

[1063] Yellow solid (21 mg, 0.053 mmol, 29.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.31 (3 H, s), 2.56-2.68 (2H, m), 2.93 (1H, t, J=8.08 Hz), 3.17 (1H, ddd, J=29.65, 11.80, 4.65 Hz), 3.99 (3 H, s), 4.20-4.37 (1H, m), 5.22 (1 H, dtd, J=55.95, 4.95, 4.95, 1.90 Hz), 6.83 (1H, d, J=7.67 Hz), 6.91 (1H, d, J=2.74 Hz), 7.70 (1H, d, J=2.74 Hz), 8.05-8.09 (1H, m), 8.10-8.14 (1H, m), 8.24 (1H, d, J=1.64 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{20}H_{20}FN_7O$ m/z 394.2 (M+1).

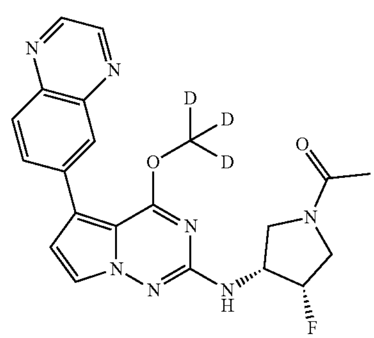
352



[1064] 1-((3S,4R)-3-Fluoro-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one 352.

[1065] Yellow solid (43 mg, 0.102 mmol, 70.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.92-2.02(3 H,m), 3.48-3.57 (1H, m), 3.58-3.76 (1H, m), 3.79-3.98 (2H, m), 4.01 (3H, d, J=1.64 Hz), 4.30-4.61 (1H, m), 5.26-5.51 (1H, m), 6.93 (1H, t, J=2.46 Hz), 7.14 (1H, t, J=6.71 Hz), 7.71 (1H, dd, J=4.11, 2.74 Hz), 8.06-8.10 (1H, m), 8.10-8.14 (1H, m), 8.25 (1 H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{21}H_2O$ FN_702 m/z 422.2 (M+1).

353

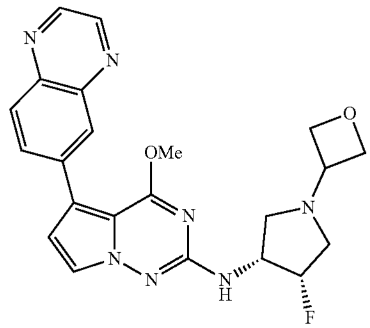


[1066] 1-((3S,4R)-3-Fluoro-4-((4-(methoxy-d_3)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one 353.

[1067] Yellow solid (66 mg, 0.156 mmol, 71.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.90-2.03(3 H,m), 3.47-3.57 (1H, m), 3.59-3.77 (1H, m), 3.79-3.99 (2H, m), 4.28-4.62 (1H, m), 5.38 (1 H, ddt, J=54.30, 37.55, 3.05, 3.05

Hz), 6.93 (1H, t, J=2.46 Hz), 7.14 (1H, t, J=6.71 Hz), 7.71 (1H, dd, J=3.97, 2.60 Hz), 8.06-8.10 (1H, m), 8.10-8.15 (1H, m), 8.25 (1 H, d, J=1.64 Hz), 8.90 (1H, d, J=1.64 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{21}H_{17}[^2H_3]FN_7O_2$ m/z 425.2 (M+1).

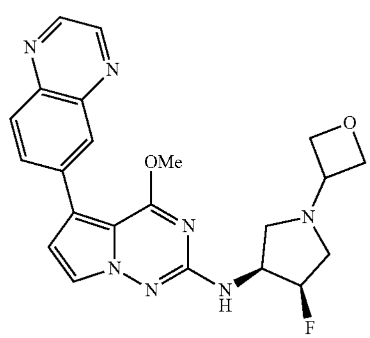
355



[1068] N-((3R,4S)-4-Fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 355.

[1069] Yellow solid (7 mg, 0.016 mmol, 11.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.70 (1H, t, J=9.03 Hz), 2.78 (1H, ddd, J=29.90, 12.10, 1.40 Hz), 3.02 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=33.20, 12.05, 4.40 Hz), 3.75-3.85 (1H, m), 4.00 (3 H, s), 4.24-4.40 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 5.26 (1 H, dtd, J=55.65, 4.65, 4.65, 1.10 Hz), 6.89 (1H, d, J=7.67 Hz), 6.91 (1H, d, J=2.74 Hz), 7.70 (1H, d, J=2.74 Hz), 8.05-8.09 (1H, m), 8.10-8.14 (1H, m), 8.25 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{22}FN_7O_2$ m/z 436.2 (M+1).

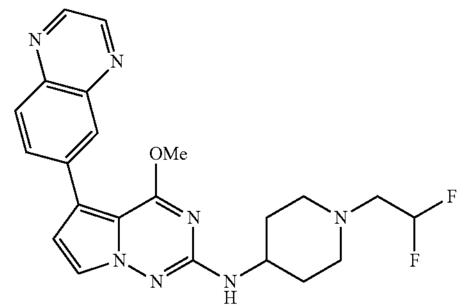
356



[1070] N-((3S,4R)-4-Fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 356.

[1071] Yellow solid (25 mg, 0.057 mmol, 49.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.70 (1H, t, J=9.03 Hz), 2.78 (1H, ddd, J=30.15, 12.35, 1.40 Hz), 3.02 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=32.90, 12.10, 4.40 Hz), 3.74-3.84 (1H, m), 4.00 (3 H, s), 4.26-4.38 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 5.26 (1 H, dtd, J=55.65, 4.40, 4.40, 1.10 Hz), 6.89 (1H, d, J=7.67 Hz), 6.91 (1H, d, J=2.46 Hz), 7.70 (1H, d, J=2.46 Hz), 8.06-8.09 (1H, m), 8.10-8.14 (1H, m), 8.25 (1H, d, J=1.64 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{22}H_{22}FN_7O_2$ m/z 436.2 (M+1).

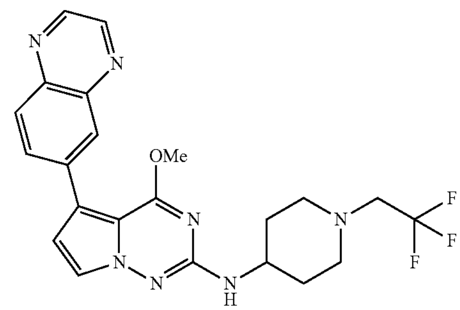
362



[1072] N-(1-(2,2-Difluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 362.

[1073] Yellow solid (27 mg, 0.061 mmol, 25.5% yield). H NMR (499 MHz, DMSO-d_6) δ ppm 1.48-1.62 (2H, m), 1.85-1.96 (2H, m), 2.20-2.33 (2H, m), 2.72 (2 H, td, J=15.74, 4.38 Hz), 2.91 (2H, br d, J=11.77 Hz), 3.55-3.67 (1H, m), 3.97 (3 H, s), 6.14 (1 H, tt, J=55.95, 4.24 Hz), 6.67 (1H, d, J=7.94 Hz), 6.87 (1H, d, J=2.46 Hz), 7.68 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.08-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{22}H_{23}F_2N_7O$ m/z 440.2 (M+1).

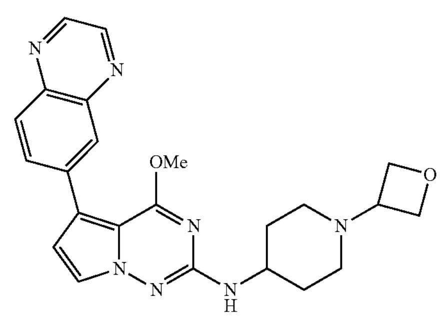
363



[1074] 4-Methoxy-5-(quinoxalin-6-yl)-N-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 363.

[1075] Yellow solid (13 mg, 0.028 mmol, 12.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.47-1.63 (2H, m), 1.91 (2H, br d, J=10.13 Hz), 2.39-2.49 (2H, m), 2.93 (2H, br d, J=11.77 Hz), 3.16 (2 H, q, J=10.31 Hz), 3.55-3.68 (1H, m), 3.97 (3 H, s), 6.67 (1H, d, J=7.94 Hz), 6.87 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=2.46 Hz), 8.05-8.08 (1H, m), 8.09-8.12 (1H, m), 8.23 (1H, d, J=1.64 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{22}F_3N_7O$ m/z 458.2 (M+1).

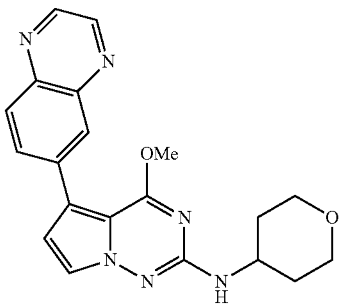
365



[1076] 4-Methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 365.

[1077] Yellow solid (6 mg, 0.0140 mmol, 4.3% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.55 (2 H, qd, J=11.64, 3.15 Hz), 1.87 (2 H, br t, J=11.36 Hz), 1.93 (2H, br d, J=11.50 Hz), 2.70(2 H, brd, J=11.23 Hz), 3.36-3.42 (1H, m), 3.56-3.68 (1H, m), 3.97(3 H, s), 4.42(2 H, t, J=6.16 Hz), 4.53 (2H, t, J=6.57 Hz), 6.69 (1H, d, J=7.94 Hz), 6.86 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.46 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{23}H_{25}N_7O_2$ m/z 432.2 (M+1).

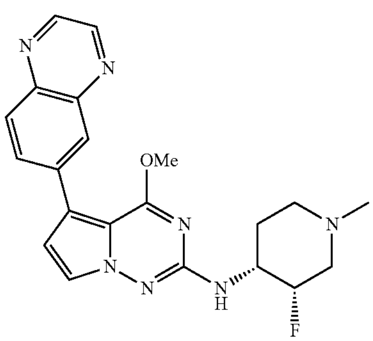
366



[1078] 4-Methoxy-5-(quinoxalin-6-yl)-N-(tetrahydro-2H-pyran-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 366.

[1079] Yellow solid (34 mg, 0.090 mmol, 46.9% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.48-1.61 (2H, m), 1.91 (2 H, br dd, J=12.59, 2.46 Hz), 3.40 (2 H, td, J=11.57, 1.78 Hz), 3.76-3.86 (1H, m), 3.86-3.92 (2H, m), 3.98 (3 H, s), 6.74 (1H, d, J=7.94 Hz), 6.87 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=2.46 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{20}H_{20}N_6O_2$ m/z 377.2 (M+1).

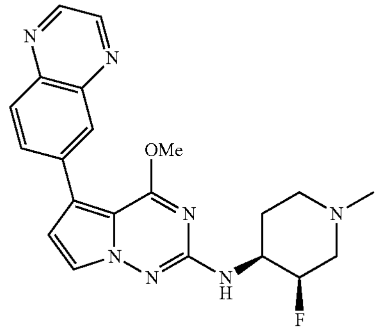
367



[1080] N-((3S,4R)-3-Fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 367.

[1081] Pale yellow solid (34 mg, 0.083 mmol, 65.7% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.66-1.74(1 H,m), 1.89-1.99(1 H,m),2.02-2.11 (1 H,m), 2.12-2.25 (1H, m), 2.19 (3 H, s), 2.80 (1H, br d, J=11.22 Hz), 3.05 (1 H, brt, J=10.95 Hz), 3.69-3.84 (1H, m), 3.99 (3 H, s), 4.92 (1H, d, J=49.65 Hz), 6.68 (1H, d, J=7.94 Hz), 6.89 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=2.46 Hz), 8.05-8.09 (1H, m), 8.09-8.14 (1H, m), 8.24 (1H, d, J=1.64 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{21}H_{22}FN_7O$ m/z 408.2 (M+1).

368



[1082] N-((3R,4S)-3-Fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 368.

[1083] Yellow solid (45 mg, 0.110 mmol, 43.0% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.76 (1H, br d, J=9.86 Hz), 1.98 (1 H, qd, J=12.41, 3.56 Hz), 2.33 (3 H, br s), 2.34-2.38 (1H, m), 2.88-3.03 (1H, m), 3.14-3.27 (1H, m), 3.27-3.30 (1H, m), 3.75-3.93 (1H, m), 3.99 (3 H, s), 5.00 (1H, d, J=49.65 Hz), 6.78 (1H, br d, J=6.30 Hz), 6.90 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.46 Hz), 8.05-8.09 (1H, m), 8.09-8.14 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{21}H_{22}FN_7O$ m/z 408.2 (M+1).

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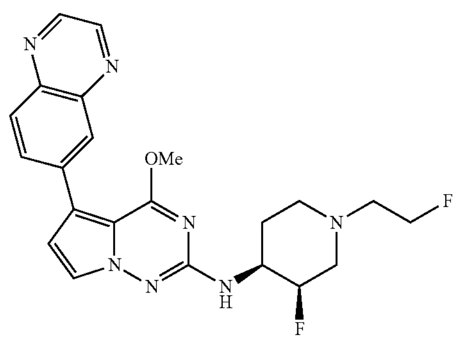
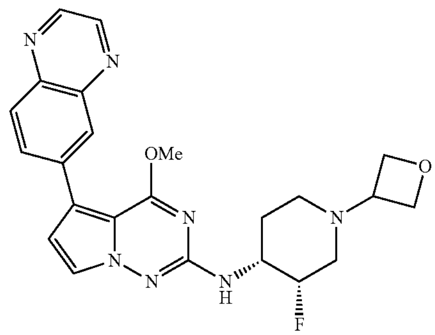


[1084] N-((3R,4S)-3-Fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 372.

[1085] Pale-yellow solid (20 mg, 0.046 mmol, 59.7% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.66-1.76 (1H, m), 1.93 (1 H, qd, J=12.23, 3.83 Hz), 2.26 (1 H, br t, J=10.95 Hz), 2.39 (1H, dd, J=37.85, 12.38 Hz), 2.64-2.73 (2H, m), 2.94 (1H, br d, J=11.23 Hz), 3.13-3.23 (1H, m), 3.74-3.90 (1H, m), 3.99 (3 H, s), 4.55 (2 H, dt, J=48.00, 4.95 Hz), 4.93 (1H, d, J=49.95 Hz), 6.71 (1H, d, J=7.67 Hz), 6.89 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=2.74 Hz), 8.05-8.09 (1H, m), 8.09-8.14 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{23}F_2N_7O$ m/z 440.2 (M+1).



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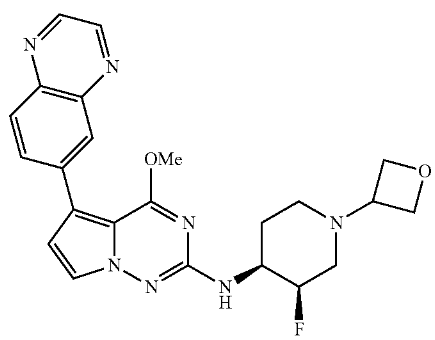
[1086] N-((3S,4R)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 373.

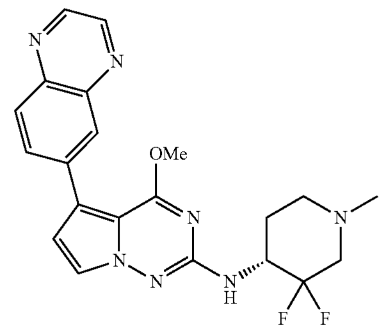
[1087] Yellow solid (39 mg, 0.087 mmol, 68.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68-1.79 (1H, m), 1.93 (1 H, qd, J=12.09, 3.15 Hz), 1.99-2.08 (1H, m), 2.10-2.25 (1H, m), 2.76 (1H, br d, J=10.40 Hz), 2.95-3.06 (1H, m), 3.50 (1 H, quin, J=6.37 Hz), 3.77-3.91 (1H, m), 3.99 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.44-4.49 (1H, m), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.95 (1H, d, J=49.65 Hz), 6.75 (1H, d, J=7.67 Hz), 6.89 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.46 Hz), 8.05-8.09 (1H, m), 8.10-8.13 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{23}H_{24}FN_7O_2$ m/z 450.2 (M+1).



374

[1088] N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 374.

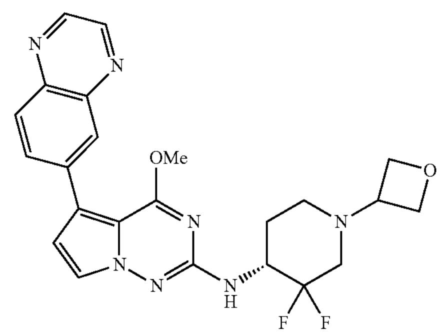
[1089] Yellow solid (51 mg, 0.114 mmol, 74.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.69-1.79 (1H, m), 1.93 (1 H, qd, J=12.14, 3.56 Hz), 2.00-2.07 (1H, m), 2.09-2.25 (1H, m), 2.76 (1H, br d, J=9.86 Hz), 2.95-3.06 (1H, m), 3.50 (1 H, quin, J=6.30 Hz), 3.75-3.94 (1H, m), 3.99 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.95 (1H, d, J=49.65 Hz), 6.76 (1H, d, J=7.67 Hz), 6.89 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.46 Hz), 8.06-8.09 (1H, m), 8.09-8.13 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{24}FN_7O_2$ m/z 450.25 (M+1).



375

[1090] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 375.

[1091] Yellow solid (14 mg, 0.033 mmol, 67.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.78-1.92 (2H, m), 2.18 (1 H, td, J=11.02, 2.60 Hz), 2.26 (3 H, s), 2.34-2.44 (1H, m), 2.79 (1H, br d, J=12.05 Hz), 3.06 (1 H, td, J=9.86, 7.94 Hz), 4.00 (3 H, s), 4.18-4.33 (1H, m), 6.89 (1H, d, J=9.31 Hz), 6.91 (1H, d, J=2.74 Hz), 7.69 (1H, d, J=2.74 Hz), 8.06-8.09 (1H, m), 8.10-8.13 (1H, m), 8.24 (1H, d, J=1.64 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{21}H_{21}F_2N_7O$ m/z 426.2 (M+1).

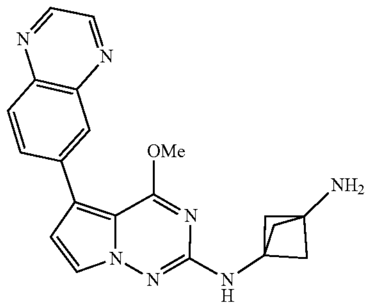


379

[1092] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 379.

[1093] Red brown fluffy solid (14 mg, 0.028 mmol, 67.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.81-1.93 (1H, m), 1.94-2.03 (1H, m), 2.18-2.44 (1H, m), 2.78-2.98 (1H, m), 3.07-3.28 (1H, m), 3.60-3.68 (1H, m), 3.68-3.84 (1H, m), 4.01 (3 H, s), 4.29-4.44 (1H, m), 4.45-4.56 (2H, m), 4.59 (2 H, br s), 6.92 (1H, d, J=2.74 Hz), 6.98-7.08 (1H, m), 7.68 (1H, d, J=2.46 Hz), 8.06-8.09 (1H, m), 8.10-8.14 (1H, m), 8.25 (1H, d, J=1.64 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{23}H_{23}F_2N_7O_2$ m/z 469.2 (M+1).

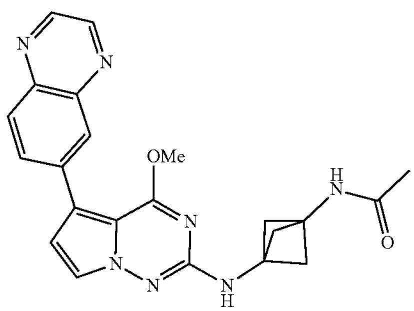
381



[1094] N_1-(4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)bicyclo[1.1.1]pentane-1,3-diamine 381.

[1095] Yellow foam (14 mg, 0.038 mmol, 42.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.02 (6 H, s), 2.24 (2 H, br s), 3.97 (3 H, s), 6.90 (1H, d, J=2.74 Hz), 7.34 (1 H, s), 7.66 (1H, d, J=2.74 Hz), 8.04-8.09 (1H, m), 8.09-8.13 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{20}H_{19}N_7O$ m/z 374.2 (M+1).

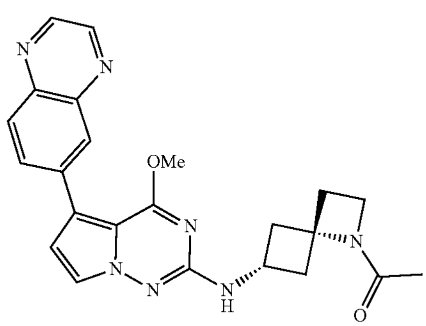
382



[1096] N-(3-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[1.1.1]pentan-1-yl)acetamide 382.

[1097] Yellow solid (10 mg, 0.024 mmol, 89.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.78 (3H, s), 2.28 (6H, s), 3.97 (3 H, s), 6.91 (1H, d, J=2.74 Hz), 7.48 (1 H, s), 7.69 (1 H, d, J=2.46 Hz), 8.05-8.09 (1H, m), 8.09-8.14 (1H, m), 8.24 (1H, d, J=1.64 Hz), 8.43 (1 H, s), 8.90 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{22}H_{21}N_7O_2$ m/z 416.2 (M+1).

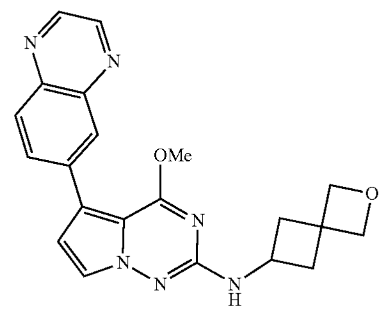
383



[1098] 1-((4s,6r)-6-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one 383.

[1099] Yellow solid (20 mg, 0.047 mmol, 60.1% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.74 (3 H, s), 2.27-2.44 (2H, m), 2.52-2.60 (2H, m), 2.62-2.70 (2H, m), 2.84-2.97 (2H, m), 3.70 (1 H, br s), 4.00 (3 H, s), 6.85 (2H, br d, J=2.20 Hz), 7.63 (1H, d, J=2.20 Hz), 8.04-8.08 (1H, m), 8.08-8.12 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.87 (1H, d, J=1.65 Hz), 8.91 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{23}N_7O_2$ m/z 430.2 (M+1).

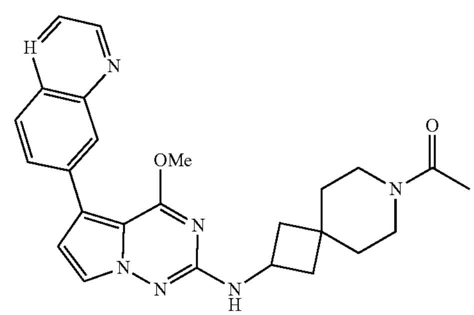
385



[1100] 4-Methoxy-5-(quinoxalin-6-yl)-N-(2-oxaspiro[3.3]heptan-6-yl)pyrrolo[2,1-f][11,2,4]triazin-2-amine 385.

[1101] Pale yellow solid (22 mg, 0.057 mmol, 26.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.14-2.24 (2H, m), 2.62 (2H, ddd, J=9.99, 7.53, 2.74 Hz), 3.96 (3 H, s), 3.97-4.06 (1H, m), 4.51 (2H, s), 4.64 (2H, s), 6.87 (1H, d, J=2.74 Hz), 7.03 (1H, d, J=7.12 Hz), 7.67 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.08-8.13 (1H, m), 8.23 (1H, d, J=1.64 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{21}H_2O\ N_6O_2$ m/z 389.2 (M+1).

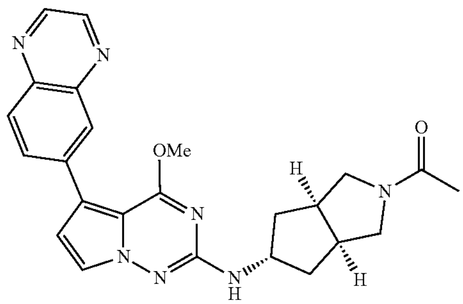
386



[1102] 1-(2-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-7-azaspiro[3.5]nonan-7-yl)ethan-1-one 386.

[1103] Off-white solid (32 mg, 0.070 mmol, 41.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.40-1.47 (1H, m), 1.52 (2 H, br t, J=10.13 Hz), 1.57-1.65 (1H, m), 1.76-1.86 (2H, m), 1.94-2.01 (3H, m), 2.23-2.33 (2H, m), 3.26-3.33 (2H, m), 3.36-3.39 (1H, m), 3.40-3.44 (1H, m), 3.97 (3 H, s), 4.15-4.27 (1H, m), 6.87 (1H, d, J=2.74 Hz), 7.05 (1H, t, J=7.12 Hz), 7.65-7.71 (1H, m), 8.05-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{25}H_{27}N_7O_2$ m/z 458.2 (M+1).

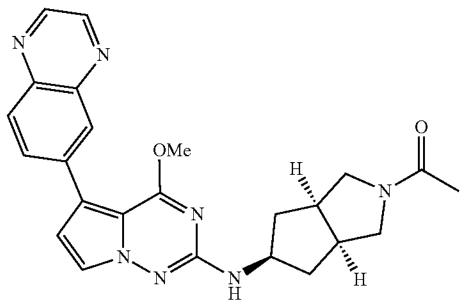
387



[1104] 1-((3aR,5s,6aS)-5-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)hexahydrocyclopenta[c]pyrrol-2(1H)-yl)ethan-1-one 387.

[1105] White solid (53 mg, 0.120 mmol, 99.95% yield). ^{1}HNMR(499 MHz, DMSO-d_6) δ ppm 1.82-1.91 (4H, m), 1.95 (3 H, s), 2.73-2.81 (1H, m), 2.82-2.91 (1H, m), 3.15 (1H, dd, J=12.32, 4.93 Hz), 3.26 (1 H, br dd, J=10.81, 4.79 Hz), 3.52 (1H, dd, J=12.18, 8.62 Hz), 3.65 (1H, dd, J=10.95, 8.21 Hz), 3.94-3.99 (3H, m), 4.25 (1 H, sxt, J=6.63 Hz), 6.83 (1H, d, J=6.84 Hz), 6.87 (1H, d, J=2.46 Hz), 7.68 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{24}H_{25}N_7O_2$ m/z 444.2 (M+1).

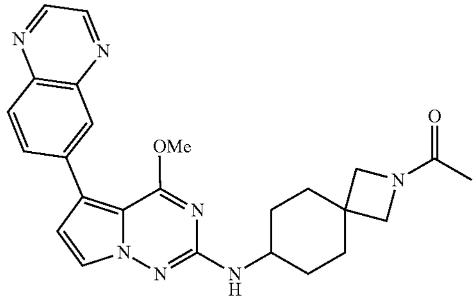
388



[1106] 1-((3aR,5r,6aS)-5-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)hexahydrocyclopenta[c]pyrrol-2(1H)-yl)ethan-1-one 388.

[1107] Off-white solid (55 mg, 0.124 mmol, 90.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.34-1.48 (2H, m), 1.95 (3 H, s), 2.24-2.38 (2H, m), 2.54-2.62 (1H, m), 2.62-2.72 (1H, m), 3.35-3.45 (3H, m), 3.59 (1H, dd, J=10.68, 7.94 Hz), 3.97 (3 H, s), 4.08-4.21 (1H, m), 6.85-6.90 (2H, m), 7.66 (1H, d, J=2.74 Hz), 8.05-8.08 (1H, m), 8.09-8.13 (1 H, m), 8.23 (1H, d, J=1.64 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{24}H_{25}N_7O_2$ m/z 444.2 (M+1).

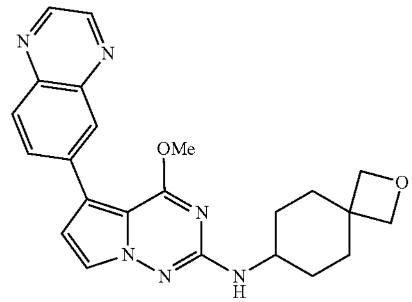
389



[1108] 1-(7-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one 389.

[1109] Off-white solid (60 mg, 0.131 mmol, 82.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.29-1.41 (2H, m), 1.49-1.62 (2H, m), 1.73-1.78 (3H, m), 1.88 (4 H, br dd, J=9.58, 4.11 Hz), 3.47(1 H, s), 3.52(1 H, s), 3.56-3.67 (1H, m), 3.75 (1H, s), 3.81 (1H, s), 3.97 (3H, d, J=1.10 Hz), 6.58 (1H, dd, J=16.15, 7.94 Hz), 6.87 (1H, d, J=2.74 Hz), 7.67 (1H, t, J=2.87 Hz), 8.04-8.08 (1H, m), 8.09-8.13 (1H, m), 8.23 (1H, d, J=1.64 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{25}H_{27}N_7O_2$ m/z 458.2 (M+1).

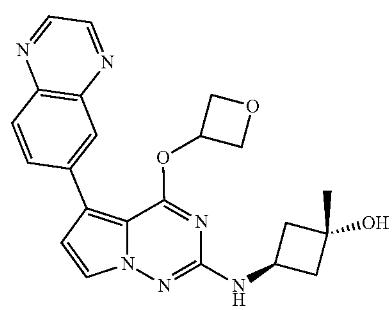
390



[1110] 4-Methoxy-5-(quinoxalin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 390.

[1111] Yellow solid (39 mg, 0.094 mmol, 48.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.20-1.36 (2H, m), 1.53 (2 H, td, J=12.87, 3.29 Hz), 1.88 (2 H, br dd, J=13.14, 3.29 Hz), 2.07 (2H, br d, J=12.87 Hz), 3.48-3.63 (1H, m), 3.96 (3H, s), 4.24 (2H, s), 4.32 (2 H, s), 6.56 (1H, d, J=8.21 Hz), 6.86 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.74 Hz), 8.04-8.08 (1H, m), 8.08-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.64 Hz); ESIMS found for $C_{23}H_{24}N_6O_2$ m/z 417.2 (M+1).

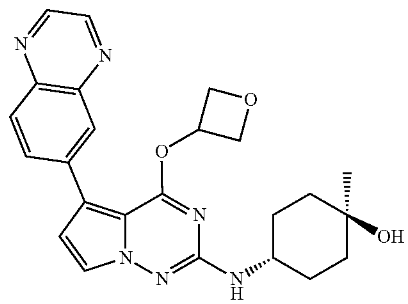
391



[1112] cis-1-Methyl-3-((4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutan-1-ol 391.

[1113] Yellow solid (10 mg, 0.024 mmol, 11.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 1.96-2.04 (2H, m), 2.28-2.40 (2H, m), 3.64-3.76 (1H, m), 4.61 (2H, dd, J=7.94, 5.20 Hz), 4.86 (2H, t, J=7.26 Hz), 4.93 (1 H, s), 5.65-5.73 (1H, m), 6.92-6.95 (2H, m), 7.71 (1H, d, J=2.74 Hz), 8.10 (1H, d, J=8.76 Hz), 8.19 (1H, dd, J=8.76, 1.92 Hz), 8.38 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.95 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{22}N_6O_3$ m/z 419.2 (M+1).

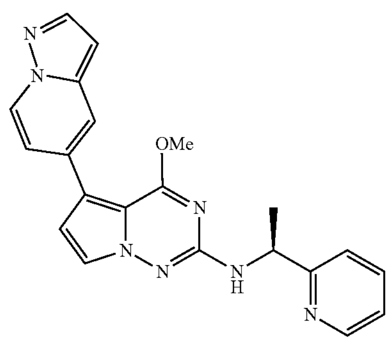
392



[1114] trans-1-Methyl-4-((4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol 392.

[1115] Yellow solid (17 mg, 0.038 mmol, 14.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.36-1.50 (4H, m), 1.54-1.64 (2H, m), 1.80-1.93 (2H, m), 3.61 (1H, br d, J=3.56 Hz), 4.25 (1 H, s), 4.62 (2H, dd, J=7.53, 5.34 Hz), 4.86 (2H, t, J=6.98 Hz), 5.72 (1 H, quin, J=5.75 Hz), 6.50 (1H, d, J=7.94 Hz), 6.93 (1H, d, J=2.46 Hz), 7.71 (1H, d, J=2.46 Hz), 8.10 (1H, d, J=8.76 Hz), 8.20 (1H, dd, J=8.76, 1.92 Hz), 8.39 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.64 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{24}H_{26}N_6O_3$ m/z 447.2 (M+1).

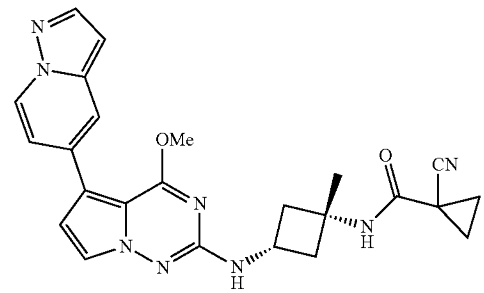
393



[1116] (S)-4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(1-(pyridin-2-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 393.

[1117] Off-white solid (14 mg, 0.036 mmol, 18.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.49 (3H, d, J=7.12 Hz), 3.98 (3 H, s), 5.00 (1 H, quin, J=7.19 Hz), 6.58 (1H, d, J=1.64 Hz), 6.74 (1H, d, J=2.46 Hz), 7.09 (1H, dd, J=7.39, 1.92 Hz), 7.19 (1H, d, J=7.94 Hz), 7.23 (1H, ddd, J=7.46, 4.86, 0.82 Hz), 7.46 (1H, d, J=7.94 Hz), 7.55 (1H, d, J=2.74 Hz), 7.74 (1 H, td, J=7.73, 1.78 Hz), 7.79 (1H, d, J=1.10 Hz), 7.96 (1H, d, J=2.19 Hz), 8.50-8.54 (1H, m), 8.61 (1H, d, J=7.12 Hz); ESIMS found for $C_{21}H_{19}N_7O$ m/z 386.2 (M+1).

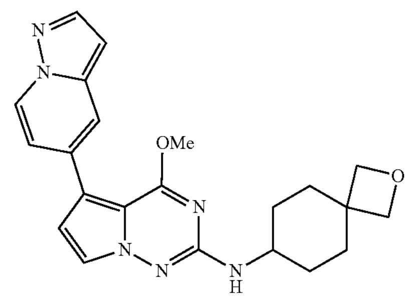
394



[1118] 1-Cyano-N-((1s,3s)-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide 394.

[1119] Beige solid (8 mg, 0.018 mmol, 25.5% yield). ^{1}HNMR (499 MHz, DMSO-d_6) δ ppm 1.37 (3 H, s), 1.44-1.49 (2H, m), 1.49-1.54 (2H, m), 2.13-2.22 (2H, m), 2.45 (2H, ddd, J=9.72, 7.39, 2.60 Hz), 3.98 (3 H, s), 4.03 (1 H, sxt, J=7.78 Hz), 6.58 (1H, dd, J=2.19, 0.82 Hz), 6.77 (1H, d, J=2.46 Hz), 7.01 (1H, d, J=6.84 Hz), 7.10 (1H, dd, J=7.26, 2.05 Hz), 7.64 (1H, d, J=2.46 Hz), 7.78-7.85 (1H, m), 7.97 (1H, d, J=2.19 Hz), 8.29 (1 H, s), 8.62 (1H, d, J=7.39 Hz); ESIMS found for $C_{24}H_{24}N_8O_2$ m/z 457.2 (M+1).

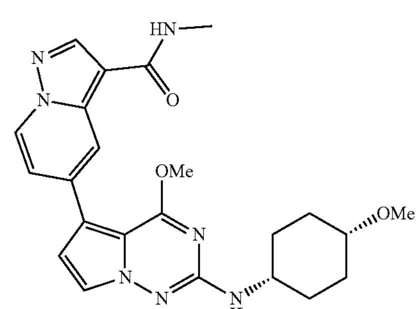
395



[1120] 4-Methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 395.

[1121] Beige solid (74 mg, 0.18 mmol, 54.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.24-1.31 (2H, m), 1.52 (2 H, td, J=12.94, 3.42 Hz), 1.80-1.92 (2H, m), 2.02-2.11 (2 H, m), 3.48-3.61 (1H, m), 3.97 (3H, s), 4.23 (2H, s), 4.32 (2 H, s), 6.51 (1H, d, J=7.94 Hz), 6.56-6.61 (1H, m), 6.75 (1H, d, J=2.74 Hz), 7.10 (1H, dd, J=7.26, 2.05 Hz), 7.62 (1H, d, J=2.74 Hz), 7.80 (1H, dd, J=1.92, 0.82 Hz), 7.96 (1H, d, J=2.19 Hz), 8.62 (1H, d, J=7.12 Hz); ESIMS found for $C_{22}H_{24}N_6O_2$ m/z 405.2 (M+1).

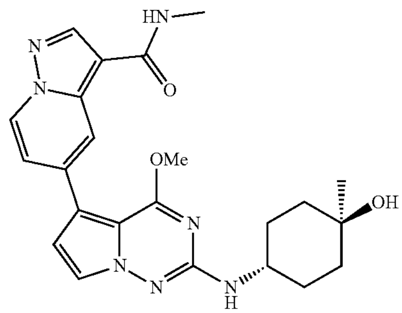
399



[1122] 5-(4-Methoxy-2-((cis-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide 399.

[1123] Beige solid (40 mg, 0.089 mmol, 55.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.54 (2H, m), 1.54-1.65 (2H, m), 1.66-1.74 (2H, m), 1.80-1.90 (2H, m), 2.79 (3H, d, J=4.38 Hz), 3.22 (3 H, s), 3.33-3.38 (1H, m), 3.58-3.71 (1H, m), 4.02 (3 H, s), 6.63 (1 H, d, J=7.67 Hz), 6.83 (1H, d, J=2.74 Hz), 7.29 (1H, dd, J=7.26, 2.05 Hz), 7.64 (1H, d, J=2.46 Hz), 8.10 (1 H, q, J=4.20 Hz), 8.45 (1 H, s), 8.49-8.55 (1H, m), 8.68 (1H, d, J=7.39 Hz); ESIMS found for $C_{23}H_{27}N_7O_3$ m/z 450.2 (M+1).

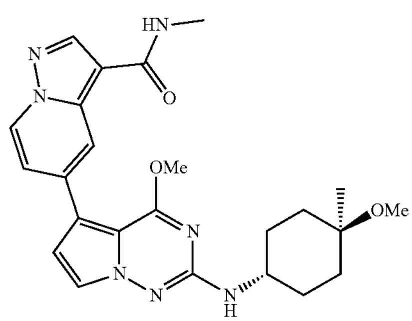
401



[1124] 5-(2-(((1r,4r)-4-Hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide 401.

[1125] Beige solid (58 mg, 0.129 mmol, 80.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.37-1.54 (4H, m), 1.57-1.66 (2H, m), 1.83-1.93 (2H, m), 2.79 (3H, d, J=4.65 Hz), 3.65 (1 H, dt, J=7.87, 3.87 Hz), 4.02 (3H, s), 4.23 (1H, s), 6.56 (1H, d, J=7.94 Hz), 6.83 (1H, d, J=2.74 Hz), 7.29 (1H, dd, J=7.26, 2.05 Hz), 7.65 (1H, d, J=2.74 Hz), 8.10 (1 H, q, J=4.56 Hz), 8.45 (1 H, s), 8.52 (1H, d, J=1.37 Hz), 8.68 (1H, d, J=7.67 Hz); ESIMS found for $C_{23}H_{27}N_7O_3$ m/z 450.25 (M+1).

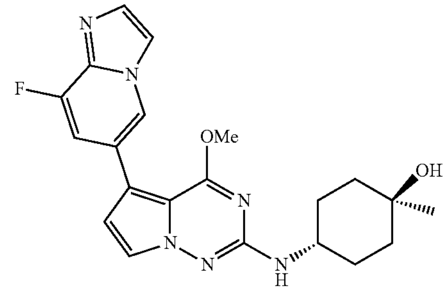
405



[1126] 5-(4-Methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide 405.

[1127] Off-white solid (47 mg, 0.101 mmol, 63.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.43-1.58 (4H, m), 1.63-1.73 (2H, m), 1.79-1.90 (2H, m), 2.79 (3H, d, J=4.65 Hz), 3.11 (3 H, s), 3.66-3.77 (1H, m), 4.03 (3 H, s), 6.61 (1H, d, J=7.94 Hz), 6.83 (1H, d, J=2.74 Hz), 7.29 (1H, dd, J=7.26, 2.05 Hz), 7.65 (1H, d, J=2.74 Hz), 8.10 (1 H, q, J=4.56 Hz), 8.45 (1 H, s), 8.52 (1H, dd, J=2.19, 0.82 Hz), 8.65-8.72 (1H, m); ESIMS found for $C_{24}H_{29}N_7O_3$ m/z 464.2 (M+1).

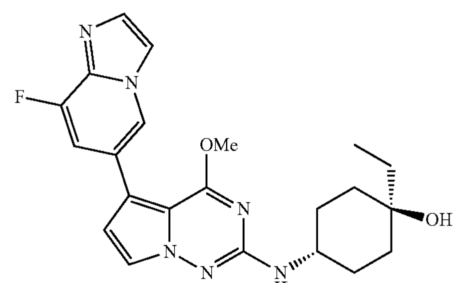
431



[1128] (1r,4r)-4-((5-(8-Fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 431.

[1129] Off-white solid (42 mg, 0.102 mmol, 32.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.37-1.52 (4H, m), 1.57-1.65 (2H, m), 1.82-1.93 (2H, m), 3.58-3.72 (1H, m), 3.98 (3H, s), 4.23 (1H, s), 6.50 (1H, d, J=7.94 Hz), 6.71 (1H, d, J=2.46 Hz), 7.38 (1H, d, J=12.59 Hz), 7.62 (1 H, s), 7.63 (1H, d, J=2.74 Hz), 8.09 (1H, d, J=2.74 Hz), 8.59 (1 H, s); ESIMS found for $C_{2}1H_{23}FN_6O_2$ m/z 411.2 (M+1).

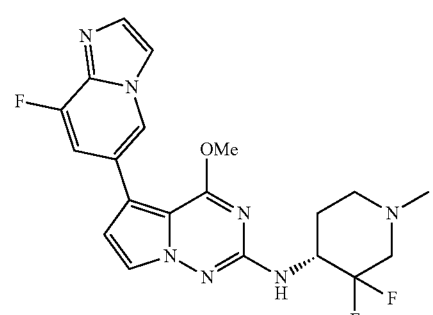
433



[1130] (1r,4r)-1-Ethyl-4-((5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol 433.

[1131] White solid (10.1 mg, 0.024 mmol, 11.6% yield). ^{1}HNMR(499 MHz, DMSO-d_6) δ ppm 0.83 (3H, t, J=7.53 Hz), 1.31-1.39 (2H, m), 1.39-1.50 (4H, m), 1.60-1.70 (2H, m), 1.80-1.89 (2H, m), 3.68 (1 H, tt, J=8.18, 4.14 Hz), 3.98 (3 H, s), 6.50 (1H, d, J=7.94 Hz), 6.71 (1H, d, J=2.74 Hz), 7.38 (1H, dd, J=12.59, 1.37 Hz), 7.62 (1H, d, J=1.37 Hz), 7.63 (1H, d, J=2.46 Hz), 8.09 (1H, dd, J=3.01, 1.10 Hz), 8.59 (1H, d, J=1.37 Hz); ESIMS found for $C_{22}H_{25}FN_6O_2$ m/z 425.2 (M+1).

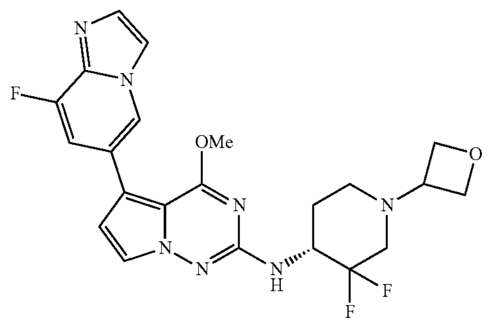
434



[1132] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 434.

[1133] Tan solid (33 mg, 0.077 mmol, 32.4% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.77-1.89 (2H, m), 2.14-2.25 (1H, m), 2.28 (3 H, br s), 2.35-2.47 (1H, m), 2.76-2.88 (1H, m), 3.01-3.15 (1H, m), 4.01 (3 H, s), 4.19-4.32 (1H, m), 6.76 (1H, d, J=2.74 Hz), 6.86 (1 H, br d, J=9.31 Hz), 7.40 (1H, dd, J=12.59, 1.37 Hz), 7.63 (1 H, s), 7.64 (1H, d, J=2.46 Hz), 8.10 (1H, d, J=2.46 Hz), 8.61 (1H, d, J=1.10 Hz); ESIMS found for $C_{20}H_{20}F_3N_7O$ m/z 432.2 (M+1).

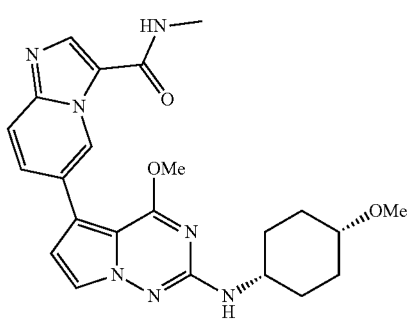
435



[1134] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 435.

[1135] Tan solid (10 mg, 0.021 mmol, 48.4% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.76-1.85 (1H, m), 1.86-1.92 (1H, m), 2.12-2.22 (1H, m), 2.35-2.45 (1H, m), 2.76(1 H, br d, J=11.50 Hz), 2.95-3.07 (1H, m), 3.60 (1 H, quin, J=6.30 Hz), 4.02 (3 H, s), 4.22-4.37 (1H, m), 4.44 (2 H, dt, J=15.26, 6.19 Hz), 4.55 (2 H, td, J=6.64, 3.70 Hz), 6.76 (1H, d, J=2.74 Hz), 6.92 (1H, d, J=9.31 Hz), 7.40 (1H, dd, J=12.59, 1.37 Hz), 7.62 (1H, d, J=1.09 Hz), 7.64 (1 H, d, J=2.46 Hz), 8.10 (1H, dd, J=3.01, 1.09 Hz), 8.61 (1H, d, J=1.37 Hz); ESIMS found for $C_{22}H_{22}F_3N_7O_2$ m/z 474.2 (M+1).

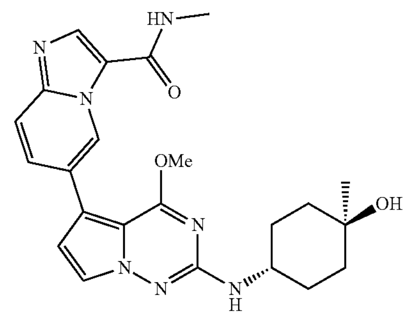
439



[1136] 6-(4-Methoxy-2-((cis-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide 439.

[1137] Beige solid (38 mg, 0.085 mmol, 52.5% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.45-1.54 (2H, m), 1.55-1.65 (2H, m), 1.66-1.74 (2H, m), 1.79-1.89 (2H, m), 2.82 (3H, d, J=4.65 Hz), 3.22 (3 H, s), 3.33-3.37 (1H, m), 3.57-3.72 (1H, m), 4.00 (3 H, s), 6.58 (1 H, d, J=7.67 Hz), 6.74 (1H, d, J=2.74 Hz), 7.63 (1H, d, J=2.46 Hz), 7.68 (2H, d, J=1.37 Hz), 8.27 (1 H, s), 8.43 (1 H, q, J=4.56 Hz), 9.80 (1H, t, J=1.37 Hz); ESIMS found for $C_{23}H_{27}N_7O_3$ m/z 450.2

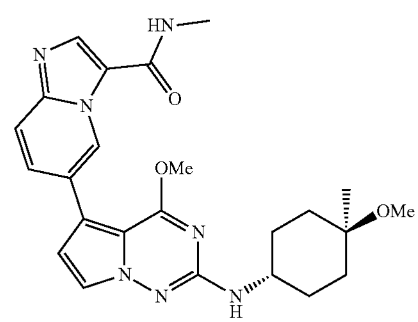
441



[1138] 6-(2-(((1r,4r)-4-Hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide 441.

[1139] Off-white solid (23 mg, 0.051 mmol, 31.8% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.14 (3 H, s), 1.34-1.52 (4H, m), 1.56-1.66 (2H, m), 1.82-1.94 (2H, m), 2.82 (3H, d, J=4.38 Hz), 3.59-3.71 (1H, m), 4.00 (3 H, s), 4.23 (1 H, br s), 6.51 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.46 Hz), 7.64 (1H, d, J=2.74 Hz), 7.68 (2H, d, J=1.10 Hz), 8.26 (1 H, s), 8.43 (1 H, q, J=4.20 Hz), 9.80 (1 H, s); ESIMS found for $C_{23}H_{27}N_7O_3$ m/z 450.2 (M+1).

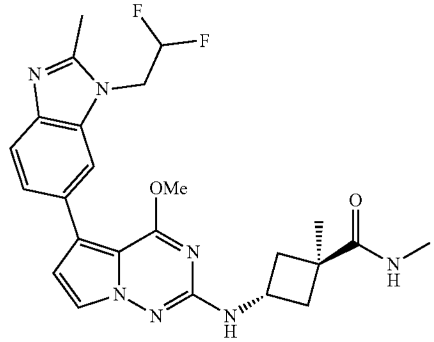
445



[1140] 6-(4-Methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide 445.

[1141] Brown solid (33 mg, 0.071 mmol, 44.5% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.14 (3 H, s), 1.41-1.58 (4H, m), 1.62-1.74 (2H, m), 1.78-1.91 (2H, m), 2.82 (3H, d, J=4.38 Hz), 3.11 (3 H, s), 3.71 (1H, br d, J=3.56 Hz), 4.01 (3 H, s), 6.56 (1H, d, J=7.67 Hz), 6.75 (1H, d, J=2.46 Hz), 7.64 (1H, d, J=2.46 Hz), 7.68 (2H, d, J=1.37 Hz), 8.27 (1 H, s), 8.43 (1 H, q, J=4.11 Hz), 9.81 (1H, t, J=1.37 Hz); ESIMS found for $C_{24}H_{29}N_7O_3$ m/z 464.25 (M+1).

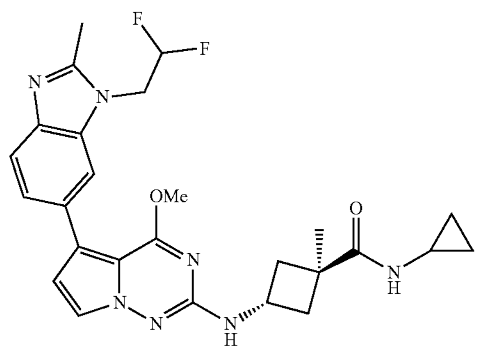
502



[1142] trans-3-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide 502.

[1143] White solid (18 mg, 0.037 mmol, 70.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.31 (3 H, s), 1.84-1.94 (2H, m), 2.57 (3 H, s), 2.62 (3H, d, J=4.38 Hz), 2.73 (2H, ddd, J=9.86, 7.80, 2.60 Hz), 3.91 (3 H, s), 3.99-4.08 (1H, m), 4.69-4.84 (2H, m), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.61 (1H, d, J=2.74 Hz), 6.90 (1H, d, J=7.39 Hz), 7.37 (1H, dd, J=8.21, 1.37 Hz), 7.51 (1H, d, J=8.21 Hz), 7.58-7.64 (2H, m), 7.71 (1 H, s); ESIMS found for $C_{24}H_{27}F_2N_7O_2$ m/z 484.2 (M+1).

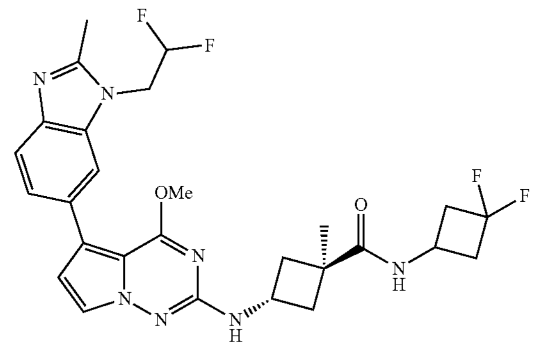
503



[1144] trans-N-Cyclopropyl-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide 503.

[1145] White solid (21 mg, 0.041 mmol, 77.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.42-0.49 (2H, m), 0.58-0.65 (2H, m), 1.29 (3 H, s), 1.82-1.91 (2H, m), 2.56 (3 H, s), 2.64-2.70 (1H, m), 2.71-2.77 (2H, m), 3.91 (3 H, s), 3.95-4.04 (1H, m), 4.74 (2 H, td, J=16.02, 2.19 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.60 (1H, d, J=2.46 Hz), 6.88 (1H, d, J=7.39 Hz), 7.35 (1H, dd, J=8.21, 1.64 Hz), 7.49 (1H, d, J=8.21 Hz), 7.61 (1H, d, J=2.46 Hz), 7.62 (1 H, d, J=4.38 Hz), 7.68 (1 H, s); ESIMS found for $C_{26}H_{29}F_2N_7O_2$ m/z 510.3 (M+1).

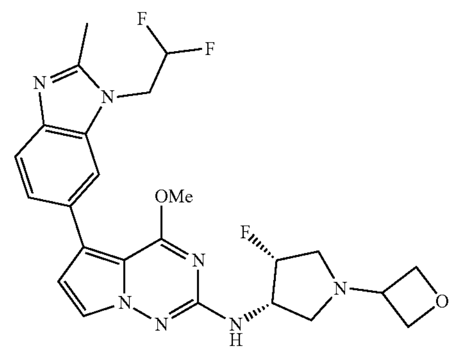
504



[1146] trans-N-(3,3-Difluorocyclobutyl)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide 504.

[1147] White solid (23 mg, 0.041 mmol, 77.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.34 (3 H, s), 1.86-1.95 (2H, m), 2.56 (3 H, s), 2.58-2.71 (2H, m), 2.76 (2H, ddd, J=10.06, 8.01, 2.46 Hz), 2.83-2.94 (2H, m), 3.91 (3 H, s), 4.01 (1 H, sxt, J=7.94 Hz), 4.10 (1 H, dt, J=14.85, 7.49 Hz), 4.68-4.80 (2H, m), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.60 (1H, d, J=2.46 Hz), 6.91 (1H, d, J=7.12 Hz), 7.35 (1H, dd, J=8.21, 1.64 Hz), 7.49 (1H, d, J=8.21 Hz), 7.60 (1 H, d, J=2.46 Hz), 7.68 (1 H, s), 8.03 (1H, d, J=6.84 Hz); ESIMS found for $C_{27}H_{29}F_4N_7O_2$ m/z 560.25 (M+1).

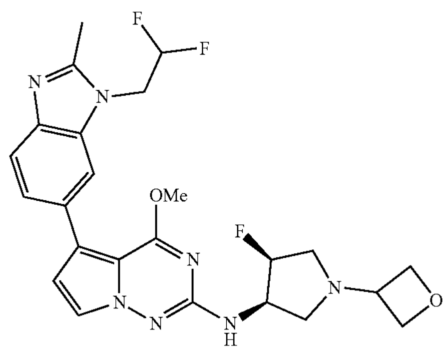
505



[1148] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 505.

[1149] White fluffy solid (14 mg, 0.028 mmol, 49.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.56 (3 H, s), 2.68 (1H, t, J=9.03 Hz), 2.77 (1H, ddd, J=30.20, 12.10, 1.40 Hz), 3.01 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=33.20, 11.91, 4.52 Hz), 3.79 (1 H, quin, J=6.23 Hz), 3.94 (3 H, s), 4.23-4.38 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 4.75 (2 H, td, J=16.02, 2.46 Hz), 5.25 (1 H, dtd, J=55.65, 4.70, 4.70, 1.35 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.65 (1H, d, J=2.74 Hz), 6.72 (1H, d, J=7.67 Hz), 7.36 (1H, dd, J=8.35, 1.51 Hz), 7.50 (1H, d, J=8.21 Hz), 7.61 (1H, d, J=2.46 Hz), 7.70 (1 H, s); ESIMS found for $C_{24}H_{26}F_3N_7O_2$ m/z 502.3 (M+1).

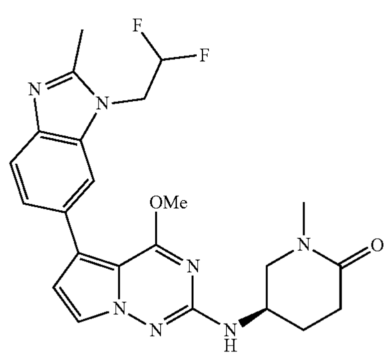
506



[1150] 5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 506.

[1151] White fluffy solid (17 mg, 0.034 mmol, 60.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.56 (3 H, s), 2.68 (1H, t, J=9.03 Hz), 2.77 (1H, ddd, J=29.90, 12.05, 1.37 Hz), 3.01 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=33.20, 11.91, 4.52 Hz), 3.73-3.84 (1H, m), 3.94 (3 H, s), 4.23-4.37 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 4.70-4.81 (2H, m), 5.25 (1 H, dtd, J=55.65, 4.45, 4.45, 1.23 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.65 (1H, d, J=2.74 Hz), 6.72 (1H, d, J=7.67 Hz), 7.36 (1H, dd, J=8.35, 1.51 Hz), 7.50 (1H, d, J=8.21 Hz), 7.61 (1 H, d, J=2.46 Hz), 7.70 (1 H, s); ESIMS found for $C_{24}H_{26}F_3N_7O_2$ m/z 502.3 (M+1).

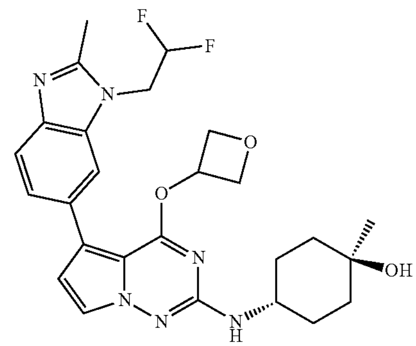
507



[1152] 5-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one 507.

[1153] White solid (25 mg, 0.053 mmol, 40.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.86-1.96 (1H, m), 1.96-2.04 (1H, m), 2.26-2.35 (1H, m), 2.35-2.43 (1H, m), 2.56 (3H, s), 2.81 (3H, s), 3.25 (1H, dd, J=11.77, 7.67 Hz), 3.57 (1H, dd, J=11.77, 4.93 Hz), 3.94 (3 H, s), 4.04-4.15 (1H, m), 4.75 (2 H, td, J=16.02, 2.46 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.63 (1H, d, J=2.74 Hz), 6.83 (1H, d, J=7.39 Hz), 7.36 (1H, dd, J=8.35, 1.51 Hz), 7.50 (1H, d, J=8.21 Hz), 7.62 (1H, d, J=2.46 Hz), 7.70 (1 H, s); ESIMS found for $C_{23}H_{25}F_2N_7O_2$ m/z 470.2 (M+1).

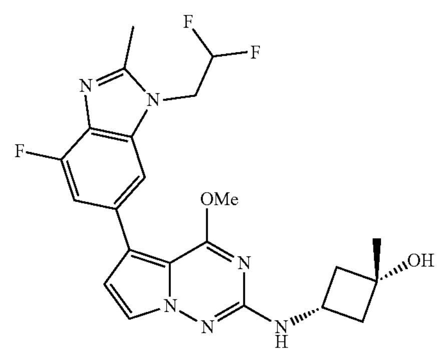
508



[1154] (1r,4r)-4-((5-(1-(2,2-Difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-(oxetan-3-yloxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 508.

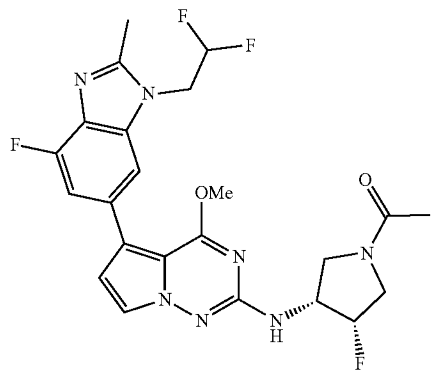
[1155] White solid (14 mg, 0.027 mmol, 38.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14(3 H, s), 1.36-1.50 (4H, m), 1.54-1.64 (2H, m), 1.80-1.90 (2H, m), 2.56(3 H, s), 3.59 (1 H, br s), 4.25 (1 H, s), 4.51 (2H, dd, J=7.67, 5.20 Hz), 4.74 (2 H, td, J=15.61, 2.19 Hz), 4.84 (2H, t, J=6.98 Hz), 5.67 (1 H, quin, J=5.68 Hz), 6.35 (1H, d, J=7.94 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.64 (1H, d, J=2.46 Hz), 7.45-7.50 (1H, m), 7.51-7.55 (1H, m), 7.62 (1H, d, J=2.46 Hz), 7.72 (1 H, s); ESIMS found for $C_{26}H_{30}F_2N_6O_3$ m/z 513.3 (M+1).

509



[1156] cis-3-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 509.

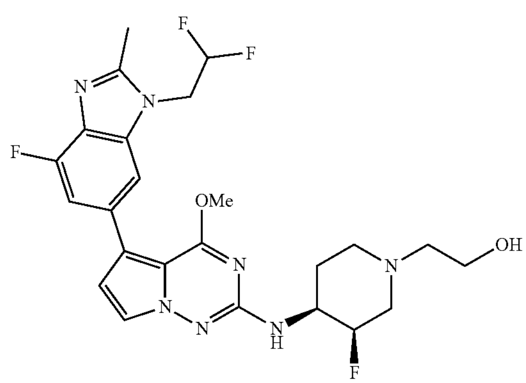
[1157] White solid (8 mg, 0.017 mmol, 11.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27 (3 H, s), 1.97-2.07 (2H, m), 2.31-2.40 (2H, m), 2.58 (3 H, s), 3.71 (1 H, sxt, J=7.67 Hz), 3.93 (3 H, s), 4.78 (2 H, td, J=16.02, 2.46 Hz), 4.91 (1 H, s), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.66 (1H, d, J=2.46 Hz), 6.88 (1H, d, J=6.57 Hz), 7.19 (1H, dd, J=12.32, 1.10 Hz), 7.57 (1 H, s), 7.60 (1H, d, J=2.74 Hz); ESIMS found for $C_{22}H_{23}F_3N_6O_2$ m/z 461.2 (M+1).



513

[1158] 1-((3R,4S)-3-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one 513.

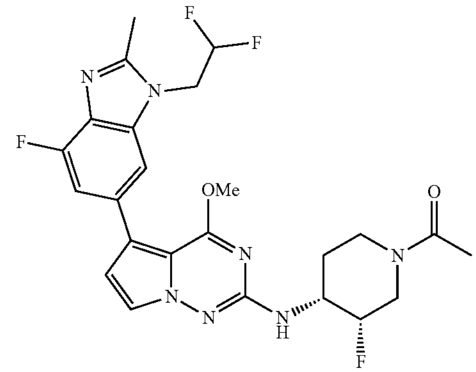
[1159] White solid (30 mg, 0.059 mmol, 32.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.93-2.01 (3H, m), 2.58(3 H, s), 3.47-3.61 (1H, m), 3.61-3.76 (1H, m), 3.78-3.85 (1H, m), 3.86-3.96 (1H, m), 3.97-3.98 (3H, m), 4.31-4.58 (1H, m), 4.78 (2 H, td, J=16.08, 2.60 Hz), 5.23-5.48 (1H, m), 6.49 (1 H, tt, J=54.30, 3.00 Hz), 6.72 (1H, t, J=2.33 Hz), 7.03 (1 H, t, J=6.98 Hz), 7.21 (1H, dd, J=12.18, 1.23 Hz), 7.59 (1 H, s), 7.63 (1H, dd, J=4.11, 2.46 Hz); ESIMS found for $C_{23}H_{23}F_4N_7O_2$ m/z 506.2 (M+1).



519

[1160] 2-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-ol 519.

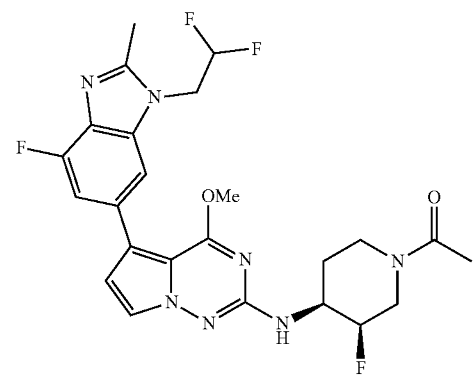
[1161] White solid (13 mg, 0.025 mmol, 23.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.64-1.72 (1H, m), 1.90 (1 H, qd, J=12.23, 3.83 Hz), 2.17 (1 H, brt, J=11.23 Hz), 2.32 (1H, dd, J=37.55, 12.59 Hz), 2.44 (2H, t, J=6.16 Hz), 2.58 (3 H, s), 2.91 (1H, br d, J=10.95 Hz), 3.15 (1 H, br t, J=9.72 Hz), 3.46-3.55 (2H, m), 3.69-3.86 (1H, m), 3.95 (3 H, s), 4.41 (1H, t, J=5.34 Hz), 4.78 (2 H, td, J=16.08, 2.33 Hz), 4.89 (1H, d, J=49.65 Hz), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.56 (1H, d, J=7.94 Hz), 6.68 (1H, d, J=2.46 Hz), 7.20 (1H, dd, J=12.18, 1.23 Hz), 7.58 (1 H, s), 7.60 (1H, d, J=2.46 Hz); ESIMS found for $C_{24}H_{27}F_4N_7O_2$ m/z 522.3 (M+1).



520

[1162] 1-((3S,4R)-4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one 520.

[1163] Fluffy white solid (5 mg, 0.010 mmol, 19.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.66-1.73 (1H, m), 1.74-1.90 (1H, m), 1.98-2.06 (3H, m), 2.58 (3 H, s), 2.66-2.97 (1H, m), 3.17-3.25 (1H, m), 3.87-4.02 (1H, m), 3.96 (3 H, s), 4.03-4.16 (1H, m), 4.39-4.72 (1H, m), 4.78 (2 H, td, J=15.88, 2.19 Hz), 4.99 (1H, d, J=49.65 Hz), 6.49 (1 H, tt, J=54.30, 3.00 Hz), 6.69 (1H, d, J=2.74 Hz), 6.73 (1H, dd, J=7.80, 1.78 Hz), 7.20 (1H, dd, J=12.18, 1.23 Hz), 7.58 (1 H, s), 7.60 (1H, d, J=2.46 Hz); ESIMS found for $C_{24}H_{25}F_4N_7O_2$ m/z 520.2 (M+1).

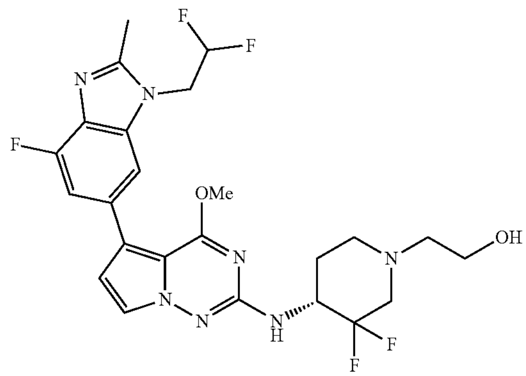


521

[1164] 1-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one 521.

[1165] White solid (25 mg, 0.048 mmol, 46.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.66-1.73 (1H, m), 1.74-1.90 (1H, m), 1.98-2.06 (3H, m), 2.58 (3 H, s), 2.65-2.97 (1H, m), 3.15-3.26 (1H, m), 3.86-4.01 (1H, m), 3.96 (3 H, s), 4.02-4.18 (1H, m), 4.39-4.73 (1H, m), 4.78 (2 H, td, J=16.02, 2.46 Hz), 4.99 (1H, d, J=49.55 Hz), 6.49 (1 H, tt, J=54.30, 3.00 Hz), 6.69 (1H, d, J=2.46 Hz), 6.73 (1H, dd, J=7.67, 1.92 Hz), 7.20 (1H, dd, J=12.18, 1.23 Hz), 7.58 (1 H, s), 7.60 (1H, d, J=2.46 Hz); ESIMS found for $C_{24}H_{25}F_4N_7O_2$ m/z 520.2 (M+1).

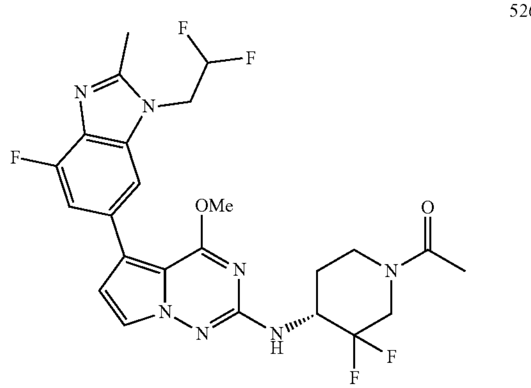
525



[1166] (R)-2-(4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-ol 525.

[1167] White solid (15 mg, 0.028 mmol, 27.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.73-1.88 (2H, m), 2.25-2.34 (1H, m), 2.51-2.54 (2H, m), 2.58 (3 H, s), 2.90 (1H, br d, J=11.50 Hz), 3.13-3.23 (1H, m), 3.30-3.32 (1H, m), 3.52 (2 H, q, J=5.84 Hz), 3.97 (3 H, s), 4.17-4.32 (1H, m), 4.49 (1H, t, J=5.20 Hz), 4.78 (2 H, td, J=16.02, 2.19 Hz), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.70 (1H, d, J=2.74 Hz), 6.77 (1H, d, J=9.31 Hz), 7.20 (1H, dd, J=12.18, 1.23 Hz), 7.58 (1 H, s), 7.61 (1H, d, J=2.74 Hz); ESIMS found for $C_{24}H_{26}F_5N_7O_2$ m/z 540.2 (M+1).

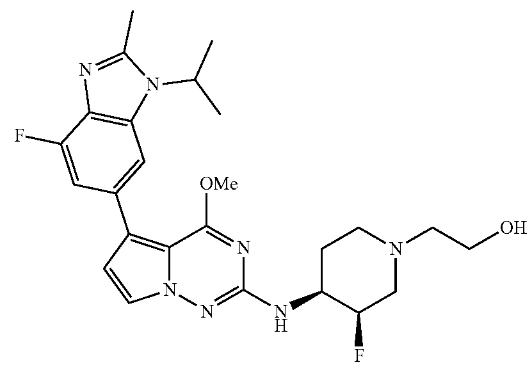
526



[1168] (R)-1-(4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one 526.

[1169] White solid (20 mg, 0.037 mmol, 36.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.58-1.83 (1H, m), 1.84-1.99 (1H, m), 2.03-2.09 (3H, m), 2.58(3 H, s), 2.92-3.05 (1H, m), 3.63-3.92 (1H, m), 3.98 (3 H, s), 4.10-4.30 (1H, m), 4.45-4.60 (2H, m), 4.78 (2 H, td, J=16.08, 2.33 Hz), 6.49 (1 H, tt, J=54.30, 3.00 Hz), 6.71 (1H, d, J=2.46 Hz), 6.95 (1H, d, J=9.31 Hz), 7.21 (1H, dd, J=12.18, 1.23 Hz), 7.59 (1 H, s), 7.61 (1H, dd, J=2.46, 1.37 Hz); ESIMS found for $C_{24}H_{24}F_5N_7O_2$ m/z 538.2 (M+1).

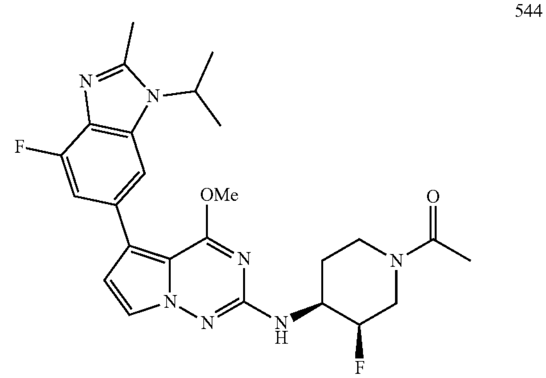
542



[1170] 2-((3R,4S)-3-Fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-ol 542.

[1171] White solid (6 mg, 0.012 mmol, 18.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.59 (6H, d, J=6.84 Hz), 1.64-1.72 (1H, m), 1.90 (1 H, qd, J=12.27, 3.70 Hz), 2.17 (1 H, br t, J=10.68 Hz), 2.32 (1H, dd, J=37.25, 12.87 Hz), 2.44 (2H, t, J=6.30 Hz), 2.58 (3 H, s), 2.91 (1H, br d, J=10.95 Hz), 3.15 (1 H, brt, J=10.13 Hz), 3.46-3.54 (2H, m), 4.41 (1H, t, J=5.34 Hz), 4.76 (1 H, spt, J=6.84 Hz), 4.89 (1H, d, J=49.90 Hz), 6.55 (1H, d, J=7.67 Hz), 6.69 (1H, d, J=2.74 Hz), 7.12 (1H, d, J=12.05 Hz), 7.59 (1H, d, J=2.46 Hz), 7.64 (1 H, s); ESIMS found for $C_{25}H_{31}F_2N_7O_2$ m/z 500.3 (M+1).

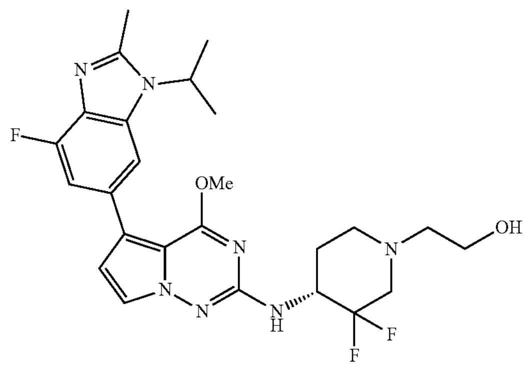
544



[1172] 1-((3R,4S)-3-Fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 544.

[1173] White solid (15 mg, 0.030 mmol, 45.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.59 (6H, d, J=6.57 Hz), 1.64-1.89 (2H, m), 1.97-2.07 (3H, m), 2.58 (3 H, s), 2.66-2.96 (1H, m), 3.17-3.26 (1H, m), 3.83-4.17 (2H, m), 3.96 (3 H, s), 4.39-4.72 (1H, m), 4.73-4.81 (1H, m), 4.92-5.06 (1H, m), 6.70 (1H, d, J=2.74 Hz), 6.72 (1H, d, J=7.94 Hz), 7.12 (1H, dd, J=12.18, 1.23 Hz), 7.59 (1H, d, J=2.46 Hz), 7.64 (1H, d, J=1.10 Hz); ESIMS found for $C_{25}H_{29}F_2N_7O_2$ m/z 498.25 (M+1).

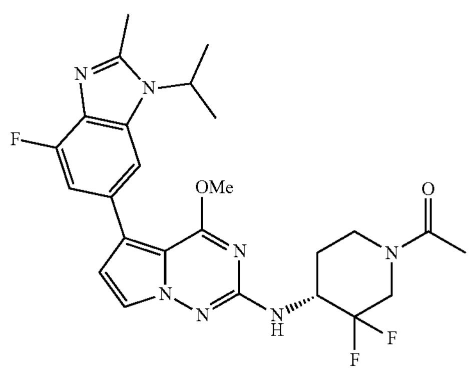
549



[1174] (R)-2-(3,3-Difluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-ol 549.

[1175] White solid (5 mg, 0.010 mmol, 15.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.59 (6H, dd, J=6.84, 2.19 Hz), 1.72-1.88 (2H, m), 2.25-2.34 (1H, m), 2.44-2.55 (1 H, m), 2.58 (3 H, s), 2.90 (1H, br d, J=11.50 Hz), 3.11-3.22 (1H, m), 3.52 (2 H, q, J=5.84 Hz), 3.97 (3 H, s), 4.17-4.32 (1H, m), 4.49 (1H, t, J=5.34 Hz), 4.76 (1 H, spt, J=6.89 Hz), 6.70 (1H, d, J=2.74 Hz), 6.76 (1H, d, J=9.31 Hz), 7.12 (1H, dd, J=12.05, 1.10 Hz), 7.61 (1H, d, J=2.74 Hz), 7.65 (1H, d, J=1.10 Hz); ESIMS found for $C_{25}H_{30}F_3N_7O_2$ m/z 518.3 (M+1).

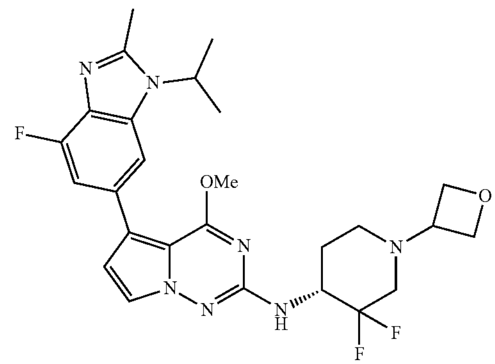
550



[1176] (R)-1-(3,3-Difluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 550.

[1177] White solid (6 mg, 0.012 mmol, 18.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.57-1.61 (6H, m), 1.62-1.83 (1H, m), 1.84-1.98 (1H, m), 2.02-2.10 (3H, m), 2.58 (3 H, s), 2.93-3.05 (1H, m), 3.63-3.77 (1H, m), 3.82-4.21 (1H, m), 3.98 (3 H, s), 4.22-4.61 (2H, m), 4.76 (1 H, spt, J=6.89 Hz), 6.72 (1H, d, J=2.74 Hz), 6.93 (1H, d, J=9.31 Hz), 7.12 (1H, dd, J=12.05, 1.10 Hz), 7.60 (1H, dd, J=2.46, 1.37 Hz), 7.65 (1H, d, J=1.10 Hz); ESIMS found for $C_{25}H_{28}F_3N_7O_2$ m/z 516.2 (M+1).

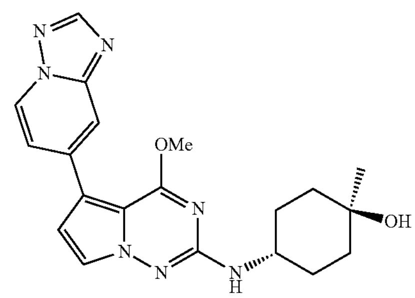
551



[1178] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 551.

[1179] White solid (8 mg, 0.015 mmol, 23.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.59 (6H, dd, J=6.98, 2.05 Hz), 1.75-1.85 (1H, m), 1.85-1.93 (1H, m), 2.16 (1 H, br t, J=10.40 Hz), 2.34-2.47 (1H, m), 2.58 (3 H, s), 2.76 (1H, br d, J=11.77 Hz), 2.96-3.07 (1H, m), 3.60 (1 H, quin, J=6.23 Hz), 3.97 (3 H, s), 4.24-4.37 (1H, m), 4.44 (2 H, dt, J=14.92, 6.23 Hz), 4.55 (2 H, td, J=6.64, 3.42 Hz), 4.76 (1 H, spt, J=6.89 Hz), 6.71 (1H, d, J=2.74 Hz), 6.83 (1 H, d, J=9.58 Hz), 7.12 (1H, dd, J=12.18, 0.96 Hz), 7.60 (1H, d, J=2.74 Hz), 7.65 (1H, d, J=1.10 Hz); ESIMS found for $C_{26}H_{30}F_3N_7O_2$ m/z 530.25 (M+1).

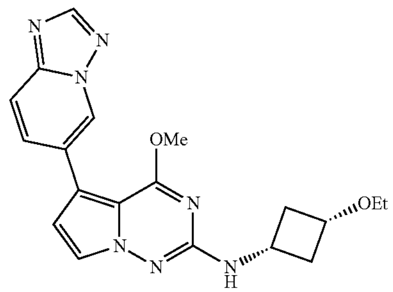
554



[1180] (1r,4r)-4-((5-([1,2,4]Triazolo[1,5-a]pyridin-7-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 554.

[1181] White solid (6.4 mg, 0.016 mmol, 8.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.37-1.53 (4H, m), 1.57-1.65 (2H, m), 1.84-1.93 (2H, m), 3.65 (1 H, br dd, J=8.08, 3.70 Hz), 3.99 (3H, s), 4.23 (1H, s), 6.58 (1H, d, J=7.94 Hz), 6.88 (1H, d, J=2.74 Hz), 7.44 (1H, dd, J=7.12, 1.64 Hz), 7.67 (1H, d, J=2.74 Hz), 7.95 (1H, dd, J=1.92, 0.82 Hz), 8.46 (1 H, s), 8.89 (1H, dd, J=7.12, 0.82 Hz); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

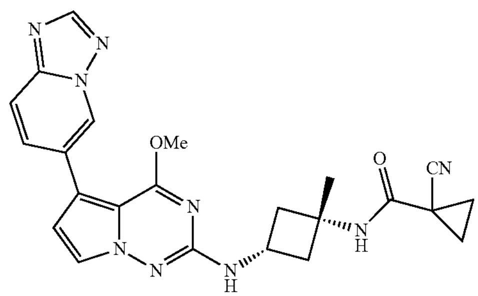
555



[1182] 5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-N-(cis-3-ethoxycyclobutyl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 555.

[1183] Off-white solid (9 mg, 0.024 mmol, 32.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.10 (3H, t, J=6.98 Hz), 1.80-1.91 (2H, m), 2.59-2.70 (2H, m), 3.34 (2 H, q, J=7.10 Hz), 3.65-3.72 (1H, m), 3.74-3.84 (1H, m), 3.96 (3 H, s), 6.81 (1H, d, J=2.74 Hz), 7.05 (1H, d, J=7.39 Hz), 7.63 (1H, d, J=2.74 Hz), 7.80-7.86 (1H, m), 7.87-7.92 (1H, m), 8.49 (1 H, s), 9.03-9.10 (1H, m); ESIMS found for $C_{1\text{-}9}H_{21}N_7O_2$ m/z 380.2 (M+1).

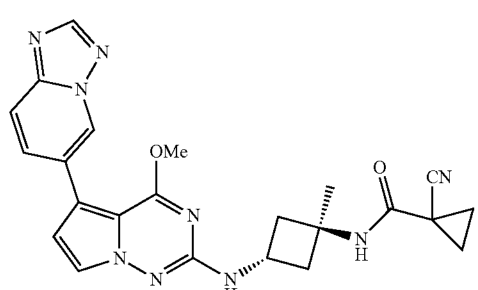
562



[1184] N-((1s,3s)-3-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-1-cyanocyclopropane-1-carboxamide 562.

[1185] Beige solid (8 mg, 0.018 mmol, 25.5% yield). ^{1}HNMR (499 MHz, DMSO-d_6) δ ppm 1.37 (3 H, s), 1.43-1.49 (2H, m), 1.49-1.55 (2H, m), 2.18 (2 H, br dd, J=11.64, 9.17 Hz), 2.45 (2H, ddd, J=9.86, 7.39, 2.46 Hz), 3.96 (3 H, s), 4.03 (1 H, sxt, J=7.78 Hz), 6.81 (1H, d, J=2.74 Hz), 7.03 (1H, d, J=7.12 Hz), 7.67 (1H, d, J=2.46 Hz), 7.82-7.86 (1H, m), 7.87-7.92 (1 H, m), 8.29 (1H, s), 8.49 (1H, s), 9.04-9.11 (1H, m); ESIMS found for $C_{23}H_{23}N_9O_2$ m/z 458.2 (M+1).

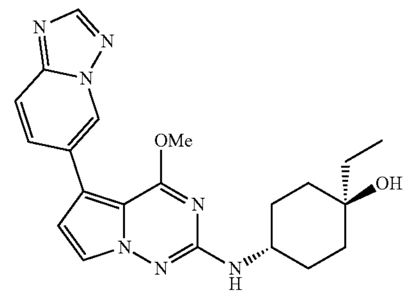
563



[1186] N-((1r,3r)-3-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-1-cyanocyclopropane-1-carboxamide 563.

[1187] Beige solid (7 mg, 0.015 mmol, 22.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.37 (3 H, s), 1.48-1.57 (4H, m), 1.93-2.06 (2H, m), 2.67-2.78 (2H, m), 3.96 (3 H, s), 4.18 (1 H, sxt, J=7.72 Hz), 6.80 (1H, d, J=2.74 Hz), 7.05 (1H, d, J=6.84 Hz), 7.67 (1H, d, J=2.74 Hz), 7.81-7.86 (1H, m), 7.87-7.92 (1H, m), 8.05 (1H, s), 8.49 (1H, s), 9.02-9.10 (1H, m); ESIMS found for $C_{23}H_{23}N_9O_2$ m/z 458.2 (M+1).

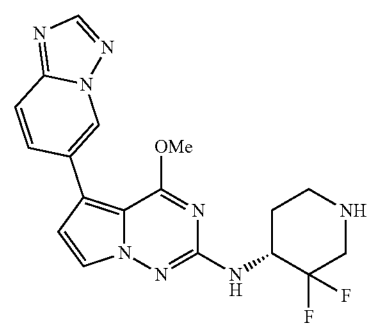
567



[1188] (1r,4r)-4-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol 567.

[1189] Off-white solid (25 mg, 0.061 mmol, 36.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.83 (3H, t, J=7.39 Hz), 1.31-1.39 (2H, m), 1.40-1.45 (2H, m), 1.46 (2 H, q, J=7.57 Hz), 1.58-1.69 (2H, m), 1.80-1.90 (2H, m), 3.68 (1 H, tt, J=8.01, 4.04 Hz), 3.96 (3H, s), 3.99 (1H, s), 6.51 (1H, d, J=7.67 Hz), 6.79 (1H, d, J=2.46 Hz), 7.65 (1H, d, J=2.74 Hz), 7.81-7.85 (1H, m), 7.87-7.91 (1H, m), 8.49 (1 H, s), 9.06 (1 H, s); ESIMS found for $C_{21}H_{25}N_7O_2$ m/z 408.2 (M+1).

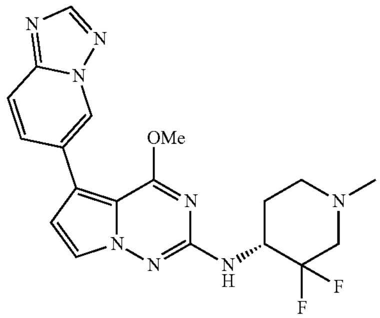
575



[1190] (R)-5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-N-(3,3-difluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 575.

[1191] Off-white solid (86 mg, 0.215 mmol, 53.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.69 (1 H, qd, J=11.82, 3.70 Hz), 1.80-1.89 (1H, m), 2.60 (1 H, br t, J=11.64 Hz), 2.81 (1H, dd, J=29.65, 13.46 Hz), 2.93 (1H, br d, J=12.87 Hz), 3.06-3.19 (1H, m), 4.00 (3 H, s), 4.25-4.42 (1H, m), 6.83 (1H, d, J=2.46 Hz), 6.89 (1H, d, J=9.31 Hz), 7.67 (1H, d, J=2.46 Hz), 7.82-7.87 (1H, m), 7.88-7.93 (1H, m), 8.50 (1 H, s), 9.08 (1 H, s); ESIMS found for $C_{18}H_{18}F_2N_8O$ m/z 401.2 (M+1).

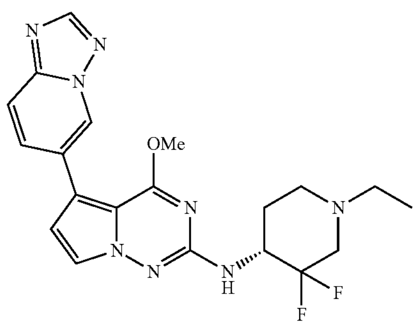
576



[1192] (R)-5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 576.

[1193] Fluffy white solid (12 mg, 0.027 mmol, 71.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.94 (2H, m), 2.10-2.47 (5H, m), 2.73-2.94 (1H, m), 3.00-3.20 (1H, m), 4.00 (3 H, s), 4.21-4.41 (1H, m), 6.84 (1H, d, J=2.74 Hz), 6.89-6.99 (1H, m), 7.67 (1H, d, J=2.74 Hz), 7.80-7.87 (1H, m), 7.88-7.94 (1H, m), 8.50 (1 H, s), 9.05-9.12 (1H, m); ESIMS found for $C_{1-9}H_2O\ F_2N_8O$ m/z 415.2 (M+1).

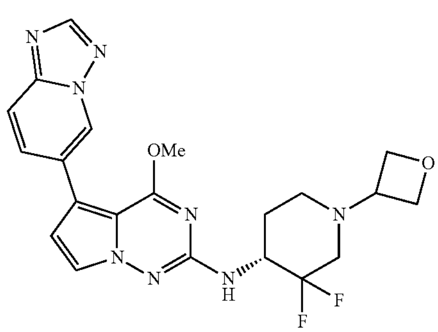
577



[1194] (R)-5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-N-(1-ethyl-3,3-difluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 577.

[1195] Fluffy white solid (16 mg, 0.034 mmol, 55.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.01 (3 H, br s), 1.71-1.94 (2H, m), 2.10-2.24 (1H, m), 2.29-2.48 (3H, m), 2.80-2.94 (1H, m), 3.01-3.18 (1H, m), 4.00 (3 H, s), 4.18-4.36 (1H, m), 6.79-6.94 (2H, m), 7.66 (1 H, br s), 7.82-7.87 (1H, m), 7.88-7.95 (1H, m), 8.50 (1 H, s), 9.09 (1 H, s); ESIMS found for $C_{20}H_{22}F_2N_8O$ m/z 429.2 (M+1).

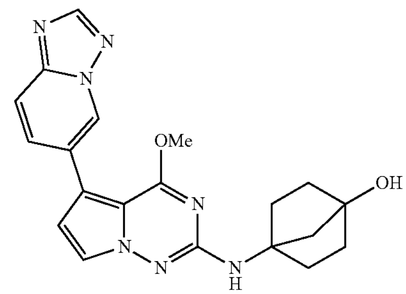
578



[1196] (R)-5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 578.

[1197] Fluffy white solid (18 mg, 0.039 mmol, 63.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.86 (1H, m), 1.86-1.93 (1H, m), 2.10-2.22 (1H, m), 2.40 (1H, dd, J=26.30, 11.77 Hz), 2.76 (1H, br d, J=11.22 Hz), 2.95-3.08 (1H, m), 3.60 (1 H, quin, J=6.30 Hz), 4.00 (3 H, s), 4.23-4.37 (1H, m), 4.44 (2 H, dt, J=15.19, 6.23 Hz), 4.55 (2 H, td, J=6.57, 3.83 Hz), 6.84 (1H, d, J=2.74 Hz), 6.94 (1H, d, J=9.31 Hz), 7.66 (1H, d, J=2.74 Hz), 7.80-7.87 (1H, m), 7.88-7.95 (1H, m), 8.50 (1 H, s), 9.08 (1 H, s); ESIMS found for $C_{21}H_{22}F_2N_8O_2$ m/z 457.2 (M+1).

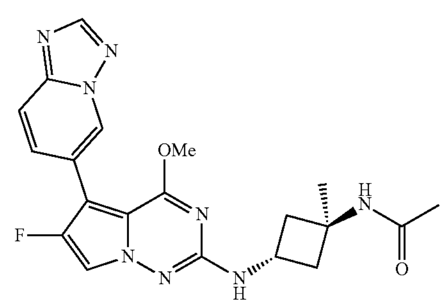
582



[1198] 4-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol 582.

[1199] Off-white solid (3 mg, 0.008 mmol, 4.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.51-1.63 (2H, m), 1.66-1.79 (2H, m), 1.85 (2 H, s), 1.86-1.92 (2H, m), 1.98-2.11 (2H, m), 3.96 (3H, s), 4.89 (1H, s), 6.77 (1 H, s), 6.80 (1H, d, J=2.74 Hz), 7.62 (1H, d, J=2.74 Hz), 7.80-7.86 (1H, m), 7.87-7.91 (1H, m), 8.49 (1 H, s), 9.03-9.10 (1H, m); ESIMS found for $C_{20}H_{21}N_7O_2$ m/z 392.2 (M+1).

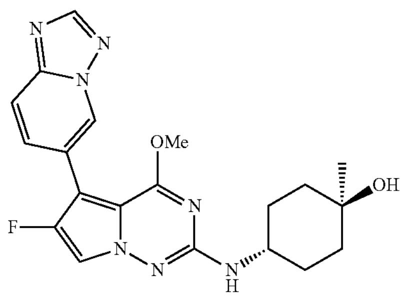
585



[1200] N-((1r,3r)-3-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 585.

[1201] Off-white solid (6 mg, 0.014 mmol, 27.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.35 (3H, s), 1.81 (3H, s), 1.89-2.00 (2H, m), 2.58-2.70 (2H, m), 3.92 (3 H, s), 4.17 (1 H, sxt, J=7.72 Hz), 7.13 (1H, d, J=7.12 Hz), 7.77-7.82 (1H, m), 7.83 (1H, d, J=3.01 Hz), 7.88 (1H, d, J=9.86 Hz), 7.93 (1H, s), 8.53 (1H, s), 9.05 (1 H, s); ESIMS found for $C_{20}H_{21}FN_8O_2$ m/z 425.2 (M+1).

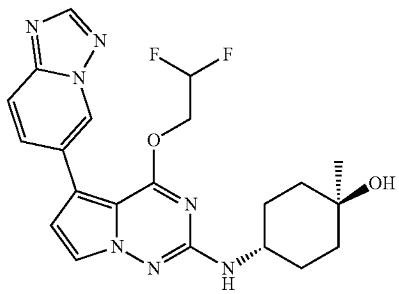
589



[1202] (1r,4r)-4-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo-[2, 1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 589.

[1203] Off-white solid (7 mg, 0.017 mmol, 23.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.36-1.51 (4H, m), 1.55-1.65 (2H, m), 1.81-1.90 (2H, m), 3.58-3.68 (1H, m), 3.92 (3H, s), 4.25 (1H, s), 6.63 (1H, d, J=7.94 Hz), 7.78-7.82 (1H, m), 7.86 (1H, d, J=3.01 Hz), 7.88 (1H, dd, J=9.31, 0.82 Hz), 8.53 (1 H, s), 9.05 (1 H, s); ESIMS found for $C_{20}H_{22}FN_7O_2$ m/z 412.2 (M+1).

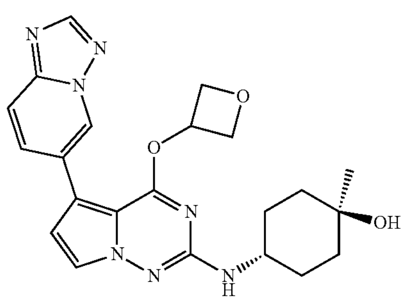
616



[1204] (1r,4r)-4-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo [2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 616.

[1205] White solid (2.92 mg, 0.007 mmol). ^{1}H NMR (400 MHz, Solvent) 6 ppm 1.28 (3 H, s), 1.46-1.66 (4H, m), 1.69-1.80 (2H, m), 1.99-2.10 (2H, m), 3.68-3.82 (1H, m), 4.69 (2 H, td, J=14.07, 3.75 Hz), 6.18 (1 H, tt, J=55.00, 3.76 Hz), 6.77 (1H, d, J=2.63 Hz), 7.57 (1H, d, J=2.50 Hz), 7.75 (1H, d, J=9.13 Hz), 7.96 (1H, dd, J=9.26, 1.38 Hz), 8.41 (1 H, s), 8.94 (1 H, s); ESIMS found for $C_{21}H_{23}F_2N_7O_2$ m/z 444.3 (M+1).

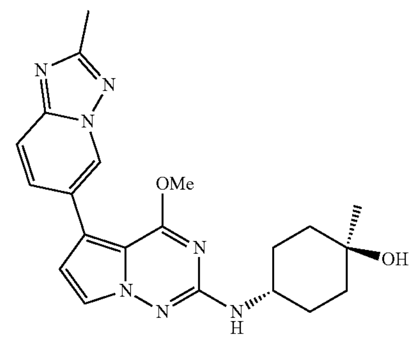
621



[1206] (1r,4r)-4-((5-([1,2,4]Triazolo[1,5-a]pyridin-6-yl)-4-(oxetan-3-yloxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 621.

[1207] White solid (11 mg, 0.025 mmol, 35.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.36-1.48 (4H, m), 1.55-1.64 (2H, m), 1.80-1.90 (2H, m), 3.59 (1H, br d, J=3.83 Hz), 4.25 (1 H, s), 4.61 (2H, dd, J=7.53, 5.34 Hz), 4.86 (2H, t, J=7.12 Hz), 5.69 (1 H, quin, J=5.75 Hz), 6.48 (1H, d, J=7.94 Hz), 6.86 (1H, d, J=2.74 Hz), 7.69 (1H, d, J=2.74 Hz), 7.88 (1H, d, J=9.31 Hz), 7.98 (1H, dd, J=9.31, 1.64 Hz), 8.51 (1 H, s), 9.21 (1 H, s); ESIMS found for $C_{22}H_{25}N_7O_3$ m/z 436.2 (M+1).

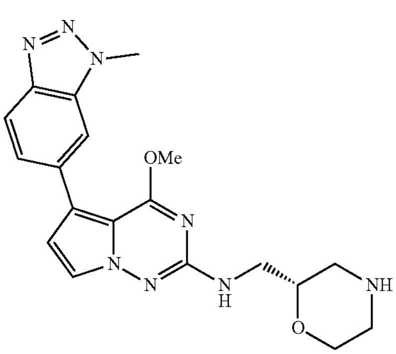
622



[1208] (1r,4r)-4-((4-Methoxy-5-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 622.

[1209] White solid (34 mg, 0.083 mmol, 35.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.37-1.52 (4H, m), 1.55-1.66 (2H, m), 1.82-1.93 (2H, m), 2.48 (3 H, s), 3.64 (1H, br d, J=4.11 Hz), 3.96 (3H, s), 4.23 (1H, s), 6.51 (1H, d, J=7.67 Hz), 6.76 (1H, d, J=2.74 Hz), 7.65 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=9.03 Hz), 7.82 (1H, dd, J=9.31, 1.64 Hz), 8.94 (1 H, s); ESIMS found for $C_{21}H_{25}N_7O_2$ m/z 408.2 (M+1).

623

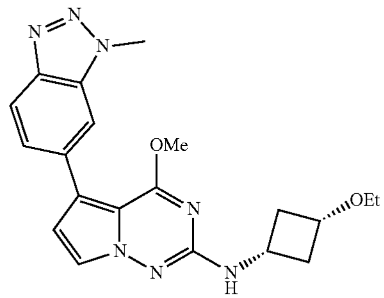


[1210] (S)-4-Methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-(morpholin-2-ylmethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 623.

[1211] White solid (54 mg, 0.137 mmol, 94.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.59 (1H, dd, J=12.32, 10.68 Hz), 2.80 (1 H, td, J=12.05, 3.56 Hz), 2.86-2.94 (1H, m), 3.06 (1H, br d, J=11.77 Hz), 3.20-3.26 (1H, m), 3.28-3.32 (1H, m), 3.54 (1 H, td, J=11.64, 2.46 Hz), 3.75 (1 H, dtd, J=10.23, 6.04, 6.04, 2.05 Hz), 3.85 (1H, dd, J=11.77, 2.19 Hz), 3.96 (3H, s), 4.31 (3H, s), 6.74 (1H, t, J=6.02 Hz), 6.76 (1H, d, J=2.46 Hz), 7.61 (1H, dd, J=8.76, 1.37 Hz), 7.65

(1H, d, J=2.74 Hz), 7.94 (1 H, s), 7.98 (1H, d, J=8.76 Hz); ESIMS found for $C_{1-9}H_{22}N_8O_2$ m/z 395.2 (M+1).

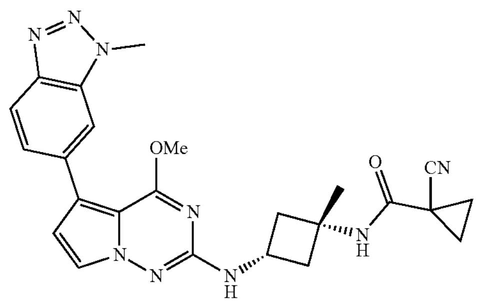
624



[1212] N-(cis-3-Ethoxycyclobutyl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 624.

[1213] Beige solid (23 mg, 0.059 mmol, 30.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.10 (3H, t, J=6.98 Hz), 1.81-1.93 (2H, m), 2.64 (2 H, tdt, J=9.02, 9.02, 6.74, 2.53, 2.53 Hz), 3.34 (2 H, q, J=6.85 Hz), 3.65-3.73 (1H, m), 3.74-3.84 (1H, m), 3.95 (3 H, s), 4.31 (3 H, s), 6.75 (1H, d, J=2.46 Hz), 7.01 (1H, d, J=7.39 Hz), 7.58-7.62 (1H, m), 7.62 (1H, d, J=2.74 Hz), 7.94 (1 H, s), 7.95-7.99 (1H, m); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

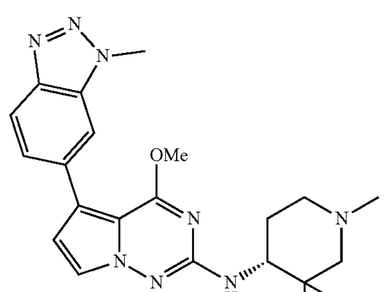
625



[1214] 1-Cyano-N-((1s,3s)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide 625.

[1215] Off-white solid (9 mg, 0.019 mmol, 28.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3 H, s), 1.43-1.49 (2H, m), 1.49-1.54 (2H, m), 2.14-2.23 (2H, m), 2.45 (2H, ddd, J=9.79, 7.46, 2.74 Hz), 3.95 (3 H, s), 4.04 (1 H, sxt, J=7.78 Hz), 4.31 (3 H, s), 6.75 (1H, d, J=2.46 Hz), 6.99 (1H, d, J=7.12 Hz), 7.60 (1H, dd, J=8.76, 1.64 Hz), 7.65 (1H, d, J=2.46 Hz), 7.94 (1 H, s), 7.97 (1H, dd, J=8.62, 0.68 Hz), 8.29 (1 H, s); ESIMS found for $C_{24}H_{25}N_9O_2$ m/z 472.2 (M+1).

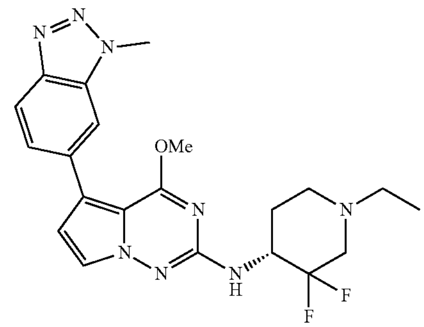
626



[1216] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 626.

[1217] Fluffy white solid (6 mg, 0.013 mmol, 35.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.77-1.90 (2H, m), 2.12-2.23 (1H, m), 2.28 (3 H, br s), 2.34-2.46 (1H, m), 2.75-2.88 (1H, m), 3.01-3.15 (1H, m), 3.98 (3 H, s), 4.19-4.30 (1H, m), 4.31 (3 H, s), 6.78 (1 H, d, J=2.46 Hz), 6.84 (1H, br d, J=6.84 Hz), 7.62 (1H, dd, J=8.62, 1.51 Hz), 7.66 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 7.98 (1H, d, J=8.76 Hz); ESIMS found for $C_{20}H_{22}F_2N_8O$ m/z 429.2 (M+1).

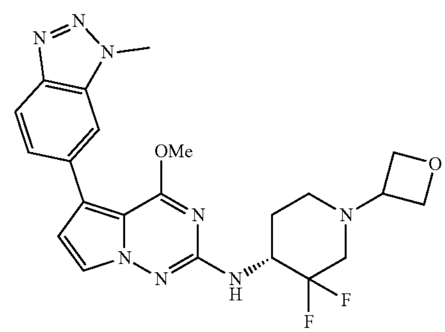
627



[1218] (R)—N-(1-Ethyl-3,3-difluoropiperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 627.

[1219] Fluffy white solid (14 mg, 0.032 mmol, 52.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.01 (3H, t, J=7.26 Hz), 1.72-1.83 (1H, m), 1.84-1.92 (1H, m), 2.18 (1 H, br t, J=10.40 Hz), 2.33-2.42 (1H, m), 2.45 (2 H, q, J=7.12 Hz), 2.88 (1H, br d, J=11.77 Hz), 3.07-3.18 (1H, m), 3.98 (3 H, s), 4.20-4.30 (1H, m), 4.31 (3 H, s), 6.78 (1H, d, J=2.46 Hz), 6.83 (1 H, d, J=9.31 Hz), 7.60-7.63 (1H, m), 7.66 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 7.98 (1H, d, J=8.49 Hz); ESIMS found for $C_{21}H_{24}F_2N_8O$ m/z 443.2 (M+1).

628

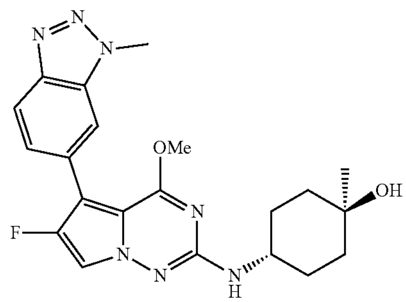


[1220] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 628.

[1221] Fluffy white solid (22 mg, 0.047 mmol, 52.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.75-1.86 (1H, m), 1.87-1.94 (1H, m), 2.11-2.22 (1H, m), 2.41 (1H, dd, J=27.15, 11.55 Hz), 2.76 (1H, br d, J=11.23 Hz), 2.96-3.07 (1H, m), 3.60 (1 H, quin, J=6.23 Hz), 3.99 (3 H, s), 4.25-4.37 (1H, m), 4.31 (3 H, s), 4.44 (2 H, dt, J=15.06, 6.16 Hz), 4.55

(2 H, td, J=6.64, 3.70 Hz), 6.78 (1H, d, J=2.46 Hz), 6.89 (1H, d, J=9.31 Hz), 7.62 (1H, dd, J=8.76, 1.64 Hz), 7.65 (1H, d, J=2.46 Hz), 7.95 (1 H, s), 7.98 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{24}F_2N_8O_2$ m/z 471.2 (M+1).

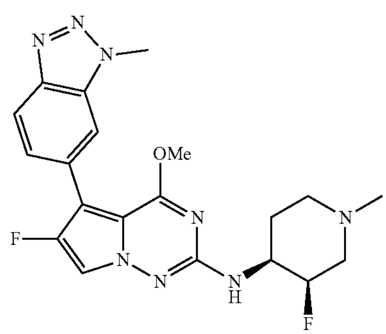
629



[1222] trans-4-((6-Fluoro-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 629.

[1223] Off-white solid (10.5 mg, 0.025 mmol, 27.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.37-1.52 (4H, m), 1.56-1.66 (2H, m), 1.82-1.92 (2H, m), 3.63 (1 H, dt, J=8.21, 4.11 Hz), 3.90 (3H, s), 4.24 (1H, s), 4.31 (3 H, s), 6.59 (1H, d, J=7.94 Hz), 7.52 (1H, d, J=8.76 Hz), 7.84 (1H, d, J=2.74 Hz), 7.90 (1 H, s), 8.02 (1H, d, J=8.76 Hz); ESIMS found for $C_{21}H_{24}FN_7O_2$ m/z 426.2 (M+1).

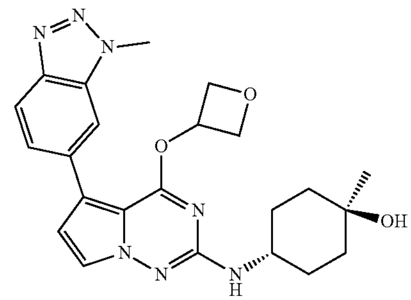
630



[1224] 6-Fluoro-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 630.

[1225] White solid (7.6 mg, 0.018 mmol, 19.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.63-1.72 (1H, m), 1.86-1.98 (1H, m), 2.01-2.10 (1H, m), 2.17 (1H, dd, J=37.55, 12.87 Hz), 2.19 (3 H, s), 2.80 (1H, br d, J=10.95 Hz), 3.00-3.11 (1H, m), 3.66-3.83 (1H, m), 3.92 (3H, s), 4.32 (3H, s), 4.89 (1H, d, J=50.20 Hz), 6.74 (1H, d, J=7.67 Hz), 7.52 (1H, d, J=8.76 Hz), 7.83 (1H, d, J=3.01 Hz), 7.91 (1 H, s), 8.03 (1H, d, J=8.49 Hz); ESIMS found for $C_{20}H_{22}F_2N_8O$ m/z 429.2 (M+1).

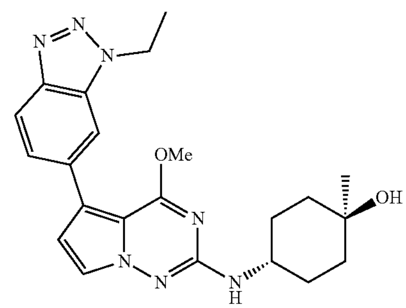
631



[1226] (1r,4r)-1-Methyl-4-((5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-(oxetan-3-yloxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol 631.

[1227] Off-white solid (11 mg, 0.025 mmol, 34.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.36-1.52 (4H, m), 1.54-1.65 (2H, m), 1.79-1.93 (2H, m), 3.60 (1 H, br s), 4.25 (1H, s), 4.32 (3H, s), 4.56 (2H, dd, J=7.39, 5.20 Hz), 4.85 (2H, t, J=6.98 Hz), 5.70 (1 H, quin, J=5.61 Hz), 6.45 (1H, br d, J=7.67 Hz), 6.79 (1H, d, J=2.46 Hz), 7.68 (1H, d, J=2.46 Hz), 7.69-7.73 (1H, m), 8.01 (1H, d, J=8.76 Hz), 8.04 (1 H, s); ESIMS found for $C_{23}H_{27}N_7O_3$ m/z 450.2 (M+1).

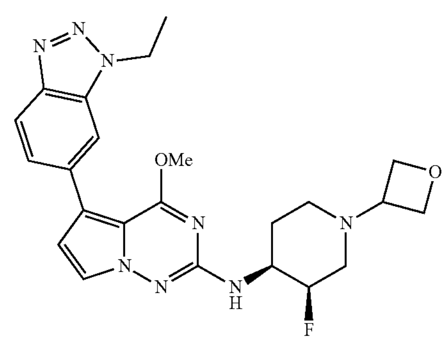
639



[1228] (1r,4r)-4-((5-(1-Ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 639.

[1229] Fluffy white solid (6 mg, 0.014 mmol, 29.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.50 (4H, m), 1.54 (3H, t, J=7.26 Hz), 1.57-1.63 (2H, m), 1.84-1.93 (2H, m), 3.65 (1 H, dt, J=8.08, 3.90 Hz), 3.95 (3H, s), 4.23 (1H, s), 4.75 (2 H, q, J=7.12 Hz), 6.49 (1H, d, J=7.94 Hz), 6.74 (1H, d, J=2.46 Hz), 7.57-7.62 (1H, m), 7.64 (1H, d, J=2.46 Hz), 7.97-7.99 (2H, m); ESIMS found for $C_{22}H_{27}N_7O_2$ m/z 422.2 (M+1).

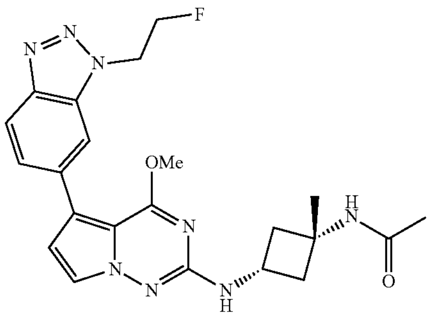
646



[1230] 5-(1-Ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 646.

[1231] Off-white solid (2 mg, 0.004 mmol, 25.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.54 (3H, t, J=7.39 Hz), 1.68-1.78 (1H, m), 1.92 (1 H, qd, J=12.14, 3.29 Hz), 1.98-2.06 (1H, m), 2.16 (1H, dd, J=37.30, 12.59 Hz), 2.76 (1H, br d, J=10.68 Hz), 2.99 (1 H, br t, J=10.13 Hz), 3.49 (1 H, quin, J=6.30 Hz), 3.74-3.91 (1H, m), 3.97 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.75 (2 H, q, J=7.12 Hz), 4.94 (1H, d, J=49.60 Hz), 6.69 (1H, d, J=7.67 Hz), 6.77 (1H, d, J=2.74 Hz), 7.59-7.62 (1H, m), 7.64 (1H, d, J=2.74 Hz), 7.97-8.00 (2H, m); ESIMS found for $C_{23}H_{27}FN_8O_2$ m/z 467.25 (M+1).

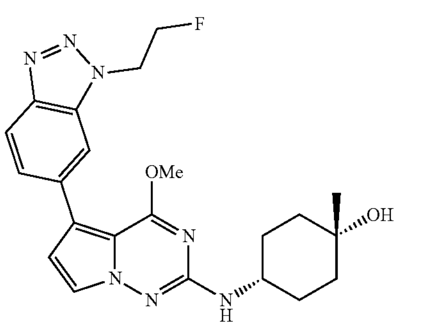
653



[1232] N-((1s,3s)-3-((5-(1-(2-Fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 653.

[1233] White solid (12 mg, 0.027 mmol, 21.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.11-2.21 (2H, m), 2.42 (2H, ddd, J=9.58, 7.39, 2.46 Hz), 3.93 (3 H, s), 4.03 (1 H, sxt, J=7.78 Hz), 4.94 (3 H, dt, J=47.15, 4.65 Hz), 5.08 (2 H, dt, J=27.70, 4.70 Hz), 6.73 (1H, d, J=2.46 Hz), 6.99 (1H, d, J=6.84 Hz), 7.61 (1H, dd, J=8.76, 1.37 Hz), 7.65 (1H, d, J=2.46 Hz), 7.98-8.04 (3H, m); ESIMS found for $C_{22}H_{25}FN_8O_2$ m/z 453.2 (M+1).

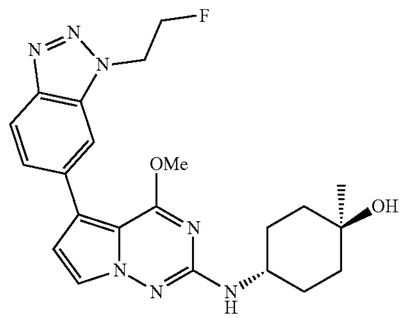
658



[1234] (1s,4s)-4-((5-(1-(2-Fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 658.

[1235] White solid (10 mg, 0.023 mmol, 23.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.37 (2 H, td, J=13.00, 4.38 Hz), 1.58 (2H, br d, J=12.05 Hz), 1.61-1.74 (4H, m), 3.46-3.58 (1H, m), 3.93 (3H, s), 4.00 (1H, s), 4.94 (2 H, dt, J=47.20, 4.65 Hz), 5.07 (2 H, dt, J=27.95, 4.65 Hz), 6.50 (1H, d, J=7.94 Hz), 6.71 (1H, d, J=2.74 Hz), 7.61 (1H, dd, J=8.62, 1.51 Hz), 7.61 (1H, d, J=2.46 Hz), 7.99 (1 H, s), 8.00 (1H, d, J=8.49 Hz); ESIMS found for $C_{22}H_{26}FN_7O_2$ m/z 440.2 (M+1).

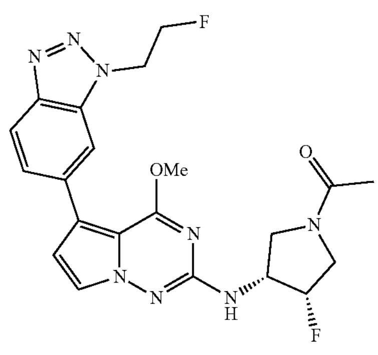
659



[1236] (1r,4r)-4-((5-(1-(2-Fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 659.

[1237] Fluffy white solid (3 mg, 0.007 mmol, 14.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.51 (4H, m), 1.56-1.65 (2H, m), 1.82-1.92 (2H, m), 3.65 (1 H, dt, J=7.73, 3.94 Hz), 3.94 (3H, s), 4.23 (1H, s), 4.94 (2 H, dt, J=47.20, 4.65 Hz), 5.07 (2 H, dt, J=27.70, 4.65 Hz), 6.49 (1H, d, J=7.94 Hz), 6.72 (1H, d, J=2.46 Hz), 7.61 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.46 Hz), 7.99 (1 H, s), 8.00 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{26}FN_7O_2$ m/z 440.2 (M+1).

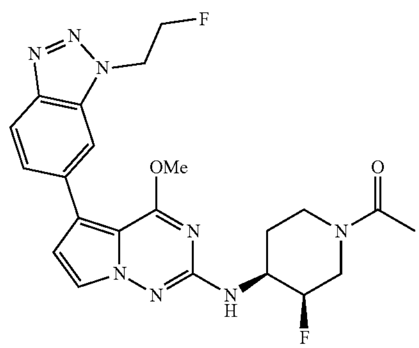
660



[1238] 1-((3S,4R)-3-Fluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one 660.

[1239] White solid (17 mg, 0.037 mmol, 20.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.93-2.01 (3H, m), 3.46-3.58 (1H, m), 3.59-3.76 (1H, m), 3.77-3.85 (1H, m), 3.85-3.96 (1H, m), 3.96-3.99 (3H, m), 4.29-4.59 (1H, m), 4.94 (2 H, dt, J=47.15, 4.65 Hz), 5.08 (2 H, dt, J=27.95, 4.65 Hz), 5.24-5.50 (1H, m), 6.79 (1H, t, J=2.46 Hz), 7.09 (1H, dd, J=7.12, 5.75 Hz), 7.61-7.65 (1H, m), 7.68 (1H, dd, J=3.97, 2.60 Hz), 8.00-8.04 (2H, m); ESIMS found for $C_{21}H_{22}F_2N_8O_2$ m/z 457.2 (M+1).

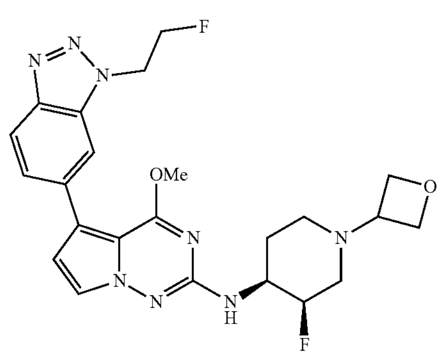
664



[1240] 1-((3R,4S)-3-Fluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 664.

[1241] Fluffy white solid (15 mg, 0.032 mmol, 64.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.66-1.92 (2H, m), 1.97-2.06 (3H, m), 2.66-3.00 (1H, m), 3.36-3.52 (1H, m), 3.86-4.18 (2H, m), 3.96 (3 H, s), 4.41-4.75 (1H, m), 4.94 (2 H, dt, J=47.20, 4.65 Hz), 4.94 (1 H, br s), 5.08 (2 H, dt, J=27.95, 4.65 Hz), 6.76 (1H, d, J=2.74 Hz), 6.80 (1H, dd, J=7.80, 3.15 Hz), 7.62 (1H, dd, J=8.62, 1.51 Hz), 7.65 (1H, d, J=2.74 Hz), 7.99-8.03 (2H, m); ESIMS found for $C_{22}H_{24}F_2N_8O_2$ m/z 471.2 (M+1).

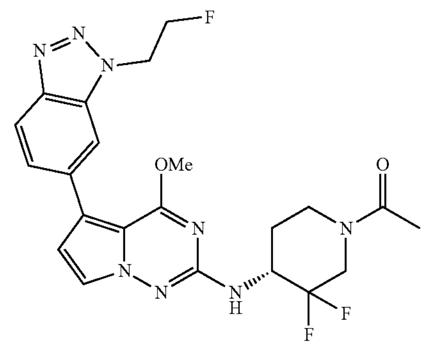
666



[1242] N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 666.

[1243] Off-white solid (2 mg, 0.004 mmol, 14.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67-1.78 (1H, m), 1.87-1.97 (1H, m), 1.99-2.05 (1H, m), 2.16 (1H, dd, J=37.00, 12.59 Hz), 2.72-2.79 (1H, m), 2.99 (1 H, br t, J=10.54 Hz), 3.49 (1 H, quin, J=6.30 Hz), 3.76-3.91 (1H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.43, 3.01 Hz), 4.94 (2 H, dt, J=47.45, 4.65 Hz), 5.08 (2 H, dt, J=28.00, 4.65 Hz), 6.70 (1H, d, J=7.67 Hz), 6.75 (1H, d, J=2.46 Hz), 7.62 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.74 Hz), 7.99-8.03 (2H, m); ESIMS found for $C_{23}H_{26}F_2N_8O_2$ m/z 485.2 (M+1).

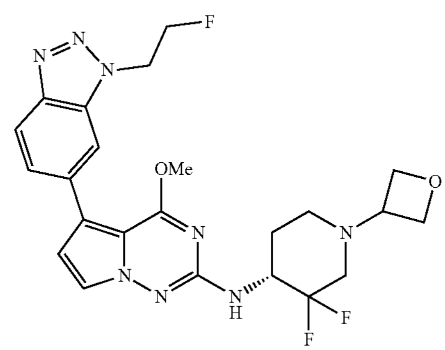
669



[1244] (R)-1-(3,3-Difluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 669.

[1245] Fluffy white solid (7 mg, 0.014 mmol, 32.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.58-1.84 (1H, m), 1.85-2.00 (1H, m), 2.02-2.10 (3H, m), 2.99 (1 H, brt, J=11.09 Hz), 3.63-3.92 (1H, m), 3.98 (3 H, s), 4.10-4.31 (1H, m), 4.46-4.63 (2H, m), 4.94 (2 H, dt, J=47.20, 4.65 Hz), 5.08 (2 H, dt, J=28.00, 4.65 Hz), 6.78 (1H, d, J=2.74 Hz), 7.00 (1H, d, J=9.31 Hz), 7.61-7.64 (1H, m), 7.65 (1H, dd, J=2.46, 1.37 Hz), 8.00-8.04 (2H, m); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).

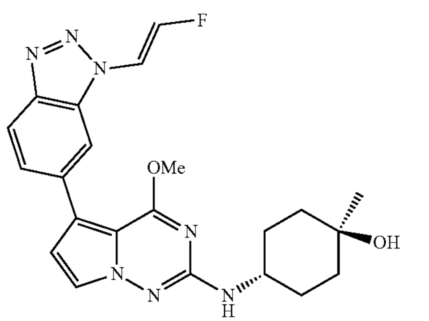
670



[1246] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 670.

[1247] Pale yellow solid (8 mg, 0.016 mmol, 33.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.86 (1H, m), 1.86-1.93 (1H, m), 2.12-2.23 (1H, m), 2.34-2.47 (1H, m), 2.76 (1H, br d, J=11.77 Hz), 2.97-3.06 (1H, m), 3.60 (1 H, quin, J=6.30 Hz), 3.97 (3 H, s), 4.24-4.38 (1H, m), 4.44 (2 H, dt, J=15.13, 6.26 Hz), 4.55 (2 H, td, J=6.57, 3.83 Hz), 4.94 (2 H, dt, J=46.90, 4.65 Hz), 5.08 (2 H, dt, J=27.70, 4.65 Hz), 6.77 (1H, d, J=2.74 Hz), 6.90 (1H, d, J=9.31 Hz), 7.61-7.64 (1H, m), 7.65 (1H, d, J=2.46 Hz), 8.00-8.03 (2H, m); ESIMS found for $C_{23}H_{25}F_3N_8O_2$ m/z 503.2 (M+1).

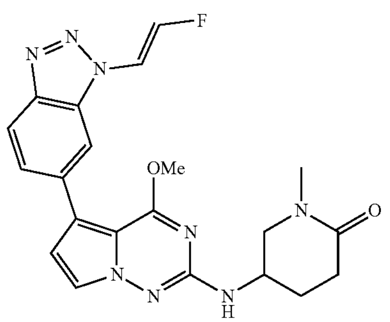
672



[1248] (1r,4r)-4-((5-(1-((E)-2-Fluorovinyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 672.

[1249] Yellow solid (7 mg, 0.016 mmol, 23.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.51 (4H, m), 1.57-1.66 (2H, m), 1.82-1.93 (2H, m), 3.59-3.71 (1H, m), 3.94 (3H, s), 4.23 (1H, s), 6.51 (1H, d, J=7.94 Hz), 6.74 (1H, d, J=2.74 Hz), 7.34 (1H, dd, J=60.90, 4.10 Hz), 7.45 (1H, dd, J=18.62, 3.83 Hz), 7.65 (1H, d, J=2.46 Hz), 7.69 (1H, d, J=9.03 Hz), 7.92 (1 H, s), 8.08 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{24}FN_7O_2$ m/z 438.2 (M+1).

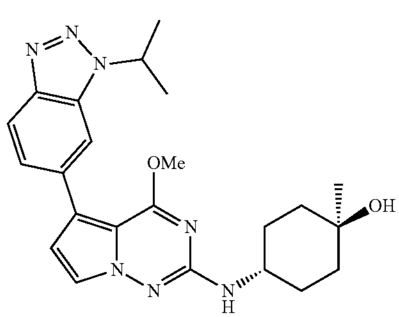
673



[1250] (E)-5-((5-(1-(2-Fluorovinyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one 673.

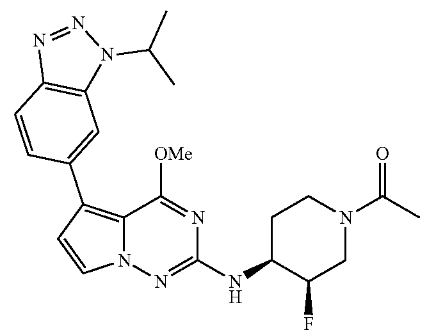
[1251] White solid (2 mg, 0.005 mmol, 4.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.82-2.06 (2H, m), 2.23-2.43 (2H, m), 2.81 (3 H, br s), 3.20-3.28 (1H, m), 3.56 (1 H, br s), 3.96 (3 H, br s), 4.10 (1 H, br s), 6.78 (1 H, br s), 6.95 (1 H, br s), 7.34 (1H, d, J=63.35 Hz), 7.45 (1H, br d, J=17.25 Hz), 7.68 (2 H, br s), 7.93 (1 H, br s), 8.08 (1H, br d, J=3.01 Hz); ESIMS found for $C_{21}H_{21}FN_8O_2$ m/z 437.2 (M+1).

681



[1252] (1r,4r)-4-((5-(1-Isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 681.

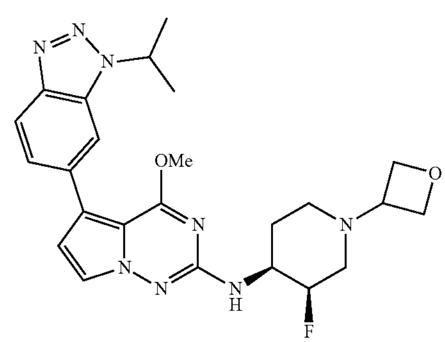
[1253] Fluffy white solid (2.7 mg, 0.006 mmol, 10.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.39-1.51 (4H, m), 1.57-1.63 (2H, m), 1.67 (6H, d, J=6.57 Hz), 1.84-1.91 (2H, m), 3.65 (1 H, br dd, J=7.80, 3.97 Hz), 3.94 (3H, s), 4.23 (1H, s), 5.24 (1 H, spt, J=6.71 Hz), 6.48 (1H, d, J=7.94 Hz), 6.74 (1H, d, J=2.46 Hz), 7.58 (1H, dd, J=8.76, 1.37 Hz), 7.64 (1H, d, J=2.46 Hz), 7.98 (1H, d, J=8.49 Hz), 8.00 (1 H, s); ESIMS found for $C_{23}H_{29}N_7O_2$ m/z 436.2 (M+1).



[1254] 1-((3R,4S)-3-Fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 686.

[1255] Fluffy white solid (9 mg, 0.019 mmol, 54.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67 (6H, d, J=6.84 Hz), 1.69-1.74 (1H, m), 1.74-1.92 (1H, m), 1.97-2.06 (3H, m), 2.67-2.98 (1H, m), 3.18-3.51 (1H, m), 3.86-4.18 (2H, m), 3.96 (3 H, s), 4.38-4.76 (1H, m), 4.99 (1H, d, J=49.90 Hz), 5.24 (1 H, spt, J=6.71 Hz), 6.78 (1H, d, J=2.74 Hz), 6.78-6.81 (1H, m), 7.59 (1H, dd, J=8.62, 1.51 Hz), 7.64 (1H, d, J=2.46 Hz), 7.99 (1H, d, J=8.76 Hz), 8.02 (1 H, s); ESIMS found for $C_{23}H_{27}FN_8O_2$ m/z 467.3 (M+1).

688

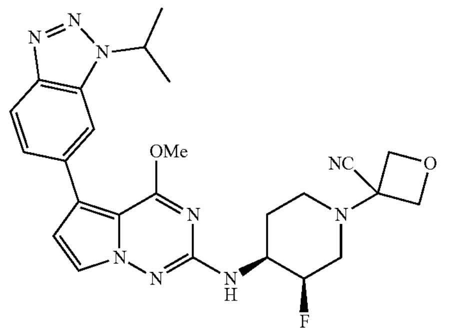


[1256] N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 688.

[1257] Fluffy white solid (11 mg, 0.023 mmol, 24.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67 (6H, d, J=6.57 Hz), 1.70-1.77 (1H, m), 1.88-1.97 (1H, m), 1.99-2.06 (1H, m), 2.16 (1H, dd, J=37.00, 12.59 Hz), 2.71-2.80 (1H, m), 2.95-3.04 (1H, m), 3.49 (1 H, quin, J=6.37 Hz), 3.74-

3.90 (1H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.43, 3.01 Hz), 4.94 (1H, d, J=49.90 Hz), 5.24 (1 H, spt, J=6.75 Hz), 6.69 (1 H, d, J=7.94 Hz), 6.77 (1H, d, J=2.74 Hz), 7.59 (1H, dd, J=8.76, 1.37 Hz), 7.64 (1H, d, J=2.46 Hz), 7.99 (1H, d, J=8.76 Hz), 8.02 (1 H, s); ESIMS found for $C_{24}H_{29}FN_8O_2$ m/z 481.25 (M+1).

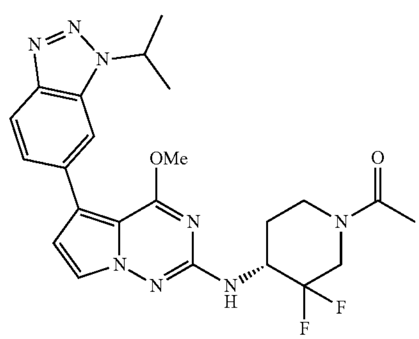
690



[1258] 3-((3R,4S)-3-Fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,14][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile 690.

[1259] Fluffy white solid (10 mg, 0.020 mmol, 21.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67 (6H, d, J=6.84 Hz), 1.82 (1 H, br dd, J=12.32, 3.01 Hz), 2.00 (1 H, qd, J=12.37, 3.70 Hz), 2.09-2.18 (1H, m), 2.26 (1H, dd, J=36.20, 12.32 Hz), 2.78-2.86 (1H, m), 3.00-3.11 (1H, m), 3.79-3.95 (1H, m), 3.97 (3 H, s), 4.52 (1H, d, J=6.84 Hz), 4.65 (1H, d, J=7.12 Hz), 4.76 (2H, t, J=6.84 Hz), 5.04 (1H, d, J=49.35 Hz), 5.24 (1 H, spt, J=6.75 Hz), 6.78 (1H, d, J=2.46 Hz), 6.81 (1H, d, J=7.67 Hz), 7.59 (1H, dd, J=8.76, 1.37 Hz), 7.66 (1H, d, J=2.46 Hz), 7.99 (1H, d, J=8.49 Hz), 8.02 (1 H, s); ESIMS found for $C_{25}H_{28}FN_9O_2$ m/z 506.2 (M+1).

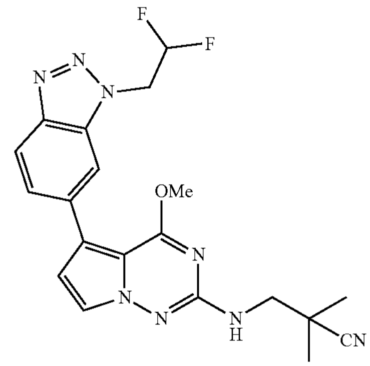
691



[1260] (R)-1-(3,3-Difluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 691.

[1261] Fluffy white solid (11 mg, 0.023 mmol, 67.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67 (6H, d, J=6.84 Hz), 1.72-1.84 (1H, m), 1.85-2.00 (1H, m), 2.02-2.10 (3H, m), 2.95-3.43 (2H, m), 3.64-3.91 (1H, m), 4.10-4.31 (1H, m), 4.46-4.61 (1H, m), 5.24 (1 H, spt, J=6.71 Hz), 6.80 (1H, d, J=2.74 Hz), 7.00 (1H, d, J=9.31 Hz), 7.60 (1H, dd, J=8.76, 1.37 Hz), 7.65 (1H, dd, J=2.46, 1.37 Hz), 7.99 (1H, d, J=8.76 Hz), 8.03 (1 H, s); ESIMS found for $C_{23}H_{26}F_2N_8O_2$ m/z 485.2 (M+1).

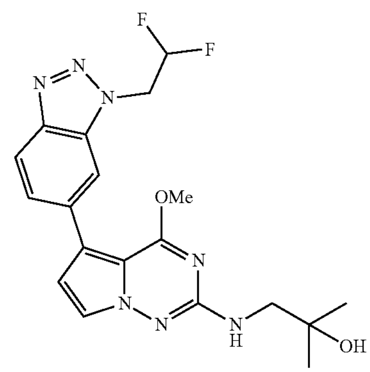
695



[1262] 3-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2,2-dimethylpropanenitrile 695.

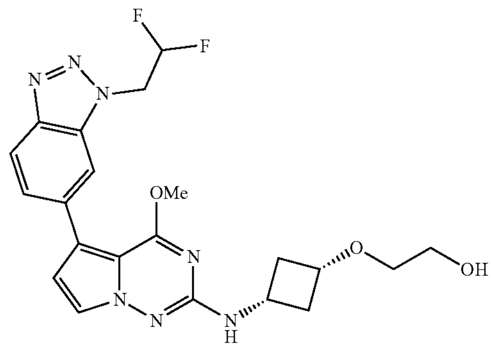
[1263] Off-white solid (30 mg, 0.070 mmol, 35.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (6 H, s), 3.49 (2H, d, J=6.57 Hz), 3.98 (3 H, s), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 7.14 (1H, t, J=6.71 Hz), 7.63-7.66 (1H, m), 7.67 (1H, d, J=2.46 Hz), 8.04 (1H, d, J=8.21 Hz), 8.04 (1 H, s); ESIMS found for $C_{20}H_{20}F_2N_8O$ m/z 427.2 (M+1).

696



[1264] 1-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-methylpropan-2-ol 696.

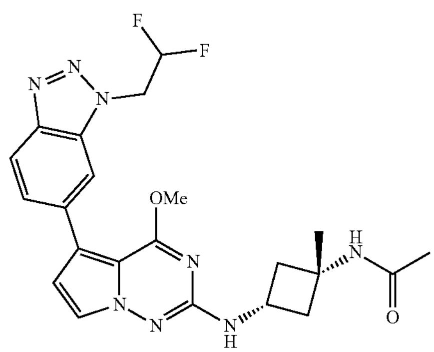
[1265] Off-white solid (6 mg, 0.014 mmol, 15.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.16 (6 H, s), 3.23 (2H, d, J=6.02 Hz), 3.96 (3H, s), 4.56 (1H, s), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.21 (1 H, brt, J=5.89 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.74 (1H, d, J=2.74 Hz), 7.63-7.65 (1H, m), 7.64 (1H, d, J=2.74 Hz), 8.02 (1 H, s), 8.03-8.05 (1H, m); ESIMS found for $C_{1-9}H_{21}F_2N_7O_2$ m/z 418.1 (M+1).



699

[1266] 2-(cis-3-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol 699.

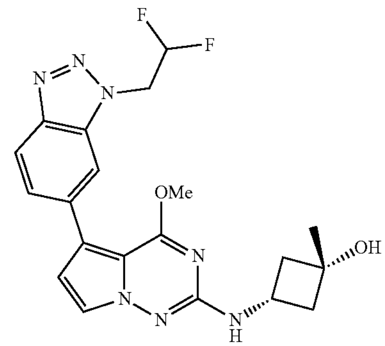
[1267] Fluffy white solid (3.5 mg, 0.008 mmol, 19.9% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.81-1.94 (2H, m), 2.59-2.70 (2H, m), 3.33-3.35 (2H, m), 3.48 (2 H, q, J=5.29 Hz), 3.70-3.75 (1H, m), 3.75-3.82 (1H, m), 3.94 (3 H, s), 4.60 (1H, t, J=5.48 Hz), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.60 (2 H, tt, J=54.30, 3.00 Hz), 6.73 (1H, d, J=2.46 Hz), 7.03 (1H, d, J=7.39 Hz), 7.63 (1H, d, J=2.46 Hz), 7.62-7.65 (1H, m), 8.01-8.04 (2H, m); ESIMS found for $C_{21}H_{23}F_2N_7O_3$ m/z 460.2 (M+1).



702

[1268] N-((1s,3s)-3-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 702.

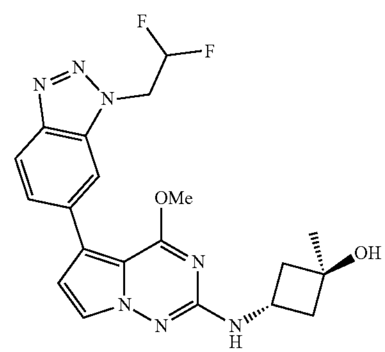
[1269] White solid (16 mg, 0.034 mmol, 27.5% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.12-2.23 (2H, m), 2.42 (2H, ddd, J=9.58, 7.39, 2.74 Hz), 3.93 (3 H, s), 4.03 (1 H, sxt, J=7.78 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.73 (1H, d, J=2.74 Hz), 7.00 (1H, d, J=6.84 Hz), 7.63 (1H, dd, J=8.62, 1.51 Hz), 7.66 (1H, d, J=2.74 Hz), 7.99-8.05 (3H, m); ESIMS found for $C_{22}H_{24}F_2N_8O_2$ m/z 471.2 (M+1).



710

[1270] (1s,3s)-3-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol710.

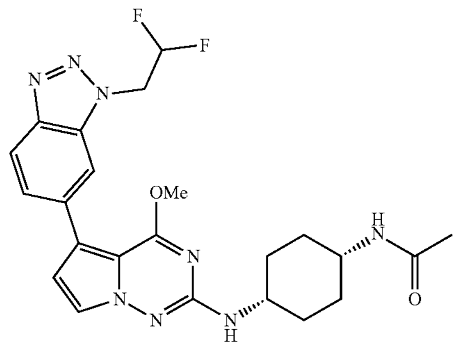
[1271] Fluffy white solid (18 mg, 0.042 mmol, 39.5% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.27 (3 H, s), 2.02 (2 H, td, J=8.90, 2.46 Hz), 2.32-2.40 (2H, m), 3.72 (1 H, dq, J=15.16, 7.72 Hz), 3.93 (3H, s), 4.91 (1H, s), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.72 (1H, d, J=2.74 Hz), 6.94 (1H, d, J=6.57 Hz), 7.63 (1H, dd, J=8.76, 1.64 Hz), 7.65 (1H, d, J=2.74 Hz), 7.99-8.06 (2H, m); ESIMS found for $C_{20}H_{21}F_2N_7O_2$ m/z 430.15



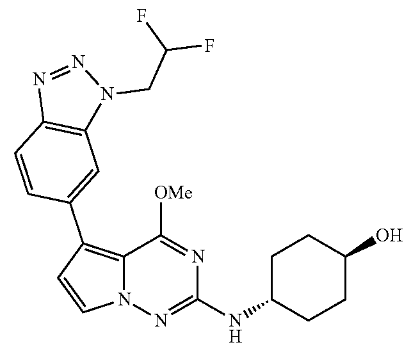
711

[1272] (1r,3r)-3-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol 711.

[1273] Fluffy white solid (20 mg, 0.047 mmol, 43.9% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.28 (3 H, s), 1.95-2.05 (2H, m), 2.27-2.35 (2H, m), 3.93 (3 H, s), 4.26 (1 H, dq, J=14.82, 7.38 Hz), 4.79 (1 H, s), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.72 (1H, d, J=2.74 Hz), 6.95 (1H, d, J=6.84 Hz), 7.63 (1H, dd, J=8.80, 1.35 Hz), 7.64 (1 H, d, J=2.74 Hz), 8.01-8.04 (2H, m); ESIMS found for $C_{20}H_{21}F_2N_7O_2$ m/z 430.2 (M+1).



717



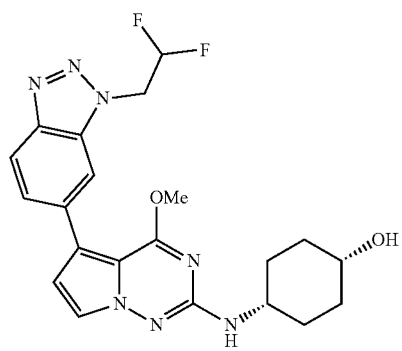
719

[1274] N-(cis-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide 717.

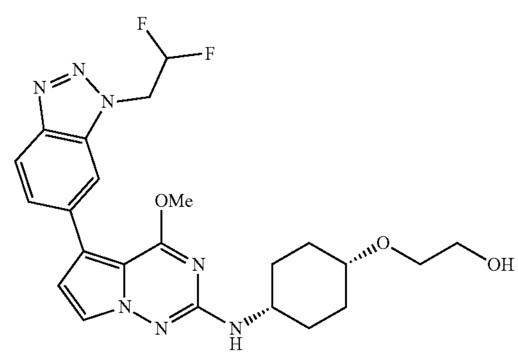
[1275] White solid (5.83 mg, 0.012 mmol). ^{1}H NMR (400 MHz, DMSO-d$_6$) δ ppm 1.50-1.59 (2H, m), 1.60-1.72 (4H, m), 1.73-1.80 (2H, m), 1.81 (3 H, s), 3.68 (2 H, br s), 3.95 (3 H, s), 5.30 (2 H, td, J=15.85, 2.69 Hz), 6.46 (1H, d, J=6.38 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.73 (1H, d, J=2.63 Hz), 7.62-7.66 (2H, m), 7.70 (1H, br d, J=7.00 Hz), 8.00-8.05 (2H, m); ESIMS found for $C_{23}H_{26}F_2N_8O_2$ m/z 485.0 (M+1).

[1278] trans-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol 719.

[1279] Fluffy white solid (7 mg, 0.016 mmol, 11.4% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.17-1.40 (4H, m), 1.79-1.89 (2H, m), 1.92-2.01 (2H, m), 3.35-3.46 (1H, m), 3.49-3.59 (1H, m), 3.93 (3 H, s), 4.55 (1H, d, J=4.38 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.51 (1H, d, J=8.21 Hz), 6.71 (1H, d, J=2.46 Hz), 7.64 (1H, dd, J=8.76, 1.64 Hz), 7.65 (1H, d, J=2.46 Hz), 8.02 (1H, d, J=9.86 Hz), 8.02 (1 H, s); ESIMS found for $C_{21}H_{23}F_2N_7O_2$ m/z 444.2 (M+1).



718



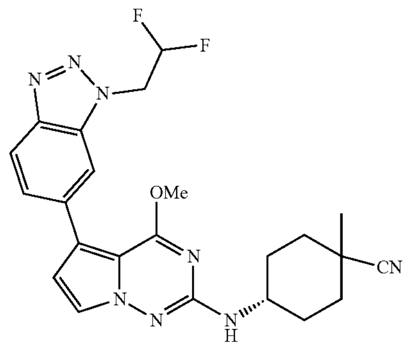
720

[1276] cis-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol 718.

[1277] Fluffy white solid (9 mg, 0.020 mmol, 14.7% yield). ^{1}H NMR (499 MHz, DMSO-d$_6$) δ ppm 1.46-1.54 (2H, m), 1.61-1.69 (4H, m), 1.70-1.79 (2H, m), 3.56-3.67 (1H, m), 3.73 (1H, br d, J=2.19 Hz), 3.94 (3 H, s), 4.34 (1H, d, J=3.01 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.53 (1H, d, J=7.39 Hz), 6.71 (1H, d, J=2.46 Hz), 7.64 (1 H, dd, J=8.50, 1.65 Hz), 7.63 (1H, d, J=2.46 Hz), 8.01-8.05 (2H, m); ESIMS found for $C_{21}H_{23}F_2N_7O_2$ m/z 444.2 (M+1).

[1280] 2-((cis-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol 720.

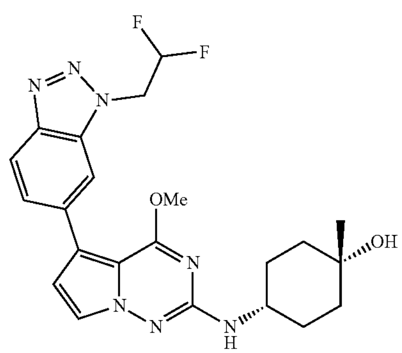
[1281] White solid (7.47 mg, 0.015 mmol). ^{1}H NMR (400 MHz, DMSO-d$_6$) δ ppm 1.46-1.57 (2H, m), 1.62-1.73 (4H, m), 1.78-1.89 (2H, m), 3.40 (2H, t, J=5.50 Hz), 3.48-3.54 (2H, m), 3.58-3.72 (2H, m), 3.94 (3 H, s), 4.52 (1H, t, J=5.50 Hz), 5.30 (2 H, td, J=15.86, 2.51 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.54 (1H, d, J=7.70 Hz), 6.71 (1H, d, J=2.57 Hz), 7.61-7.66 (2H, m), 7.99-8.05 (2H, m); ESIMS found for $C_{23}H_{27}F_2N_7O_3$ m/z 488.2 (M+1).



721

[1282] 4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile 721.

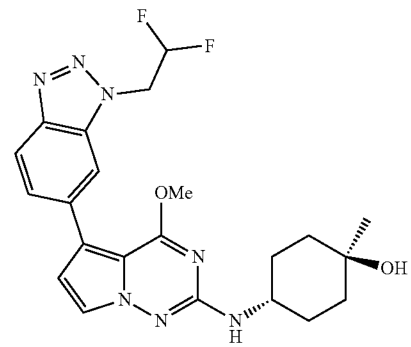
[1283] White solid (15 mg, 0.032 mmol, 51.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.34 (3 H, s), 1.45-1.63 (4H, m), 1.95 (2H, br d, J=10.68 Hz), 1.99-2.08 (2H, m), 3.56-3.63 (1H, m), 3.94 (3 H, s), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.72 (1H, d, J=2.46 Hz), 6.78 (1H, d, J=7.94 Hz), 7.62 (1H, d, J=2.74 Hz), 7.63-7.66 (1H, m), 8.01-8.05 (2H, m); ESIMS found for $C_{23}H_{24}F_2N_8O$ m/z 467.2 (M+1).



724

[1284] (1s,4s)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 724.

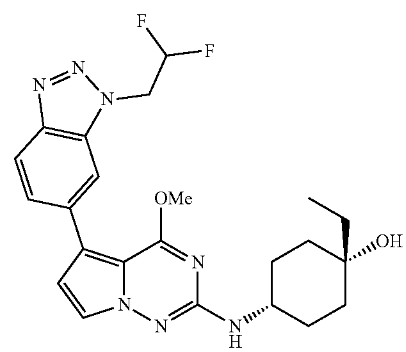
[1285] Fluffy white solid (15 mg, 0.033 mmol, 34.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.37 (2 H, td, J=13.07, 4.52 Hz), 1.58 (2H, br d, J=12.32 Hz), 1.61-1.69 (2H, m), 1.69-1.75 (2H, m), 3.46-3.59 (1H, m), 3.93 (3H, s), 4.00 (1H, s), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.51 (1H, d, J=7.94 Hz), 6.71 (1H, d, J=2.74 Hz), 7.62 (1H, d, J=2.46 Hz), 7.62-7.65 (1H, m), 8.00-8.04 (2H, m); ESIMS found for $C_{22}H_{25}F_2N_7O_2$ m/z 458.2 (M+1).



725

[1286] (1r,4r)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 725.

[1287] Fluffy white solid (9 mg, 0.020 mmol, 55.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.53 (4H, m), 1.56-1.65 (2H, m), 1.81-1.93 (2H, m), 3.60-3.72 (1H, m), 3.94 (3H, s), 4.23 (1H, s), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.50 (1H, d, J=7.94 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.72 (1 H, s), 7.62-7.65 (1H, m), 7.65 (1H, d, J=2.74 Hz), 8.01-8.04 (2H, m); ESIMS found for $C_{22}H_{25}F_2N_7O_2$ m/z 458.2 (M+1).

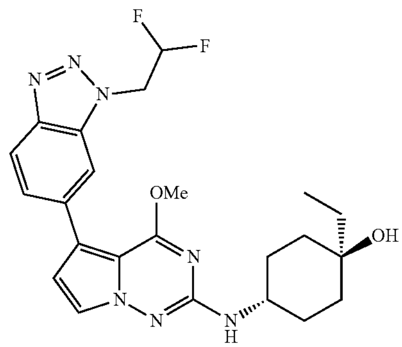


726

[1288] (1s,4s)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol726.

[1289] Fluffy white solid (24 mg, 0.051 mmol, 36.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.85 (3H, t, J=7.53 Hz), 1.30 (2 H, td, J=13.21, 3.97 Hz), 1.37 (2 H, q, J=7.39 Hz), 1.56 (2H, br d, J=12.32 Hz), 1.60-1.70 (2H, m), 1.71-1.77 (2H, m), 3.45-3.59 (1H, m), 3.80 (1H, s), 3.93 (3H, s), 5.30 (2 H, td, J=15.81, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.54 (1H, d, J=7.94 Hz), 6.71 (1H, d, J=2.74 Hz), 7.62 (1H, d, J=2.46 Hz), 7.64 (1H, dd, J=8.76, 1.64 Hz), 8.00-8.04 (2H, m); ESIMS found for $C_{23}H_{27}F_2N_7O_2$ m/z 472.2 (M+1).

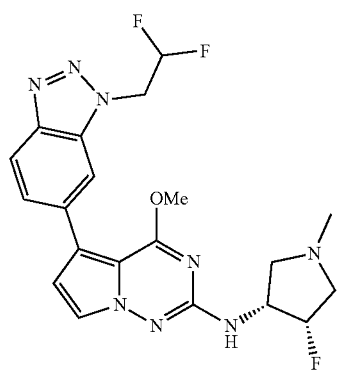
727



[1290] (1r,4r)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol727.

[1291] Fluffy white solid (28 mg, 0.059 mmol, 42.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.83 (3H, t, J=7.39 Hz), 1.32-1.39 (2H, m), 1.40-1.46 (2H, m), 1.47 (2 H, q, J=7.39 Hz), 1.60-1.71 (2H, m), 1.80-1.91 (2H, m), 3.69 (1 H, tt, J=8.08, 4.11 Hz), 3.94 (3H, s), 3.98 (1H, s), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.49 (1H, d, J=7.94 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.72 (1H, d, J=2.46 Hz), 7.64 (1H, dd, J=8.50, 1.65 Hz), 7.65 (1H, d, J=2.74 Hz), 8.00-8.06 (2H, m); ESIMS found for $C_{23}H_{27}F_2N_7O_2$ m/z 472.2 (M+1).

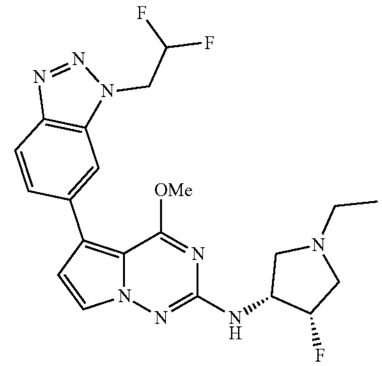
730



[1292] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 730.

[1293] Fluffy white solid (12 mg, 0.027 mmol, 58.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.31 (3 H, s), 2.60 (1H, ddd, J=31.55, 11.64, 2.05 Hz), 2.61 (1 H, br t, J=8.90 Hz), 2.92 (1H, t, J=8.08 Hz), 3.17 (1H, ddd, J=29.35, 11.50, 4.93 Hz), 3.96 (3 H, s), 4.20-4.36 (1H, m), 5.14-5.28 (1H, m), 5.25-5.35 (2H, m), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.78 (1H, d, J=7.67 Hz), 7.64 (1H, dd, J=8.90, 0.96 Hz), 7.67 (1H, d, J=2.74 Hz), 8.04 (1H, d, J=8.21 Hz), 8.03 (1 H, s); ESIMS found for $C_{20}H_{21}F_3N_8O$ m/z 447.2 (M+1).

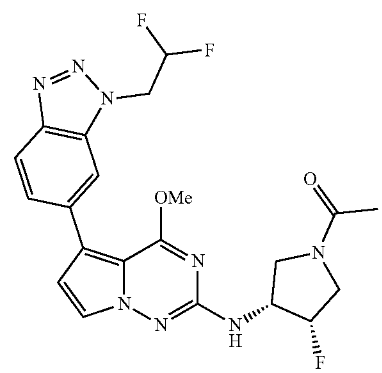
732



[1294] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-1-ethyl-4-fluoropyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 732.

[1295] Fluffy white solid (2 mg, 0.004 mmol, 6.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.03 (3H, t, J=7.26 Hz), 2.47-2.54 (2H, m), 2.59-2.70 (2H, m), 2.97 (1H, t, J=8.21 Hz), 3.18 (1H, ddd, J=30.95, 11.91, 4.79 Hz), 3.96 (3 H, s), 4.19-4.33 (1H, m), 5.13-5.27 (1H, m), 5.27-5.35 (2H, m), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.75-6.77 (1H, m), 6.76 (1 H, d, J=2.74 Hz), 7.63-7.66 (1H, m), 7.67 (1H, d, J=2.46 Hz), 8.04 (1H, d, J=7.94 Hz), 8.03 (1 H, s); ESIMS found for $C_{21}H_{23}F_3N_8O$ m/z 461.2 (M+1).

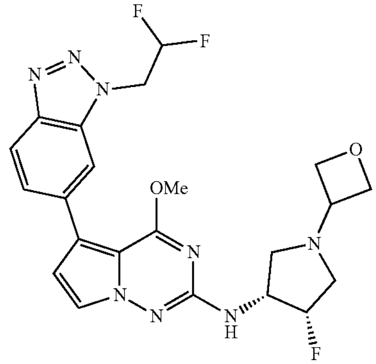
734



[1296] 1-((3R,4S)-3-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one 734.

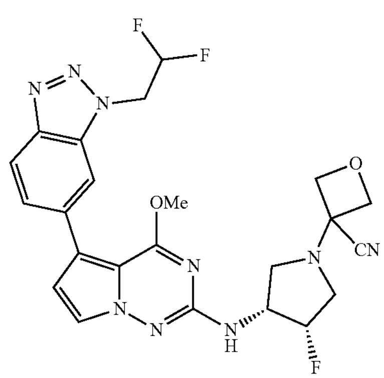
[1297] Fluffy white solid (19 mg, 0.040 mmol, 69.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.92-2.02 (3H, m), 3.47-3.75 (2H, m), 3.78-3.96 (2H, m), 3.97 (3H, d, J=1.37 Hz), 4.30-4.59 (1H, m), 5.25-5.48 (3H, m), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.78 (1H, t, J=2.46 Hz), 7.10 (1H, dd, J=7.12, 5.20 Hz), 7.63-7.67 (1H, m), 7.68 (1H, dd, J=3.97, 2.60 Hz), 8.03-8.06 (2H, m); ESIMS found for $C_{21}H_{21}F_3N_8O_2$ m/z 475.2 (M+1).

739



[1298] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 739.

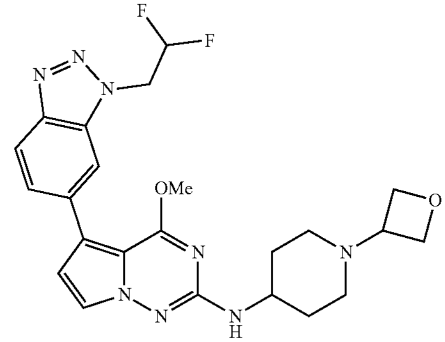
[1299] Fluffy white solid (14 mg, 0.029 mmol, 27.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.69 (1H, t, J=9.17 Hz), 2.77 (1H, ddd, J=30.20, 12.10, 1.40 Hz), 3.02 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=32.90, 12.05, 4.38 Hz), 3.79 (1 H, quin, J=6.16 Hz), 3.96 (3 H, s), 4.23-4.37 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 5.18-5.32 (1H, m), 5.31 (2 H, td, J=15.95, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.77 (1H, d, J=2.46 Hz), 6.84 (1H, d, J=7.67 Hz), 7.63-7.66 (1H, m), 7.67 (1H, d, J=2.46 Hz), 8.04 (1H, d, J=8.21 Hz), 8.04 (1 H, s); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).



[1300] 3-((3R,4S)-3-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)oxetane-3-carbonitrile 741.

[1301] Fluffy white solid (14 mg, 0.027 mmol, 26.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.82 (1H, t, J=9.05 Hz), 2.88 (1H, ddd, J=29.60, 11.77, 0.82 Hz), 3.09 (1H, t, J=8.35 Hz), 3.26 (1H, ddd, J=34.05, 12.05, 4.38 Hz), 3.97 (3 H, s), 4.32-4.46 (1H, m), 4.58 (1 H, d, J=6.84 Hz), 4.62 (1H, d, J=6.84 Hz), 4.81 (2H, d, J=6.84 Hz), 5.26-5.41 (3H, m), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.78 (1H, d, J=2.46 Hz), 7.02 (1H, d, J=7.39 Hz), 7.63-7.67 (1H, m), 7.69 (1H, d, J=2.74 Hz), 8.04 (1H, br d, J=8.21 Hz), 8.04 (1 H, s); ESIMS found for $C_{23}H_{22}F_3N_902$ m/z 514.2 (M+1).

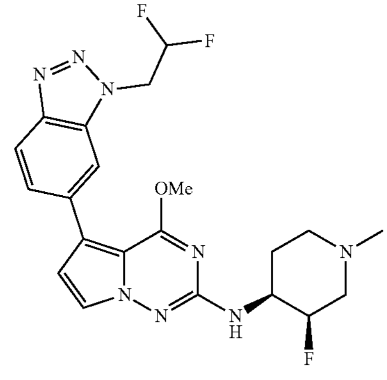
750



[1302] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 750.

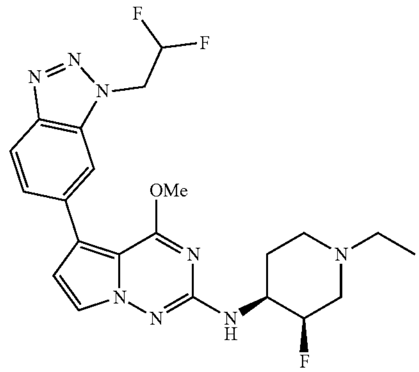
[1303] Fluffy white solid (4 mg, 0.008 mmol, 6.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.54 (2 H, qd, J=11.64, 3.42 Hz), 1.86 (2 H, br t, J=11.50 Hz), 1.92 (2H, br d, J=11.50 Hz), 2.69 (2H, br d, J=11.50 Hz), 3.35-3.42 (1H, m), 3.54-3.66 (1H, m), 3.94 (3 H, s), 4.42 (2H, t, J=6.02 Hz), 4.50-4.57 (2H, m), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.65 (1H, d, J=7.94 Hz), 6.72 (1H, d, J=2.46 Hz), 7.64 (1 H, br dd, J=8.50, 1.65 Hz), 7.64 (1H, d, J=2.74 Hz), 8.03 (1H, d, J=10.40 Hz), 8.02 (1 H, s); ESIMS found for $C_{23}H_{26}F_2N_8O_2$ m/z 485.2 (M+1).

754

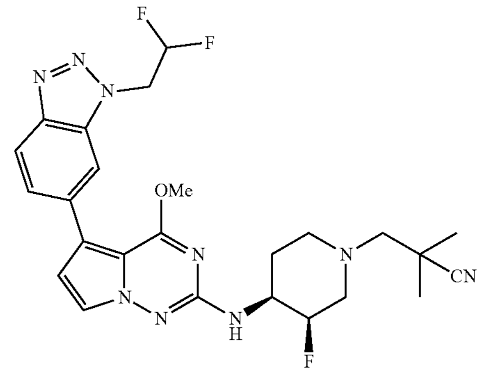


[1304] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 754.

[1305] Fluffy white solid (3 mg, 0.007 mmol, 19.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.64-1.74 (1H, m), 1.93 (1 H, qd, J=12.32, 3.56 Hz), 2.02-2.10 (1H, m), 2.18 (1H, dd, J=37.85, 12.32 Hz), 2.19 (3 H, s), 2.80 (1H, br d, J=11.23 Hz), 3.00-3.10 (1H, m), 3.69-3.85 (1H, m), 3.95 (3 H, s), 4.92 (1H, d, J=50.20 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.64 (1H, d, J=7.67 Hz), 6.75 (1H, d, J=2.74 Hz), 7.63-7.66 (1H, m), 7.65 (1H, d, J=2.46 Hz), 8.01-8.05 (2H, m); ESIMS found for $C_{21}H_{23}F_3N_8O$ m/z 461.2 (M+1).



755



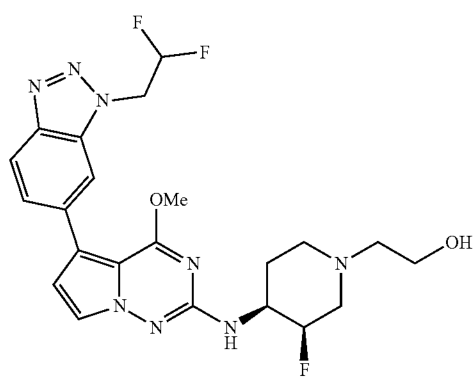
757

[1306] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-1-ethyl-3-fluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 755.

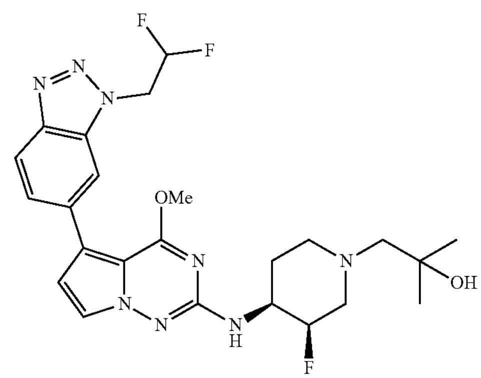
[1307] Fluffy white solid (2.6 mg, 0.006 mmol, 12.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.00 (3H, t, J=7.12 Hz), 1.66-1.75 (1H, m), 1.90 (1 H, qd, J=12.23, 3.56 Hz), 2.06 (1 H, brt, J=11.09 Hz), 2.19 (1H, dd, J=37.85, 12.32 Hz), 2.37 (2 H, q, J=7.30 Hz), 2.89 (1 H, br d, J=10.95 Hz), 3.08-3.17 (1H, m), 3.71-3.86 (1H, m), 3.95 (3 H, s), 4.92 (1H, d, J=49.90 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.63 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.74 Hz), 7.63-7.65 (1H, m), 7.65 (1H, d, J=2.74 Hz), 8.01-8.05 (2H, m); ESIMS found for $C_{22}H_{25}F_3N_8O$ m/z 475.2 (M+1).

[1310] 3-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2,2-dimethylpropanenitrile 757.

[1311] Fluffy white solid (2 mg, 0.004 mmol, 20.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.16 (6 H, s), 1.65-1.74 (1H, m), 1.86-1.98 (1H, m), 2.02-2.10 (1H, m), 2.13-2.25 (1H, m), 2.19 (2 H, s), 2.75-2.83 (1H, m), 2.99-3.08 (1H, m), 3.70-3.86 (1H, m), 4.46 (3 H, s), 4.91 (1H, d, J=50.20 Hz), 5.29 (2 H, td, J=15.67, 3.15 Hz), 6.59 (1 H, tt, J=54.30, 3.00 Hz), 6.70 (1H, d, J=7.67 Hz), 6.74 (1H, d, J=2.46 Hz), 7.70 (1H, d, J=2.74 Hz), 7.71 (1H, dd, J=8.50, 1.65 Hz), 7.98 (1 H, s), 8.00 (1H, d, J=8.49 Hz); ESIMS found for $C_{25}H_{28}F_3N_90$ m/z 528.3 (M+1).



756



758

[1308] 2-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-ol 756.

[1309] Fluffy white solid (8 mg, 0.016 mmol, 37.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.63-1.72 (1H, m), 1.85-1.97 (1H, m), 2.14-2.22 (1H, m), 2.32 (1H, dd, J=37.55, 12.59 Hz), 2.44 (2H, t, J=6.30 Hz), 2.91 (1H, br d, J=11.77 Hz), 3.16 (1 H, br dd, J=11.23, 10.13 Hz), 3.50 (2H, t, J=6.30 Hz), 3.71-3.88 (1H, m), 3.95 (3 H, s), 4.42 (1 H, br s), 4.90 (1H, d, J=50.15 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (2 H, tt, J=54.30, 3.00 Hz), 6.63 (1H, d, J=7.94 Hz), 6.74 (1H, d, J=2.74 Hz), 7.62-7.66 (2H, m), 8.01-8.05 (2H, m); ESIMS found for $C_{22}H_{25}F_3N_8O_2$ m/z 491.2 (M+1).

[1312] 1-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2-methylpropan-2-ol 758.

[1313] Fluffy white solid (2 mg, 0.004 mmol, 26.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.09 (6 H, s), 1.60-1.69 (1H, m), 1.95 (1 H, qd, J=12.46, 3.70 Hz), 2.26-2.32 (1H, m), 2.33-2.46 (1H, m), 2.98 (1H, br d, J=10.13 Hz), 3.25-3.29 (1H, m), 3.33 (2 H, s), 3.70-3.85 (1H, m), 3.95 (3 H, s), 4.08 (1 H, br s), 4.86 (1H, d, J=49.65 Hz), 5.30 (2 H, td, J=16.02, 2.74 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.61 (1H, d, J=7.94 Hz), 6.74 (1H, d, J=2.46 Hz), 7.63-7.66 (1H, m), 7.65 (1H, d, J=2.46 Hz), 8.01-8.05 (2H, m); ESIMS found for $C_{24}H_{29}F_3N_8O_2$ m/z 519.2 (M+1).

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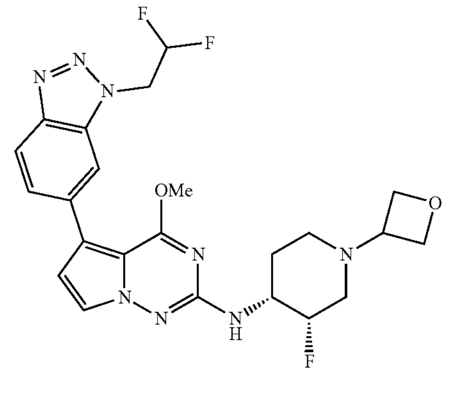
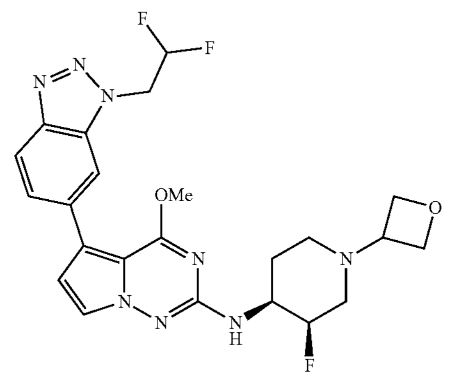


[1314] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 761.

[1315] Fluffy white solid (11 mg, 0.022 mmol, 32.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68-1.78 (1H, m), 1.92 (1 H, qd, J=12.18, 3.42 Hz), 1.99-2.06 (1H, m), 2.16 (1H, dd, J=37.05, 12.59 Hz), 2.76 (1H, br d, J=9.31 Hz), 2.94-3.05 (1H, m), 3.50 (1 H, quin, J=6.30 Hz), 3.74-3.91 (1H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.94 (1H, d, J=49.65 Hz), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.70 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.74 Hz), 7.64 (1H, dd, J=8.76, 1.64 Hz), 7.64 (1H, d, J=2.74 Hz), 8.01-8.05 (2H, m); ESIMS found for $C_{23}H_{25}F_3N_8O_2$ m/z 503.2 (M+1).

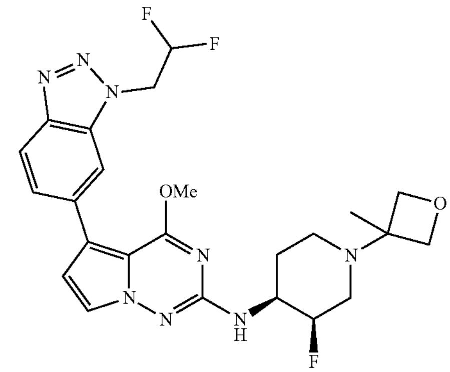
762



[1316] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 762.

[1317] Fluffy white solid (12 mg, 0.024 mmol, 18.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68-1.78 (1H, m), 1.92 (1 H, qd, J=12.09, 3.42 Hz), 1.99-2.06 (1H, m), 2.16 (1H, dd, J=37.05, 12.59 Hz), 2.76 (1H, br d, J=9.86 Hz), 2.94-3.04 (1H, m), 3.50 (1 H, quin, J=6.43 Hz), 3.75-3.91 (1H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.94 (1H, d, J=49.90 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.70 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.74 Hz), 7.64 (1H, dd, J=8.50, 1.35 Hz), 7.64 (1H, d, J=2.74 Hz), 8.01-8.05 (2H, m); ESIMS found for $C_{23}H_{25}F_3N_8O_2$ m/z 503.2 (M+1).

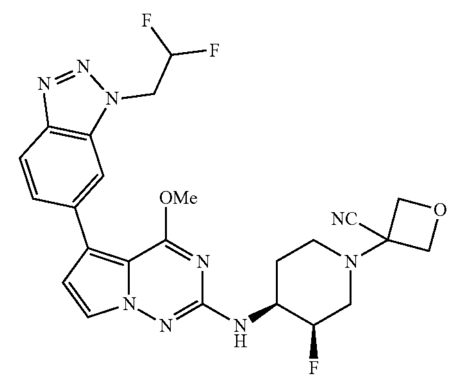
764



[1318] 5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 764.

[1319] Fluffy white solid (1 mg, 0.002 mmol, 5.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.29 (3 H, s), 1.69-1.78 (1H, m), 1.91 (1 H, qd, J=11.96, 3.83 Hz), 2.20 (1 H, br t, J=10.81 Hz), 2.35 (1H, dd, J=35.35, 11.77 Hz), 2.54-2.59 (1H, m), 2.75-2.84 (1H, m), 3.74-3.90 (1H, m), 3.96 (3 H, s), 4.13 (2H, dd, J=7.26, 5.61 Hz), 4.34 (1H, d, J=5.48 Hz), 4.42 (1H, d, J=5.75 Hz), 4.93 (1H, d, J=49.90 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.70 (1H, d, J=7.94 Hz), 6.75 (1H, d, J=2.74 Hz), 7.64 (1H, dd, J=8.80, 1.35 Hz), 7.64 (1H, d, J=2.74 Hz), 8.01-8.05 (2H, m); ESIMS found for $C_{24}H_{27}F_3N_8O_2$ m/z 517.25 (M+1).

769

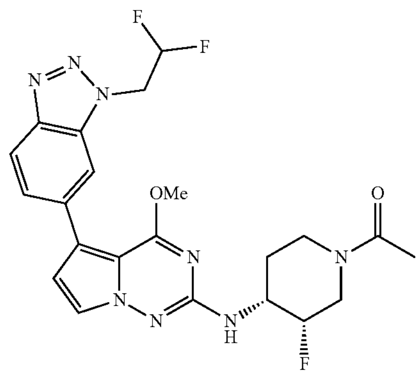


[1320] 3-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile 769.

[1321] Fluffy white solid (14 mg, 0.027 mmol, 20.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.82 (1 H, br dd, J=13.00, 3.15 Hz), 2.00 (1 H, qd, J=12.32, 3.83 Hz), 2.10-2.17 (1H, m), 2.26 (1H, dd, J=36.20, 12.05 Hz), 2.77-2.86 (1H, m), 3.00-3.11 (1H, m), 3.79-3.94 (1H, m), 3.97 (3 H, s), 4.52 (1H, d, J=7.12 Hz), 4.65 (1H, d, J=7.12

Hz), 4.76 (2H, t, J=6.84 Hz), 5.04 (1H, d, J=49.90 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.46 Hz), 6.82 (1H, d, J=7.67 Hz), 7.63-7.66 (1H, m), 7.67 (1H, d, J=2.46 Hz), 8.02-8.05 (2H, m); ESIMS found for $C_{24}H_{24}F_3N_9O_2$ m/z 528.2 (M+1).

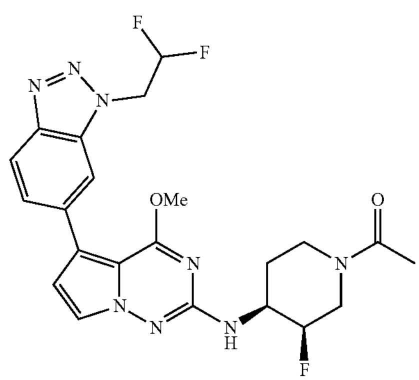
770



[1322] 1-((3S,4R)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one 770.

[1323] Fluffy white solid (8 mg, 0.016 mmol, 32.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.65-1.74 (1H, m), 1.75-1.92 (1H, m), 1.98-2.06 (3H, m), 2.67-2.98 (1H, m), 3.17-3.26 (1H, m), 3.87-4.04 (1H, m), 3.96 (3 H, s), 4.04-4.17 (1H, m), 4.42-4.74 (1H, m), 4.99 (1H, d, J=48.80 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.61 (2 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.80 (1H, dd, J=7.80, 2.60 Hz), 7.63-7.66 (1H, m), 7.65 (1H, d, J=2.46 Hz), 8.02-8.05 (2H, m); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).

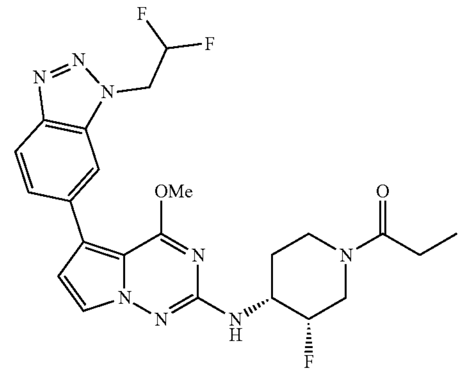
771



[1324] 1-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one 771.

[1325] Fluffy white solid (7 mg, 0.014 mmol, 53.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.64-1.90 (2H, m), 1.97-2.08 (3H, m), 2.66-3.28 (1H, m), 2.82-3.50 (1H, m), 3.86-4.02 (1H, m), 3.96 (3 H, s), 4.02-4.17 (1H, m), 4.41-4.75 (1H, m), 5.00 (1H, d, J=49.90 Hz), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.81 (1H, dd, J=7.80, 3.42 Hz), 7.63-7.66 (1H, m), 7.65 (1H, d, J=2.74 Hz), 8.02-8.05 (2 H, m); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).

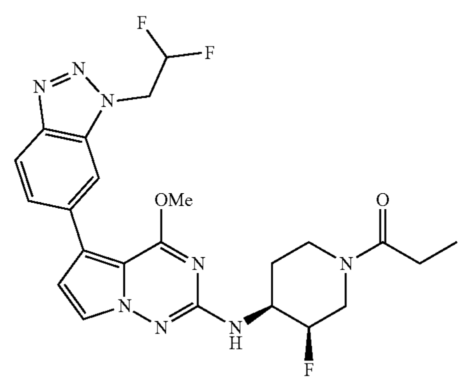
772



[1326] 1-((3S,4R)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,14][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)propan-1-one 772.

[1327] Fluffy white solid (7 mg, 0.014 mmol, 27.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.00 (3H, t, J=7.39 Hz), 1.66-1.89 (2H, m), 2.26-2.41 (2H, m), 2.67-2.98 (1H, m), 3.14-3.23 (1H, m), 3.90-4.05 (1H, m), 3.96 (3 H, s), 4.05-4.22 (1H, m), 4.43-4.79 (1H, m), 4.99 (1H, d, J=49.65 Hz), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.61 (2 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.46 Hz), 6.79 (1H, d, J=7.67 Hz), 7.64 (1H, dd, J=6.30, 1.35 Hz), 7.65 (1 H, s), 8.01-8.06 (2H, m); ESIMS found for $C_{23}H_{25}F_3N_8O_2$ m/z 503.2 (M+1).

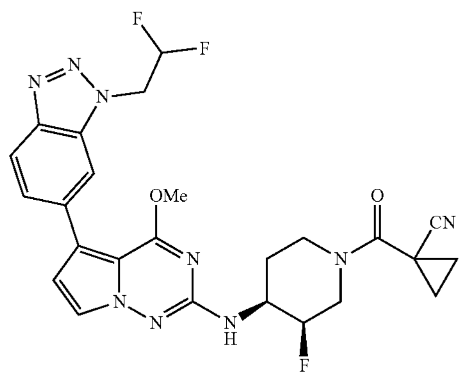
773



[1328] 1-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)propan-1-one 773.

[1329] Fluffy white solid (9.1 mg, 0.018 mmol, 46.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.00 (3H, t, J=7.39 Hz), 1.66-1.90 (2H, m), 2.24-2.42 (2H, m), 2.69-3.00 (1H, m), 3.12-3.24 (1H, m), 3.91-4.00 (1H, m), 3.96 (3 H, s), 4.04-4.22 (1H, m), 4.43-4.78 (1H, m), 4.99 (1H, d, J=49.35 Hz), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.79 (1H, d, J=7.94 Hz), 7.63-7.66 (2H, m), 8.02-8.05 (2H, m); ESIMS found for $C_{23}H_{25}F_3N_8O_2$ m/z 503.2 (M+1).

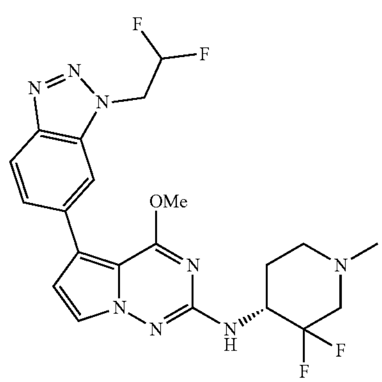
776



[1330] 1-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidine-1-carbonyl)cyclopropane-1-carbonitrile 776.

[1331] Beige solid (4 mg, 0.007 mmol, 23.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.23 (2 H, s), 1.35-1.52 (1H, m), 1.52-1.65 (2H, m), 1.63-1.75 (1H, m), 1.75-1.94 (1 H, in), 1.94-2.12 (1H, m), 3.96 (3 H, s), 4.05-4.17 (1H, m), 4.26-4.38 (1H, m), 4.51-4.62 (1 H, m), 5.09 (1H, d, J=48.55 Hz), 5.30 (2 H, td, J=15.81, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.88 (1 H, br s), 7.63-7.67 (2H, m), 8.02-8.06 (2H, m); ESIMS found for $C_{25}H_{24}F_3N_9O_2$ m/z 540.2 (M+1).

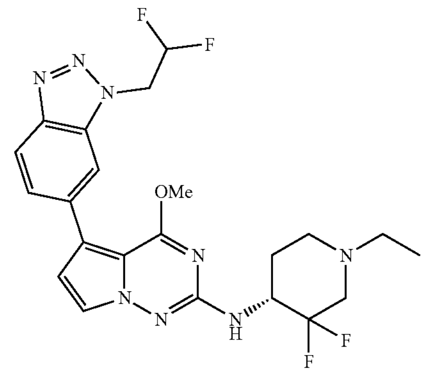
777



[1332] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 777.

[1333] Off-white solid (7 mg, 0.015 mmol, 31.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.75-1.89 (2H, m), 2.18 (1 H, td, J=11.16, 2.87 Hz), 2.26 (3 H, s), 2.38 (1H, ddd, J=27.15, 11.50, 1.40 Hz), 2.79 (1H, br d, J=11.77 Hz), 2.99-3.12 (1H, m), 3.97 (3 H, s), 4.17-4.32 (1H, m), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.46 Hz), 6.84 (1H, d, J=9.31 Hz), 7.63-7.66 (1H, m), 7.66 (1H, d, J=2.46 Hz), 8.03 (1 H, s), 8.04 (1H, d, J=6.57 Hz); ESIMS found for $C_{21}H_{22}F_4N_8O$ m/z 479.2 (M+1).

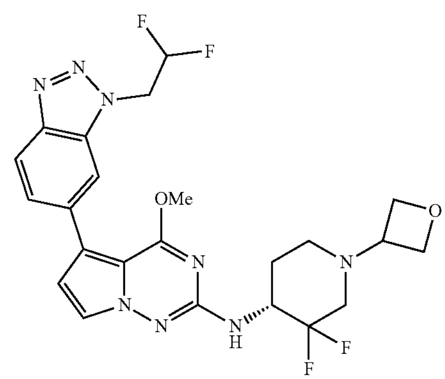
780



[1334] (R)-5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-(1-ethyl-3,3-difluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 780.

[1335] Off-white solid (8 mg, 0.016 mmol, 36.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.01 (3H, t, J=7.26 Hz), 1.73-1.83 (1H, m), 1.84-1.90 (1H, m), 2.12-2.24 (1H, m), 2.34-2.43 (1H, m), 2.45 (2 H, q, J=7.12 Hz), 2.88 (1H, br d, J=12.05 Hz), 3.05-3.17 (1H, m), 3.97 (3 H, s), 4.19-4.35 (1H, m), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.85 (1H, d, J=9.58 Hz), 7.63-7.66 (1H, m), 7.66 (1H, d, J=2.74 Hz), 8.03 (1 H, s), 8.04 (1H, d, J=6.55 Hz); ESIMS found for $C_{22}H_{24}F_4N_8O$ m/z 493.25 (M+1).

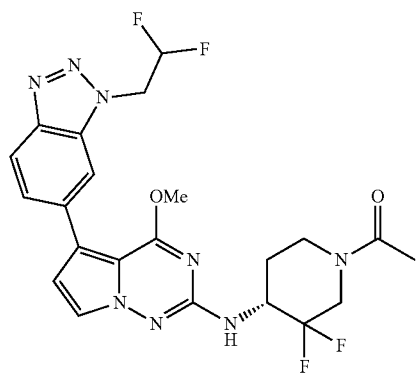
785



[1336] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 785.

[1337] Off-white solid (8 mg, 0.015 mmol, 22.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.77-1.86 (1H, m), 1.86-1.93 (1H, m), 2.12-2.22 (1H, m), 2.41 (1H, ddd, J=26.60, 11.50, 1.65 Hz), 2.76 (1H, br d, J=11.50 Hz), 2.95-3.08 (1H, m), 3.60 (1 H, quin, J=6.30 Hz), 3.97 (3 H, s), 4.24-4.37 (1H, m), 4.44 (2 H, dt, J=15.06, 6.16 Hz), 4.55 (2 H, td, J=6.57, 3.56 Hz), 5.30 (2 H, td, J=15.88, 2.74 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.46 Hz), 6.91 (1H, d, J=9.31 Hz), 7.63-7.66 (1H, m), 7.66 (1H, d, J=2.46 Hz), 8.03 (1 H, s), 8.04 (1H, d, J=6.30 Hz); ESIMS found for $C_{23}H_{24}F_4N_8O_2$ m/z 521.2 (M+1).

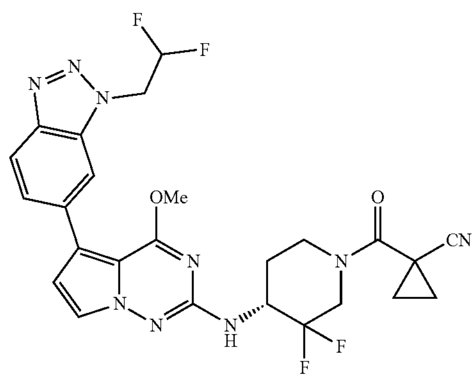
788



[1338] (R)-1-(4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one 788.

[1339] Fluffy white solid (20 mg, 0.040 mmol, 79.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.58-1.84 (1H, m), 1.85-2.00 (1H, m), 2.02-2.10 (3H, m), 3.32 (1 H, s), 3.39-3.78(1 H,m), 3.84-4.30 (1H, m), 3.98(3 H, s), 4.10-4.61 (2H, m), 5.30 (2H,td,J=15.81, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.77 (1H, d, J=2.74 Hz), 7.01 (1H, d, J=9.31 Hz), 7.63-7.67 (2H, m), 8.02-8.06 (2H, m); ESIMS found for $C_{22}H_{22}F_4N_8O_2$ m/z 507.2 (M+1).

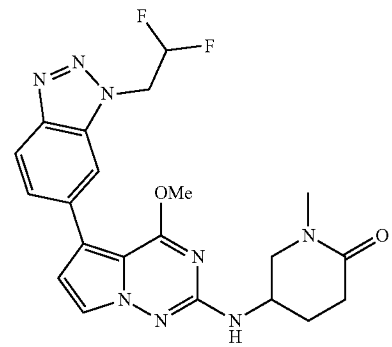
791



[1340] (R)-1-(4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidine-1-carbonyl)cyclopropane-1-carbonitrile 791.

[1341] Off-white solid (3 mg, 0.005 mmol, 13.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36-1.52 (2H, m), 1.61-1.81 (3H, m), 1.86-2.08 (2H, m), 3.04-3.11 (1H, m), 3.98 (3 H, s), 4.18-4.31 (1H, m), 4.38-4.49 (1H, m), 4.56-4.70 (1H, m), 5.30 (2 H, td, J=15.74, 2.74 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.78 (1H, d, J=2.46 Hz), 7.08 (1H, br d, J=9.31 Hz), 7.64-7.66 (1H, m), 7.67 (1H, d, J=2.74 Hz), 8.03 (1 H, s), 8.04-8.06 (1H, m); ESIMS found for $C_{25}H_{23}F_4N_9O_2$ m/z 558.2 (M+1).

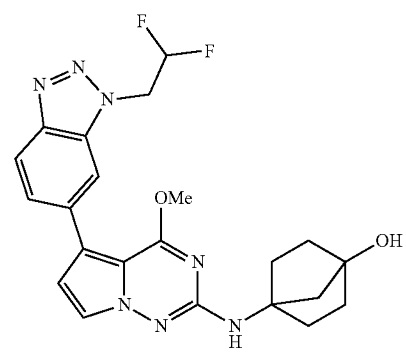
793



[1342] 5-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one 793.

[1343] White solid (11 mg, 0.024 mmol, 22.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.87-1.96 (1H, m), 1.97-2.04 (1H, m), 2.27-2.35 (1H, m), 2.36-2.44 (1H, m), 2.81 (3 H, s), 3.26 (1H, dd, J=11.77, 7.67 Hz), 3.57 (1H, dd, J=11.91, 4.52 Hz), 3.96 (3 H, s), 4.05-4.15 (1H, m), 5.30 (2 H, td, J=15.95, 2.60 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.46 Hz), 6.94 (1H, d, J=7.12 Hz), 7.63-7.66 (1H, m), 7.68 (1H, d, J=2.74 Hz), 8.02-8.05 (2 H, m); ESIMS found for $C_{21}H_{22}F_2N_8O_2$ m/z 457.2 (M+1).

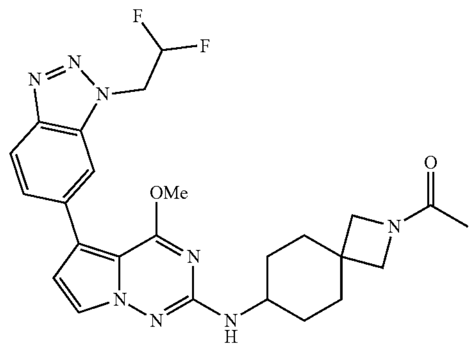
798



[1344] 4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol 798.

[1345] Fluffy white solid (2.4 mg, 0.005 mmol, 3.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.52-1.63 (2H, m), 1.65-1.77 (2H, m), 1.86 (2 H, s), 1.87-1.93 (2H, m), 1.99-2.09 (2H, m), 3.93 (3H, s), 4.88 (1H, s), 5.30 (2 H, td, J=16.02, 3.01 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.73 (1H, d, J=2.74 Hz), 6.75 (1 H, s), 7.61 (1H, d, J=2.46 Hz), 7.64 (1H, dd, J=8.62, 1.51 Hz), 8.01-8.04 (2H, m); ESIMS found for $C_{22}H_{23}F_2N_7O_2$ m/z 456.2 (M+1).

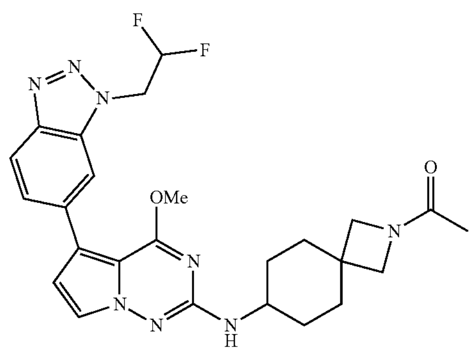
799



[1346] 1-(7-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one 799.

[1347] White solid (8 mg, 0.016 mmol, 8.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.27-1.41 (2H, m), 1.50-1.61 (2H, m), 1.73-1.78 (3H, m), 1.82-1.94 (4H, m), 3.45-3.54 (2H, m), 3.55-3.64 (1H, m), 3.72-3.82 (2H, m), 3.93 (3H, d, J=1.10 Hz), 5.30 (2 H, td, J=15.74, 2.46 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.53 (1H, dd, J=16.43, 7.94 Hz), 6.72 (1H, d, J=2.46 Hz), 7.62-7.65 (2H, m), 8.00-8.05 (2H, m); ESIMS found for $C_{25}H_{28}F_2N_8O_2$ m/z 511.2

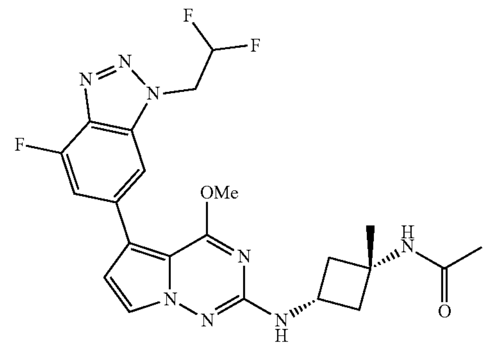
799



[1348] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 801.

[1349] Colorless semi-solid (2 mg, 0.004 mmol, 4.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.41-1.49 (1H, m), 1.53 (2 H, td, J=12.94, 3.42 Hz), 1.83-1.92 (2H, m), 1.96-2.03 (1H, m), 2.07 (2H, br d, J=12.87 Hz), 3.49-3.61 (1H, m), 3.93 (3H, s), 4.24 (2H, s), 4.32 (2 H, s), 5.30 (2 H, td, J=15.88, 3.01 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.51 (1H, d, J=8.21 Hz), 6.72 (1H, d, J=2.74 Hz), 7.63 (1H, dd, J=8.80, 1.35 Hz), 7.64 (1H, d, J=2.74 Hz), 8.02 (1 H, d, J=9.86 Hz), 8.02 (1 H, s); ESIMS found for $C_{23}H_{25}F_2N_7O_2$ m/z 470.2 (M+1).

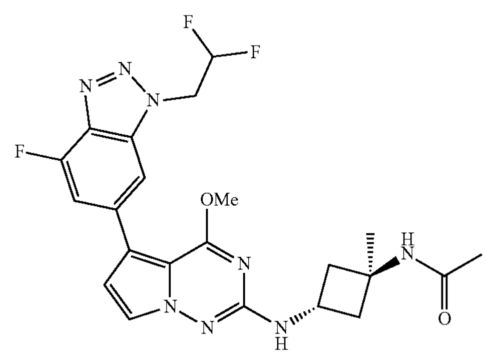
805



[1350] N-((1s,3s)-3-((5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 805.

[1351] White solid (16 mg, 0.033 mmol, 26.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.12-2.21 (2H, m), 2.42 (2H, ddd, J=9.65, 7.32, 2.46 Hz), 3.96 (3 H, s), 4.03 (1 H, sxt, J=7.72 Hz), 5.34 (2 H, td, J=15.88, 2.74 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.78 (1H, d, J=2.46 Hz), 7.05 (1H, d, J=6.84 Hz), 7.50 (1H, dd, J=12.18, 0.96 Hz), 7.66 (1H, d, J=2.46 Hz), 7.90 (1 H, s), 8.02 (1 H, s); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).

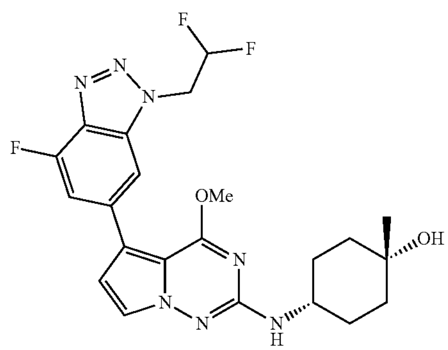
806



[1352] N-((1r,3r)-3-((5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 806.

[1353] White solid (5 mg, 0.010 mmol, 13.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.81 (3H, s), 1.91-2.00 (2H, m), 2.59-2.68 (2H, m), 3.95 (3 H, s), 4.19 (1 H, sxt, J=7.78 Hz), 5.34 (2 H, td, J=15.88, 2.74 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.78 (1H, d, J=2.74 Hz), 7.05 (1H, d, J=7.39 Hz), 7.50 (1H, dd, J=12.18, 0.96 Hz), 7.64 (1H, d, J=2.46 Hz), 7.89 (1 H, s), 7.93 (1 H, s); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).

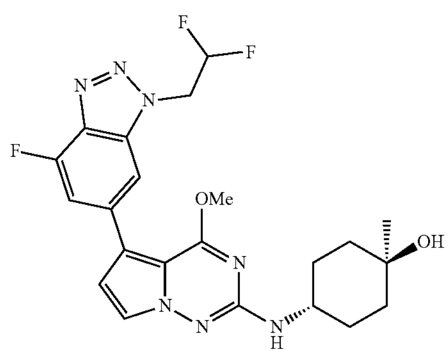
810



[1354] (1s,4s)-4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 810.

[1355] White solid (15 mg, 0.032 mmol, 32.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.37 (2 H, td, J=13.00, 4.38 Hz), 1.53-1.62 (2H, m), 1.63-1.74 (4H, m), 3.47-3.57 (1H, m), 3.96 (3H, s), 4.00 (1H, s), 5.34 (2 H, td, J=15.88, 2.74 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.56 (1H, d, J=8.21 Hz), 6.76 (1H, d, J=2.46 Hz), 7.50 (1H, dd, J=12.05, 1.10 Hz), 7.63 (1H, d, J=2.46 Hz), 7.90 (1 H, s); ESIMS found for $C_{22}H_{24}F_3N_7O_2$ m/z 476.2 (M+1).

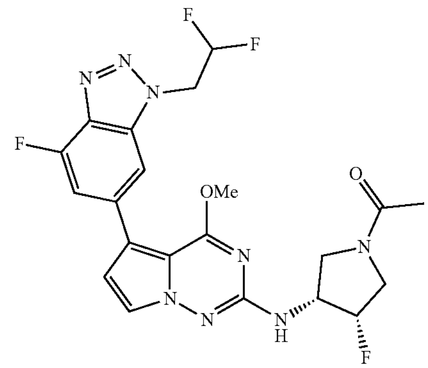
811



[1356] (1r,4r)-4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 811.

[1357] Fluffy white solid (14 mg, 0.029 mmol, 61.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.52 (4H, m), 1.56-1.64 (2H, m), 1.83-1.92 (2H, m), 3.64 (1 H, br dd, J=8.62, 3.97 Hz), 3.96 (3H, s), 4.23 (1H, s), 5.34 (2 H, td, J=15.95, 2.60 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.54 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.46 Hz), 7.50 (1H, dd, J=12.05, 0.82 Hz), 7.66 (1H, d, J=2.74 Hz), 7.90 (1 H, s); ESIMS found for $C_{22}H_{24}F_3N_7O_2$ m/z 476.2 (M+1).

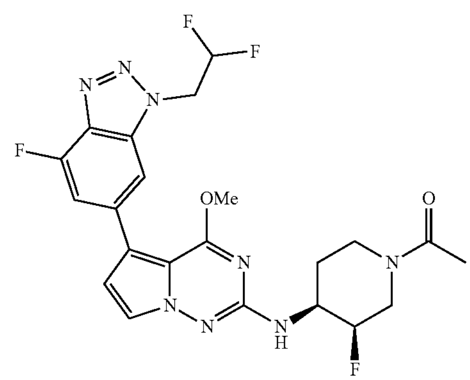
812



[1358] 1-((3R,4S)-3-((5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one 812.

[1359] White solid (30 mg, 0.061 mmol, 33.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.93-2.01 (3H, m), 3.47-3.64 (1H, m), 3.65-3.77 (1H, m), 3.78-3.85 (1H, m), 3.86-3.97 (1H, m), 3.98-4.01 (3H, m), 4.36-4.56 (1H, m), 5.25-5.48 (1H, m), 5.35 (2 H, td, J=16.02, 3.01 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.84 (1H, t, J=2.46 Hz), 7.14 (1H, dd, J=7.26, 4.24 Hz), 7.52 (1H, dd, J=12.18, 0.96 Hz), 7.69 (1H, dd, J=3.83, 2.74 Hz), 7.92 (1 H, s); ESIMS found for $C_{21}H_2O F_4N_8O_2$ m/z 493.2 (M+1).

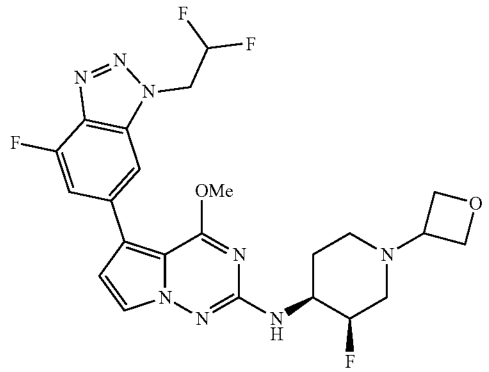
816



[1360] 1-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one 816.

[1361] Fluffy white solid (10 mg, 0.020 mmol, 39.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.66-1.73 (1H, m), 1.74-1.93 (1H, m), 1.98-2.06 (3H, m), 2.67-2.98 (1H, m), 3.17-3.26 (1H, m), 3.87-4.04 (1H, m), 3.98 (3 H, s), 4.04-4.17 (1H, m), 4.41-4.76 (1H, m), 4.99 (1H, d, J=49.65 Hz), 5.34 (2 H, td, J=15.88, 2.74 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.81 (1H, d, J=2.46 Hz), 6.85 (1H, dd, J=7.67, 3.29 Hz), 7.51 (1H, dd, J=12.05, 1.10 Hz), 7.66 (1H, d, J=2.74 Hz), 7.91 (1 H, s); ESIMS found for $C_{22}H_{22}F_4N_8O_2$ m/z 507.2 (M+1).

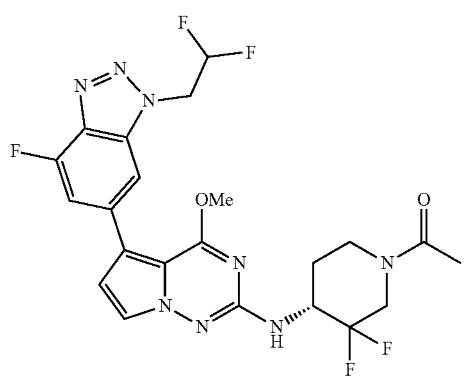
818



[1362] 5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 818.

[1363] Fluffy white solid (4 mg, 0.008 mmol, 23.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68-1.77 (1H, m), 1.92 (1 H, qd, J=12.00, 3.42 Hz), 1.98-2.06 (1H, m), 2.16 (1H, dd, J=37.30, 12.05 Hz), 2.76 (1H, br d, J=10.13 Hz), 2.94-3.03 (1H, m), 3.49 (1 H, quin, J=6.23 Hz), 3.74-3.91 (1H, m), 3.98 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.50, 3.15 Hz), 4.93 (1H, d, J=49.35 Hz), 5.34 (2 H, td, J=15.95, 2.87 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=7.94 Hz), 6.80 (1H, d, J=2.74 Hz), 7.51 (1H, dd, J=12.18, 0.96 Hz), 7.65 (1H, d, J=2.46 Hz), 7.91 (1 H, s); ESIMS found for $C_{23}H_{24}F_4N_8O_2$ m/z 521.2 (M+1).

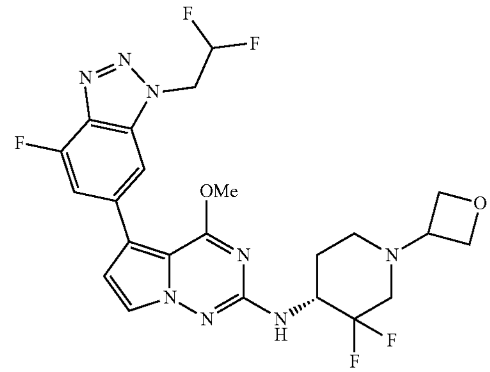
821



[1364] (R)-1-(4-((5-(1-(2,2-Difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one 821.

[1365] Fluffy white solid (11 mg, 0.021 mmol, 44.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.58-1.84 (1H, m), 1.85-1.99 (1H, m), 2.03-2.09 (3H, m), 2.94-3.04 (1H, m), 3.64-3.92 (1H, m), 4.00 (3 H, s), 4.09-4.31 (1H, m), 4.46-4.61 (2H, m), 5.34 (2 H, td, J=15.88, 2.46 Hz), 6.62 (1 H, tt, J=54.30, 3.00 Hz), 6.83 (1H, d, J=2.74 Hz), 7.06 (1H, d, J=9.31 Hz), 7.52 (1H, dd, J=12.18, 0.96 Hz), 7.67 (1H, dd, J=2.46, 1.37 Hz), 7.92 (1 H, s); ESIMS found for $C_{22}H_{21}F_5N_8O_2$ m/z 525.2 (M+1).

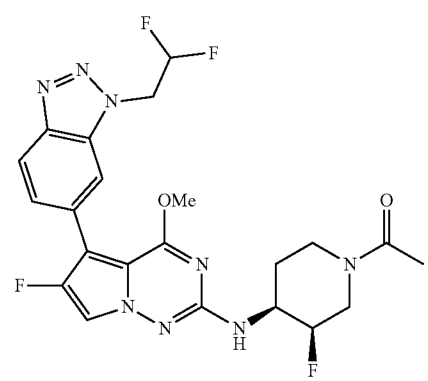
822



[1366] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 822.

[1367] Fluffy white solid (3 mg, 0.006 mmol, 11.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.77-1.86 (1H, m), 1.86-1.93 (1H, m), 2.12-2.21 (1H, m), 2.40 (1H, dd, J=26.90, 11.88 Hz), 2.76 (1H, br d, J=11.50 Hz), 2.96-3.07 (1H, m), 3.60 (1 H, quin, J=6.23 Hz), 4.00 (3 H, s), 4.23-4.37 (1H, m), 4.44 (2 H, dt, J=15.19, 6.23 Hz), 4.55 (2 H, td, J=6.64, 3.70 Hz), 5.34 (2 H, td, J=15.88, 2.74 Hz), 6.62 (2 H, tt, J=54.30, 3.00 Hz), 6.82 (1H, d, J=2.74 Hz), 6.96 (1H, d, J=9.31 Hz), 7.52 (1H, dd, J=12.05, 1.10 Hz), 7.67 (1H, d, J=2.46 Hz), 7.91 (1 H, s); ESIMS found for $C_{23}H_{23}F_5N_8O_2$ m/z 539.2 (M+1).

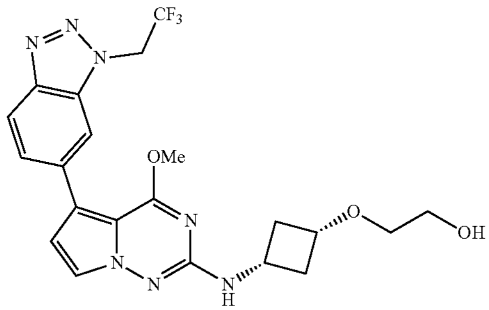
856



[1368] 1-((3R,4S)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one 856.

[1369] White solid (4 mg, 0.008 mmol, 21.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67-1.73(1 H,m), 1.74-1.90 (1H, m), 1.98-2.06 (3H, m), 2.66-2.98 (1H, m), 3.13-3.26 (1H, m), 3.87-4.01 (1H, m), 3.91 (3 H, s), 4.02-4.16 (1H, m), 4.39-4.76 (1H, m), 4.97 (1H, d, J=49.40 Hz), 5.32 (2 H, td, J=16.02, 2.74 Hz), 6.59 (1 H, tt, J=54.30, 3.00 Hz), 6.91 (1H, dd, J=7.67, 4.11 Hz), 7.57 (1H, d, J=8.76 Hz), 7.83 (1H, d, J=3.01 Hz), 7.99 (1 H, s), 8.09 (1H, d, J=8.76 Hz); ESIMS found for $C_{22}H_{22}F_4N_8O_2$ m/z 507.2 (M+1).

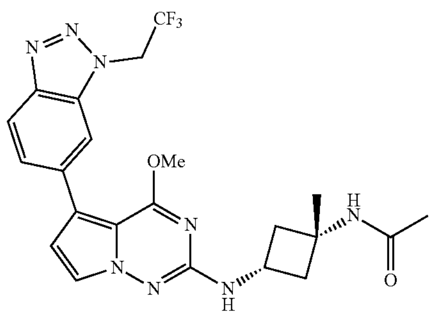
904



[1370] 2-(cis-3-((4-Methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol904.

[1371] Fluffy white solid (1.8 mg, 0.004 mmol, 9.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.81-1.95 (2H, m), 2.59-2.71 (2H, m), 3.36-3.43 (2H, m), 3.48 (2 H, br s), 3.69-3.75 (1H, m), 3.75-3.81 (1H, m), 3.93 (3 H, s), 5.87 (2 H, q, J=9.13 Hz), 6.73 (1H, d, J=2.46 Hz), 7.05 (1H, d, J=7.39 Hz), 7.63 (1H, d, J=2.46 Hz), 7.65-7.69 (1H, m), 8.07 (1H, d, J=8.76 Hz), 8.09 (1 H, s); ESIMS found for $C_{21}H_{22}F_3N_7O_3$ m/z 478.2 (M+1).

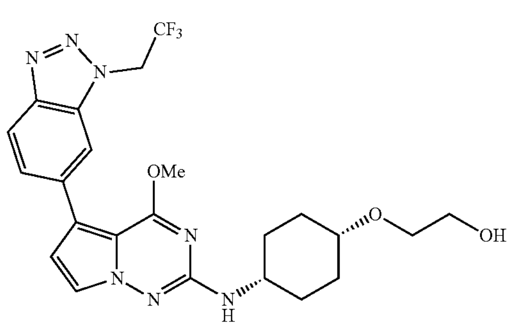
905



[1372] N-((1s,3s)-3-((4-Methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 905.

[1373] White solid (18 mg, 0.037 mmol, 29.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.12-2.22 (2H, m), 2.42 (2H, ddd, J=9.58, 7.39, 2.46 Hz), 3.93 (3 H, s), 4.03 (1 H, sxt, J=7.72 Hz), 5.87 (2 H, q, J=9.03 Hz), 6.73 (1H, d, J=2.46 Hz), 7.02 (1H, d, J=6.84 Hz), 7.67 (1H, dd, J=8.50, 1.65 Hz), 7.66 (1H, d, J=2.74 Hz), 8.02 (1 H, s), 8.07 (1H, d, J=8.76 Hz), 8.09 (1 H, s); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).

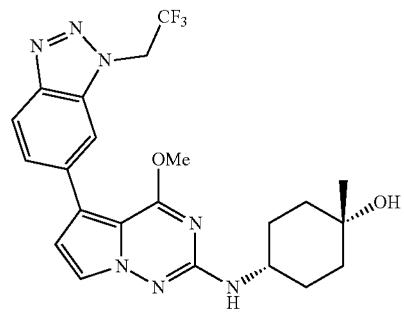
909



[1374] 2-((cis-4-((4-Methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol 909.

[1375] White solid (14.88 mg, 0.029 mmol, % yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.40-1.57 (2H, m), 1.61-1.76 (4H, m), 1.78-1.90 (2H, m), 3.38-3.43 (2H, m), 3.48-3.54 (2H, m), 3.57-3.71 (2H, m), 3.93 (3 H, s), 4.52 (1H, t, J=5.44 Hz), 5.87 (2 H, q, J=9.01 Hz), 6.56 (1H, br d, J=7.46 Hz), 6.71 (1H, d, J=2.57 Hz), 7.64 (1H, d, J=2.57 Hz), 7.67 (1H, dd, J=8.68, 1.22 Hz), 8.07 (1H, d, J=8.68 Hz), 8.09 (1 H, s); ESIMS found for $C_{23}H_{26}F_3N_7O_3$ m/z 506.2 (M+1).

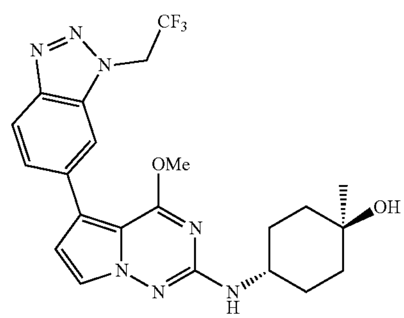
910



[1376] (1s,4s)-4-((4-Methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol910.

[1377] White solid (15 mg, 0.032 mmol, 32.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.12 (3 H, s), 1.37 (2 H, td, J=13.07, 4.24 Hz), 1.58 (2H, br d, J=12.05 Hz), 1.61-1.75 (4H, m), 3.45-3.56 (1H, m), 3.92 (3H, s), 4.00 (1H, s), 5.87 (2 H, q, J=8.94 Hz), 6.53 (1H, d, J=7.94 Hz), 6.71 (1H, d, J=2.74 Hz), 7.63 (1H, d, J=2.46 Hz), 7.67 (1H, dd, J=8.76, 1.37 Hz), 8.06 (1H, d, J=8.76 Hz), 8.09 (1 H, s); ESIMS found for $C_{22}H_{24}F_3N_7O_2$ m/z 476.2 (M+1).

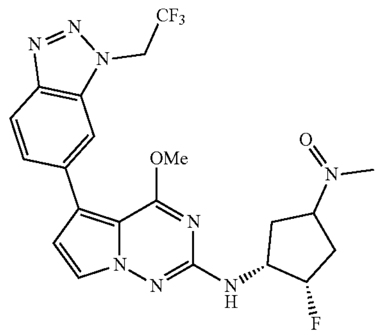
911



[1378] (1r,4r)-4-((4-Methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 911.

[1379] Fluffy white solid (15 mg, 0.032 mmol, 65.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.38-1.51 (4H, m), 1.56-1.66 (2H, m), 1.83-1.93 (2H, m), 3.65 (1 H, dt, J=7.87, 3.87 Hz), 3.93 (3H, s), 4.24 (1H, s), 5.87 (2 H, q, J=8.94 Hz), 6.51 (1H, d, J=7.94 Hz), 6.71 (1H, d, J=2.74 Hz), 7.66 (1H, d, J=2.46 Hz), 7.66-7.68 (1H, m), 8.07 (1H, d, J=8.76 Hz), 8.09 (1 H, s); ESIMS found for $C_{22}H_{24}F_3N_7O_2$ m/z 476.2 (M+1).

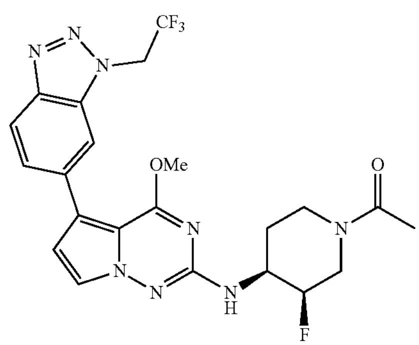
912



[1380] 1-((3S,4R)-3-Fluoro-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one 912.

[1381] White solid (18 mg,0.037 mmol, 20.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.92-2.02 (3H, m), 3.47-3.56 (1H, m), 3.58-3.75 (1H, m), 3.79-3.86 (1H, m), 3.86-3.95 (1H, m), 3.95-3.98 (3H, m), 4.28-4.60 (1H, m), 5.22-5.51 (1H, m), 5.88 (2 H, q, J=8.94 Hz), 6.78 (1H, t, J=2.46 Hz), 7.11 (1H, dd, J=7.12, 5.20 Hz), 7.67-7.70 (2H, m), 8.08 (1H, d, J=8.76 Hz), 8.11 (1 H, s); ESIMS found for $C_{21}H_2O\ F_4N_8O_2$ m/z 493.2 (M+1).

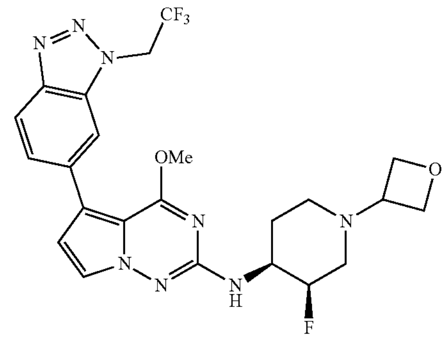
916



[1382] 1-((3R,4S)-3-Fluoro-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo [2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 916.

[1383] Fluffy white solid (12 mg, 0.024 mmol, 47.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67-1.74 (1H, m), 1.74-1.91 (1H, m), 1.98-2.06 (3H, m), 2.67-2.99 (1H, m), 3.16-3.26 (1H, m), 3.88-4.02 (1H, m), 3.95 (3 H, s), 4.03-4.17 (1H, m), 4.40-4.75 (1H, m), 5.00 (1H, d, J=49.65 Hz), 5.88 (2 H, q, J=9.22 Hz), 6.75 (1H, d, J=2.74 Hz), 6.82 (1H, dd, J=7.67, 3.01 Hz), 7.66 (1H, d, J=2.46 Hz), 7.68 (1H, dd, J=8.76, 1.64 Hz), 8.08 (1H, d, J=8.76 Hz), 8.10 (1 H, s); ESIMS found for $C_{22}H_{22}F_4N_8 02$ m/z 507.2 (M+1).

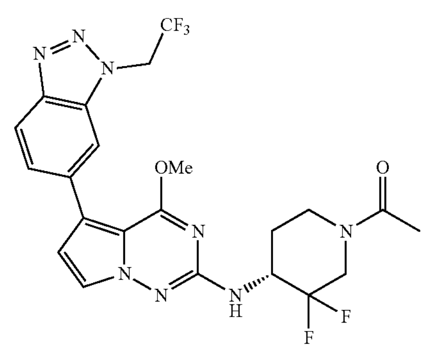
918



[1384] N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 918.

[1385] Fluffy white solid (10 mg, 0.019 mmol, 45.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68-1.78 (1H, m), 1.87-1.97 (1H, m), 1.99-2.06 (1H, m), 2.16 (1H, dd, J=37.00, 12.59 Hz), 2.76 (1H, br d, J=10.95 Hz), 2.94-3.05 (1H, m), 3.49 (1 H, quin, J=6.30 Hz), 3.73-3.90 (1H, m), 3.95 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.43, 3.01 Hz), 4.94 (1H, d, J=49.60 Hz), 5.87 (2 H, q, J=8.94 Hz), 6.73 (1H, d, J=7.94 Hz), 6.74 (1H, d, J=2.74 Hz), 7.65 (1H, d, J=2.46 Hz), 7.67 (1H, dd, J=8.49, 1.37 Hz), 8.07 (1 H, d, J=8.76 Hz), 8.10 (1 H, s); ESIMS found for $C_{23}H_{24}F_4N_8O_2$ m/z 521.2 (M+1).

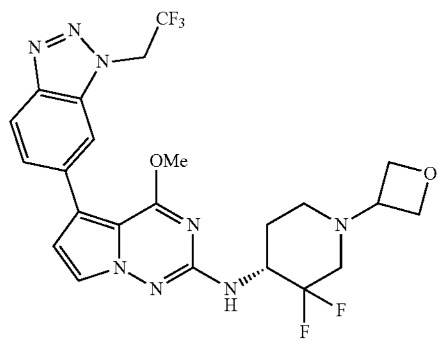
921



[1386] (R)-1-(3,3-Difluoro-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d]1[1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 921.

[1387] Fluffy white solid (7 mg, 0.013 mmol, 43.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.58-1.84 (1H, m), 1.84-2.01 (1H, m), 2.03-2.09 (3H, m), 2.99 (1 H, br t, J=11.36 Hz), 3.61-3.90 (1H, m), 3.97(3 H, s), 4.10-4.31 (1H, m), 4.45-4.63 (2H, m), 5.88 (2 H, q, J=9.22 Hz), 6.77 (1H, d, J=2.46 Hz), 7.03 (1H, d, J=9.03 Hz), 7.67 (1H, dd, J=2.60, 1.23 Hz), 7.67-7.70 (1H, m), 8.08 (1H, d, J=8.76 Hz), 8.11 (1 H, s); ESIMS found for $C_{22}H_{21}F_5N_8O_2$ m/z 525.2 (M+1).

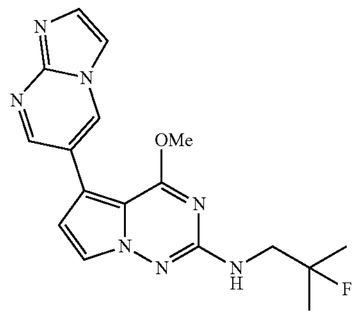
922



[1388] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 922.

[1389] Fluffy white solid (3 mg, 0.006 mmol, 11.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.86 (1H, m), 1.86-1.93 (1H, m), 2.12-2.20 (1H, m), 2.41 (1H, dd, J=27.15, 11.23 Hz), 2.76 (1H, br d, J=11.77 Hz), 2.95-3.08 (1H, m), 3.61 (1 H, quin, J=6.09 Hz), 3.96 (3 H, s), 4.22-4.37 (1H, m), 4.44 (2 H, dt, J=15.19, 6.09 Hz), 4.55 (2 H, td, J=6.57, 3.56 Hz), 5.87 (2 H, q, J=9.03 Hz), 6.76 (1H, d, J=2.74 Hz), 6.93 (1H, d, J=9.31 Hz), 7.66 (1H, d, J=2.74 Hz), 7.68 (1H, dd, J=8.80, 1.35 Hz), 8.08 (1H, d, J=8.76 Hz), 8.11 (1 H, s); ESIMS found for $C_{23}H_{23}F_5N_8O_2$ m/z 539.2 (M+1).

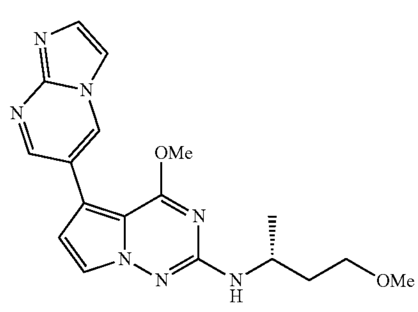
924



[1390] N-(2-Fluoro-2-methylpropyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 924.

[1391] Beige solid (6 mg, 0.017 mmol, 8.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.37 (6H, d, J=21.40 Hz), 3.47 (2H, dd, J=18.89, 6.57 Hz), 4.00 (3 H, s), 6.79 (1H, d, J=2.74 Hz), 6.86 (1H, t, J=6.43 Hz), 7.67 (1H, d, J=2.46 Hz), 7.73 (1H, d, J=1.10 Hz), 7.93 (1 H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.10 (1H, d, J=2.46 Hz); ESIMS found for $C_{17}H_{18}FN_7O$ m/z 356.2 (M+1).

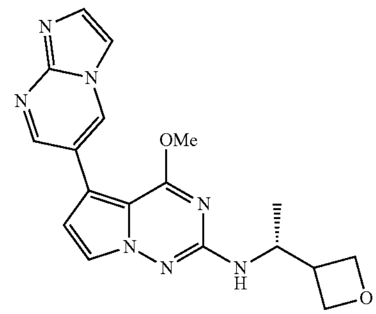
926



[1392] (R)-5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(4-methoxybutan-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 926.

[1393] Beige solid (4 mg, 0.011 mmol, 5.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.16 (3H, d, J=6.57 Hz), 1.63-1.73(1 H,m), 1.77-1.88 (1H, m), 3.22 (3H, s), 3.36-3.45 (2H, m), 3.88-3.96 (1H, m), 3.97 (3 H, s), 6.58 (1H, d, J=8.49 Hz), 6.77 (1H, d, J=2.46 Hz), 7.66 (1H, d, J=2.46 Hz), 7.75 (1 H, br s), 7.95 (1 H, br s), 8.74 (1H, d, J=2.19 Hz), 9.10 (1H, d, J=1.64 Hz); ESIMS found for $C_{18}H_{21}N_7O_2$ m/z 368.2 (M+1).

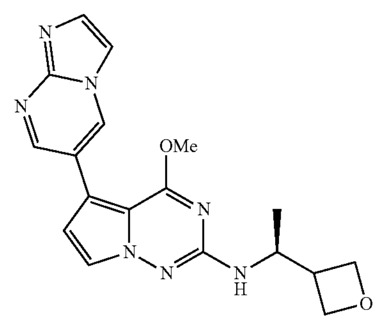
927



[1394] (R)-5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 927.

[1395] Beige solid (13 mg, 0.036 mmol, 17.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.10 (3H, d, J=6.57 Hz), 3.04-3.14 (1H, m), 3.98 (3 H, s), 4.14-4.26 (1H, m), 4.35 (1H, t, J=6.30 Hz), 4.43 (1H, t, J=6.16 Hz), 4.58-4.65 (2H, m), 6.70 (1H, d, J=8.76 Hz), 6.78 (1H, d, J=2.46 Hz), 7.69 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.2 (M+1).

928

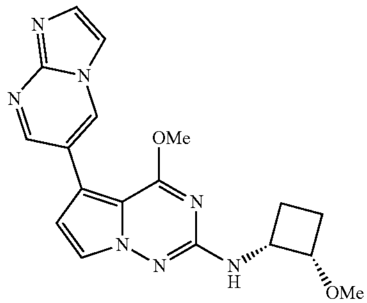


[1396] (S)-5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 928.

[1397] Off-white solid (14 mg, 0.038 mmol, 19.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.10 (3H, d, J=6.57 Hz), 3.04-3.17 (1H, m), 4.15-4.26 (1H, m), 4.35 (1H, t, J=6.16 Hz), 4.43 (1H, t, J=6.16 Hz), 4.55-4.66 (2H, m), 6.70 (1H, d, J=8.49 Hz), 6.78 (1H, d, J=2.46 Hz), 7.69 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37

Hz), 8.74 (1 H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.2 (M+1).

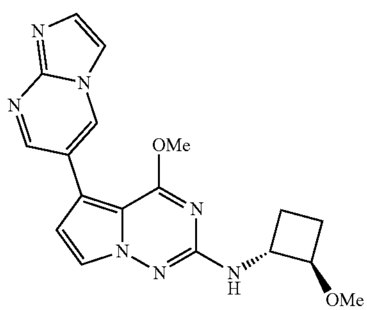
929



[1398] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((1R,2S)-2-methoxycyclobutyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 929.

[1399] White solid (10 mg, 0.027 mmol, 27.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.92-2.05 (3H, m), 2.05-2.12 (1H, m), 3.19 (3H, s), 4.00 (3H, s), 4.00-4.04 (1H, m), 4.30-4.41 (1H, m), 6.59 (1H, d, J=7.67 Hz), 6.79 (1H, d, J=2.74 Hz), 7.68 (1H, d, J=2.46 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.10 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.2 (M+1).

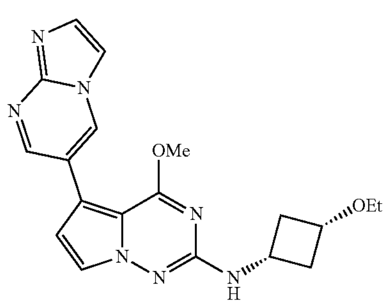
930



[1400] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((1R,2R)-2-methoxycyclobutyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 930.

[1401] Off-white solid (25 mg, 0.068 mmol, 41.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38-1.48 (2H, m), 1.95-2.02 (1H, m), 2.02-2.10 (1H, m), 3.22 (3 H, s), 3.81 (1 H, q, J=7.48 Hz), 3.98 (3 H, s), 4.06-4.16 (1H, m), 6.79 (1H, d, J=2.46 Hz), 7.19 (1H, d, J=8.76 Hz), 7.68 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.10 Hz), 8.73 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.2 (M+1).

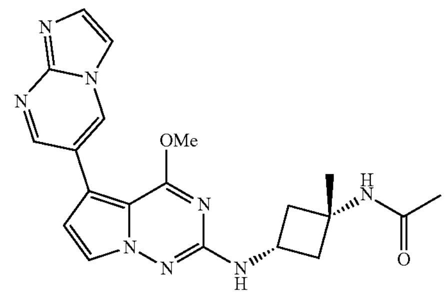
931



[1402] N-(cis-3-Ethoxycyclobutyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 931.

[1403] Off-white solid (10 mg, 0.026 mmol, 13.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.10 (3H, t, J=6.98 Hz), 1.79-1.92 (2H, m), 2.57-2.69 (2H, m), 3.33-3.37 (2H, m), 3.64-3.72 (1H, m), 3.74-3.83 (1H, m), 3.97 (3 H, s), 6.78 (1H, d, J=2.46 Hz), 7.07 (1 H, d, J=7.39 Hz), 7.65 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.74 Hz); ESIMS found for $C_{1-9}H_{21}N_7O_2$ m/z 380.2 (M+1).

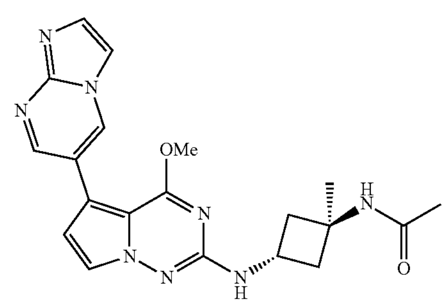
934



[1404] N-((1s,3s)-3-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 934.

[1405] Beige solid (26 mg, 0.064 mmol, 93.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.12-2.21 (2H, m), 2.42 (2H, ddd, J=9.58, 7.39, 2.74 Hz), 3.97 (3 H, s), 3.98-4.07 (1H, m), 6.77 (1H, d, J=2.74 Hz), 7.05 (1H, d, J=7.12 Hz), 7.68 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.02 (1 H, s), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{22}N_8O_2$ m/z 407.2 (M+1).

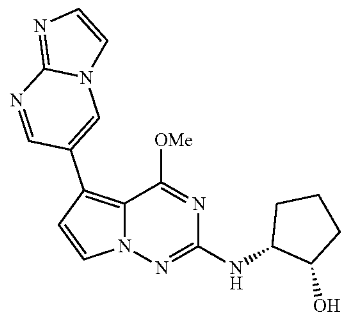
935



[1406] N-((1r,3r)-3-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 935.

[1407] Off-white solid (26 mg, 0.064 mmol, 93.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (3H, s), 1.81 (3H, s), 1.90-2.00 (2H, m), 2.58-2.69 (2H, m), 3.97 (3 H, s), 4.19 (1 H, sxt, J=7.78 Hz), 6.77 (1H, d, J=2.46 Hz), 7.05 (1H, d, J=7.12 Hz), 7.65 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 7.94 (1 H, s), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{22}N_8O_2$ m/z 407.2 (M+1).

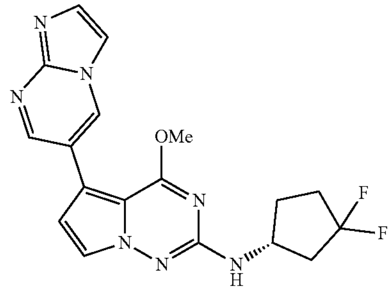
942



[1408] (1S,2R)-2-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclopentan-1-ol 942.

[1409] Beige solid (16 mg, 0.044 mmol, 26.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.46-1.56 (1H, m), 1.57-1.67 (2H, m), 1.69-1.77 (1H, m), 1.77-1.86 (1H, m), 1.92-2.01 (1H, m), 3.79-3.91 (1H, m), 3.98 (3 H, s), 4.09-4.19 (1H, m), 4.74 (1H, d, J=4.38 Hz), 5.98 (1H, d, J=7.67 Hz), 6.79 (1H, d, J=2.46 Hz), 7.68 (1H, d, J=2.46 Hz), 7.73 (1 H, s), 7.93 (1 H, s), 8.73 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.15 (M+1).

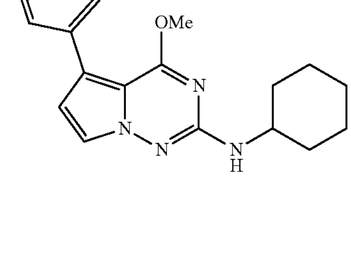
943



[1410] (R)—N-(3,3-Difluorocyclopentyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 943.

[1411] White solid (17 mg, 0.044 mmol, 26.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.82 (1 H, dq, J=12.25, 8.42 Hz), 2.02-2.23 (3H, m), 2.23-2.35 (1H, m), 2.54-2.62 (1H, m), 3.98 (3 H, s), 4.23 (1 H, sxt, J=7.34 Hz), 6.80 (1H, d, J=2.46 Hz), 7.07 (1H, d, J=6.84 Hz), 7.70 (1H, d, J=2.46 Hz), 7.73 (1H, s), 7.93 (1H, s), 8.74 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{17}F_2N_7O$ m/z 386.2 (M+1).

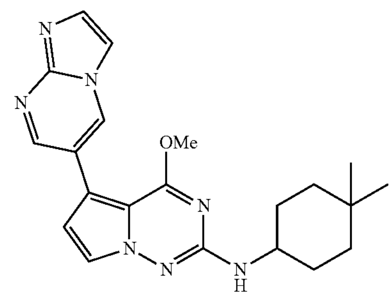
944



[1412] N-Cyclohexyl-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 944.

[1413] Beige solid (43 mg, 0.118 mmol, 59.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.08-1.19 (1H, m), 1.21-1.38 (4H, m), 1.54-1.65 (1H, m), 1.70-1.78 (2H, m), 1.95 (2H, br d, J=10.40 Hz), 3.53-3.65 (1H, m), 3.97 (3 H, s), 6.58 (1H, d, J=8.21 Hz), 6.76 (1H, d, J=2.74 Hz), 7.66 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.92 (1H, d, J=1.10 Hz), 8.73 (1 H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{19}H_{21}N_7O$ m/z 364.15 (M+1).

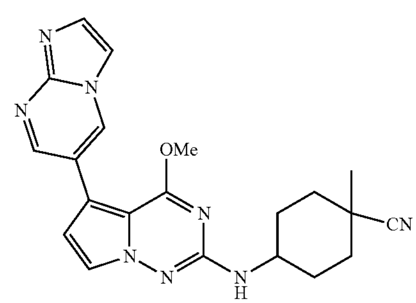
947



[1414] N-(4,4-Dimethylcyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 947.

[1415] Off-white solid (12 mg, 0.031 mmol, 15.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.93 (3H, s), 0.93 (3H, s), 1.26 (2 H, td, J=13.21, 3.70 Hz), 1.35-1.43 (1H, m), 1.44-1.54 (1H, m), 1.62-1.72 (1H, m), 1.73-1.83 (2H, m), 1.90 (1H, br d, J=3.56 Hz), 3.48-3.61 (1H, m), 3.97 (3 H, s), 6.56 (1H, d, J=8.21 Hz), 6.76 (1H, d, J=2.74 Hz), 7.65 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{25}N_7O$ m/z 392.2 (M+1).

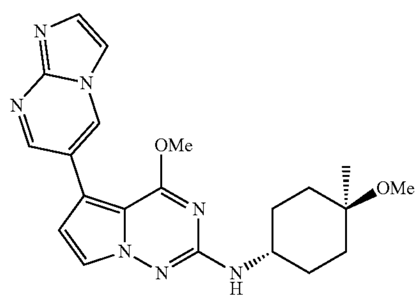
948



[1416] 4-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile 948.

[1417] Off-white solid (34 mg, 0.085 mmol, 42.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.34 (3 H, s), 1.45-1.60 (4H, m), 1.95 (2H, br d, J=10.68 Hz), 2.00-2.07 (2 H, m), 3.52-3.65 (1H, m), 3.98 (3 H, s), 6.77 (1H, d, J=2.46 Hz), 6.83 (1H, d, J=7.94 Hz), 7.65 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.10 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{22}N_8O$ m/z 403.2 (M+1).

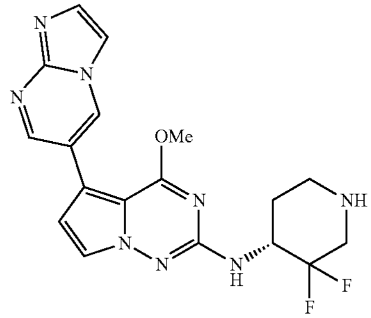
954



[1418] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((1r,4r)-4-methoxy-4-methylcyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 954.

[1419] Off-white solid (22 mg, 0.054 mmol, 27.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.14 (3 H, s), 1.42-1.57 (4H, m), 1.63-1.74 (2H, m), 1.78-1.90 (2H, m), 3.11 (3 H, s), 3.65-3.77 (1H, m), 3.98 (3 H, s), 6.60 (1H, d, J=7.94 Hz), 6.77 (1H, d, J=2.74 Hz), 7.67 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{25}N_7O_2$ m/z 408.2 (M+1).

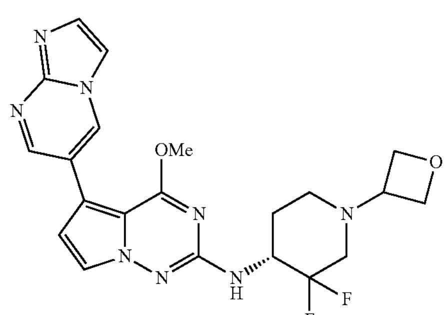
964



[1420] (R)—N-(3,3-Difluoropiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 964.

[1421] Beige solid (18 mg, 0.045 mmol, 75.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.69 (1 H, qd, J=11.96, 3.56 Hz), 1.79-1.90 (1H, m), 2.55-2.67 (1H, m), 2.81 (1H, dd, J=29.35, 14.00 Hz), 2.93 (1H, br d, J=12.05 Hz), 3.06-3.15 (1H, m), 4.01 (3 H, s), 4.26-4.41 (1H, m), 6.80 (1H, d, J=2.74 Hz), 6.91 (1H, d, J=9.31 Hz), 7.68 (1H, d, J=2.46 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.10 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{18}F_2N_8O$ m/z 401.2 (M+1).

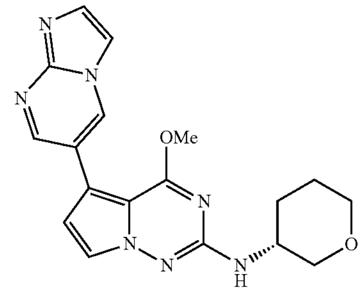
968



[1422] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 968.

[1423] Off-white solid (15 mg, 0.033 mmol, 72.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.86 (1H, m), 1.86-1.92 (1H, m), 2.12-2.22 (1H, m), 2.35-2.46 (1H, m), 2.76 (1H, br d, J=11.50 Hz), 2.96-3.08 (1H, m), 3.60 (1 H, quin, J=6.30 Hz), 4.01 (3 H, s), 4.23-4.37 (1H, m), 4.44 (2 H, dt, J=15.19, 6.23 Hz), 4.55 (2 H, td, J=6.57, 3.83 Hz), 6.81 (1H, d, J=2.46 Hz), 6.96 (1H, d, J=9.31 Hz), 7.68 (1H, d, J=2.46 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.10 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{22}F_2N_8O_2$ m/z 457. (M+1).

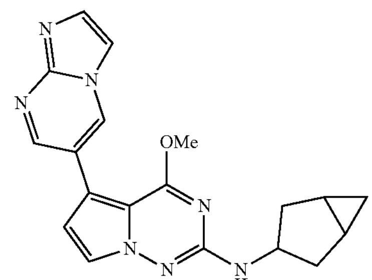
975



[1424] (R)-5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(tetrahydro-2H-pyran-3-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 975.

[1425] White solid (7 mg, 0.019 mmol, 11.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.53-1.65 (2H, m), 1.67-1.76 (1H, m), 1.99 (1H, br d, J=7.39 Hz), 3.11 (1H, t, J=9.99 Hz), 3.23-3.30 (1H, m), 3.70-3.80 (2H, m), 3.94 (1 H, br dd, J=10.54, 3.15 Hz), 3.98 (3 H, s), 6.66 (1H, d, J=7.94 Hz), 6.78 (1H, d, J=2.46 Hz), 7.69 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=0.82 Hz), 7.93 (1H, d, J=1.10 Hz), 8.73 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{19}N_7O_2$ m/z 366.2 (M+1).

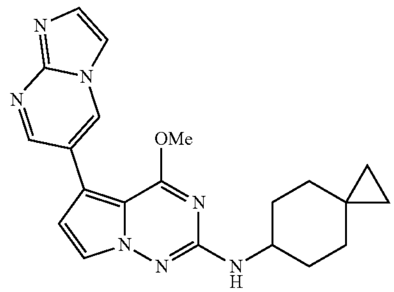
976



[1426] N-(Bicyclo[3.1.0]hexan-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 976.

[1427] Beige solid (18 mg, 0.050 mmol, 25.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.39 (1 H, q, J=4.11 Hz), 0.55 (1 H, td, J=8.08, 4.93 Hz), 1.26-1.30 (2H, m), 1.74 (2 H, dd, J=13.69, 3.01 Hz), 2.18-2.28 (2H, m), 3.97 (3 H, s), 4.18 (1 H, tdt, J=8.30, 8.30, 5.51, 2.91, 2.91 Hz), 6.62 (1H, d, J=5.48 Hz), 6.76 (1H, d, J=2.46 Hz), 7.65 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.92 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{19}H_{19}N_7O$ m/z 362.2 (M+1).

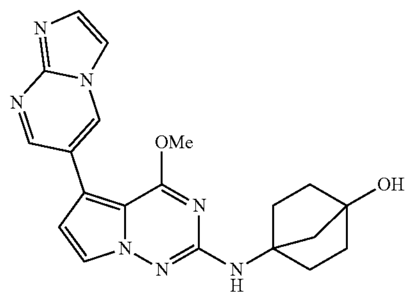
977



[1428] 5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(spiro[2.5]octan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 977.

[1429] Off-white solid (8 mg, 0.021 mmol, 10.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.17-0.25 (2H, m), 0.26-0.35 (2H, m), 0.98 (2H, br d, J=13.42 Hz), 1.45 (2 H, qd, J=11.65, 3.30 Hz), 1.67-1.79 (2H, m), 1.88-1.97 (2H, m), 3.57-3.73 (1H, m), 3.98 (3 H, s), 6.64 (1H, d, J=8.21 Hz), 6.76 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{21}H_{23}N_7O$ m/z 390.2 (M+1).

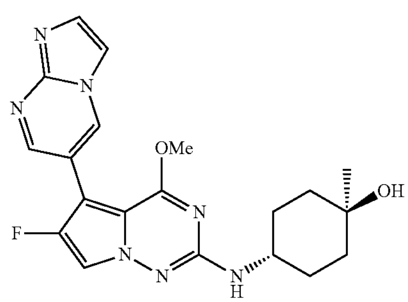
978



[1430] 4-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol 978.

[1431] Beige solid (17 mg, 0.043 mmol, 21.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.57 (2 H, td, J=9.79, 3.70 Hz), 1.65-1.77 (2H, m), 1.85 (2 H, s), 1.87-1.93 (2H, m), 1.97-2.07 (2H, m), 3.97 (3H, s), 4.89 (1H, s), 6.77 (1H, d, J=2.46 Hz), 6.79 (1 H, s), 7.63 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.10 Hz), 7.93 (1H, d, J=1.10 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{21}N_7O_2$ m/z 392.2 (M+1).

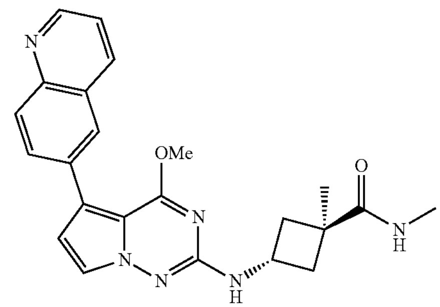
996



[1432] (1r,4r)-4-((6-Fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol996.

[1433] Off-white solid (1 mg, 0.002 mmol, 4.3% yield). ^{1}H NMR (499 MHz, METHANOL-d_4) δ ppm 1.28 (3 H, s), 1.48-1.56 (2H, m), 1.56-1.63 (2H, m), 1.68-1.78 (2H, m), 1.98-2.09 (2H, m), 3.74 (1 H, tt, J=8.80, 4.21 Hz), 4.01 (3 H, s), 4.58 (1 H, br s), 7.54 (1H, d, J=3.01 Hz), 7.75 (1H, s), 7.88 (1H, s), 8.72 (1H, d, J=2.19 Hz), 9.00 (1H, d, J=2.19 Hz); ESIMS found for $C_{20}H_{22}FN_7O_2$ m/z 412.2 (M+1).

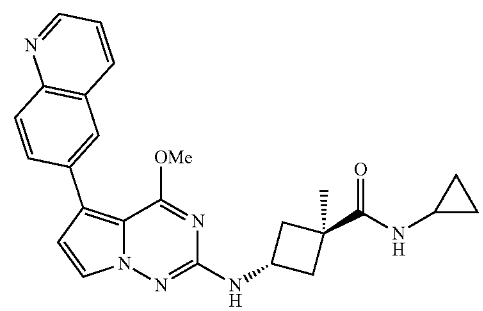
1038



[1434] trans-3-((4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide 1038.

[1435] Yellow solid (23 mg, 0.055 mmol, 44.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.32 (3 H, s), 1.85-1.95 (2H, m), 2.63 (3H, d, J=4.65 Hz), 2.71-2.80 (2H, m), 3.95 (3 H, s), 4.05 (1 H, sxt, J=7.94 Hz), 6.77 (1H, d, J=2.46 Hz), 6.99 (1H, d, J=7.39 Hz), 7.52 (1H, dd, J=8.21, 4.11 Hz), 7.62 (1 H, q, J=4.11 Hz), 7.66 (1H, d, J=2.74 Hz), 7.94-8.03 (2H, m), 8.10 (1H, d, J=1.37 Hz), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, br d, J=2.74 Hz); ESIMS found for $C_{23}H_{24}N_6O_2$ m/z 417.2 (M+1).

1039

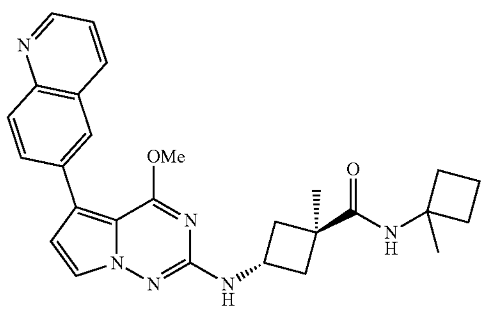


[1436] trans-N-Cyclopropyl-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide 1039.

[1437] Light yellow solid (20 mg, 0.045 mmol, 36.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 0.42-0.48 (2H, m), 0.58-0.64 (2H, m), 1.30 (3 H, s), 1.84-1.90 (2H, m), 2.68 (1 H, tq, J=7.41, 3.91 Hz), 2.72-2.78 (2H, m), 3.95 (3 H, s), 3.96-4.06 (1H, m), 6.77 (1H, d, J=2.74 Hz), 6.98 (1H, d, J=7.39 Hz), 7.53 (1H, dd, J=8.35, 4.24 Hz), 7.63 (1H, d, J=4.11 Hz), 7.67 (1H, d, J=2.46 Hz), 7.94-8.04 (2H, m), 8.11

(1 H, s), 8.37 (1H, dd, J=8.21, 1.37 Hz), 8.87 (1H, br d, J=2.46 Hz); ESIMS found for $C_{25}H_{26}N_6O_2$ m/z 443.2 (M+1).

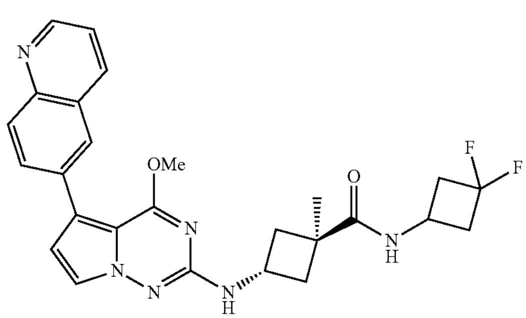
1040



[1438] trans-3-((4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methyl-N-(1-methylcyclobutyl)cyclobutane-1-carboxamide 1040.

[1439] Tan solid (21 mg, 0.045 mmol, 36.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.33 (3H, s), 1.39 (3H, s), 1.71-1.82 (2H, m), 1.83-1.97 (4H, m), 2.16-2.28 (2H, m), 2.71-2.82 (2H, m), 3.96 (3 H, s), 3.97-4.04 (1H, m), 6.77 (1H, d, J=2.74 Hz), 6.97 (1H, br d, J=7.12 Hz), 7.51-7.56 (2H, m), 7.67 (1H, d, J=2.74 Hz), 7.95-8.04 (2H, m), 8.12 (1 H, s), 8.38 (1H, br d, J=7.94 Hz), 8.84-8.92 (1H, m); ESIMS found for $C_{27}H_{30}N_6O_2$ m/z 471.3 (M+1).

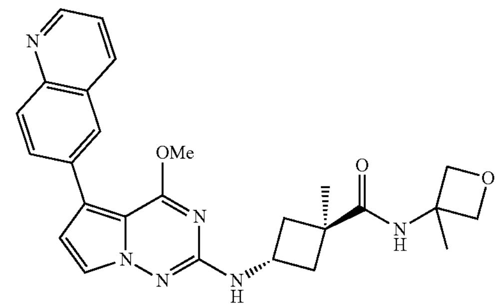
1041



[1440] trans-N-(3,3-Difluorocyclobutyl)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide ?1041

[1441] Yellow solid (33 mg, 0.067 mmol, 54.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.34 (3 H, s), 1.87-1.98 (2H, m), 2.58-2.71 (2H, m), 2.77 (2H, ddd, J=9.99, 7.80, 2.46 Hz), 2.83-2.96 (2H, m), 3.96 (3 H, s), 3.99-4.06 (1H, m), 4.07-4.15 (1H, m), 6.78 (1H, d, J=2.74 Hz), 7.02 (1H, br d, J=7.12 Hz), 7.59 (1H, dd, J=8.21, 4.11 Hz), 7.67 (1H, d, J=2.46 Hz), 8.02 (2 H, s), 8.04 (1H, d, J=6.84 Hz), 8.14 (1 H, s), 8.45 (1H, br d, J=7.94 Hz), 8.91 (1H, br d, J=3.01 Hz); ESIMS found for $C_{26}H_{26}F_2N_6O_2$ m/z 493.25 (M+1).

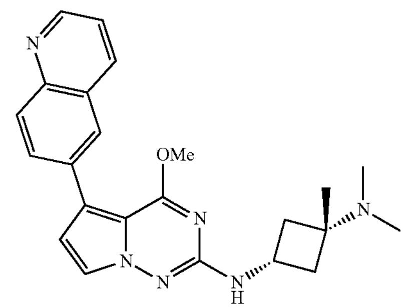
1042



[1442] trans-3-((4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methyl-N-(3-methyloxetan-3-yl)cyclobutane-1-carboxamide 1042.

[1443] Tan solid (21 mg, 0.044 mmol, 35.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.35 (3H, s), 1.52 (3H, s), 1.87-1.98 (2H, m), 2.71-2.80 (2H, m), 3.96 (3 H, s), 4.05 (1 H, sxt, J=7.94 Hz), 4.31 (2H, d, J=6.30 Hz), 4.60 (2H, d, J=6.30 Hz), 6.77 (1H, d, J=2.74 Hz), 7.00 (1H, d, J=7.39 Hz), 7.46-7.57 (1H, m), 7.67 (1H, d, J=2.46 Hz), 7.93-8.03 (2H, m), 8.08 (1 H, s), 8.10 (1H, d, J=1.37 Hz), 8.36 (1H, dd, J=8.21, 1.64 Hz), 8.86 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{26}H_{28}N_6O_3$ m/z 473.3 (M+1).

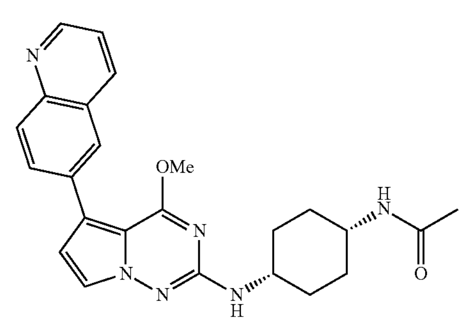
1043



[1444] cis-N_3-(4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-N_1,$N_{1,1}$-trimethylcyclobutane-1,3-diamine 1043.

[1445] Beige solid (28 mg, 0.070 mmol, 57.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.07 (3 H, s), 1.82-1.92 (2H, m), 2.03 (6 H, s), 2.15-2.25 (2H, m), 3.92-4.03 (1H, m), 3.96 (3 H, s), 6.77 (1H, d, J=2.74 Hz), 6.96 (1H, d, J=7.12 Hz), 7.52 (1H, dd, J=8.35, 4.24 Hz), 7.65 (1H, d, J=2.46 Hz), 7.94-8.03 (2H, m), 8.11 (1 H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.38, 1.64 Hz); ESIMS found for $C_{23}H_{26}N_{60}$ m/z 403.25 (M+1).

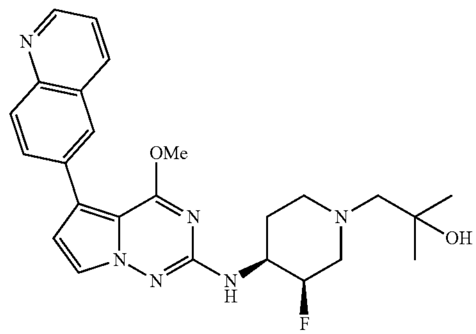
1044



[1446] N-(cis-4-((4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl) amino)cyclohexyl)acetamide 1044.

[1447] White solid (4.16 mg, 0.010 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.50-1.60 (2H, m), 1.60-1.73 (4H, m), 1.73-1.81 (2H, m), 1.81 (3 H, s), 3.40-3.47 (1H, m), 3.68 (2 H, br s), 3.97 (3 H, s), 6.46 (1H, d, J=6.38 Hz), 6.77 (1H, d, J=2.63 Hz), 7.53 (1H, dd, J=8.32, 4.19 Hz), 7.65 (1H, d, J=2.63 Hz), 7.73 (1H, br d, J=7.00 Hz), 7.99 (2H, s), 8.11 (1H, s), 8.36 (1H, dd, J=8.25, 1.50 Hz), 8.86 (1H, dd, J=4.19, 1.69 Hz); ESIMS found for $C_{24}H_{26}N_6O_2$ m/z 431.1 (M+1).

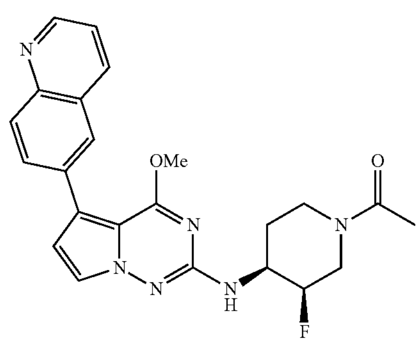
1045



[1448] 1-((3R,4S)-3-Fluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol 1045.

[1449] White solid (5 mg, 0.011 mmol, 14.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.10 (6 H, s), 1.61-1.71 (1H, m), 1.95 (1 H, qd, J=12.18, 3.42 Hz), 2.20-2.29 (2H, m), 2.29-2.35 (1H, m), 2.43 (1H, dd, J=37.55, 12.87 Hz), 2.98 (1H, br d, J=12.32 Hz), 3.23-3.30 (2H, m), 3.71-3.86 (1H, m), 3.98 (3 H, s), 4.08 (1 H, br s), 4.87 (1H, d, J=49.90 Hz), 6.59 (1H, d, J=7.94 Hz), 6.79 (1H, d, J=2.74 Hz), 7.53 (1H, dd, J=8.21, 4.11 Hz), 7.65 (1H, d, J=2.46 Hz), 7.95-8.03 (2H, m), 8.11 (1H, d, J=1.37 Hz), 8.36 (1H, dd, J=8.35, 1.78 Hz), 8.86 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{25}H_{29}FN_6O_2$ m/z 465.3 (M+1).

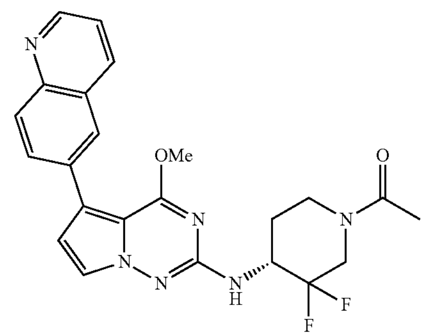
1047



[1450] 1-((3R,4S)-3-Fluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl) ethan-1-one 1047.

[1451] Light orange solid (20 mg, 0.046 mmol, 60.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67-1.75 (1H, m), 1.75-1.91 (1H, m), 1.99-2.07 (3H, m), 2.67-2.97 (1H, m), 3.15-3.27 (1H, m), 3.87-3.95 (1H, m), 3.98 (3 H, s), 4.03-4.17 (1H, m), 4.40-4.77 (1H, m), 5.00 (1H, d, J=49.35 Hz), 6.80 (2H, d, J=2.46 Hz), 7.53 (1H, dd, J=8.21, 4.11 Hz), 7.65 (1 H, d, J=2.74 Hz), 7.96-8.02 (2H, m), 8.12 (1 H, s), 8.36 (1H, dd, J=8.21, 1.64 Hz), 8.86 (1H, dd, J=4.38, 1.64 Hz); ESIMS found for $C_{23}H_{23}FN_6O_2$ m/z 435.2 (M+1).

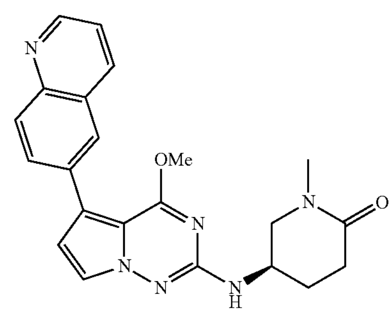
1048



[1452] (R)-1-(3,3-Difluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl) ethan-1-one 1048.

[1453] Light yellow solid (5 mg, 0.011 mmol, 37.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.55-1.85 (1H, m), 1.86-2.01 (1H, m), 2.03-2.10 (3H, m), 2.92-3.06 (1H, m), 3.80-3.94 (1H, m), 4.00 (3 H, s), 4.11-4.32 (1H, m), 4.46-4.62 (2H, m), 6.82 (1H, d, J=2.74 Hz), 7.00 (1H, d, J=9.31 Hz), 7.53 (1H, dd, J=8.21, 4.11 Hz), 7.66 (1H, dd, J=2.46, 1.37 Hz), 7.94-8.04 (2H, m), 8.12 (1 H, s), 8.37 (1H, dd, J=8.35, 1.51 Hz), 8.87 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{23}H_{22}F_2N_6O_2$ m/z 453.2 (M+1).

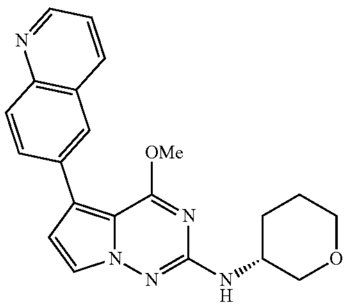
1049



[1454] (R)-5-((4-Methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one 1049.

[1455] Beige solid (23 mg, 0.057 mmol, 44.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.88-1.97 (1H, m), 1.97-2.04 (1H, m), 2.27-2.36 (1H, m), 2.37-2.44 (1H, m), 2.81 (3 H, s), 3.26 (1H, dd, J=12.05, 7.67 Hz), 3.58 (1H, dd, J=12.05, 4.38 Hz), 3.98 (3 H, s), 4.05-4.17 (1H, m), 6.80 (1H, d, J=2.74 Hz), 6.92 (1H, d, J=7.39 Hz), 7.53 (1H, dd, J=8.21, 4.11 Hz), 7.69 (1H, d, J=2.74 Hz), 7.94-8.04 (2H, m), 8.12 (1 H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{22}H_{22}N_6O_2$ m/z 403.2 (M+1).

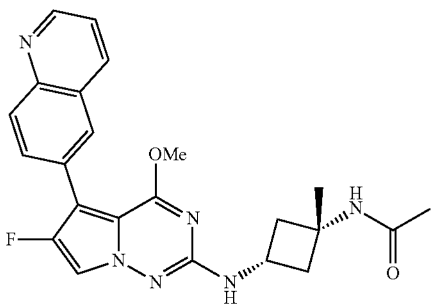
1050



[1456] (R)-4-Methoxy-5-(quinolin-6-yl)-N-(tetrahydro-2H-pyran-3-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1050.

[1457] Off-white solid (59 mg, 0.157 mmol, 46.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.51-1.63 (2H, m), 1.67-1.76 (1H, m), 1.95-2.04 (1H, m), 3.06-3.17 (1H, m), 3.25-3.32 (1H, m), 3.72-3.81 (2H, m), 3.93-3.98 (1H, m), 3.96 (3 H, s), 6.60 (1H, d, J=8.21 Hz), 6.78 (1H, d, J=2.46 Hz), 7.52 (1H, dd, J=8.35, 4.24 Hz), 7.67 (1H, d, J=2.46 Hz), 7.94-8.03 (2H, m), 8.11 (1 H, s), 8.36 (1H, dd, J=8.35, 1.51 Hz), 8.86 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{21}H_{21}N_5O_2$ m/z 376.2 (M+1).

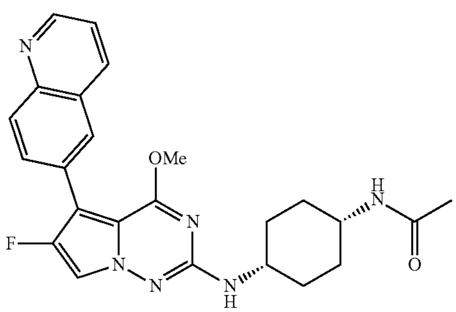
1052



[1458] N-(cis-3-((6-Fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide 1052.

[1459] Off-white solid (14 mg, 0.032 mmol, 90.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.38 (3H, s), 1.76 (3H, s), 2.11-2.21 (2H, m), 2.42 (2H, ddd, J=9.65, 7.46, 2.60 Hz), 3.91 (3 H, s), 4.01 (1 H, sxt, J=7.83 Hz), 7.09 (1H, d, J=6.84 Hz), 7.55 (1H, dd, J=8.35, 4.24 Hz), 7.85 (1H, d, J=2.74 Hz), 7.88 (1H, dd, J=8.76, 1.64 Hz), 8.01-8.05 (2H, m), 8.06 (1 H, s), 8.39 (1H, dd, J=8.49, 1.10 Hz), 8.90 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{23}H_{23}FN_6O_2$ m/z 435.2 (M+1).

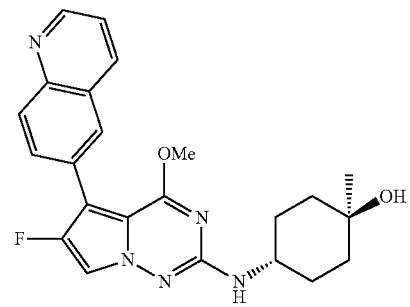
1054



[1460] N-(cis-4-((6-Fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide 1054.

[1461] Off-white solid (8.6 mg, 0.019 mmol, 70.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.50-1.59 (2H, m), 1.61-1.72 (4H, m), 1.73-1.81 (2H, m), 1.81 (3 H, s), 3.67 (2H, br d, J=3.29 Hz), 3.93 (3 H, s), 6.56 (1H, d, J=6.30 Hz), 7.50-7.59 (1H, m), 7.70 (1 H, d, J=7.12 Hz), 7.84 (1H, d, J=2.74 Hz), 7.89 (1H, dd, J=8.76, 1.64 Hz), 8.03 (1H, d, J=8.76 Hz), 8.07 (1 H, s), 8.39 (1H, dd, J=8.35, 1.23 Hz), 8.90 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{24}H_{25}FN_6O_2$ m/z 449.2 (M+1).

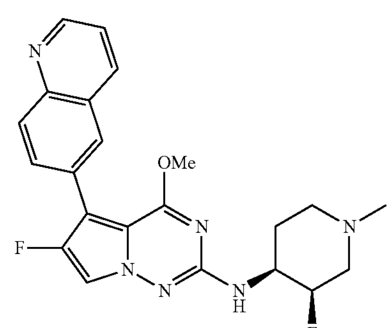
1056



[1462] trans-4-((6-Fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 1056.

[1463] Off-white solid (9.7 mg, 0.023 mmol, 30.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.36-1.53 (4H, m), 1.56-1.65 (2H, m), 1.80-1.92 (2H, m), 3.63 (1 H, br dd, J=8.21, 3.83 Hz), 3.91 (3H, s), 4.23 (1H, s), 6.59 (1H, d, J=7.94 Hz), 7.55 (1H, dd, J=8.35, 4.24 Hz), 7.85 (1H, d, J=2.74 Hz), 7.89 (1H, dd, J=8.76, 1.64 Hz), 8.03 (1H, d, J=8.76 Hz), 8.06 (1 H, s), 8.39 (1H, dd, J=8.49, 1.10 Hz), 8.90 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{23}H_{24}FN_5O_2$ m/z 422.2 (M+1).

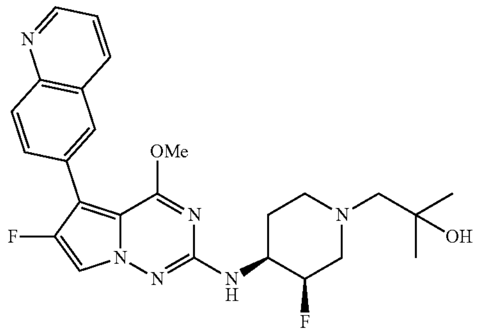
1057



[1464] 6-Fluoro-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1057.

[1465] White solid (6 mg, 0.014 mmol, 18.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.64-1.73 (1H, m), 1.93 (1 H, qd, J=12.23, 3.83 Hz), 2.06 (1 H, br t, J=11.09 Hz), 2.17 (1H, dd, J=37.60, 12.59 Hz), 2.19 (3 H, s), 2.80 (1H, br d, J=11.23 Hz), 3.05 (1 H, br t, J=10.54 Hz), 3.69-3.83 (1H, m), 3.93 (3 H, s), 4.90 (1H, d, J=49.65 Hz), 6.74 (1H, d, J=7.67 Hz), 7.55 (1H, dd, J=8.35, 4.24 Hz), 7.84 (1H, d, J=2.74 Hz), 7.89 (1H, dd, J=8.62, 1.51 Hz), 8.04 (1H, d, J=8.76 Hz), 8.07 (1 H, s), 8.39 (1H, dd, J=8.49, 1.09 Hz), 8.90 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{22}H_{22}F_2N_6O$ m/z 425.2 (M+1).

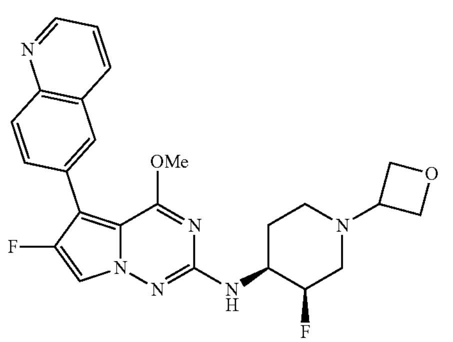
1058



[1466] 1-((3R,4S)-3-Fluoro-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol 1058.

[1467] White solid (3 mg, 0.006 mmol, 23.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.09 (6 H, s), 1.60-1.70 (1H, m), 1.95 (1 H, qd, J=12.18, 3.70 Hz), 2.20-2.28 (2 H, m), 2.29-2.35 (1H, m), 2.37-2.48 (1H, m), 2.92-3.03 (1H, m), 3.23-3.31 (1H, m), 3.68-3.85 (1H, m), 3.93 (3H, s), 4.08 (1H, s), 4.85 (1H, d, J=49.60 Hz), 6.71 (1H, d, J=7.67 Hz), 7.55 (1 H, dd, J=8.21, 4.11 Hz), 7.84 (1H, d, J=3.01 Hz), 7.89 (1H, dd, J=8.62, 1.78 Hz), 8.04 (1H, d, J=8.76 Hz), 8.07 (1 H, s), 8.40 (1H, d, J=8.49 Hz), 8.90 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{25}H_{28}F_2N_6O_2$ m/z 483.2 (M+1).

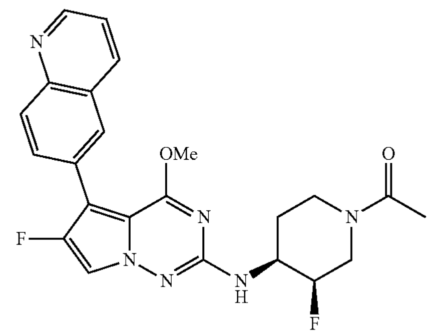
1059



[1468] 6-Fluoro-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1059.

[1469] White solid (14 mg, 0.030 mmol, 21.2% yield). ^{1}H NMR (500 MHz, DMSO-d_6) δ ppm 1.67-1.77 (1H, m), 1.92 (1 H, qd, J=12.21, 3.43 Hz), 1.98-2.06 (1H, m), 2.15 (1H, dd, J=36.80, 12.62 Hz), 2.76 (1H, br d, J=10.15 Hz), 2.99 (1 H, br t, J=10.02 Hz), 3.49 (1 H, quin, J=6.31 Hz), 3.71-3.88 (1H, m), 3.93 (3 H, s), 4.40 (1H, t, J=6.17 Hz), 4.46 (1H, t, J=6.17 Hz), 4.54 (2 H, td, J=6.52, 2.88 Hz), 4.92 (1H, d, J=49.45 Hz), 6.81 (1H, d, J=7.96 Hz), 7.55 (1H, dd, J=8.23, 4.12 Hz), 7.84 (1H, d, J=3.02 Hz), 7.89 (1H, dd, J=8.64, 1.51 Hz), 8.04 (1H, d, J=8.78 Hz), 8.07 (1 H, s), 8.36-8.43 (1H, m), 8.90 (1H, dd, J=4.12, 1.65 Hz); ESIMS found for $C_{24}H_{24}F_2N_6O_2$ m/z 467.2 (M+1).

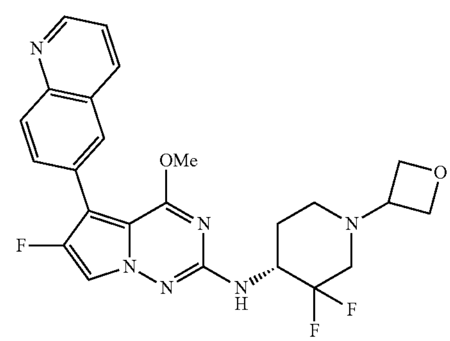
1061



[1470] 1-((3R,4S)-3-Fluoro-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 1061.

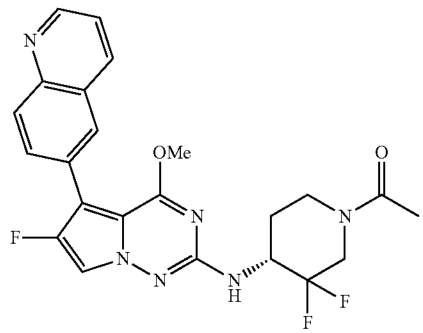
[1471] Tan solid (7 mg, 0.016 mmol, 63.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.67-1.74 (1H, m), 1.74-1.91 (1H, m), 2.00(3 H, s), 2.66-2.97 (1H, m), 3.86-4.17(3 H, m), 3.93 (3 H, s), 4.41-4.76 (1H, m), 4.98 (1H, d, J=49.35 Hz), 6.90 (1H, dd, J=7.80, 3.15 Hz), 7.55 (1H, dd, J=8.35, 4.24 Hz), 7.83 (1H, d, J=3.01 Hz), 7.90 (1H, dd, J=8.62, 1.51 Hz), 8.04 (1H, d, J=8.76 Hz), 8.08 (1 H, s), 8.40 (1H, dd, J=8.35, 1.23 Hz), 8.90 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{23}H_{22}F_2N_6O_2$ m/z 453.2 (M+1).

1062



[1472] (R)—N-(3,3-Difluoro-1-(oxetan-3-yl)piperidin-4-yl)-6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1062.

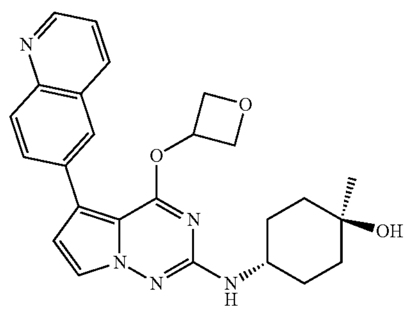
[1473] Yellow solid (1.6 mg, 0.003 mmol, 14.1% yield). ^{1}HNMR(499 MHz, DMSO-d_6) δ ppm 1.75-1.96 (2H, m), 2.13-2.24 (1H, m), 2.74-2.83 (1H, m), 2.98-3.10 (1H, m), 3.62 (1H, br d, J=6.02 Hz), 3.95 (3H, s), 3.96 (1H, s), 4.20-4.37 (1H, m), 4.45 (2 H, dt, J=14.99, 6.19 Hz), 4.56 (2 H, td, J=6.57, 3.83 Hz), 7.02 (1H, d, J=9.31 Hz), 7.58 (1H, dd, J=8.21, 4.11 Hz), 7.82-7.88 (1H, m), 7.92 (1H, br d, J=8.76 Hz), 8.05 (1H, d, J=8.49 Hz), 8.10 (1 H, s), 8.44 (1H, d, J=7.94 Hz), 8.93 (1 H, br s); ESIMS found for $C_{24}H_{23}F_3N_6O_2$ m/z 485.2 (M+1).



1064

[1474] (R)-1-(3,3-Difluoro-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 1064.

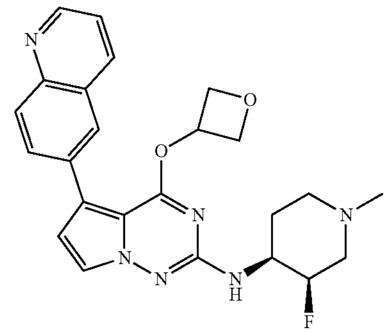
[1475] Off-white solid (7.7 mg, 0.016 mmol, 70.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.55-1.83 (1H, m), 1.85-2.00 (1H, m), 2.03-2.10 (3H, m), 2.92-3.04 (1H, m), 3.61-3.91 (1H, m), 3.95 (3 H, s), 4.12-4.31 (1H, m), 4.44-4.60 (2H, m), 7.10 (1H, dd, J=9.31, 1.92 Hz), 7.51-7.60 (1H, m), 7.85 (1H, t, J=2.33 Hz), 7.90 (1H, dd, J=8.76, 1.64 Hz), 8.04 (1H, d, J=8.76 Hz), 8.08 (1 H, s), 8.40 (1H, dd, J=8.49, 1.09 Hz), 8.90 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{23}H_{21}F_3N_6O_2$ m/z 471.2 (M+1).



1089

[1476] (1r,4r)-1-Methyl-4-((4-(oxetan-3-yloxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol 1089.

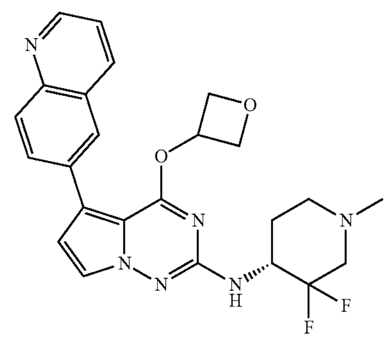
[1477] White solid (20 mg, 0.045 mmol, 27.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.37-1.48 (4H, m), 1.55-1.65 (2H, m), 1.81-1.90 (2H, m), 3.55-3.67 (1H, m), 4.25 (1 H, s), 4.56 (2H, dd, J=7.80, 5.34 Hz), 4.86 (2H, t, J=7.12 Hz), 5.66-5.74 (1H, m), 6.44 (1H, d, J=7.67 Hz), 6.82 (1H, d, J=2.46 Hz), 7.51-7.57 (1H, m), 7.69 (1H, d, J=2.46 Hz), 7.98-8.05 (1H, m), 8.06-8.12 (1H, m), 8.21 (1H, d, J=1.92 Hz), 8.36 (1H, dd, J=8.35, 1.23 Hz), 8.87 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{25}H_{27}N_5O_3$ m/z 446.2 (M+1).



1090

[1478] N-((3R,4S)-3-Fluoro-1-methylpiperidin-4-yl)-4-(oxetan-3-yloxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1090.

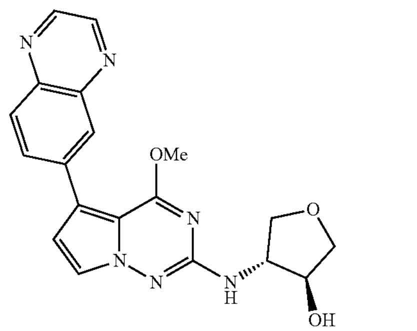
[1479] Off-white solid (19 mg, 0.042 mmol, 21.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.63-1.75 (1H, m), 1.90 (1 H, qd, J=12.23, 3.56 Hz), 2.06 (1 H, br t, J=11.36 Hz), 2.18 (1H, dd, J=37.85, 12.87 Hz), 2.19 (3 H, s), 2.80 (1H, br d, J=12.05 Hz), 3.00-3.10 (1 H, m), 3.64-3.82 (1H, m), 4.57 (2H, dd, J=7.53, 5.34 Hz), 4.87 (1H, d, J=49.60 Hz), 4.85-4.89 (2H, m), 5.71 (1 H, quin, J=5.75 Hz), 6.64 (1H, d, J=7.94 Hz), 6.85 (1H, d, J=2.46 Hz), 7.54 (1 H, dd, J=8.35, 4.24 Hz), 7.69 (1H, d, J=2.46 Hz), 8.01-8.04 (1H, m), 8.07-8.11 (1H, m), 8.22 (1H, d, J=1.92 Hz), 8.36 (1H, dd, J=8.35, 1.23 Hz), 8.87 (1H, dd, J=4.24, 1.78 Hz); ESIMS found for $C_{24}H_{25}FN_6O_2$ m/z 449.2 (M+1).



1091

[1480] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-4-(oxetan-3-yloxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1091.

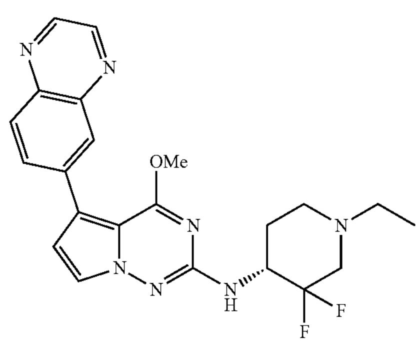
[1481] Tan solid (14 mg, 0.030 mmol, 15.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.72-1.90 (2H, m), 2.12-2.23 (1H, m), 2.26 (3 H, s), 2.39 (1H, dd, J=26.90, 12.05 Hz), 2.79 (1H, br d, J=11.50 Hz), 2.99-3.11 (1H, m), 4.09-4.27 (1H, m), 4.57 (2H, ddd, J=12.73, 7.26, 5.48 Hz), 4.88 (2 H, q, J=7.12 Hz), 5.73 (1 H, quin, J=5.75 Hz), 6.84 (1H, br d, J=9.31 Hz), 6.87 (1H, d, J=2.46 Hz), 7.54 (1H, dd, J=8.21, 4.11 Hz), 7.70 (1H, d, J=2.74 Hz), 7.99-8.06 (1 H, m), 8.07-8.14 (1H, m), 8.23 (1H, d, J=2.19 Hz), 8.37 (1H, dd, J=8.35, 1.23 Hz), 8.87 (1H, dd, J=4.11, 1.64 Hz); ESIMS found for $C_{24}H_{24}F_2N_6$02 m/z 467.2 (M+1).



1093

[1482] (3S,4R)-4-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)tetrahydrofuran-3-ol 1093.

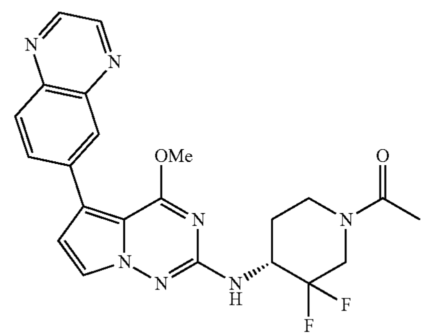
[1483] Yellow solid (30 mg,0 0.079 mmol, 33.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 3.55 (1H, dd, J=9.31, 1.92 Hz), 3.66-3.72 (1H, m), 3.92 (1H, dd, J=9.31, 4.65 Hz), 3.99 (3 H, s), 4.01-4.06 (2H, m), 4.27 (1 H, dt, J=3.76, 2.09 Hz), 5.19 (1H, d, J=3.83 Hz), 6.89 (1H, d, J=2.74 Hz), 6.96 (1H, d, J=5.48 Hz), 7.71 (1H, d, J=2.46 Hz), 8.05-8.09 (1H, m), 8.09-8.13 (1H, m), 8.24 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{19}H_{18}N_6O_3$ m/z 379.2 (M+1).



1095

[1484] (R)—N-(1-Ethyl-3,3-difluoropiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1095.

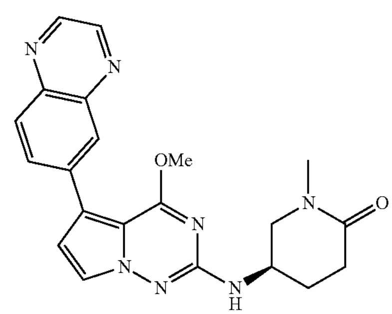
[1485] Fluffy yellow solid (8 mg, 0.017 mmol, 49.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.02 (3 H, br s), 1.79 (1H, br d, J=10.95 Hz), 1.87 (1 H, br s), 2.12-2.25 (1H, m), 2.37-2.49 (3H, m), 2.88 (1H, br d, J=9.58 Hz), 3.12 (1 H, br dd, J=4.38, 1.64 Hz), 4.01 (3 H, s), 4.20-4.36 (1H, m), 6.85-6.96 (2H, m), 7.69 (1H, br d, J=2.19 Hz), 8.05-8.09 (1H, m), 8.10-8.14 (1H, m), 8.25 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{22}H_{23}F_2N_7O$ m/z 440.2 (M+1).



1096

[1486] (R)-1-(3,3-Difluoro-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one 1096.

[1487] Fluffy yellow solid (4 mg, 0.009 mmol, 60.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.57-1.85 (1H, m), 1.86-2.02 (1H, m), 2.03-2.11 (3H, m), 3.33-3.43 (1H, m), 3.65-3.94 (1H, m), 3.98-4.05 (3H, m), 4.10-4.64 (3H, m), 6.92 (1H, d, J=2.74 Hz), 7.05 (1H, d, J=9.31 Hz), 7.69 (1H, dd, J=2.46, 1.37 Hz), 8.05-8.09 (1H, m), 8.10-8.14 (1H, m), 8.25 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{22}H_{21}F_2N_7O_2$ m/z 454.2 (M+1).

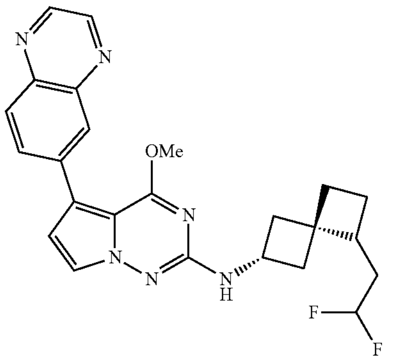


1097

[1488] (R)-5-((4-Methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one 1097.

[1489] Yellow solid (26 mg, 0.064 mmol, 33.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.88-1.96 (1H, m), 1.97-2.05 (1H, m), 2.27-2.36 (1H, m), 2.37-2.45 (1H, m), 2.81 (3 H, s), 3.26 (1H, dd, J=12.05, 7.67 Hz), 3.58 (1H, dd, J=11.64, 4.79 Hz), 3.99 (3 H, s), 4.06-4.17 (1H, m), 6.90 (1H, d, J=2.74 Hz), 6.98 (1H, d, J=7.39 Hz), 7.71 (1H, d, J=2.74 Hz), 8.06-8.09 (1H, m), 8.10-8.13 (1H, m), 8.24 (1H, d, J=1.64 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.64 Hz); ESIMS found for $C_{21}H_{21}N_7O_2$ m/z 404.2 (M+1).

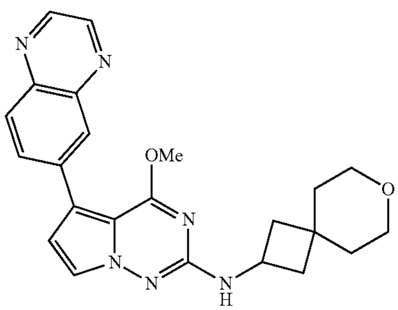
1099



[1490] N-((4s,6r)-1-(2,2-Difluoroethyl)-1-azaspiro[3.3]heptan-6-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1099.

[1491] Yellow solid (1 mg, 0.024 mmol, 31.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.11-2.22 (4H, m), 2.41 (2H, ddd, J=9.31, 6.98, 2.87 Hz), 2.83 (2 H, td, J=16.08, 4.24 Hz), 3.17 (2H, t, J=6.71 Hz), 3.87-3.96 (1H, m), 3.97 (3 H, s), 6.00 (1 H, tt, J=56.25, 4.40 Hz), 6.88 (1H, d, J=2.74 Hz), 6.92 (1H, d, J=7.94 Hz), 7.68 (1H, d, J=2.74 Hz), 8.05-8.08 (1H, m), 8.09-8.12 (1H, m), 8.23 (1H, d, J=1.64 Hz), 8.89 (1H, d, J=1.92 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{23}F_2N_7O$ m/z 452.2 (M+1).

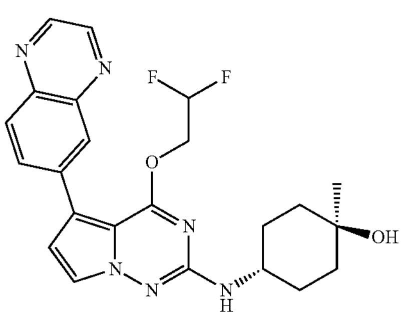
1100



[1492] 4-Methoxy-5-(quinoxalin-6-yl)-N-(7-oxaspiro[3.5]nonan-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1100.

[1493] Yellow solid (18 mg, 0.043 mmol, 44.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.48-1.54 (2H, m), 1.56-1.63 (2H, m), 1.76-1.85 (2H, m), 2.24-2.34 (2H, m), 3.42-3.48 (2H, m), 3.51-3.59 (2H, m), 3.97 (3 H, s), 4.19 (1 H, sxt, J=7.83 Hz), 6.87 (1H, d, J=2.74 Hz), 7.04 (1H, d, J=7.12 Hz), 7.68 (1H, d, J=2.74 Hz), 8.05-8.08 (1H, m), 8.08-8.13 (1H, m), 8.23 (1H, d, J=1.92 Hz), 8.89 (1H, d, J=1.64 Hz), 8.93 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{24}N_6O_2$ m/z 417.2 (M+1).

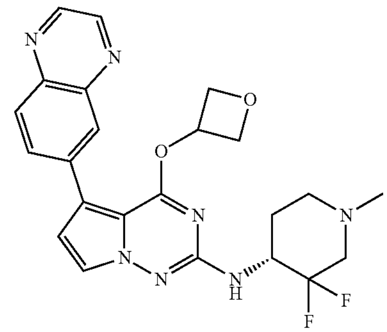
1130



[1494] (1r,4r)-4-((4-(2,2-Difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 1130.

[1495] White solid (10.45 mg, 0.023 mmol). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.47 (3 H, s), 0.62-0.85 (4H, m), 0.87-1.01 (2H, m), 1.18-1.31 (2H, m), 2.88-3.02 (1H, m), 3.86 (2 H, td, J=13.88, 3.88 Hz), 5.35 (1 H, tt, J=55.00, 3.84 Hz), 5.99 (1H, d, J=2.63 Hz), 6.76 (1 H, d, J=2.63 Hz), 7.19-7.26 (1H, m), 7.28-7.36 (1H, m), 7.42 (1H, d, J=1.75 Hz), 8.01 (1H, d, J=1.88 Hz), 8.05 (1H, d, J=1.88 Hz); ESIMS found for $C_{23}H_{24}F_2N_6O_2$ m/z 455.1 (M+1).

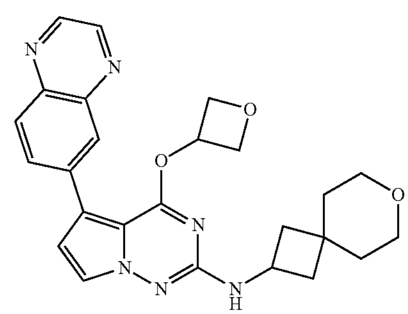
1136



[1496] (R)—N-(3,3-Difluoro-1-methylpiperidin-4-yl)-4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1136.

[1497] Tan solid (16 mg, 0.034 mmol, 15.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.73-1.90 (2H, m), 2.13-2.24 (1H, m), 2.26 (3 H, s), 2.39 (1H, dd, J=27.45, 11.25 Hz), 2.79 (1H, br d, J=11.50 Hz), 3.00-3.12 (1H, m), 4.13-4.29 (1H, m), 4.62 (2H, ddd, J=16.22, 7.60, 5.48 Hz), 4.88 (2 H, q, J=6.94 Hz), 5.70-5.80 (1H, m), 6.89 (1H, br d, J=9.31 Hz), 6.97 (1 H, d, J=2.46 Hz), 7.73 (1H, d, J=2.74 Hz), 8.11 (1H, d, J=8.76 Hz), 8.21 (1H, dd, J=8.76, 1.92 Hz), 8.40 (1H, d, J=1.92 Hz), 8.91 (1H, d, J=1.92 Hz), 8.95 (1H, d, J=1.92 Hz); ESIMS found for $C_{23}H_{23}F_2N_7O_2$ m/z 468.2 (M+1).

1137

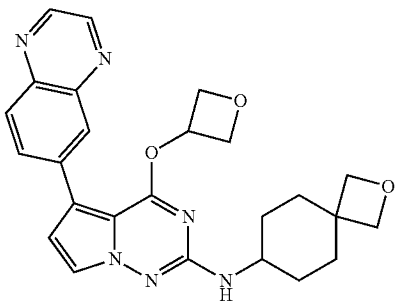


[1498] 4-(Oxetan-3-yloxy)-5-(quinoxalin-6-yl)-N-(7-oxaspiro[3.5]nonan-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1137.

[1499] Beige solid (20 mg, 0.044 mmol, 40.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.45-1.55 (2H, m), 1.56-1.63 (2H, m), 1.72-1.84 (2H, m), 2.22-2.33 (2H, m), 3.42-3.49 (2H, m), 3.50-3.59 (2H, m), 4.16 (1 H, sxt, J=7.88

Hz), 4.61 (2H, dd, J=7.67, 5.20 Hz), 4.87 (2H, t, J=7.12 Hz), 5.71 (1 H, quin, J=5.68 Hz), 6.94 (1H, d, J=2.74 Hz), 6.98 (1H, d, J=7.39 Hz), 7.71 (1H, d, J=2.74 Hz), 8.10 (1H, d, J=8.76 Hz), 8.19 (1H, dd, J=8.76, 1.92 Hz), 8.39 (1 H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.95 (1H, d, J=1.92 Hz); ESIMS found for $C_{25}H_{26}N_6O_3$ m/z 459.25 (M+1).

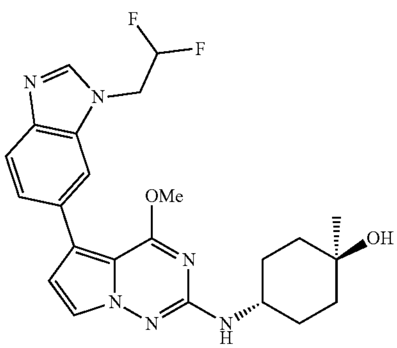
1138



[1500] 4-(Oxetan-3-yloxy)-5-(quinoxalin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1138.

[1501] Yellow solid (14 mg, 0.031 mmol, 28.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.18-1.31 (2H, m), 1.53 (2 H, td, J=12.87, 3.29 Hz), 1.86 (2 H, br dd, J=13.28, 3.15 Hz), 2.07 (2H, br d, J=13.14 Hz), 3.47-3.59 (1H, m), 4.24 (2H, s), 4.32 (2H, s), 4.62 (2H, dd, J=7.67, 5.48 Hz), 4.85 (2H, t, J=7.12 Hz), 5.70 (1 H, quin, J=5.75 Hz), 6.50 (1H, d, J=7.94 Hz), 6.93 (1H, d, J=2.74 Hz), 7.70 (1H, d, J=2.74 Hz), 8.10 (1H, d, J=8.76 Hz), 8.19 (1H, dd, J=8.76, 1.92 Hz), 8.39 (1H, d, J=1.92 Hz), 8.90 (1H, d, J=1.92 Hz), 8.94 (1H, d, J=1.92 Hz); ESIMS found for $C_{25}H_{26}N_6O_3$ m/z 459.25 (M+1).

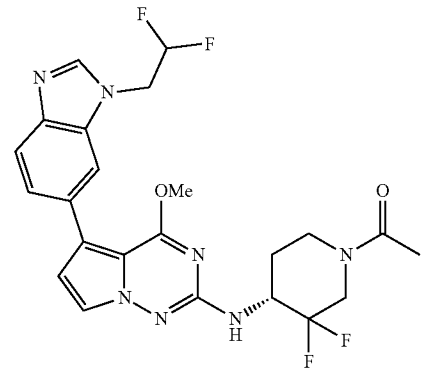
1139



[1502] (1r,4r)-4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol 1139.

[1503] Fluffy white solid (11 mg, 0.024 mmol, 49.9% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.15 (3 H, s), 1.37-1.53 (4H, m), 1.56-1.66 (2H, m), 1.82-1.93 (2H, m), 3.64 (1 H, br dd, J=8.21, 3.56 Hz), 3.92 (3H, s), 4.23 (1H, s), 4.81 (2 H, td, J=15.95, 2.87 Hz), 6.47 (1 H, tt, J=54.30, 3.00 Hz), 6.39 (1H, d, J=7.94 Hz), 6.61 (1H, d, J=2.46 Hz), 7.42 (1H, dd, J=8.35, 1.51 Hz), 7.60 (1H, d, J=2.46 Hz), 7.63 (1H, d, J=8.49 Hz), 7.80 (1 H, s), 8.20 (1 H, s); ESIMS found for $C_{23}H_{26}F_2N_6O_2$ m/z 457.2 (M+1).

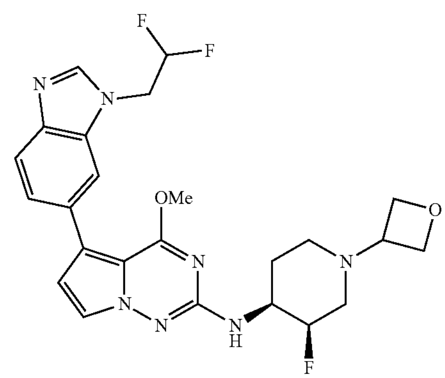
1140



[1504] (R)-1-(4-((5-(1-(2,2-Difluoroethyl)-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one 1140.

[1505] Fluffy white solid (5 mg, 0.010 mmol, 32.4% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.57-1.83 (1H, m), 1.85-2.00 (1H, m), 2.03-2.09 (3H, m), 2.93-3.06 (1H, m), 3.61-3.92 (2H, m), 3.96 (3 H, s), 4.09-4.31 (1H, m), 4.45-4.62 (2H, m), 4.81 (2 H, td, J=16.15, 3.01 Hz), 6.48 (1 H, tt, J=54.30, 3.00 Hz), 6.67 (1H, d, J=2.46 Hz), 6.91 (1H, d, J=9.31 Hz), 7.43 (1H, dd, J=8.35, 1.51 Hz), 7.61 (1H, dd, J=2.46, 1.37 Hz), 7.64 (1H, d, J=8.21 Hz), 7.82 (1 H, s), 8.21 (1 H, s); ESIMS found for $C_{23}H_{23}F_4N_7O_2$ m/z 506.2 (M+1).

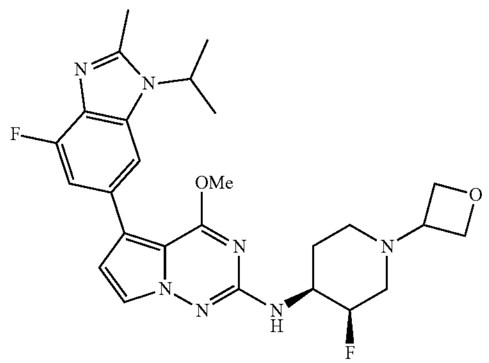
1141



[1506] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1141.

[1507] Fluffy white solid (13 mg, 0.026 mmol, 61.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.68-1.75 (1H, m), 1.91 (1 H, qd, J=12.14, 3.56 Hz), 1.98-2.06 (1H, m), 2.16 (1H, dd, J=37.55, 12.32 Hz), 2.76 (1H, br d, J=11.23 Hz), 2.95-3.05 (1H, m), 3.49 (1 H, quin, J=6.30 Hz), 3.71-3.89 (1H, m), 3.94 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.81 (2 H, td, J=15.95, 2.87 Hz), 4.94 (1H, d, J=50.50 Hz), 6.47 (1 H, tt, J=54.85, 3.30 Hz), 6.60 (1H, d, J=7.94 Hz), 6.65 (1H, d, J=2.74 Hz), 7.42 (1H, dd, J=8.49, 1.64 Hz), 7.60 (1H, d, J=2.46 Hz), 7.64 (1H, d, J=8.49 Hz), 7.81 (1 H, s), 8.21 (1 H, s); ESIMS found for $C_{24}H_{26}F_3N_7O_2$ m/z 502.2 (M+1).

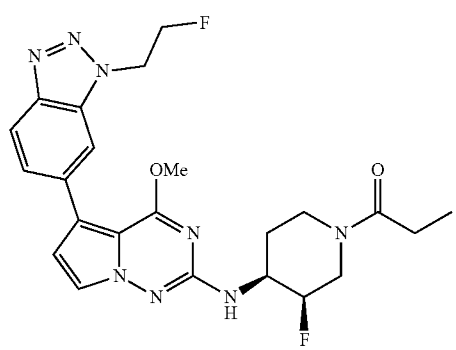
1142



[1508] N-((3R,4S)-3-Fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1142.

[1509] White solid (14 mg, 0.027 mmol, 41.6% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.59 (6H, d, J=6.84 Hz), 1.69-1.78 (1H, m), 1.85-1.97 (1H, m), 1.97-2.06 (1H, m), 2.15 (1H, dd, J=36.75, 12.59 Hz), 2.58 (3 H, s), 2.76 (1H, br d, J=11.22 Hz), 2.94-3.04 (1H, m), 3.49 (1 H, quin, J=6.43 Hz), 3.73-3.91 (1H, m), 3.96 (3 H, s), 4.40 (1H, t, J=6.16 Hz), 4.46 (1 H, t, J=6.16 Hz), 4.54 (2 H, td, J=6.57, 3.01 Hz), 4.76 (1 H, spt, J=6.94 Hz), 4.93 (1H, d, J=49.65 Hz), 6.62 (1H, d, J=7.94 Hz), 6.69 (1H, d, J=2.46 Hz), 7.12 (1H, dd, J=12.05, 1.10 Hz), 7.59 (1 H, d, J=2.74 Hz), 7.64 (1H, d, J=1.09 Hz); ESIMS found for $C_{26}H_{31}F_2N_7O_2$ m/z 512.3 (M+1).

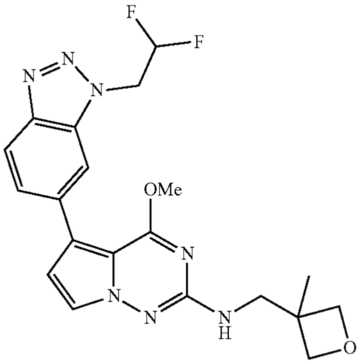
1143



[1510] 1-((3R,4S)-3-Fluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)propan-1-one 1143.

[1511] Fluffy white solid (8.8 mg, 0.018 mmol, 46.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.00 (3H, t, J=7.39 Hz), 1.67-1.90 (2H, m), 2.27-2.42 (2H, m), 2.70-2.99 (1H, m), 3.13-3.22 (1H, m), 3.91-4.00 (1H, m), 3.96 (3 H, s), 4.05-4.22 (1H, m), 4.44-4.77 (1H, m), 4.94 (2 H, dt, J=47.15, 4.65 Hz), 4.99 (1H, d, J=49.35 Hz), 5.08 (2 H, dt, J=27.70, 4.65 Hz), 6.76 (1H, d, J=2.46 Hz), 6.78 (1H, d, J=7.67 Hz), 7.62 (1H, dd, J=8.62, 1.51 Hz), 7.65 (1 H, d, J=2.74 Hz), 8.01 (1H, d, J=10.40 Hz), 8.01 (1 H, s); ESIMS found for $C_{23}H_{26}F_2N_8O_2$ m/z 485.2 (M+1).

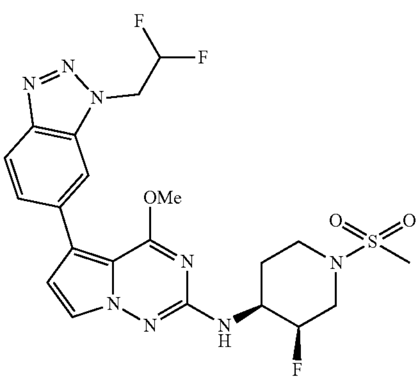
1144



[1512] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-((3-methyloxetan-3-yl)methyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1144.

[1513] White solid (33 mg, 0.077 mmol, 38.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.30 (3 H, s), 3.46 (2H, d, J=6.02 Hz), 3.96 (3 H, s), 4.22 (2H, d, J=5.75 Hz), 4.51 (2 H, d, J=5.75 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.60 (1 H, tt, J=54.30, 3.00 Hz), 6.73 (1H, d, J=2.74 Hz), 6.95 (1H, t, J=6.16 Hz), 7.63-7.66 (1H, m), 7.64 (1H, d, J=2.46 Hz), 8.01-8.05 (2 H, m); ESIMS found for $C_{20}H_{21}F_2N_7O_2$ m/z 430.2 (M+1).

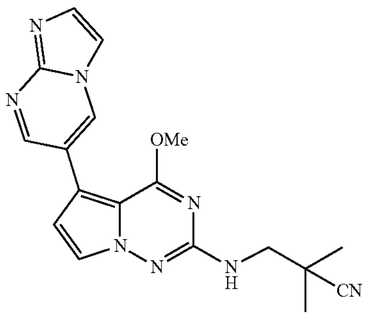
1145



[1514] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(methylsulfonyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1145.

[1515] Fluffy white solid (6 mg, 0.011 mmol, 33.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.77-1.88 (1H, m), 1.96 (1 H, qd, J=12.50, 4.38 Hz), 2.93 (3 H, s), 3.02 (1 H, td, J=12.25, 2.60 Hz), 3.20 (1H, dd, J=37.55, 12.59 Hz), 3.61-3.70 (1H, m), 3.80-3.89 (1H, m), 3.90-4.04 (1H, m), 3.96 (3 H, s), 5.05 (1H, d, J=49.10 Hz), 5.30 (2 H, td, J=15.95, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.76 (1H, d, J=2.74 Hz), 6.88 (1H, d, J=7.94 Hz), 7.63 (1H, d, J=2.46 Hz), 7.64-7.66 (1H, m), 8.02-8.05 (2H, m); ESIMS found for $C_{21}H_{23}F_3N_8O_3S$ m/z 525.15

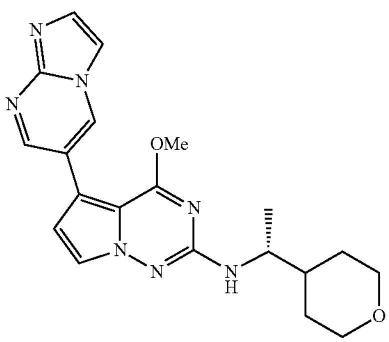
1146



[1516] 3-((5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2,2-dimethylpropanenitrile 1146.

[1517] Beige solid (20 mg, 0.055 mmol, 27.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.36 (6 H, s), 3.49 (2H, d, J=6.57 Hz), 4.02 (3 H, s), 6.81 (1H, d, J=2.74 Hz), 7.17 (1 H, t, J=6.57 Hz), 7.69 (1H, d, J=2.46 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.10 (1H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{18}N_8O$ m/z 363.3 (M+1).

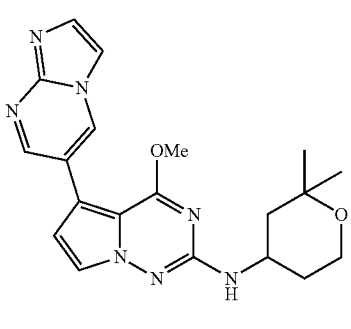
1147



[1518] (R)-5-(Imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(tetrahydro-2H-pyran-4-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1147.

[1519] Beige solid (14 mg, 0.036 mmol, 17.8% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.13 (3H, d, J=6.57 Hz), 1.20-1.33 (3H, m), 1.58-1.65 (1H, m), 1.66-1.73 (2H, m), 3.18-3.30 (2H, m), 3.69 (1 H, br dd, J=14.92, 7.26 Hz), 3.83-3.92 (2H, m), 3.98 (3 H, s), 6.61 (1H, d, J=9.03 Hz), 6.76 (1H, d, J=2.46 Hz), 7.64 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.08 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

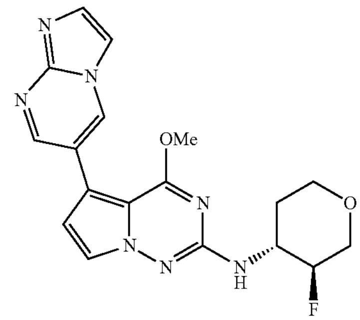
1148



[1520] N-(2,2-Dimethyltetrahydro-2H-pyran-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1148.

[1521] Off-white solid (20 mg, 0.051 mmol, 25.5% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.16 (3H, s), 1.22 (3H, s), 1.32 (1H, t, J=12.32 Hz), 1.35-1.43 (1H, m), 1.81-1.86 (1H, m), 1.87-1.92 (1H, m), 3.59-3.71 (2H, m), 3.91-4.02 (1H, m), 3.98 (3 H, s), 6.64 (1H, d, J=8.21 Hz), 6.77 (1H, d, J=2.46 Hz), 7.66 (1H, d, J=2.46 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.73 (1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{23}N_7O_2$ m/z 394.2 (M+1).

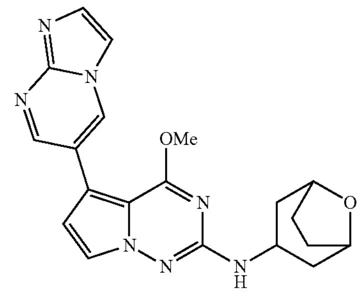
1149



[1522] N-((3S,4R)-3-Fluorotetrahydro-2H-pyran-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1149.

[1523] Off-white solid (14 mg, 0.037 mmol, 18.3% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.55-1.68 (1H, m), 2.03-2.13 (1H, m), 3.39-3.44 (1H, m), 3.44-3.51 (1H, m), 3.80-3.88 (1H, m), 3.98-4.02 (1H, m), 4.00 (3 H, s), 4.05-4.10 (1H, m), 4.58 (1 H, dtd, J=48.55, 8.21, 8.21, 4.38 Hz), 6.80 (1H, d, J=2.74 Hz), 7.03 (1H, d, J=8.21 Hz), 7.69 (1H, d, J=2.46 Hz), 7.73 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.37 Hz), 8.74 (1H, d, J=2.46 Hz), 9.09 (1 H, d, J=2.46 Hz); ESIMS found for $C_{18}H_{18}FN_7O_2$ m/z 384.2 (M+1).

1150

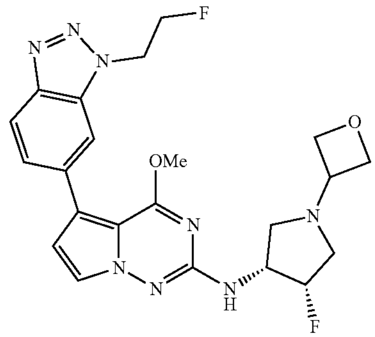


[1524] N-(8-Oxabicyclo[3.2.1]octan-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1150.

[1525] Off-white solid (7 mg, 0.018 mmol, 9.0% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 1.76-1.82 (2H, m), 1.87-1.92 (2H, m), 2.00-2.07 (2H, m), 2.11-2.18 (2H, m), 3.78-3.87 (1H, m), 4.00 (3 H, s), 4.27 (2 H, br s), 6.62 (1H, d, J=4.11 Hz), 6.78 (1H, d, J=2.46 Hz), 7.67 (1H, d, J=2.74 Hz), 7.72 (1H, d, J=1.37 Hz), 7.93 (1H, d, J=1.64 Hz), 8.74

(1H, d, J=2.46 Hz), 9.09 (1H, d, J=2.46 Hz); ESIMS found for $C_{20}H_{21}N_7O_2$ m/z 392.15 (M+1).

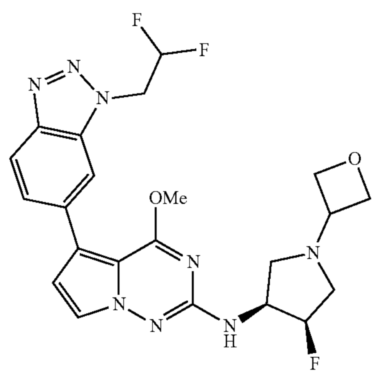
1151



[1526] N-((3R,4S)-4-Fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1151.

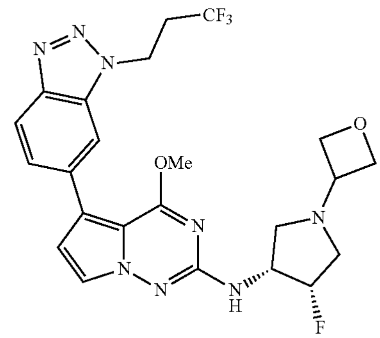
[1527] Fluffy white solid (6 mg, 0.013 mmol, 18.2% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.68 (1H, t, J=9.03 Hz), 2.77 (1H, ddd, J=29.90, 12.05, 1.10 Hz), 3.02 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=33.20, 12.05, 4.38 Hz), 3.79 (1 H, quin, J=6.16 Hz), 3.96 (3 H, s), 4.22-4.38 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 4.94 (2 H, dt, J=47.15, 4.65 Hz), 5.08 (2 H, dt, J=28.00, 4.65 Hz), 5.25 (1 H, dtd, J=55.95, 4.65, 4.65, 1.40 Hz), 6.77 (1H, d, J=2.74 Hz), 6.82 (1H, d, J=7.67 Hz), 7.61-7.64 (1H, m), 7.66 (1H, d, J=2.46 Hz), 8.00-8.03 (2 H, m); ESIMS found for $C_{22}H_{24}F_2N_8O_2$ m/z 471.2 (M+1).

1152



[1528] 5-(1-(2,2-Difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine 1152.

[1529] Fluffy white solid (15 mg, 0.031 mmol, 43.7% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.69 (1H, t, J=9.03 Hz), 2.77 (1H, ddd, J=29.90, 12.05, 1.37 Hz), 3.02 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=33.20, 12.05, 4.38 Hz), 3.74-3.84 (1H, m), 3.96 (3 H, s), 4.24-4.38 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.55-4.64 (2H, m), 5.25 (1 H, dtd, J=55.95, 4.65, 4.65, 1.40 Hz), 5.31 (2 H, td, J=15.81, 2.87 Hz), 6.61 (1 H, tt, J=54.30, 3.00 Hz), 6.77 (1H, d, J=2.46 Hz), 6.84 (1H, d, J=7.67 Hz), 7.63-7.66 (1H, m), 7.67 (1H, d, J=2.74 Hz), 8.04 (1H, d, J=7.94 Hz), 8.04 (1H, d, J=1.10 Hz); ESIMS found for $C_{22}H_{23}F_3N_8O_2$ m/z 489.2 (M+1).



[1530] N-((3R,4S)-4-Fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine 1153.

[1531] Fluffy white solid (10 mg, 0.020 mmol, 28.1% yield). ^{1}H NMR (499 MHz, DMSO-d_6) δ ppm 2.69 (1H, t, J=9.03 Hz), 2.77 (1H, ddd, J=29.90, 12.05, 1.37 Hz), 3.02 (1H, t, J=8.35 Hz), 3.18 (1H, ddd, J=32.90, 11.91, 4.52 Hz), 3.74-3.84 (1H, m), 3.95 (3 H, s), 4.23-4.39 (1H, m), 4.47 (2H, t, J=6.02 Hz), 4.60 (2H, t, J=6.57 Hz), 5.25 (1 H, dtd, J=55.95, 4.65, 4.65, 1.40 Hz), 5.88 (2 H, q, J=9.13 Hz), 6.77 (1H, d, J=2.46 Hz), 6.86 (1H, d, J=7.67 Hz), 7.68 (1H, dd, J=8.62, 1.51 Hz), 7.68 (1H, d, J=2.74 Hz), 8.08 (1H, d, J=8.49 Hz), 8.11 (1 H, s); ESIMS found for $C_{22}H_{22}F_4N_8O_2$ m/z 507.2 (M+1).

Example 12

[1532] Representative compounds were screened using the assay procedure for DYRK1A kinase activity as described below.

[1533] Each compound was dissolved in DMSO as a 10 mM stock and used to prepare compound source plates. Serial dilution (1:3, 11-point dose-response curves from 10 μM to 0.00016 μM) and compound transfer was performed using the ECHO 550 (Labcyte, Sunnyvale, CA) into 1536-well black-walled round bottom plates (Coming).

[1534] The DYRK1A kinase assay was run using the Ser/Thr 18 peptide Z-lyte assay kit according to manufacturer's instructions (Life Technologies-a Division of Thermo-Fisher). This is a non-radioactive assay using fluorescence resonance energy transfer (FRET) between coumarin and fluorescein to detect kinase activity which is represented as a ratio of coumarin emission/fluorescein emission.

[1535] Briefly, recombinant DYRK1A kinase, ATP and Ser/Thr peptide 18 were prepared in 1X Kinase buffer to final concentrations of 0.25 μg/mL, 15 μM, and 4 μM respectively. The mixture was allowed to incubate with the representative compounds for one hour at room temperature. All reactions were performed in duplicate. Unphosphorylated ("0% Control") and phosphorylated ("100% control") forms of Ser/Thr 18 served as control reactions. Additionally, an 11-point dose-response curve of Staurosporine (luM top) was run to serve as a positive compound control.

[1536] After incubation, Development Reagent A was diluted in Development Buffer then added to the reaction and allowed to further incubate for one hour at room temperature. The plate was read at Ex 400 Em 455 to detect the coumarin signal and Ex 400 Em 520 to measure the signal (EnVision Multilabel Plate Reader, PerkinElmer).

[1537] The Emission ratio (Em) was calculated as a ratio of the coumarin (C) emission signal (at 445 nm)/Fluorescein (F) emission signal (at 520 nm). The percent phosphorylation was then calculated using the following formula: [1−((Em ratio X F100%)-C100%)/((C0%-C100%) +(Em ratio X (F100%−F0%)))]. Dose-response curves were generated, and inhibitory concentration (IC_{50}) values were calculated using non-linear regression curve fit in the Dotmatics' Studies Software (Bishops Stortford, UK).

[1538] Table 2 shows the measured activity for representative compounds of Formula I as described herein.

TABLE 2

Compound	EC_{50} (μM)
1	0.0224
3	0.0015
4	0.0011
6	0.0011
7	0.0046
8	0.0006
9	9.9633
10	0.0938
13	0.0055
15	0.0337
16	0.0344
17	0.0175
18	0.0074
19	0.0141
20	0.0034
24	0.0143
26	0.0071
27	9.9633
29	0.0092
30	0.0221
31	0.0077
34	0.0062
36	0.0121
37	0.0025
39	0.0029
40	0.0016
43	0.0013
44	0.0032
45	0.0093
49	0.0026
51	0.0067
52	0.0052
53	0.0007
54	0.0012
55	0.0067
56	0.0013
61	0.0049
62	0.0085
63	0.0046
67	0.0056
74	0.0052
80	0.0562
91	0.0016
92	0.0626
93	0.1944
94	0.0041
95	0.0082
96	0.0010
97	0.0011
98	0.0256
99	0.0045
102	0.0019
103	0.0059
104	0.0012
107	0.0009
108	0.0033
109	0.0010
112	0.0026
113	0.0033
114	0.0019
122	0.0016
124	0.0028
127	0.0022
129	0.0026
137	0.0019
138	0.0043
139	0.0069
140	0.0107
141	0.0218
142	0.0027
143	0.0108
148	0.0018
149	0.0015
151	0.0017
159	0.0029
161	0.0030
164	0.0021
168	0.0027
169	0.0021
170	0.0086
171	0.0029
172	0.0025
173	0.0017
174	0.0030
187	0.1003
188	0.0503
189	0.0188
190	0.0115
191	0.0053
192	0.0009
193	0.0199
194	0.0022
195	0.0039
196	0.0011
197	0.0296
198	0.0045
199	0.0057
200	0.0038
201	0.0020
202	0.0109
203	0.0075
204	0.0035
205	0.0043
206	0.0004
207	0.0013
208	0.0005
209	0.0088
210	0.0015
211	0.0066
212	0.0014
214	0.0022
217	0.0093
218	0.0029
222	0.0035
223	0.0016
224	0.0113
225	0.0117
226	0.0032
227	0.0036
228	0.0034
229	0.0019
230	0.0042
231	0.0072
233	0.0068
236	0.0005
239	0.0029
242	0.0044
243	0.0012
245	0.0007
250	0.0006
252	0.0025
254	0.0018
257	0.0004

TABLE 2-continued

Compound	EC_{50} (μM)
258	0.0008
261	0.1532
262	0.0032
263	0.1117
264	0.0035
265	0.0589
266	0.0029
267	0.0048
268	0.0050
269	0.0023
270	0.0051
271	0.0038
272	0.0013
273	0.0018
274	0.0010
275	0.0034
276	0.0006
277	0.0633
280	0.0334
281	0.0066
282	0.0136
283	0.1099
284	0.2352
287	0.0022
288	0.0026
290	0.0018
304	0.0143
305	0.0807
306	0.0282
310	0.0047
314	0.0041
318	0.0042
319	0.0022
320	0.0082
321	0.0021
322	0.0066
326	0.0073
328	0.0054
329	0.0019
330	0.0023
331	0.0012
332	0.0028
333	0.0011
334	0.0009
335	0.0020
336	0.0013
337	0.0115
338	0.0012
339	0.0048
341	0.0093
342	0.0032
343	0.0007
344	0.0018
345	0.0037
346	0.0344
347	0.0017
348	0.0023
349	0.0066
350	0.0014
351	0.0081
352	0.0022
353	0.0022
355	0.0027
356	0.0088
362	0.0060
363	0.0401
365	0.0028
366	0.0025
367	0.0033
368	0.0040
372	0.0041
373	0.0029
374	0.0029
375	0.0033

TABLE 2-continued

Compound	EC_{50} (μM)
379	0.0033
381	0.0025
382	0.0018
383	0.0014
385	0.0017
386	0.0009
387	0.0007
388	0.0012
389	0.0013
390	0.0030
391	0.0072
392	0.0014
393	0.1779
394	0.0021
395	0.0062
399	0.0035
401	0.0027
405	0.0007
431	0.0023
433	0.0026
434	0.0049
435	0.0089
439	0.0023
441	0.0011
445	0.0021
502	0.0014
503	0.0023
504	0.0014
505	0.0038
506	0.0023
507	0.0031
508	0.0243
509	0.0014
513	0.0028
519	0.0027
520	0.0030
521	0.0026
525	0.0024
526	0.0016
542	0.0011
544	0.0009
549	0.0026
550	0.0016
551	0.0016
554	0.0077
555	0.0050
562	0.0011
563	0.0010
567	0.0037
575	0.0069
576	0.0073
577	0.0064
578	0.0080
582	0.0409
585	0.0022
589	0.0009
616	0.0029
621	0.0354
622	0.0141
623	0.0051
624	0.0086
625	0.0009
626	0.0027
627	0.0039
628	0.0063
629	0.0024
630	0.0049
631	0.0245
639	0.0013
646	0.0034
653	0.0013
658	0.0045
659	0.0009
660	<0.0002

TABLE 2-continued

Compound	EC_{50} (μM)
664	0.0016
666	0.0011
669	0.0016
670	0.0008
672	0.0059
673	0.0053
681	0.0019
686	0.0034
688	0.0023
690	0.0078
691	0.0014
695	0.0013
696	0.0013
699	0.0014
702	0.0012
710	0.0009
711	0.0005
717	0.0023
718	0.0005
719	0.0003
721	0.0057
724	0.0011
725	0.0006
726	0.0018
727	0.0028
730	0.0046
732	0.0010
734	0.0008
739	0.0046
741	0.0012
750	0.0003
754	0.0017
755	0.0023
756	0.0014
757	0.0367
758	0.0011
761	0.0017
762	0.0013
764	0.0004
769	0.0029
770	0.0015
771	0.0001
772	0.0020
773	0.0007
776	0.0005
777	0.0016
780	0.0019
785	0.0005
788	0.0007
791	0.0022
793	0.0013
798	0.0003
799	0.0017
801	0.0032
805	0.0016
806	0.0014
810	0.0109
811	0.0017
812	0.0028
816	0.0028
818	0.0008
821	0.0019
822	0.0018
856	0.0019
904	0.0018
905	0.0004
910	0.0077
911	0.0021
912	0.0008
916	0.0014
918	0.0007
921	0.0014
922	0.0009
924	0.0021

TABLE 2-continued

Compound	EC_{50} (μM)
926	0.0056
927	0.0012
928	0.0020
929	0.0198
930	0.0069
931	0.0015
934	0.0016
935	0.0012
942	0.0189
943	0.0036
944	0.0015
947	0.0022
948	0.0004
954	0.0009
964	0.0043
968	0.0028
975	0.0076
976	0.0025
977	0.0018
978	0.0024
996	0.0029
1038	0.0005
1039	0.0017
1040	0.0027
1041	0.0009
1042	0.0012
1043	0.0028
1044	0.0032
1045	0.0045
1047	0.0021
1048	0.0013
1049	0.0049
1050	0.0135
1052	0.0045
1054	0.0020
1056	0.0011
1057	0.0017
1058	0.0023
1059	0.0019
1061	0.0009
1062	0.0037
1064	0.0020
1089	0.0045
1090	0.0057
1091	0.0018
1093	0.0043
1095	0.0040
1096	0.0030
1097	0.0027
1099	0.0007
1100	0.0067
1130	0.0008
1136	0.0038
1137	0.0048
1138	0.0033
1139	0.0005
1140	0.0013
1141	0.0014
1142	0.0023
1143	0.0018
1144	0.0020
1145	0.0014
1146	0.0020
1147	0.0027
1148	0.0006
1149	0.0045
1150	0.0044

Example 13

[1539] Representative compounds were screened using the assay procedure for tau phosphorylation activity described below.

[1540] HEK293T cells (ATCC, CRL3216) cultured in DMEM (Thermo Fisher Scientific, 10566024) supplemented with 10% FBS (Coming, 35-011—CV) and Penicillin/Streptomycin (Thermo Fisher Scientific, 15140163) were seeded in a 75 cm^2 flask at 8.1×10^6 cells/flask. The HEK293T cells were then transiently transfected with 5 µg DYRK1A (NM_001396) human untagged clone (OriGene, SC314641) and 2.5 µg MAPT (441 a.a. Tau gene) (NM_005910) human untagged clone (OriGene, TP313312) using Lipofectamine 3000 (Thermo Fisher Scientific, L30000015) and incubated for 20-30 hours in a humidified incubator at 37° C. and 5% CO^2. Post-incubation, HEK293T cells transfected with the DYRK1A and MAPT expression vectors were harvested and seeded in BioCoat poly-D lysine coated 96-well plates (Coming, 354461) at 3×10^4 cells/well.

[1541] The above synthesized compounds were screened using the cell assay procedure to assess decreased Tau phosphorylation at Thr212 (pThr212) described below.

[1542] Each compound was dissolved in DMSO (Sigma-Aldrich, D8418-100 mL) as a 10 mM stock. 10 mM stocks were serially diluted 1:3, 10-point dose-response curve and added to the cells with a final concentration ranging from 20 µM to 1.1 nM. Cells were treated with compounds in duplicate and incubated for 18-24 hours in a humidified incubator at 37° C. and 5% CO^2.

[1543] Following the overnight compound treatment, cells were lysed with 1X Alpha Surefire Ultra Lysis Buffer (Perkin Elmer, ALSU-LB-100ML) complemented with 1X Halt Phosphatase Inhibitor Cocktail (Thermo Fisher Scientific, 78427) and 1X Halt Protease Inhibitor Cocktail (Thermo Fisher Scientific, 78438). Lysates were spun down at 12,000 g for 10 min to remove any cellular debris and 5 µL of lysates were dispensed into a 384-well Opti-Plate (Perkin Elmer, 6007290) for the measurement of Tau phosphorylation in the phosphoTau (Thr212) AlphaLISA assay. Donor antibody, biotinylated HT7Tau (Thermo Fisher Scientific, MN1000B), and acceptor antibody, pThr212Tau (Thermo Fisher Scientific, 44740G) were both added to the cell lysates at a final concentration of 3 nM and incubated for 1 hour at room temperature. Following incubation of the lysates with the donor and acceptor antibodies, anti-rabbit IgG(Fc specific) AlphaLISA acceptor beads (Perkin Elmer, AL104C) were added at a 10 ug/mL final concentration and incubated for 1 hour at room temperature protected from light. Lastly, AlphaScreen streptavidin donor beads (PerkinElmer, 6760002) were added at 40 ug/mL final concentration and incubated for 1 hour at room temperature protected from light. Plates were read at Ex=665 nm, and Em=615 nm on the EnVision Multilabel Plate Reader (Perkin Elmer). The phospho-Tau (Thr212) AlphaLISA signal was used to plot, draw the curve fitting, and determine each compound's EC_{50} in Prism (GraphPad).

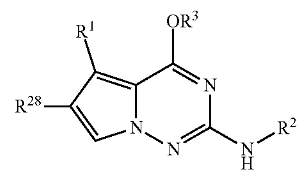
[1544] Table 3 shows the measured activity for representative compounds of Formula I as described herein.

TABLE 3

Compound	pTau (Thr212) EC_{50} (µM)
1	0.0216
3	0.1966
20	0.1068
44	0.0482
54	0.0257
56	0.0357
192	0.0181
194	0.1071
200	0.1299
210	0.0197
257	0.0151
258	0.0089
272	0.0134
276	0.0101
310	0.1090
318	0.0754
352	0.0394
392	0.0252
431	0.1288
943	0.0575

What is claimed is:

1. A compound, or a pharmaceutically acceptable salt thereof, of Formula I:



I

wherein:

R^1 is heteroaryl optionally substituted with 1-10 R^4;

R^2 is selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR, —(C_{1-5}alkylene)CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^6, —(C_{1-5} alkylene)$_p$aryl optionally substituted with 1-10 R^{26}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^7, and —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

R^3 is selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and heterocyclyl optionally substituted with 1-10 R^{18};

each R^4 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), unsubstituted —(C_{2-9} haloalkenyl), —(C_{1-5} alkylene)$_p$OR^9, —(C_{1-5} alkylene)$_p$CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{10}, -carbocyclyl optionally substituted with 1-12 R^{11}, —(C_{1-5} alkylene)$_p$heteroaryl optionally substituted with 1-10 R^{20}, —(C_{1-5} alkylene)$_p$C(=O)N(R^{12})$_2$, and —C(=O)R^{13}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

each R^5 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^6 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl),-heterocyclyl optionally substituted with 1-10 R^{16}, -carbocyclyl optionally substituted with 1-12 R^{17}, —(C_{1-5} alkylene)$_p$OR^{21}, —(C_{1-5} alkylene)CN, —SO$_2$R^{23}, and —C(═O)R^{24}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

alternatively, two R^6 attached to the same carbon atom are taken together to form a carbonyl group;

each R^7 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —OMe;

each R^8 is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —N(R^{14})$_2$, —(C_{1-5} alkylene)$_p$OR^{15}, —CN, —(C_{1-5} alkylene)pheterocyclyl optionally substituted with 1-10 R^{16}, —C(═O)R^{22}, and —NR^{14}C(═O)R^{23}, wherein each —(C_{1-5} alkylene) is, independently, optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

each R^9 is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{10} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{11} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{12} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^{21}, —(C_{1-5} alkylene)$_p$carbocyclyl optionally substituted with 1-12 R^{17}, -heterocyclyl optionally substituted with 1-10 R^{17}, and -heteroaryl optionally substituted with 1-10 R^{19}, wherein the —(C_{1-5} alkylene) is optionally substituted with 1-5 halide and/or 1-3 unsubstituted —(C_{1-3} alkyl);

each R^{13} is -heterocyclyl optionally substituted with 1-10 R^{18};

each R^{14} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{15} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —(C_{1-5} alkylene)$_p$OR^{21};

each R^{16} is independently selected from the group consisting of halide, —CN, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and -carbocyclyl optionally substituted with 1-12 R^{27};

alternatively, two R^{16} attached to the same carbon atom are taken together to form a carbonyl group;

each R^{17} is independently selected from the group consisting of halide, —OMe, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{18} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{19} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{20} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{21} is independently selected from the group consisting of H, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

each R^{22} is independently selected from the group consisting of -heterocyclyl optionally substituted with 1-10 R^{18}, —N(R^{12})$_2$, and —OR^{21};

each R^{23} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —(C_{1-5} alkylene)$_p$OR^{21}, and -carbocyclyl optionally substituted with 1-12 R^{25};

each R^{24} is independently selected from the group consisting of unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), —OR^{21}, and -carbocyclyl optionally substituted with 1-12 R^{25};

each R^{25} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), unsubstituted —(C_{1-9} haloalkyl), and —CN;

each R^{26} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

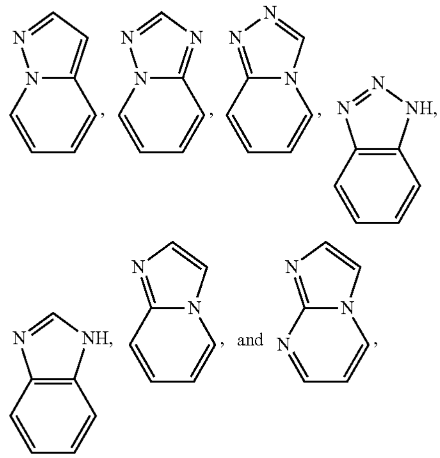
each R^{27} is independently selected from the group consisting of halide, unsubstituted —(C_{1-9} alkyl), unsubstituted —(C_{2-9} alkenyl), unsubstituted —(C_{2-9} alkynyl), and unsubstituted —(C_{1-9} haloalkyl);

R^{28} is independently selected from the group consisting of H and halide; and

each p is independently 0 or 1;

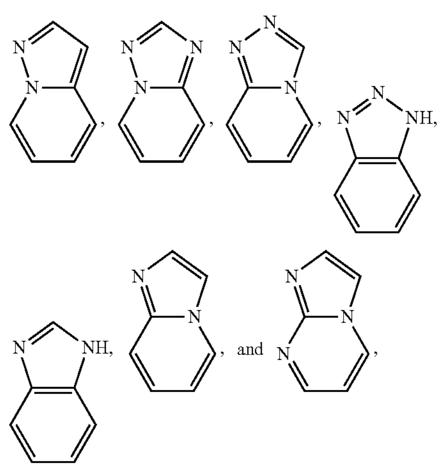
wherein each H atom is optionally, independently replaced by ^{2}H (D) (deuterium).

2. The compound of claim **1**, wherein R^1 is selected from the group consisting of:



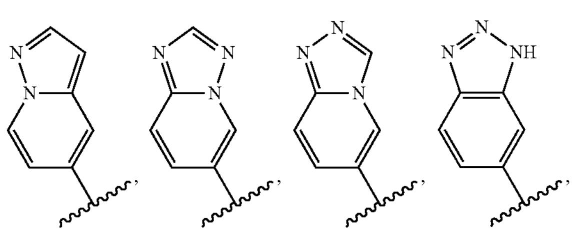
optionally substituted with 1-10 R^4.

3. The compound according to claim **2**, wherein R^1 is selected from the group consisting of:



optionally substituted with 1-3 R^4.

4. The compound according to claim **3**, wherein R^1 is selected from the group consisting of:



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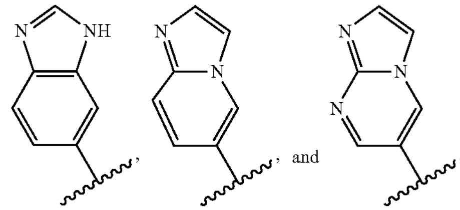
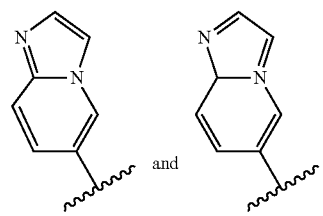


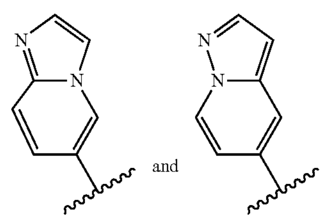
optionally substituted with 1-3 R^4.

5. The compound according to claim **4**, wherein R^1 is selected from the group consisting of:



optionally substituted with 1-3 R^4.

6. The compound according to claim **5**, wherein R^1 is selected from the group consisting of: unsubstituted



7. The compound according to claim **1**, wherein R^4 is selected from the group consisting of halide, unsubstituted —(C_{1-3} alkyl), unsubstituted —(C_{1-3} haloalkyl), —(C_{1-3} alkylene)OH, —(C_{1-3} alkylene)OMe, —CN, and —C(═O)N(R^{12})$_2$.

8. The compound according to claim **1**, wherein R^2 is selected from the group consisting of -heterocyclyl optionally substituted with 1-3 R^8, —(C_{1-2} alkylene)$_p$carbocyclyl optionally substituted with 1-3 R, and —(C_{1-2} alkylene)aryl optionally substituted with 1-2 R^7 wherein each —(C_{1-2} alkylene) is, independently, optionally substituted with 1-2 halide.

9. The compound according to claim **1**, wherein R^3 is selected from the group consisting of unsubstituted —(C_{1-5} alkyl), unsubstituted —(C_{1-5} haloalkyl), and -heterocyclyl optionally substituted with 1-2 R^{18}.

10. The compound according to claim **9**, wherein R^3 is selected from the group consisting of unsubstituted —(C_{1-3} alkyl) and unsubstituted —(C_{1-3} haloalkyl).

11. The compound according to claim **10**, wherein R^3 is methyl.

12. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-imidazo[4,5-b]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1];
(1r,4r)-4-((5-(3-(2,2-difluoroethyl)-2-methyl-3H-imidazo[4,5-b]pyridin-5-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [2];
(1r,4r)-4-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [3];
(1s,4s)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [4];
1-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-methylpropan-2-ol [5];
2-(cis-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [6];
(1s,3s)-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [7];
(1r,3r)-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [8];
4-methoxy-N-(cis-4-methoxycyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [9];
4-methoxy-N-(trans-4-methoxycyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [10];
N-(cis-4-(difluoromethoxy)cyclohexyl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [11];
N-(trans-4-(difluoromethoxy)cyclohexyl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [12];
2-((cis-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [13];
2-((trans-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [14];
4-methoxy-N-(cis-4-(2-methoxyethoxy)cyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [15];
4-methoxy-N-(trans-4-(2-methoxyethoxy)cyclohexyl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [16];
N-(cis-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [17];
N-(trans-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [18];
(1s,4s)-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [19];
(1r,4r)-4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [20];
1-(3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)azetidin-1-yl)ethan-1-one [21];
N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [22];
N-((3S,4R)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [23];
N-(1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [24];
N-(1-(2,2-difluoroethyl)piperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [25];
4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [26];
1-(4-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [27];
4-methoxy-N-(1-(methylsulfonyl)piperidin-4-yl)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [28];
N-((3S,4R)-3-fluoropiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [29];
N-((3R,4S)-3-fluoropiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [30];
N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [31];
N-((3S,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [32];
N-((3R,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [33];
N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [34];
(S)-5-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [35];
4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(tetrahydro-2H-pyran-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [36];
1-(6-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.3]heptan-2-yl)ethan-1-one [37];
4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(2-oxaspiro[3.3]heptan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [38];
1-(2-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-7-azaspiro[3.5]nonan-7-yl)ethan-1-one [39];
1-(7-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [40];
1-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-methylpropan-2-ol [41];
2-(cis-3-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [42];

(1s,3s)-3-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [43];
(1r,3r)-3-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [44];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(cis-4-methoxycyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [45];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(trans-4-methoxycyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [46];
N-(cis-4-(difluoromethoxy)cyclohexyl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [47];
N-(trans-4-(difluoromethoxy)cyclohexyl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [48];
2-((cis-4-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [49];
2-((trans-4-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [50];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(cis-4-(2-methoxyethoxy)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [51];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(trans-4-(2-methoxyethoxy)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [52];
N-(cis-4-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [53];
N-(trans-4-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [54];
(1s,4s)-4-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [55];
(1r,4r)-4-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [56];
1-(3-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)azetidin-1-yl)ethan-1-one [57];
N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [58];
N-((3S,4R)-4-fluoro-1-methylpyrrolidin-3-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [59];
N-(1-(2-fluoroethyl)piperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [60];
N-(1-(2,2-difluoroethyl)piperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [61];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [62];
1-(4-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [63];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(1-(methylsulfonyl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [64];
N-((3S,4R)-3-fluoropiperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [65];
N-((3R,4S)-3-fluoropiperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [66];
N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [67];
N-((3R,4R)-3-fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [68];
N-((3S,4S)-3-fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [69];
N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [70];
(S)-5-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [71];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(tetrahydro-2H-pyran-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [72];
1-(6-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.3]heptan-2-yl)ethan-1-one [73];
5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxy-N-(2-oxaspiro[3.3]heptan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [74];
1-(2-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-7-azaspiro[3.5]nonan-7-yl)ethan-1-one [75];
1-(7-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [76];
1-((1R,5S,6s)-6-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-azabicyclo[3.1.0]hexan-3-yl)ethan-1-one [77];
1-((1R,5S,6r)-6-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-azabicyclo[3.1.0]hexan-3-yl)ethan-1-one [78];
N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [79];
N-((1R,5S,6s)-3-oxabicyclo[3.1.0]hexan-6-yl)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [80];
1-((1R,5S,6s)-6-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-azabicyclo[3.1.0]hexan-3-yl)ethan-1-one [81];
1-((1R,5S,6r)-6-((5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-azabicyclo[3.1.0]hexan-3-yl)ethan-1-one [82];
N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [83];
N-((1R,5S,6s)-3-oxabicyclo[3.1.0]hexan-6-yl)-5-(imidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [84];

N-((1R,5S,6r)-3-oxabicyclo[3.1.0]hexan-6-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-imidazo[4,5-b]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [85];
N-((1R,5S,6s)-3-oxabicyclo[3.1.0]hexan-6-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-imidazo[4,5-b]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [86];
(1s,4s)-4-((4-(difluoromethoxy)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [87];
(1r,4r)-4-((4-(difluoromethoxy)-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [88];
(1s,4s)-4-((4-(difluoromethoxy)-5-(imidazo[1,2-a]pyridin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [89];
(1r,4r)-4-((4-(difluoromethoxy)-5-(imidazo[1,2-a]pyridin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [90];
2-(cis-3-((4-ethoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [91];
1 tert-butyl 6-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.3]heptane-2-carboxylate [92];
(R)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(1-(pyridin-2-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [93];
(1r,3r)-N_1-(4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine [94];
(1s,3s)-N_1-(4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine [95];
N-((1r,3r)-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [96];
N-((1s,3s)-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [97];
1 tert-butyl ((1r,3r)-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)carbamate [98];
1-(6-((4-ethoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.3]heptan-2-yl)ethan-1-one [99]; and
5-(2-(((1s,4s)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)pyrazolo[1,5-a]pyridine-3-carboxamide [100];

or a pharmaceutically acceptable salt thereof.

13. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

5-(2-(((1s,4s)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)pyrazolo[1,5-a]pyridine-3-carboxamide [101];
5-(2-((2-oxaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [102];
6-(2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a]pyridine-3-carbonitrile [103];
6-(2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)imidazo[1,2-a]pyridine-3-carboxamide [104];
6-(2-((4,4-difluorocyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [105];
6-(2-(((1s,4s)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [106];
6-(2-((2-oxaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [107];
N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [108];
(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide [109];
azetidin-1-yl((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)methanone [110];
((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)(pyrrolidin-1-yl)methanone [111];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [112];
5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [113];
5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [114];
1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [115];
1-((3S,4R)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [116];
(S)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [117];
(R)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [118];
5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-(1-(2-fluoroethyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [119];
5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-(1-(2,2-difluoroethyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [120];
5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxy-N-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [121];
1-(4-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [122];

N-(1-(3,3-difluorocyclobutyl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [123];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [124];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [125];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [126];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [127];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-1-ethyl-3-fluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [128];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [129];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4R)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [130];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4S)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [131];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [132];

N-((3R,4S)-1-cyclopropyl-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [133];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [134];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [135];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [136];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [137];

(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [138];

(S)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [139];

(R)—N-(1-cyclobutyl-3,3-difluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [140];

(S)—N-(1-cyclobutyl-3,3-difluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [141];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [142];

(S)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [143];

1-((4s,6r)-6-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [144];

1-((4r,6s)-6-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [145];

1-(7-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [146];

5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [147];

N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [148];

N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [149];

(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [150];

(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [151];

(S)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [152];

(R)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [153];

5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [154];

5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [155];

5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [156];

5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [157];
5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [158];
5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [159];
5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [160];
5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [161];
(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [162];
(S)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [163];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [164];
(S)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [165];
1-((4s,6r)-6-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [166];
1-((4r,6s)-6-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [167];
(1r,4r)-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [168];
(1s,3s)-3-((5-(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [169];
(1r,3r)-3-((5-(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [170];
N-((1r,3r)-3-((5-(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [171];
(1r,4r)-4-((5-(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [172];
1-(7-((5-(1-(2-hydroxyethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [173];
2-(6-(2-((2-oxaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-2-methyl-1H-benzo[d]imidazol-1-yl)ethan-1-ol [174];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [175];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3R,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [176];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [177];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3S,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [178];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [179];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3R,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [180];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3S,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [181];
5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [182];
(R)-5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [183];
(S)-5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [184];
(R)-5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [185];
(S)-5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [186];
(1r,4r)-4-((5-([1,2,4]triazolo[4,3-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [187];
5-([1,2,4]triazolo[4,3-a]pyridin-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [188];
(1s,3s)-N_1-(5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine [189];
(1r,3r)-N_1-(5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine [190];
N-((1s,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [191];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [192];
5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-N-(4,4-difluorocyclohexyl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [193];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [194];

5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxy-N-(2-azaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [195];

1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [196];

1 tert-butyl 7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonane-2-carboxylate [197];

5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [198];

(1s,3s)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [199]; and

(1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [200];

or a pharmaceutically acceptable salt thereof.

14. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of 2-(cis-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [201];

(1s,3s)-N_1-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine [202];

(1r,3r)-N_1-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine [203];

(1s,3s)-N^3-(4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-N_1,N_1,1-trimethylcyclobutane-1,3-diamine [204];

N-((1s,3s)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [205];

N-((1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [206];

N-((1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)propionamide [207];

2-methoxy-N-((1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [208];

(1s,3s)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [209];

(1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [210];

(1s,3s)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide [211];

(1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide [212];

(1s,3s)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N-(2-methoxyethyl)-1-methylcyclobutane-1-carboxamide [213];

(1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N-(2-methoxyethyl)-1-methylcyclobutane-1-carboxamide [214];

(1r,3r)-N-(2-fluoroethyl)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [215];

(1r,3r)-N-(2,2-difluoroethyl)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [216];

(1s,3s)-N-cyclopropyl-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [217];

(1r,3r)-N-cyclopropyl-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [218];

(1r,3r)-N-cyclobutyl-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [219];

(1r,3r)-N-(3,3-difluorocyclobutyl)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [220];

(1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methyl-N-(oxetan-3-yl)cyclobutane-1-carboxamide [221];

((1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)(pyrrolidin-1-yl)methanone [222];

1-((1r,3r)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)pyrrolidin-2-one [223];

(1s,4s)-4-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [224];

(1s,4s)-4-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclohexane-1-carboxamide [225];

3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N-methylbicyclo[1.1.1]pentane-1-carboxamide [226];

1-(2-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-7-azaspiro[3.5]nonan-7-yl)ethan-1-one [227];

1-((3aR,5r,6aS)-5-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)hexahydrocyclopenta[c]pyrrol-2(1H)-yl)ethan-1-one [228];

1-(7-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [229];

4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [230];

(R)—N-(1-cyclopropylethyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [231];

(S)—N-(1-cyclopropylethyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [232];
(R)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-phenylethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [233];
(R)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(pyridin-2-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [234];
(S)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(pyridin-2-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [235];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-3-methoxycyclobutyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [236];
N-((1R,2S)-2-fluorocyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [237];
N-((1S,2R)-2-fluorocyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [238];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-(trifluoromethyl)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [239];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(trans-4-(trifluoromethyl)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [240];
2-(cis-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [241];
2-(trans-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [242];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-methoxycyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [243];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(trans-4-methoxycyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [244];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-(methoxy-d_3)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [245];
N-(cis-4-ethoxycyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [246];
N-(trans-4-ethoxycyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [247];
5-(imidazo[1,2-a]pyrimidin-6-yl)-N-(cis-4-isopropoxycyclohexyl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [248];
5-(imidazo[1,2-a]pyrimidin-6-yl)-N-(trans-4-isopropoxycyclohexyl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [249];
N-(cis-4-(difluoromethoxy)cyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [250];
N-(trans-4-(difluoromethoxy)cyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [251];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(cis-4-(trifluoromethoxy)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [252];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(trans-4-(trifluoromethoxy)cyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [253];
N-(4,4-difluorocyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [254];
(R)—N-(2,2-difluorocyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [255];
(S)—N-(2,2-difluorocyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [256];
(1r,4r)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [257];
(1r,4r)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [258];
1-(3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)azetidin-1-yl)ethan-1-one [259];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)azetidin-3-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [260];
2-(((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol [261];
N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [262];
1-((3S,4R)-3-fluoro-4-((4-hydroxy-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [263];
1-((3S,4R)-3-fluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [264];
2-(((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)amino)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol [265];
N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [266];
N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [267];
N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [268];
N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [269];
N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [270];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(tetrahydro-2H-pyran-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [271];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(2-oxaspiro[3.3]heptan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [272];
1-(7-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [273];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((4s,7s)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [274];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((4r,7r)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [275];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [276];
(1s,3s)-3-((4-methoxy-5-(1H-pyrrolo[3,2-b]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [277];
(1r,3r)-3-((4-methoxy-5-(1H-pyrrolo[3,2-b]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [278];
(1s,4s)-4-((4-methoxy-5-(1H-pyrrolo[3,2-b]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [279];
(1r,4r)-4-((4-methoxy-5-(1H-pyrrolo[3,2-b]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [280];
(1s,3s)-3-((4-methoxy-5-(1H-pyrrolo[3,2-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [281];
(1r,4r)-4-((4-methoxy-5-(1H-pyrrolo[3,2-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [282];
(1s,3s)-3-((4-methoxy-5-(1H-pyrrolo[2,3-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [283];
(1r,4r)-4-((4-methoxy-5-(1H-pyrrolo[2,3-c]pyridin-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [284];
(R)-4-methoxy-N-(1-(pyridin-2-yl)ethyl)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [285];
2-((1s,3s)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutyl)propan-2-ol [286];
2-((1r,3r)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutyl)propan-2-ol [287];
N-((1s,3s)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [288];
N-((1s,3s)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-N-methylacetamide [289];
(1r,3r)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide [290];
azetidin-1-yl((1r,3r)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)methanone [291];
((1r,3r)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)(pyrrolidin-1-yl)methanone [292];
(1s,4s)-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [293];
(1r,4r)-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [294];
N-((3S,4R)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [295];
N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [296];
1-((3R,4S)-3-fluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [297];
1-((3S,4R)-3-fluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [298];
N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [299]; and
N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [300];
or a pharmaceutically acceptable salt thereof.

15. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:
(S)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [301];
(R)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [302];
N-(1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [303];
N-(1-(2,2-difluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [304];
4-methoxy-5-(quinolin-6-yl)-N-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [305];
N-(1-(3,3-difluorocyclobutyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [306];
N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [307];
N-((3R,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [308];
N-((3S,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [309];
N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [310];
N-((3S,4R)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [311];
N-((3R,4R)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [312];
N-((3S,4S)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [313];
N-((3R,4S)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [314];

N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [315];
N-((3R,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [316];
N-((3S,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [317];
N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [318];
(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [319];
(S)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [320];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [321];
(S)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [322];
1-((4s,6r)-6-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [323];
1-((4r,6s)-6-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [324];
1-(7-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [325];
4-methoxy-5-(quinolin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [326];
2-(cis-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutyl)propan-2-ol [327];
2-(trans-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutyl)propan-2-ol [328];
2-(cis-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [329];
(1r,3r)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [330];
(1r,3r)-3-((4-(methoxy-d_3)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [331];
(1s,3s)-N_1-(4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-3-methylcyclobutane-1,3-diamine [332];
N-((1s,3s)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [333];
N-((1r,3r)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [334];
N-((1s,3s)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)propionamide [335];
2-methoxy-N-((1s,3s)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [336];
1 tert-butyl ((1s,3s)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)carbamate [337];
(1r,3r)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [338];
(1r,3r)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,N,1-trimethylcyclobutane-1-carboxamide [339];
((1r,3r)-3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)(pyrrolidin-1-yl)methanone [340];
2-(cis-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [341];
2-(trans-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [342];
2-((cis-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [343];
N-(trans-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [344];
(1s,4s)-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [345];
2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-4-ol [346];
(1r,4r)-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [347];
(1r,4r)-4-((4-(methoxy-d_3)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [348];
(1r,4r)-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-(trifluoromethyl)cyclohexan-1-ol [349];
N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [350];
N-((3S,4R)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [351];
1-((3S,4R)-3-fluoro-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [352];
1-((3S,4R)-3-fluoro-4-((4-(methoxy-d_3)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [353];
1-((3R,4S)-3-fluoro-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [354];
N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [355];
N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [356];

(R)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [357];
(S)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [358];
(R)—N-(4,4-difluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [359];
(S)—N-(4,4-difluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [360];
N-(1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [361];
N-(1-(2,2-difluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [362];
4-methoxy-5-(quinoxalin-6-yl)-N-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [363];
N-(1-(3,3-difluorocyclobutyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [364];
4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [365];
4-methoxy-5-(quinoxalin-6-yl)-N-(tetrahydro-2H-pyran-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [366];
N-((3S,4R)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [367];
N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [368];
N-((3S,4R)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [369];
N-((3R,4R)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [370];
N-((3S,4S)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [371];
N-((3R,4S)-3-fluoro-1-(2-fluoroethyl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [372];
N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [373];
N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [374];
(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [375];
(S)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [376];
(R)—N-(1-cyclobutyl-3,3-difluoropiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [377];
(S)—N-(1-cyclobutyl-3,3-difluoropiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [378];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [379];
(S)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [380];
N_1-(4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)bicyclo[1.1.1]pentane-1,3-diamine [381];
N-(3-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[1.1.1]pentan-1-yl)acetamide [382];
1-((4s,6r)-6-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [383];
1-((4r,6s)-6-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-azaspiro[3.3]heptan-1-yl)ethan-1-one [384];
4-methoxy-5-(quinoxalin-6-yl)-N-(2-oxaspiro[3.3]heptan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [385];
1-(2-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-7-azaspiro[3.5]nonan-7-yl)ethan-1-one [386];
1-((3aR,5s,6aS)-5-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)hexahydrocyclopenta[c]pyrrol-2(1H)-yl)ethan-1-one [387];
1-((3aR,5r,6aS)-5-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)hexahydrocyclopenta[c]pyrrol-2(1H)-yl)ethan-1-one [388];
1-(7-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [389];
4-methoxy-5-(quinoxalin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [390];
(1s,3s)-1-methyl-3-((4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutan-1-ol [391];
(1r,4r)-1-methyl-4-((4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [392];
(S)-4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(1-(pyridin-2-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [393];
1-cyano-N-((1s,3s)-3-((4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide [394];
4-methoxy-5-(pyrazolo[1,5-a]pyridin-5-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [395];
(R)-5-(4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [396];
(S)-5-(4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [397];
5-(2-(cyclohexylamino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [398];
5-(4-methoxy-2-(((1s,4s)-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [399]; and

5-(2-((4,4-dimethylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [400];

or a pharmaceutically acceptable salt thereof.

16. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

5-(2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [401];

5-(2-(((1s,4s)-4-ethyl-4-hydroxycyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [402];

5-(2-(((1r,4r)-4-ethyl-4-hydroxycyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [403];

5-(4-methoxy-2-(((1s,4s)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [404];

5-(4-methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [405];

5-(2-(((1s,4s)-4-cyano-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [406];

5-(2-(((1r,4r)-4-cyano-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [407];

5-(2-(bicyclo[3.1.0]hexan-3-ylamino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [408];

5-(2-((4-hydroxybicyclo[2.2.1]heptan-1-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [409];

5-(4-methoxy-2-(spiro[2.5]octan-6-ylamino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [410];

(R)-5-(6-fluoro-4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [411];

(S)-5-(6-fluoro-4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [412];

5-(2-(cyclohexylamino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [413];

5-(6-fluoro-4-methoxy-2-((cis-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [414];

5-(2-((4,4-dimethylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [415];

5-(6-fluoro-2-(((1s,4s)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [416];

5-(6-fluoro-2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [417];

5-(2-(((1s,4s)-4-ethyl-4-hydroxycyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [418];

5-(2-(((1r,4r)-4-ethyl-4-hydroxycyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [419];

5-(6-fluoro-4-methoxy-2-(((1s,4s)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [420];

5-(6-fluoro-4-methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [421];

5-(2-(((1s,4s)-4-cyano-4-methylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [422];

5-(2-(((1r,4r)-4-cyano-4-methylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [423];

5-(2-(bicyclo[3.1.0]hexan-3-ylamino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [424];

5-(6-fluoro-2-((4-hydroxybicyclo[2.2.1]heptan-1-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [425];

5-(6-fluoro-4-methoxy-2-(spiro[2.5]octan-6-ylamino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [426];

5-(2-((2-oxaspiro[3.5]nonan-7-yl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylpyrazolo[1,5-a]pyridine-3-carboxamide [427];

N-((1s,3s)-3-((5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [428];

N-((1r,3r)-3-((5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [429];

(1s,4s)-4-((5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [430];

(1r,4r)-4-((5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [431];

(1s,4s)-1-ethyl-4-((5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [432];

(1r,4r)-1-ethyl-4-((5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [433];

(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [434];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(8-fluoroimidazo[1,2-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [435];

(R)-6-(4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [436];

(S)-6-(4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [437];

6-(2-(cyclohexylamino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [438];

6-(4-methoxy-2-((cis-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [439];

6-(2-((4,4-dimethylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [440];

6-(2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [441];
6-(2-(((1s,4s)-4-ethyl-4-hydroxycyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [442];
6-(2-(((1r,4r)-4-ethyl-4-hydroxycyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [443];
6-(4-methoxy-2-(((1s,4s)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [444];
6-(4-methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [445];
6-(2-(((1s,4s)-4-cyano-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [446];
6-(2-(((1r,4r)-4-cyano-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [447];
6-(2-(bicyclo[3.1.0]hexan-3-ylamino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [448];
6-(2-((4-hydroxybicyclo[2.2.1]heptan-1-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [449];
6-(4-methoxy-2-(spiro[2.5]octan-6-ylamino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [450];
(R)-8-fluoro-6-(4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [451];
(S)-8-fluoro-6-(4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [452];
6-(2-(cyclohexylamino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [453];
8-fluoro-6-(4-methoxy-2-((cis-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [454];
6-(2-((4,4-dimethylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [455];
8-fluoro-6-(2-(((1s,4s)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [456];
8-fluoro-6-(2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [457];
6-(2-(((1s,4s)-4-ethyl-4-hydroxycyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [458];
6-(2-(((1r,4r)-4-ethyl-4-hydroxycyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [459];
8-fluoro-6-(4-methoxy-2-(((1s,4s)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [460];
8-fluoro-6-(4-methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [461];
6-(2-(((1s,4s)-4-cyano-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [462];
6-(2-(((1r,4r)-4-cyano-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [463];
6-(2-(bicyclo[3.1.0]hexan-3-ylamino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [464];
8-fluoro-6-(2-((4-hydroxybicyclo[2.2.1]heptan-1-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [465];
8-fluoro-6-(4-methoxy-2-(spiro[2.5]octan-6-ylamino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [466];
6-(2-((2-oxaspiro[3.5]nonan-7-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [467];
(R)-6-(6-fluoro-4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [468];
(S)-6-(6-fluoro-4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [469];
6-(2-(cyclohexylamino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [470];
6-(6-fluoro-4-methoxy-2-((cis-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [471];
6-(2-((4,4-dimethylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [472];
6-(6-fluoro-2-(((1s,4s)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [473];
6-(6-fluoro-2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [474];
6-(2-(((1s,4s)-4-ethyl-4-hydroxycyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [475];
6-(2-(((1r,4r)-4-ethyl-4-hydroxycyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [476];
6-(6-fluoro-4-methoxy-2-(((1s,4s)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [477];
6-(6-fluoro-4-methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [478];
6-(2-(((1s,4s)-4-cyano-4-methylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [479];
6-(2-(((1r,4r)-4-cyano-4-methylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [480];
6-(2-(bicyclo[3.1.0]hexan-3-ylamino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [481];
6-(6-fluoro-2-((4-hydroxybicyclo[2.2.1]heptan-1-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [482];

6-(6-fluoro-4-methoxy-2-(spiro[2.5]octan-6-ylamino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [483];
6-(2-((2-oxaspiro[3.5]nonan-7-yl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [484];
(R)-8-fluoro-6-(6-fluoro-4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [485];
(S)-8-fluoro-6-(6-fluoro-4-methoxy-2-((1-(oxetan-3-yl)ethyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [486];
6-(2-(cyclohexylamino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [487];
8-fluoro-6-(6-fluoro-4-methoxy-2-((cis-4-methoxycyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [488];
6-(2-((4,4-dimethylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [489];
8-fluoro-6-(6-fluoro-2-(((1s,4s)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [490];
8-fluoro-6-(6-fluoro-2-(((1r,4r)-4-hydroxy-4-methylcyclohexyl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [491];
6-(2-(((1s,4s)-4-ethyl-4-hydroxycyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [492];
6-(2-(((1r,4r)-4-ethyl-4-hydroxycyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [493];
8-fluoro-6-(6-fluoro-4-methoxy-2-(((1s,4s)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [494];
8-fluoro-6-(6-fluoro-4-methoxy-2-(((1r,4r)-4-methoxy-4-methylcyclohexyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [495];
6-(2-(((1s,4s)-4-cyano-4-methylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [496];
6-(2-(((1r,4r)-4-cyano-4-methylcyclohexyl)amino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [497];
6-(2-(bicyclo[3.1.0]hexan-3-ylamino)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [498];
8-fluoro-6-(6-fluoro-2-((4-hydroxybicyclo[2.2.1]heptan-1-yl)amino)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [499]; and
8-fluoro-6-(6-fluoro-4-methoxy-2-(spiro[2.5]octan-6-ylamino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)-N-methylimidazo[1,2-a]pyridine-3-carboxamide [500];

or a pharmaceutically acceptable salt thereof.

17. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

6-(2-((2-oxaspiro[3.5]nonan-7-yl)amino)-6-fluoro-4-methoxypyrrolo[2,1]-[1,2,4]triazin-5-yl)-8-fluoro-N-methylimidazo[1,2-a]pyridine-3-carboxamide [501];
(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [502];
(1r,3r)-N-cyclopropyl-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [503];
(1r,3r)-N-(3,3-difluorocyclobutyl)-3-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [504];
5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [505];
5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [506];
5-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [507];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-2-methyl-1H-benzo[d]imidazol-6-yl)-4-(oxetan-3-yloxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [508];
(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [509];
(1s,3r)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [510];
(1r,3s)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [511];
N-((1s,4s)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [512];
1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [513];
1-((3S,4R)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [514];
5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [515];

5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [516];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropyrrolidin-1-yl)ethan-1-one [517];

(R)—N-(4,4-difluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [518];

2-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-ol [519];

1-((3S,4R)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [520];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [521];

5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3S,4R)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [522];

5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [523];

3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [524];

(R)-2-(4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,14][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-ol [525];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [526];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [527];

(S)-5-((5-(1-(2,2-difluoroethyl)-4-fluoro-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [528];

N-((1s,3s)-3-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [529];

N-((1r,3r)-3-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [530];

(1s,3r)-1-ethyl-3-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutan-1-ol [531];

(1r,3s)-1-ethyl-3-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutan-1-ol [532];

N-((1s,4s)-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [533];

(1s,4s)-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [534];

1-((3S,4R)-3-fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [535];

1-((3R,4S)-3-fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [536];

N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [537];

N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [538];

(R)-1-(3,3-difluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [539];

(R)—N-(4,4-difluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [540];

5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [541];

2-((3R,4S)-3-fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-ol [542];

1-((3S,4R)-3-fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [543];

1-((3R,4S)-3-fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [544];

N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [545];

N-((3S,4R)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [546];

N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [547];

3-((3R,4S)-3-fluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile [548];

(R)-2-(3,3-difluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-ol [549];
(R)-1-(3,3-difluoro-4-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [550];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [551];
(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [552];
(S)-5-((5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [553];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-7-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [554];
5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-N-(cis-3-ethoxycyclobutyl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [555];
2-(cis-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [556];
(1s,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [557];
(1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [558];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide-2,2,2-d_3 [559];
N-((1s,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-N-methylacetamide [560];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-N-methylacetamide [561];
N-((1s,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-1-cyanocyclopropane-1-carboxamide [562];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-1-cyanocyclopropane-1-carboxamide [563];
(1s,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [564];
(1r,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [565];
2-((cis-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [566];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [567];
(1s,4s)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [568];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [569];
(R)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpyrrolidin-2-one [570];
(S)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpyrrolidin-2-one [571];
1-(4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [572];
1-(4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidine-1-carbonyl)cyclopropane-1-carbonitrile [573];
1-((3R,4S)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidine-1-carbonyl)cyclopropane-1-carbonitrile [574];
(R)-5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-N-(3,3-difluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [575];
(R)-5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [576];
(R)-5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-N-(1-ethyl-3,3-difluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [577];
(R)-5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [578];
(R)-1-(4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidine-1-carbonyl)cyclopropane-1-carbonitrile [579];
(R)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [580];
(S)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [581];
4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [582];
5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-N-(bicyclo[3.1.0]hexan-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [583];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [584];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [585];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide-2,2,2-d_3 [586];
(1s,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [587];

(1r,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [588];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [589];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [590];
1-(4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [591];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [592];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [593];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutyl)acetamide [594];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutyl)acetamide-2,2,2-d_3 [595];
(1s,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-ethylcyclobutan-1-ol [596];
(1r,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-ethylcyclobutan-1-ol [597];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclohexan-1-ol [598];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-ethylcyclohexan-1-ol [599]; and
1-(4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)piperidin-1-yl)ethan-1-one [600];

or a pharmaceutically acceptable salt thereof.

18. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [601];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [602];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [603];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide-2,2,2-d_3 [604];
(1s,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [605];
(1r,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [606];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [607];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [608];
1-(4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [609];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [610];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [611];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [612];
N-((1r,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide-2,2,2-d_3 [613];
(1s,3r)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [614];
(1r,3s)-3-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [615];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [616];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [617];
1-(4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [618];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [619];
1-(7-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(2,2-difluoroethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [620];
(1r,4r)-4-((5-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-(oxetan-3-yloxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [621];
(1r,4r)-4-((4-methoxy-5-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [622];
(S)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-(morpholin-2-ylmethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [623];
N-(cis-3-ethoxycyclobutyl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [624];
1-cyano-N-((1s,3s)-3-((4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide [625];
(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [626];
(R)—N-(1-ethyl-3,3-difluoropiperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [627];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [628];

(1r,4r)-4-((6-fluoro-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [629];
6-fluoro-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [630];
(1r,4r)-1-methyl-4-((5-(1-methyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-(oxetan-3-yloxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [631];
2-(cis-3-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [632];
N-((1s,3s)-3-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [633];
N-((1r,3r)-3-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [634];
(1s,3s)-3-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [635];
(1r,3r)-3-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [636];
2-((cis-4-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [637];
(1s,4s)-4-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [638];
(1r,4r)-4-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [639];
1-((3R,4S)-3-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [640];
5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [641];
5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [642];
5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [643];
1-((3R,4S)-4-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [644];
N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [645];
5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [646];
5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [647];
3-((3R,4S)-4-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [648];
(R)-1-(4-((5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [649];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [650];
(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-ethyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [651];
2-(cis-3-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [652];
N-((1s,3s)-3-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [653];
N-((1r,3r)-3-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [654];
(1s,3s)-3-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [655];
(1r,3r)-3-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [656];
2-((cis-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [657];
(1s,4s)-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [658];
(1r,4r)-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [659];
1-((3S,4R)-3-fluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [660];
5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [661];
5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [662];
N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [663];
1-((3R,4S)-3-fluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [664];
N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [665];
N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [666];
N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [667];
3-((3R,4S)-3-fluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile [668];
(R)-1-(3,3-difluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [669];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [670];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [671];

(1r,4r)-4-((5-(1-((E)-2-fluorovinyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [672];

(E)-5-((5-(1-(2-fluorovinyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [673];

2-(cis-3-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [674];

N-((1s,3s)-3-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [675];

N-((1r,3r)-3-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [676];

(1s,3s)-3-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [677];

(1r,3r)-3-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [678];

2-((cis-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [679];

(1s,4s)-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [680];

(1r,4r)-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [681];

1-((3S,4R)-3-fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [682];

5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [683];

5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [684];

N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [685];

1-((3R,4S)-3-fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [686];

N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [687];

N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [688];

N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [689];

3-((3R,4S)-3-fluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile [690];

(R)-1-(3,3-difluoro-4-((5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [691];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [692];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-isopropyl-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [693];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-(2-fluoro-2-methylpropyl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [694];

3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2,2-dimethylpropanenitrile [695];

1-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-methylpropan-2-ol [696];

(R)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [697];

(S)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [698];

2-(cis-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [699]; and

(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [700];

or a pharmaceutically acceptable salt thereof.

19. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of (1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [701];

N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [702];

N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [703];

N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-N-methylacetamide [704];

N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-N-methylacetamide [705];

1-cyano-N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide [706];

1-cyano-N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide [707];

(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carbonitrile [708];
(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carbonitrile [709];
(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [710];
(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [711];
(1s,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [712];
(1r,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclobutan-1-ol [713];
(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-(trifluoromethyl)cyclobutan-1-ol [714];
(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-(trifluoromethyl)cyclobutan-1-ol [715];
2-(trans-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [716];
N-(cis-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [717];
cis-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [718];
trans-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [719];
2-((cis-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [720];
4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [721];
(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [722];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [723];
(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [724];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [725];
(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [726];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [727];
(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-(trifluoromethyl)cyclohexan-1-ol [728];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-(trifluoromethyl)cyclohexan-1-ol [729];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [730];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-4-fluoro-1-methylpyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [731];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-1-ethyl-4-fluoropyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [732];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-1-ethyl-4-fluoropyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [733];
1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [734];
1-((3S,4R)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [735];
1-((3S,4R)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one-2,2,2-d_3 [736];
1-((3S,4R)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)propan-1-one [737];
N-((3S,4R)-1-cyclopropyl-4-fluoropyrrolidin-3-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [738];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [739];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-4-fluoro-1-(3-methyloxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [740];
3-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)oxetane-3-carbonitrile [741];
(R)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [742];
(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropyrrolidin-1-yl)ethan-1-one [743];
(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropyrrolidin-1-yl)ethan-1-one-2,2,2-d_3 [744];
(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropyrrolidin-1-yl)propan-1-one [745];
(R)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpyrrolidin-2-one [746];

(S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpyrrolidin-2-one [747];

2-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-ol [748];

3-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2,2-dimethylpropanenitrile [749];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [750];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [751];

3-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile [752];

1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidine-1-carbonyl)cyclopropane-1-carbonitrile [753];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [754];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-1-ethyl-3-fluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [755];

2-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-ol [756];

3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2,2-dimethylpropanenitrile [757];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2-methylpropan-2-ol [758];

N-((3R,4S)-1-cyclopropyl-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [759];

N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [760];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [761];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [762];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [763];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [764];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-1-(3-ethyloxetan-3-yl)-3-fluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [765];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-1-(3-ethynyloxetan-3-yl)-3-fluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [766];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-isopropyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [767];

N-((3R,4S)-1-(3-cyclopropyloxetan-3-yl)-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [768];

3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [769];

1-((3S,4R)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [770];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [771];

1-((3S,4R)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)propan-1-one [772];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)propan-1-one [773];

1-((3S,4R)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one-2,2,2-d_3 [774];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one-2,2,2-d_3 [775];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidine-1-carbonyl)cyclopropane-1-carbonitrile [776];

(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [777];

(R)—N-(3,3-difluoro-1-(methyl-d2)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [778];

(R)—N-(3,3-difluoro-1-(methyl-d_3)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [779];

(R)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-(1-ethyl-3,3-difluoropiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [780];

(R)-2-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-ol [781];

(R)-3-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)-2,2-dimethylpropanenitrile [782];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)-2-methylpropan-2-ol [783];

(R)—N-(1-cyclopropyl-3,3-difluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [784];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [785];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [786];

(R)-3-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)oxetane-3-carbonitrile [787];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [788];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one-2,2,2-d_3 [789];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)propan-1-one [790];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidine-1-carbonyl)cyclopropane-1-carbonitrile [791];

(S)-1-(5-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [792];

5-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [793];

(S)-5-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [794];

(R)-5-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [795];

(R)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [796];

(S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [797];

4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [798];

1-(7-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [799]; and

1-(7-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [800];

or a pharmaceutically acceptable salt thereof.

20. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [801];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-((4r,7r)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [802];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-((4s,7s)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [803];

2-(cis-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [804];

N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [805];

N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [806];

(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [807];

(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [808];

2-((cis-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [809];

(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [810];

(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [811];

1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [812];

5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [813];

5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [814];

5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [815];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [816];

N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [817];

5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [818];

5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [819];

3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [820];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [821];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [822];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-4-fluoro-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [823];

2-(cis-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)cyclobutoxy)ethan-1-ol [824];

N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutyl)acetamide [825];

N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutyl)acetamide [826];

(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutan-1-ol [827];

(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutan-1-ol [828];

2-((cis-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)cyclohexyl)oxy)ethan-1-ol [829];

(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclohexan-1-ol [830];

(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclohexan-1-ol [831];

1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [832];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [833];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [834];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [835];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-3-fluoropiperidin-1-yl)ethan-1-one [836];

N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [837];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [838];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [839];

3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [840];

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [841];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [842];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [843];

2-(cis-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [844];

N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [845];

N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [846];

(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [847];

(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [848];

2-((cis-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [849];

(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [850];

(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [851];

1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [852];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [853];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [854];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [855];
1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [856];
N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [857];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [858];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [859];
3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [860];
(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [861];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [862];
(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [863];
2-(cis-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)cyclobutoxy)ethan-1-ol [864];
N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutyl)acetamide [865];
N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutyl)acetamide [866];
(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutan-1-ol [867];
(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclobutan-1-ol [868];
2-((cis-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)cyclohexyl)oxy)ethan-1-ol [869];
(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclohexan-1-ol [870];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclohexan-1-ol [871];
1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [872];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [873];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [874];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [875];
1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-3-fluoropiperidin-1-yl)ethan-1-one [876];
N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [877];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [878];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [879];
3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [880];
(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [881];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [882];
(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-6-fluoro-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [883];
2-(cis-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [884];

N-((1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [885];

N-((1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [886];

(1s,3s)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [887];

(1r,3r)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [888];

2-((cis-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [889];

(1s,4s)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [890];

(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [891];

1-((3R,4S)-3-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-4-fluoropyrrolidin-1-yl)ethan-1-one [892];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)-N-(1-(oxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [893];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [894];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-amine [895];

1-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [896];

N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-amine [897];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-amine [898];

5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-amine [899]; and

3-((3R,4S)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)oxetane-3-carbonitrile [900];

or a pharmaceutically acceptable salt thereof.

21. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [901];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-amine [902];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-amine [903];

2-(cis-3-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutoxy)ethan-1-ol [904];

N-((1s,3s)-3-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [905];

N-((1r,3r)-3-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [906];

(1s,3s)-3-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [907];

(1r,3r)-3-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutan-1-ol [908];

2-((cis-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)oxy)ethan-1-ol [909];

(1s,4s)-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [910];

(1r,4r)-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [911];

1-((3S,4R)-3-fluoro-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)pyrrolidin-1-yl)ethan-1-one [912];

4-methoxy-N-(1-(oxetan-3-yl)piperidin-4-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [913];

4-methoxy-N-(1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [914];

N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [915];

1-((3R,4S)-3-fluoro-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [916];

N-((3R,4S)-1-(3,3-difluorocyclobutyl)-3-fluoropiperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [917];

N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [918];

N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [919];

3-((3R,4S)-3-fluoro-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)oxetane-3-carbonitrile [920];

(R)-1-(3,3-difluoro-4-((4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [921];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [922];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [923];

N-(2-fluoro-2-methylpropyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [924];

(R)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1,1,1-trifluoropropan-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [925];

(R)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(4-methoxybutan-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [926];

(R)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [927];

(S)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(oxetan-3-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [928];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((1R,2S)-2-methoxycyclobutyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [929];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((1R,2R)-2-methoxycyclobutyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [930];

N-(cis-3-ethoxycyclobutyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [931];

(1s,3s)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [932];

(1r,3r)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [933];

N-((1s,3s)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [934];

N-((1r,3r)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [935];

N-((1s,3s)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-N-methylacetamide [936];

N-((1r,3r)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)-N-methylacetamide [937];

1-cyano-N-((1s,3s)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide [938];

1-cyano-N-((1r,3r)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)cyclopropane-1-carboxamide [939];

(1s,3r)-1-ethyl-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutan-1-ol [940];

(1r,3s)-1-ethyl-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclobutan-1-ol [941];

(1S,2R)-2-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclopentan-1-ol [942];

(R)—N-(3,3-difluorocyclopentyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [943];

N-cyclohexyl-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [944];

2-(trans-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [945];

N-(cis-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [946];

N-(4,4-dimethylcyclohexyl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [947];

4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [948];

(1s,4s)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [949];

(1r,4r)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexane-1-carbonitrile [950];

(1s,4s)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [951];

(1s,4s)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [952];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((1s,4s)-4-methoxy-4-methylcyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [953];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((1r,4r)-4-methoxy-4-methylcyclohexyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [954];

(R)—N-(4,4-difluoro-1-methylpyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [955];

(R)—N-(1-ethyl-4,4-difluoropyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [956];

(R)—N-(1-cyclopropyl-4,4-difluoropyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [957];

(R)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpyrrolidin-2-one [958];

(S)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpyrrolidin-2-one [959];

1-(4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [960];
1-(4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidine-1-carbonyl)cyclopropane-1-carbonitrile [961];
1-((3R,4S)-3-fluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [962];
1-((3R,4S)-3-fluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidine-1-carbonyl)cyclopropane-1-carbonitrile [963];
(R)—N-(3,3-difluoropiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [964];
(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [965];
(R)—N-(1-ethyl-3,3-difluoropiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [966];
(R)—N-(1-cyclopropyl-3,3-difluoropiperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [967];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [968];
(R)-1-(3,3-difluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [969];
(R)-1-(3,3-difluoro-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidine-1-carbonyl)cyclopropane-1-carbonitrile [970];
(S)-5-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [971];
(R)-5-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [972];
(R)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [973];
(S)-3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [974];
(R)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(tetrahydro-2H-pyran-3-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [975];
N-(bicyclo[3.1.0]hexan-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [976];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(spiro[2.5]octan-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [977];
4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [978];
1-(7-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [979];
cyclopropyl(7-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)methanone [980];
(1-fluorocyclopropyl)(7-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)methanone [981];
2-(trans-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)cyclohexyl)propan-2-ol [982];
(1s,4s)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclohexan-1-ol [983];
(1r,4r)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-1-methylcyclohexan-1-ol [984];
(1s,4s)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)cyclohexan-1-ol [985];
(1r,4r)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)cyclohexan-1-ol [986];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [987];
1-(7-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl-7-d)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [988];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [989];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((4r,7r)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [990];
5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-((4s,7s)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-7-d-2-amine [991];
N-((1s,3s)-3-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [992];
N-((1r,3r)-3-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [993];
2-(trans-4-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [994];
(1s,4s)-4-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [995];
(1r,4r)-4-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [996];
(1s,4s)-1-ethyl-4-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [997];
(1r,4r)-1-ethyl-4-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [998];
6-fluoro-N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [999]; and
1-(4-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1000]; or a pharmaceutically acceptable salt thereof.

22. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

6-fluoro-N-((3S,4R)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1001];

6-fluoro-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1002];

6-fluoro-N-((3S,4R)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1003];

6-fluoro-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1004];

(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1005];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1006];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1007];

1-(7-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [1008];

1-(7-((6-fluoro-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one-2,2,2-d_3 [1009];

2-(trans-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)propan-2-ol [1010];

(1s,4s)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1011];

(1r,4r)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1012];

(1s,4s)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1013];

(1r,4r)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1014];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1015];

1-(7-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [1016];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1017];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)-N-((4r,7r)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1018];

5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(methoxy-d_3)-N-((4s,7s)-1-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1019];

(1s,4s)-4-((4-(difluoromethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1020];

(1r,4r)-4-((4-(difluoromethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1021];

(1s,4s)-4-((4-(difluoromethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [1022];

(1r,4r)-4-((4-(difluoromethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [1023];

1-(7-((4-(difluoromethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [1024];

4-(difluoromethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1025];

(1s,4s)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1026];

(1r,4r)-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1027];

(1s,4s)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1028];

(1r,4r)-1-ethyl-4-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1029];

1-(7-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [1030];

5-(imidazo[1,2-a]pyrimidin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1031];

(1s,4s)-4-((4-(2,2-difluoroethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1032];

(1r,4r)-4-((4-(2,2-difluoroethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1033];

(1s,4s)-4-((4-(2,2-difluoroethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [1034];

(1r,4r)-4-((4-(2,2-difluoroethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-ethylcyclohexan-1-ol [1035];

1-(7-((4-(2,2-difluoroethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2-azaspiro[3.5]nonan-2-yl)ethan-1-one [1036];

4-(2,2-difluoroethoxy)-5-(imidazo[1,2-a]pyrimidin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1037];

(1r,3r)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-N,1-dimethylcyclobutane-1-carboxamide [1038];

(1r,3r)-N-cyclopropyl-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [1039];

(1r,3r)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methyl-N-(1-methylcyclobutyl)cyclobutane-1-carboxamide [1040];

(1r,3r)-N-(3,3-difluorocyclobutyl)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutane-1-carboxamide [1041];

(1r,3r)-3-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methyl-N-(3-methyloxetan-3-yl)cyclobutane-1-carboxamide [1042];

(1s,3s)-N^3-(4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)-N^1,N^1,1-trimethylcyclobutane-1,3-diamine [1043];

N-(cis-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1044];

1-((3R,4S)-3-fluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol [1045];

N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1046];

1-((3R,4S)-3-fluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1047];

(R)-1-(3,3-difluoro-4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1048];

(R)-5-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [1049];

(R)-4-methoxy-5-(quinolin-6-yl)-N-(tetrahydro-2H-pyran-3-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1050];

4-((4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1051];

N-((1s,3s)-3-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [1052];

N-((1r,3r)-3-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [1053];

N-(cis-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1054];

(1s,4s)-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1055];

(1r,4r)-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1056];

6-fluoro-N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1057];

1-((3R,4S)-3-fluoro-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol [1058];

6-fluoro-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1059];

6-fluoro-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1060];

1-((3R,4S)-3-fluoro-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1061];

(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1062];

(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1063];

(R)-1-(3,3-difluoro-4-((6-fluoro-4-methoxy-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1064];

N-(cis-4-((4-(difluoromethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1065];

(1s,4s)-4-((4-(difluoromethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1066];

(1r,4r)-4-((4-(difluoromethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1067];

1-((3R,4S)-4-((4-(difluoromethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2-methylpropan-2-ol [1068];

4-(difluoromethoxy)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1069];

1-((3R,4S)-4-((4-(difluoromethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [1070];

(R)-1-(4-((4-(difluoromethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [1071];

4-((4-(difluoromethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1072];

N-(cis-4-((5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1073];

(1s,4s)-1-methyl-4-((5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1074];

(1r,4r)-1-methyl-4-((5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1075];

1-((3R,4S)-3-fluoro-4-((5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol [1076];

N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1077];

1-((3R,4S)-3-fluoro-4-((5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1078];

(R)-1-(3,3-difluoro-4-((5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1079];

4-((5-(quinolin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1080];

N-(cis-4-((4-(2,2-difluoroethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1081];

(1s,4s)-4-((4-(2,2-difluoroethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1082];

(1r,4r)-4-((4-(2,2-difluoroethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1083];

1-((3R,4S)-4-((4-(2,2-difluoroethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2-methylpropan-2-ol [1084];

4-(2,2-difluoroethoxy)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1085];
1-((3R,4S)-4-((4-(2,2-difluoroethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [1086];
(R)-1-(4-((4-(2,2-difluoroethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [1087];
4-((4-(2,2-difluoroethoxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1088];
(1r,4r)-1-methyl-4-((4-(oxetan-3-yloxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1089];
N-((3R,4S)-3-fluoro-1-methylpiperidin-4-yl)-4-(oxetan-3-yloxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1090];
(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-(oxetan-3-yloxy)-5-(quinolin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1091];
N-(cis-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1092];
(3S,4R)-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)tetrahydrofuran-3-ol [1093];
1-((3R,4S)-3-fluoro-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol [1094];
(R)—N-(1-ethyl-3,3-difluoropiperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1095];
(R)-1-(3,3-difluoro-4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1096];
(R)-5-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylpiperidin-2-one [1097];
4-((4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1098];
N-((4s,6r)-1-(2,2-difluoroethyl)-1-azaspiro[3.3]heptan-6-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1099]; and
4-methoxy-5-(quinoxalin-6-yl)-N-(7-oxaspiro[3.5]nonan-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1100]; or a pharmaceutically acceptable salt thereof.

23. The compound according to claim **1**, wherein the compound of Formula I is selected from the group consisting of:

N-((1s,3s)-3-((6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [1101];
N-((1r,3r)-3-((6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclobutyl)acetamide [1102];
N-(cis-4-((6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1103];
(1s,4s)-4-((6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1104];
1-((3R,4S)-3-fluoro-4-((6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol [1105];
6-fluoro-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1106];
6-fluoro-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1107];
1-((3R,4S)-3-fluoro-4-((6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1108];
(R)—N-(3,3-difluoro-1-(oxetan-3-yl)piperidin-4-yl)-6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1109];
(R)—N-(3,3-difluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1110];
(R)-1-(3,3-difluoro-4-((6-fluoro-4-methoxy-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1111];
N-(cis-4-((4-(difluoromethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1112];
(1s,4s)-4-((4-(difluoromethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1113];
(1r,4r)-4-((4-(difluoromethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1114];
1-((3R,4S)-4-((4-(difluoromethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2-methylpropan-2-ol [1115];
4-(difluoromethoxy)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1116];
1-((3R,4S)-4-((4-(difluoromethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [1117];
(R)-1-(4-((4-(difluoromethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [1118];
4-((4-(difluoromethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1119];
N-(cis-4-((5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1120];
(1s,4s)-1-methyl-4-((5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1121];
(1r,4r)-1-methyl-4-((5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexan-1-ol [1122];
1-((3R,4S)-3-fluoro-4-((5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)-2-methylpropan-2-ol [1123];
N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1124];
1-((3R,4S)-3-fluoro-4-((5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1125];
(R)-1-(3,3-difluoro-4-((5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)ethan-1-one [1126];

4-((5-(quinoxalin-6-yl)-4-(trifluoromethoxy)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1127];
N-(cis-4-((4-(2,2-difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)cyclohexyl)acetamide [1128];
(1s,4s)-4-((4-(2,2-difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1129];
(1r,4r)-4-((4-(2,2-difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1130];
1-((3R,4S)-4-((4-(2,2-difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)-2-methylpropan-2-ol [1131];
4-(2,2-difluoroethoxy)-N-((3R,4S)-3-fluoro-1-(3-methyloxetan-3-yl)piperidin-4-yl)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1132];
1-((3R,4S)-4-((4-(2,2-difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3-fluoropiperidin-1-yl)ethan-1-one [1133];
(R)-1-(4-((4-(2,2-difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [1134];
4-((4-(2,2-difluoroethoxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)bicyclo[2.2.1]heptan-1-ol [1135];
(R)—N-(3,3-difluoro-1-methylpiperidin-4-yl)-4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1136];
4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)-N-(7-oxaspiro[3.5]nonan-2-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1137];
4-(oxetan-3-yloxy)-5-(quinoxalin-6-yl)-N-(2-oxaspiro[3.5]nonan-7-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1138];
(1r,4r)-4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-1-methylcyclohexan-1-ol [1139];
(R)-1-(4-((5-(1-(2,2-difluoroethyl)-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-3,3-difluoropiperidin-1-yl)ethan-1-one [1140];
5-(1-(2,2-difluoroethyl)-1H-benzo[d]imidazol-6-yl)-N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1141];
N-((3R,4S)-3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-5-(4-fluoro-1-isopropyl-2-methyl-1H-benzo[d]imidazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1142];
1-((3R,4S)-3-fluoro-4-((5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)piperidin-1-yl)propan-1-one [1143];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxy-N-((3-methyloxetan-3-yl)methyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1144];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3R,4S)-3-fluoro-1-(methylsulfonyl)piperidin-4-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1145];
3-((5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-yl)amino)-2,2-dimethylpropanenitrile [1146];
(R)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxy-N-(1-(tetrahydro-2H-pyran-4-yl)ethyl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1147];
N-(2,2-dimethyltetrahydro-2H-pyran-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1148];
N-((3S,4R)-3-fluorotetrahydro-2H-pyran-4-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1149];
N-(8-oxabicyclo[3.2.1]octan-3-yl)-5-(imidazo[1,2-a]pyrimidin-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1150];
N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-5-(1-(2-fluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1151];
5-(1-(2,2-difluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)-N-((3S,4R)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxypyrrolo[2,1-f][1,2,4]triazin-2-amine [1152]; and
N-((3R,4S)-4-fluoro-1-(oxetan-3-yl)pyrrolidin-3-yl)-4-methoxy-5-(1-(2,2,2-trifluoroethyl)-1H-benzo[d][1,2,3]triazol-6-yl)pyrrolo[2,1-f][1,2,4]triazin-2-amine [1153]; or a pharmaceutically acceptable salt thereof.

24. A pharmaceutical composition comprising a therapeutically effective amount of a compound according to claim **1**, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

25. A method of treating a disorder or disease in a patient, wherein the disorder or disease is selected from the group consisting of: a neurological disorder, diabetes, and cancer, the method comprising administering to the patient a therapeutically effective amount of a compound according to claim **1** or a pharmaceutically acceptable salt.

26. The method of claim **25**, wherein the disorder or disease is cancer.

27. The method of claim **25**, wherein the disorder or disease is diabetes.

28. The method of claim **25**, wherein the disorder or disease is a neurological disorder.

29. The method according to claim **26**, wherein the cancer is selected from the group consisting of: brain tumors, glioblastoma, ovarian, breast, head and neck squamous cell carcinoma, hepatocellular carcinoma, pancreatic cancer, acute lymphoblastic leukemia, acute megakaryoblastic leukemia, and chronic myeloid leukemia.

30. The method according to claim **28**, wherein the disorder or disease is a neurological disorder, wherein the neurological disorder is selected from the group consisting of: Alzheimer's disease, amyotrophic lateral sclerosis, CDKL5 deficiency disorder, Down syndrome, frontotemporal dementia with parkinsonism-17 (FTDP-17), Lewy body dementia, Parkinson's disease, Pick's disease, and additional diseases with pronounced neurodegeneration such as autism, dementia, epilepsy, Huntington's disease, multiple sclerosis; diseases and disorders associated with acquired brain injury such as chronic traumatic encephalopathy, traumatic brain injury, tumor, stroke, Pick disease, progressive supranuclear palsy, corticobasal degeneration, argyrophilic grain disease, globular glial tauopathies, primary age-related tauopathy, neurofibrillary tangle dementia, chronic traumatic encephalopathy (CTE), frontotemporal lobar degeneration with tau inclusions (FTLD-tau), and aging-related tau astrogliopathy.

31. The method according to claim **30**, wherein the disorder or disease is Alzheimer's disease.

32. The method according to claim **25**, wherein the patient is a human.

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