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(54) **[1,2,4]TRIAZOLO[1,5-A]PYRIDINYL SUBSTITUTED INDOLE COMPOUNDS**

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CPC A61K 31/4196; A61K 31/437; A61K 31/4427; A61K 45/06; C07D 249/00; C07D 471/04; A61P 19/02; A61P 25/00; A61P 29/00; A61P 35/00; A61P 37/00; A61P 37/02; A61P 43/00

See application file for complete search history.

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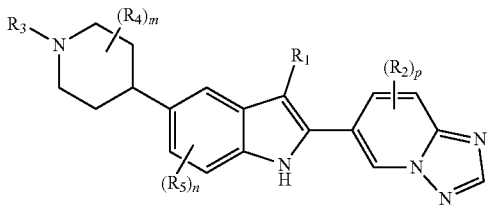
(57) **ABSTRACT**

Disclosed are compounds of Formula (I)

(I)



or a salt thereof, wherein R_1, R_2, R_3, R_4, R_5, m, n, and p are defined herein. Also disclosed are methods of using such compounds as inhibitors of signaling through Toll-like receptor 7, or 8, or 9, and pharmaceutical compositions comprising such compounds. These compounds are useful in treating inflammatory and autoimmune diseases.

17 Claims, No Drawings

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[1,2,4]TRIAZOLO[1,5-A]PYRIDINYL SUBSTITUTED INDOLE COMPOUNDS

Matter enclosed in heavy brackets [ ] appears in the original patent but forms no part of this reissue specification; matter printed in italics indicates the additions made by reissue; a claim printed with strikethrough indicates that the claim was canceled, disclaimed, or held invalid by a prior post-patent action or proceeding.

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation application of U.S. patent application Ser. No. 16/042,116 filed Jul. 23, 2018, which is a continuation application of U.S. patent application Ser. No. 15/635,055 filed Jun. 27, 2017, which claims the benefit of Indian Provisional Application Serial No. 201611022328, filed Jun. 29, 2016.

DESCRIPTION

The present invention generally relates to [1,2,4]triazolo [1,5-a]pyridinyl substituted indole compounds useful as inhibitors of signaling through Toll-like receptor 7, 8, or 9 (TLR7, TLR8, TLR9) or combinations thereof. Provided herein are [1,2,4]triazolo[1,5-a]pyridinyl substituted indole compounds, compositions comprising such compounds, and methods of their use. The invention further pertains to pharmaceutical compositions containing at least one compound according to the invention that are useful for the treatment of conditions related to TLR modulation, such as inflammatory and autoimmune diseases, and methods of inhibiting the activity of TLRs in a mammal.

Toll/IL-1 receptor family members are important regulators of inflammation and host resistance. The Toll-like receptor family recognizes molecular patterns derived from infectious organisms including bacteria, fungi, parasites, and viruses (reviewed in Kawai, T. et al., Nature Immunol., 11:373-384-(2010)). Ligand binding to the receptor induces dimerization and recruitment of adaptor molecules to a conserved cytoplasmic motif in the receptor termed the Toll/IL-1 receptor (TIR) domain. With the exception of TLR_3, all TLRs recruit the adaptor molecule MyD88. The IL-1 receptor family also contains a cytoplasmic TIR motif and recruits MyD88 upon ligand binding (reviewed in Sims, J. E. et al., Nature Rev. Immunol., 10:89-102 (2010)).

Toll-like receptors (TLRs) are a family of evolutionarily conserved, transmembrane innate immune receptors that participate in the first-line defense. As pattern recognition receptors, the TLRs protect against foreign molecules, activated by pathogen associated molecular patterns (PAMPs), or from damaged tissue, activated by danger associated molecular patterns (DAMPs). A total of 13 TLR family members have been identified, 10 in human, that span either the cell surface or the endosomal compartment. TLR7-9 are among the set that are endosomally located and respond to single-stranded RNA (TLR7 and TLR8) or unmethylated single-stranded DNA containing cytosinephosphateguanine (CpG) motifs (TLR9).

Activation of TLR7/8/9 can initiate a variety of inflammatory responses (cytokine production, B cell activation and IgG production, Type I interferon response). In the case of autoimmune disorders, the aberrant sustained activation of TLR7/8/9 leads to worsening of disease states. Whereas overexpression of TLR7 in mice has been shown to exacerbate autoimmune disease, knockout of TLR7 in mice was found to be protective against disease in lupusprone MRL/lpr mice. Dual knockout of TLR7 and 9 showed further enhanced protection.

As numerous conditions may benefit by treatment involving modulation of cytokines, IFN production and B cell activity, it is immediately apparent that new compounds capable of modulating TLR7 and/or TLR8 and/or TLR9 and methods of using these compounds could provide substantial therapeutic benefits to a wide variety of patients.

The present invention relates to a new class of [1,2,4] triazolo[1,5-a]pyridinyl substituted indole compounds found to be effective inhibitors of signaling through TLR7/8/9. These compounds are provided to be useful as pharmaceuticals with desirable stability, bioavailability, therapeutic index, and toxicity values that are important to their drugability.

SUMMARY OF THE INVENTION

The present invention provides compounds of Formula (I) that are useful as inhibitors of signaling through Toll-like receptor 7, 8, or 9 and are useful for the treatment of proliferative diseases, allergic diseases, autoimmune diseases and inflammatory diseases, or stereoisomers, tautomers, pharmaceutically acceptable salts, solvates or prodrugs thereof.

The present invention also provides pharmaceutical compositions comprising a pharmaceutically acceptable carrier and at least one of the compounds of the present invention or stereoisomers, tautomers, pharmaceutically acceptable salts, solvates, or prodrugs thereof.

The present invention also provides a method for inhibition of Toll-like receptor 7, 8, or 9 comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or stereoisomers, tautomers, pharmaceutically acceptable salts, solvates, or prodrugs thereof.

The present invention also provides a method for treating proliferative, metabolic, allergic, autoimmune and inflammatory diseases, comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or stereoisomers, tautomers, pharmaceutically acceptable salts, solvates, or prodrugs thereof.

The present invention also provides a method of treating a disease or disorder associated with Toll-like receptor 7, 8, or 9 activity, the method comprising administering to a mammal in need thereof, at least one of the compounds of Formula (I) or salts, solvates, and prodrugs thereof.

The present invention also provides processes and intermediates for making the compounds of Formula (I) including salts, solvates, and prodrugs thereof.

The present invention also provides at least one of the compounds of Formula (I) or salts, solvates, and prodrugs thereof, for use in therapy.

The present invention also provides the use of at least one of the compounds of Formula (I) or salts, solvates, and prodrugs thereof, for the manufacture of a medicament for the treatment of prophylaxis of Toll-like receptor 7, 8, or 9 related conditions, such as allergic disease, autoimmune diseases, inflammatory diseases, and proliferative diseases.

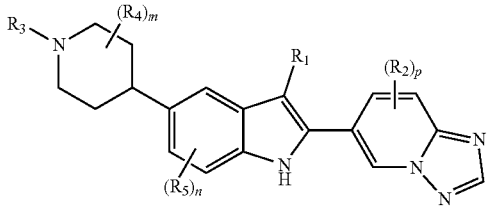
The compound of Formula (I) and compositions comprising the compounds of Formula (I) may be used in treating, preventing, or curing various Toll-like receptor 7, 8, or 9 related conditions. Pharmaceutical compositions comprising these compounds are useful for treating, preventing, or

slowing the progression of diseases or disorders in a variety of therapeutic areas, such as allergic disease, autoimmune diseases, inflammatory diseases, and proliferative diseases.

These and other features of the invention will be set forth in expanded form as the disclosure continues.

DETAILED DESCRIPTION

The first aspect of the present invention provides at least one compound of Formula (I):



or a salt thereof, wherein:

R_1 is H, Cl, —CN, C_{1-4} alkyl, C_{1-3} fluoroalkyl, C_{1-3} hydroxy-fluoroalkyl, $—CR_z═CH_2$, C_{3-6} cycloalkyl, $—CH_2(C_{3-6}$ cycloalkyl), $—C(O)O(C_{1-3}$ alkyl), or tetrahydropyranyl;

each R_2 is independently halo, —CN, —OH, $—NO_2^+$, C_{1-3} alkyl, $—CD_3$, C_{1-2} fluoroalkyl, C_{1-2} cyanoalkyl, C_{1-3} hydroxyalkyl, C_{1-3} aminoalkyl, $—O(CH_2)_{1-2}OH$, $—(CH_2)_{0-4}O(C_{1-4}$ alkyl), C_{1-3} fluoroalkoxy, $—(CH_2)_{1-4}O(C_{1-3}$alkyl), $—O(CH_2)_{1-2}OC(O)(C_{1-3}$alkyl), $—O(CH_2)_{1-2}NR_xR_x$, $—C(O)O(C_{1-3}$ alkyl), $—C(O)NR_yR_y$, $—NR_yR_y$, $—NR_y(C_{1-3}$ fluoroalkyl), $—NR_y(C_{1-4}$ hydroxyalkyl), $—NR_xCH_2$(phenyl), $—NR_xS(O)_2(C_{3-6}$ cycloalkyl), $—NR_xC(O)(C_{1-3}$ alkyl), $—NR_x(CH_2$-cyclopropyl), C_{3-6} cycloalkyl, morpholinyl, dioxothiomorpholinyl, methylpiperidinyl, methylpiperazinyl, amino-oxadiazolyl, imidazolyl, triazolyl, or —C(O)(thiazolyl);

R_3 is:

(a) $-L_1$-A; or

(b) H, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} cyanoalkyl, C_{1-6} hydroxyalkyl, C_{1-3} hydroxy-fluoroalkyl, $—CR_xR_xCR_x(OH)CR_x═CR_xR_x$, $—C═N(NR_xR_x)$, $—(CR_xR_x)_{1-4}O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-4}O(CR_xR_x)_{1-3}O(C_{1-3}$ alkyl), $—CH_2CH(OH)CH_2O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-3}S(C_{1-3}$ alkyl), $—(CH_2)_{1-3}C(O)OC(CH_3)_3$, $—(CR_xR_x)_{0-3}NR_xR_y$, $—(CR_xR_x)_{0-3}NR_x(C_{1-4}$ hydroxyalkyl), $—CH_2CH(OH)CH_2NR_xR_y$, —C(O)H, $—C(O)(C_{1-6}$ alkyl), $—C(O)(C_{1-4}$ hydroxyalkyl), $—C(O)(C_{1-3}$ fluoroalkyl), $—C(O)(C_{1-3}$ chloroalkyl), $—C(O)(C_{1-3}$ cyanoalkyl), $—(CR_xR_x)_{0-3}C(O)OH$, $—C(O)(CH_2)_{0-2}O(C_{1-4}$ alkyl), $—C(O)(CR_xR_x)_{0-2}O(CR_xR_x)_{1-2}O(C_{1-3}$ alkyl), $—C(O)(CR_xR_x)_{0-2}O(CR_xR_x)_{1-2}NR_yR_y$, $—C(O)CR_xR_xS(O)_2(C_{1-3}$ alkyl), $—C(O)CR_xR_xNR_xS(O)_2(C_{1-3}$ alkyl), $—C(O)CR_xR_xOC(O)(C_{1-3}$ alkyl), $—C(O)(CR_xR_x)_{0-3}NR_yR_y$, $—C(O)(CR_xR_x)_{0-1}NR_xC_{1-3}$ cyanoalkyl), $—C(O)(CR_xR_x)_{0-2}NR_y(C_{1-6}$ hydroxyalkyl), $—C(O)(CR_xR_x)_{0-2}NR_x(C_{1-3}$ fluoroalkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(C_{1-5}$ hydroxy-fluoroalkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}O(C_{1-3}$ hydroxyalkyl), $—C(O)(CR_xR_x)_{0-2}NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-2}$ alkyl), $—C(O)(CR_xR_x)_{0-2}NR_x((CR_xR_x)_{1-2}O(C_{1-2}$ alkyl)), $—C(O)(CR_xR_x)_{0-2}N((CR_xR_x)_{1-2}O(C_{1-2}$ alkyl))$_2$, $—C(O)(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{1-3}NR_xR_x$, $—C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xR_x$, $—C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xC(O)NR_xR_x$, $—C(O)(CR_xR_x)_{0-3}NR_x(CH_2)_{0-1}C(O)(C_{3}$alkyl), $—C(O)(CR_xR_x)_{0-3}N((CH_2)_{0-1}C(O)(C_{1-3}$alkyl))$_2$, $—C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$cyanoalkyl), $—C(O)(CR_xR_x)_{0-2}NR_x(CH_2)_{1-2}C(O)NR_yR_y$, $—C(O)(CR_xR_x)_{1-3}C(O)NR_yR_y$, $—C(O)(CR_xR_x)_{1-3}S(O)_2NR_yR_y$, $—C(O)(CR_xR_x)_{0-2}NR_x(CHR_y(CH_2OH))$, $—(CR_xR_x)_{1-2}C(O)NR_yR_y$, —CH(CN)C(O)$NR_yR_y$, $—(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ fluoroalkyl), $—(CR_xR_x)_{1-2}C(O)NR_y(C_{1-4}$ hydroxyalkyl), $—(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ cyanoalkyl), $—(CR_xR_x)_{1-2}C(O)NR_x(CH_2)_{1-2}O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-2}C(O)NR_xCH(C_{1-4}$ alkyl)$(C_{1-3}$ hydroxyalkyl), $—(CR_xR_x)_{1-2}C(O)NR_xCH(C_{1-3}$ hydroxyalkyl)$(C_{3-6}$ cycloalkyl), $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}C(O)NR_xR_x$, $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(C_{1-3}$ alkyl), $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(O)_2OH$, $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-3}$ alkyl), $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-3}NR_xR_x$, $—(CH_2)_{1-2}C(O)N(CH_2CH_3)(CH_2)_{1-3}NR_xR_x$, $—(CR_xR_x)_{0-3}S(O)_2(C_{1-4}$ alkyl), $—(CH_2)_{0-2}S(O)_2(C_{1-3}$ fluoroalkyl), $—(CR_xR_x)_{0-2}S(O)_2NR_yR_y$, $—(CR_xR_x)_{0-2}NR_xS(O)_2(C_{1-3}$ alkyl), —C(O)C(O)OH, —C(O)C(O)NR_yR_y, or $—C(O)C(O)NR_y(CR_xR_x)_{1-2}NR_yR_y$;

L_1 is a bond, $—(CR_xR_x)_{1-2}—$, $—(CR_xR_x)_{1-2}CR_x(OH)—$, $—(CR_xR_x)_{1-2}O—$, $—CR_xR_xC(O)—$, $—(CR_xR_x)_2NR_x(CR_xR_x)_{0-1}—$, $—CR_xR_xC(O)NR_x(CR_xR_x)_{0-4}—$, $—C(O)(CR_xR_x)_{0-3}—$, $—C(O)(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{0-2}—$, $—C(O)(CR_xR_x)_{0-2}N(C_{1-2}$ hydroxyalkyl)$(CR_xR_x)_{0-2}—$, $—C(O)(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{1-2}CR_x(OH)—$, $—C(O)(CR_xR_x)_{1-2}C(O)NR_x—$, $—(CR_xR_x)_{0-2}C(O)NR_x(CR_xR_x)_{1-2}CR_x(OH)—$, $—(CR_xR_x)_{0-2}C(O)N(C_{1-2}$ hydroxyalkyl)$(CR_xR_x)_{1-2}—$, $—C(O)(CR_xR_x)_{0-1}O—$, $—C(O)(CR_xR_x)_{1-2}NHS(O)_2—$, $—C(O)CR_x(NH_2)CR_xR_x—$, $—C(O)C(O)(CR_xR_x)_{0-2}—$, $—C(O)NR_x(CR_xR_x)_{1-2}—$, or $—S(O)_2—$; A is 2-oxa-6-azaspiro[3,3]heptanyl, 4-oxaspiro[2.5]octanyl, 7-azaspiro[3.5]nonanyl, 8-azabicyclo[3.2.1]octanyl, 8-oxa-3-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, adamantanyl, azepanyl, azetidinyl, C_{3-6} cycloalkyl, diazepanyl, dihydroinonyl, dihydropyrimidinonyl, dioxanyl, dioxidothiadiazinanyl, dioxidothiazolidinyl, dioxidothiomorpholinyl, dioxoisothiazolidinyl, dioxidothiazinanyl, dioxotetrahydrothiophenyl, dioxotetrahydrothiopyranyl, dioxothiomorpholinyl, furanyl, imidazolyl, imidazolidinonyl, indolyl, isoquinolinyl, isoxazolyl, morpholinyl, morpholinonyl, naphthalenyl, octahydrocyclopenta[b]pyranyl, octahydropyrrolo[3,4-b]pyridinyl, oxazolidinonyl, oxadiazolyl, oxazolyl, oxetanyl, phenyl, piperidinyl, piperidinonyl, piperazinyl, piperazinonyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridazinonyl, pyridinonyl, pyridinyl, pyrimidinyl, pyrrolidinonyl, pyrrolidinyl, pyrrolyl, quinolinyl, quinolizinonyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrazolyl, thiadiazolyl, thiazolyl, triazolonyl, or triazolyl, each substituted wtih $-L_2R_a$ and zero to 4 R_b; L_2 is a bond or CR_xR_x;

R_a 1S:

(a) H, F, Cl, —CN, —OH, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-5} hydroxyalkyl, $—(CH_2)_{0-4}O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-3}S(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-3}NHC(O)O(C_{1-4}$ alkyl), $—(CR_xR_x)_{1-3}NR_yR_y$, $—(CR_xR_x)_{1-3}C(O)NR_yR_y$, $—O(C_{1-3}$ fluoroalkyl), $—S(O)_2NR_xR_x$, $—O(CR_xR_x)_{1-3}NR_xR_x$, $—NHS(O)_2(C_{1-3}$ alkyl), $—NR_xR_x$, $—NR_x(C_{1-4}$ alkyl), $—NR_xC(O)(C_{1-4}$ alkyl), $—(CR_xR_x)_{0-3}C(O)OH$, $—C(O)(C_{1-5}$ alkyl), $—C(O)(C_{1-3}$ fluoroalkyl), $—C(O)O(C_{1-4}$ alkyl), —C(O)NH$(C_{1-3}$ cyanoalkyl), $—C(O)NR_yR_y$, $—C(O)NR_xCH_2C(O)NR_xR_x$, or $—C(O)NR_xCH_2CH_2NHC(O)(C_{1-3}$ alkyl);

(b) C_{3-6} cycloalkyl or C(O)NH(C_{3-6} cycloalkyl), wherein each cycloalkyl is substituted with zero to 2 substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, and —C(O)O(C_{1-3} alkyl); or

(c) A_1, —CH_2A_1, —C(O)A_1, —NR_xA_1, or —C(O)NR_xA_1, wherein A_1 is furanyl, imidazolyl, indolyl, isoxazolyl, morpholinyl, octahydropyrrolo[3,4-c]pyrrolyl, oxazolyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolidinyl, pyrrolyl, tetrahydrofuranyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophenyl, or triazolyl, each substituted with zero to three substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, —C(O)(C_{1-2} alkyl), —C(O)O(C_{1-3} alkyl), —NR_xR_x, phenyl, trifluoromethyl-phenyl, —CH_2(bromophenyl), and —CH_2CH_2(pyrrolidinyl);

each R_b is independently F, —OH, —CH_3, —CF_3, or —OCH_3;

each R_x is independently H or —CH_3;

each R_y is independently H or C_{1-6} alkyl;

R_z is H, C_{1-2} alkyl, or C_{1-2} fluoroalkyl;

each R_4 is independently F, —OH, C_{1-2} alkyl, or —OCH_3; or two R_4 attached to the same carbon atom form =O; or wherein when m is at least 2, two R_4, each attached to a different carbon atom adjacent to the nitrogen atom in the piperidinyl ring, can form a —CH_2CH_2— bridge;

each R_5 is independently F, Cl, —CN, C_{1-2} alkyl, C_{1-2} fluoroalkyl, or —OCH_3;

m is zero, 1, 2, 3, or 4;

n is zero, 1, or 2; and

p is zero, 1, 2, 3, or 4.

The second aspect of the present invention provides at least one compound of Formula (I) or a salt thereof, wherein:

R_1 is H, Cl, —CN, C_{1-4} alkyl, C_{1-3} fluoroalkyl, C_{1-3} hydroxy-fluoroalkyl, —CR_z=CH_2, C_{3-6} cycloalkyl, —CH_2(C_{3-6} cycloalkyl), —C(O)O(C_{1-3} alkyl), or tetrahydropyranyl;

each R_2 is independently halo, —CN, —OH, —NO_2^+, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, C_{1-3} aminoalkyl, $(CH_2)_{0-4}$O(C_{1-3} alkyl), C_{1-3} fluoroalkoxy, C_{2-4} alkoxyalkoxy, —O$(CH_2)_{1-2}NR_xR_x$, —C(O)O(C_{1-3} alkyl), —C(O)NR_yR_y, —NR_yR_y, —NR_xC(O)(C_{1-3} alkyl), —NR_x(CH_2-cyclopropyl), C_{3-6} cycloalkyl, methylpiperidinyl, methylpiperazinyl, amino-oxadiazolyl, imidazolyl, triazolyl, or C(O)(thiazolyl);

R_3 is:

(a) -L_1-A; or

(b) H, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} cyanoalkyl, C_{1-6} hydroxyalkyl, C_{1-3} hydroxy-fluoroalkyl, —$CR_xR_xCR_x$(OH)CR_x=CR_xR_x, —$(CR_xR_x)_{1-4}$O(C_{1-3} alkyl), —$(CR_xR_x)_{1-4}$O$(CR_xR_x)_{1-3}$O(C_{1-3} alkyl), —CH_2CH(OH)CH_2O(C_{1-3} alkyl), —$(CR_xR_x)_{1-3}$S(C_{1-3} alkyl), —$(CH_2)_{1-3}$C(O)OC$(CH_3)_3$, —$(CR_xR_x)_{0-3}NR_xR_y$, —$(CR_xR_x)_{0-3}NR_x$(C_{1-4} hydroxyalkyl), —CH_2CH(OH)$CH_2NR_xR_y$, —C(O)H, —C(O)(C_{1-6} alkyl), —C(O)(C_{1-3} hydroxyalkyl), —C(O)(C_{1-3} fluoroalkyl), —C(O)(C_{1-3} chloroalkyl), —C(O)(C_{1-3} cyanoalkyl), —$(CR_xR_x)_{0-3}$C(O)OH, —C(O)$(CH_2)_{0-2}$O(C_{1-4} alkyl), —C(O)$(CR_xR_x)_{0-2}$O$(CR_xR_x)_{1-2}$O(C_{1-3} alkyl), —C(O)CR_xR_xS(O)$_2$(C_{1-3} alkyl), —C(O)$CR_xR_xNR_xS$(O)$_2$(C_{1-3} alkyl), —C(O)CR_xR_xOC(O)(C_{1-3} alkyl), —C(O)$(CR_xR_x)_{0-3}NR_yR_y$, —C(O)$(CR_xR_x)_{0-1}NR_x$(C_{1-3} cyanoalkyl), —C(O)$(CR_xR_x)_{0-2}NR_y$(C_{1-6} hydroxyalkyl), —C(O)$(CR_xR_x)_{0-1}NR_x$(C_{1-3} fluoroalkyl), —C(O)$(CR_xR_x)_{0-1}NR_x$(C_{1-5} hydroxy-fluoroalkyl), —C(O)$(CR_xR_x)_{0-1}NR_x$$(CH_2)_{1-2}$O($C_{1-3}$ hydroxyalkyl), —C(O)$(CR_xR_x)_{0-1}NR_x$$(CH_2)_{1-2}NR_xC$(O)($C_{1-2}$ alkyl), —C(O)$(CR_xR_x)_{0-1}NR_x$(($CR_xR_x)_{1-2}$O(C_{1-2} alkyl)), —C(O)$CR_x$$(NH_2)(CR_xR_x)_{1-4}NR_xR_x$, —C(O)$CR_x$$(NH_2)(CR_xR_x)_{1-4}NR_xC(O)NR_xR_x$, —C(O)$(CR_xR_x)_{0-3}NR_x$$(CH_2)_{0-1}$C(O)($C_{1-3}$ alkyl), —C(O)$(CR_xR_x)_{0-1}NR_x$$(CH_2)_{0-1}$C(O)($C_{1-3}$ cyanoalkyl), —C(O)$(CR_xR_x)_{0-1}$$NR_x(CH_2)_{1-2}$ C(O)NR_yR_y, —C(O)$(CR_xR_x)_{1-3}$C(O)NR_yR_y, —C(O)$(CR_xR_x)_{0-1}NR_x$(CHR$_y$(CH_2OH)), —$(CR_xR_x)_{1-2}$C(O)NR_yR_y, —$(CR_xR_x)_{1-2}$C(O)NR_y(C_{1-3} fluoroalkyl), —$(CR_xR_x)_{1-2}$C(O)NR_y(C_{1-4} hydroxyalkyl), —$(CR_xR_x)_{1-2}$C(O)NR_y(C_{1-3} cyanoalkyl), —$(CR_xR_x)_{1-2}$C(O)$NR_x(CH_2)_{1-2}$O(C_{1-3} alkyl), —$(CR_xR_x)_{1-2}$C(O)NR_xCH(C_{1-4} alkyl)(C_{1-3} hydroxyalkyl), —$(CH_2)_{1-2}$C(O)$NR_x(CH_2)_{1-2}$C(O)NR_xR_x, —$(CH_2)_{1-2}$C(O)$NR_x(CH_2)_{1-2}$S(O)$_2$OH, —$(CH_2)_{1-2}$C(O)$NR_x(CH_2)_{1-2}NR_xC$(O)(C_{1-3} alkyl), —$(CH_2)_{1-2}$C(O)$NR_x(CH_2)_{1-3}NR_xR_x$, —$(CH_2)_{1-2}$C(O)N(CH_2CH_3)$(CH_2)_{1-3}NR_xR_x$, —$(CH_2)_{0-2}$S(O)$_2$(C_{1-4} alkyl), —$(CH_2)_{0-2}$S(O)$_2$(C_{1-3} fluoroalkyl), —$(CH_2)_{0-2}$S(O)$_2NR_xR_x$, —C(O)C(O)OH, —C(O)C(O)NR_yR_y, or —C(O)C(O)$NR_y(CR_xR_x)_{1-2}NR_yR_y$;

L_1 is a bond, —$(CR_xR_x)_{1-2}$—, —$(CR_xR_x)_{1-2}CR_x$(OH)—, —$(CR_xR_x)_{1-2}$O—, —CR_xR_xC(O)—, —$(CR_xR_x)_2NR_x$$(CR_xR_x)_{0-1}$—, —$CR_xR_xC(O)NR_x(CR_xR_x)_{0-4}$—, —C(O)$(CR_xR_x)_{0-3}$—, —C(O)$(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{0-2}$—, —C(O)$(CR_xR_x)_{0-2}N$($C_{1-2}$ hydroxyalkyl)$(CR_xR_x)_{0-2}$—, —C(O)$(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{1-2}CR_x$(OH)—, —C(O)$(CR_xR_x)_{1-2}$C(O)$NR_x$—, —$(CR_xR_x)_{0-2}$C(O)$NR_x(CR_xR_x)_{1-2}CR_x$(OH)—, —$(CR_xR_x)_{0-2}$C(O)N($C_{1-2}$ hydroxyalkyl)$(CR_xR_x)_{1-2}$—, —C(O)$(CR_xR_x)_{01}$O—, —C(O)$(CR_xR_x)_{1-2}$NHS(O)$_2$—, —C(O)$CR_x$$(NH_2)CR_xR_x$—, —C(O)C(O)$(CR_xR_x)_{0-2}$—, —C(O)$NR_x(CR_xR_x)_{1-2}$—, or —S(O)$_2$—;

A is 2-oxa-6-azaspiro[3,3]heptanyl, 4-oxaspiro[2.5]octanyl, 7-azaspiro[3.5]nonanyl, 8-azabicyclo[3.2.1]octanyl, 8-oxa-3-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, adamantanyl, azepanyl, azetidinyl, C_{3-6} cycloalkyl, diazepanyl, dihydroinonyl, dihydropyrimidinonyl, dioxidothiadiazinanyl, dioxidoisothiazolidinyl, dioxidothiazinanyl, dioxotetrahydrothiophenyl, dioxotetrahydrothiopyranyl, dioxothiomorpholinyl, furanyl, imidazolyl, imidazolidinonyl, indolyl, isoquinolinyl, isoxazolyl, morpholinyl, morpholinonyl, naphthalenyl, octahydrocyclopenta[b]pyranyl, oxazolidinonyl, oxadiazolyl, oxetanyl, oxazolyl, phenyl, piperidinyl, piperidinonyl, piperazinyl, piperazinonyl, pyrazinyl, pyrazolyl, pyridazinonyl, pyridinonyl, pyridinyl, pyrimidinyl, pyrrolidinonyl, pyrrolidinyl, pyrrolyl, quinolinyl, quinolizinonyl, tetrahydrofuranyl, tetrahydropyranyl, tetrazolyl, thiadiazolyl, thiazolyl, or triazolyl, each substituted wtih -L_2R_a and zero to 4 R_b;

L_2 is a bond or —CR_xR_x—,

R_a is:

(a) H, F, Cl, —CN, —OH, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-5} hydroxyalkyl, —$(CH_2)_{0-4}$O(C_{1-3} alkyl), —$(CR_xR_x)_{1-3}$S(C_{1-3} alkyl), —$(CR_xR_x)_{1-3}$NHC(O)O(C_{1-4} alkyl), —$(CR_xR_x)_{1-3}NR_yR_y$, —$(CR_xR_x)_{1-3}$C(O)NR_yR_y, —O(C_{1-3} fluoroalkyl), —S(O)$_2NR_xR_x$, —O$(CR_xR_x)_{1-3}NR_xR_x$, —NHS(O)$_2$(C_{1-3} alkyl), —NR_xR_x, —NR_x(C_{1-4} alkyl), —NR_xC(O)(C_{1-4} alkyl), —$(CR_xR_x)_{0-3}$C(O)OH, —C(O)(C_{1-5} alkyl), —C(O)(C_{1-3} fluoroalkyl), —C(O)O(C_{1-4} alkyl), —C(O)NH(C_{1-3} cyanoalkyl), —C(O)NR_yR_y, —C(O)NR_xCH_2C(O)NR_xR_x, or —C(O)$NR_xCH_2CH_2NHC$(O)(C_{1-3} alkyl);

(b) C_{3-6} cycloalkyl or —C(O)NH(C_{3-6} cycloalkyl), wherein each cycloalkyl is substituted with zero to 2 substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, and —C(O)O(C_{1-3} alkyl); or

(c) A_1, —CH_2A_1, —C(O)A_1, —NR_xA_1, or —C(O)NR_xA_1, wherein A_1 is furanyl, imidazolyl, indolyl, isoxazolyl, morpholinyl, octahydropyrrolo[3,4-c]pyrrolyl, oxazolyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolidinyl, pyrrolyl, tetrahydrofuranyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophenyl, or triazolyl, each substituted with zero to three substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, —C(O)(C_{1-2} alkyl), —C(O)O(C_{1-3} alkyl), —NR_xR_x, phenyl, trifluoromethyl-phenyl, —CH_2(bromophenyl), and —CH_2CH_2(pyrrolidinyl);

each R_b is independently F, —CH_3, —CF_3, or —OCH_3;

each R_x is independently H or —CH_3;

each R_y is independently H or C_{1-6} alkyl;

R_z is H, C_{1-2} alkyl, or C_{1-2} fluoroalkyl;

each R_4 is independently F, —OH, C_{1-2} alkyl, or —OCH_3; or two R_4 attached to the same carbon atom form =O;

each R_5 is independently F, Cl, —CN, C_{1-2} alkyl, C_{1-2} fluoroalkyl, or —OCH_3;

m is zero, 1, 2, 3, or 4;

n is zero, 1, or 2; and

p is zero, 1, 2, 3, or 4.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_1 is H, Cl, —CN, C_{1-4} alkyl, C_{1-3} fluoroalkyl, C_{1-3} hydroxy-fluoroalkyl, C_{3-6} cycloalkyl, —CH_2(C_{3-6} cycloalkyl), or tetrahydropyranyl; and R_2, R_3, R_4, R_5, m, n, and p are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is H, Cl, —CN, C_{1-4} alkyl, or C_{1-2} fluoroalkyl. Also included are compounds in which R_1 is —CH_2CH_3, —$CH(CH_3)_2$, or —CH_2CHF_2; and compounds in which R_1 is —$CH(CH_3)_2$. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein each R_2 is independently F, Cl, —CN, —OH, C_{1-3} alkyl, —CD_3, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, C_{1-2} cyanoalkyl, C_{1-3} aminoalkyl, C_{1-4} alkoxy, C_{1-2} fluoroalkoxy, —$O(CH_2)_{1-2}$OH, —$(CH_2)_{1-4}$O(C_{1-3} alkyl), —$O(CH_2)_{1-2}$OC(O)(C_{1-3} alkyl), —$O(CH_2)_{1-2}NR_xR_x$, —C(O)O(C_{1-3} alkyl), —C(O)NR_yR_y, —NR_yR_y, —NR_y(C_{1-3} fluoroalkyl), —NR_y(C_{1-4} hydroxyalkyl), —NR_xCH_2(phenyl), —$NR_xS(O)_2$(C_{3-6} cycloalkyl), C_{3-6} cycloalkyl, —$NR_xC(O)$(C_{1-3} alkyl), —NR_x(CH_2-cyclopropyl), C_{3-6} cycloalkyl, morpholinyl, dioxothiomorpholinyl, methylpiperidinyl, methylpiperazinyl, amino-oxadiazolyl, imidazolyl, triazolyl, or —C(O)(thiazolyl); and R_1, R_3, R_4, R_5, R_x, R_y, m, n, and p are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which each R_2 is independently F, Cl, —CN, C_{1-3} alkyl, —CD_3, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, C_{1-2} cyanoalkyl, C_{1-4} alkoxy, C_{1-2} fluoroalkoxy, —$O(CH_2)_{1-2}$OH, —$(CH_2)_{1-4}$O(C_{1-3} alkyl), —$O(CH_2)_{1-2}$OC(O)(C_{1-3} alkyl), —NR_yR_y, —NR_y(C_{1-3} fluoroalkyl), —NR_y(C_{1-4} hydroxyalkyl), —NR_xCH_2(phenyl), —$NR_xS(O)_2$(C_{3-6} cycloalkyl), C_{3-6} cycloalkyl, morpholinyl, di oxothiomorpholinyl, or methylpiperazinyl. Also included in this embodiment are compounds in which each R_2 is independently F, Cl, —CN, —CH_3, —CH_2CH_3, —$CH(CH_3)_2$, —CD_3, —CF_3, —CH_2CN, —CH_2OH, —CH_2CH_2OH, —$CH(CH_3)OH$, —$C(CH_3)_2OH$, —OCH_2CH_2OH, —OCH_3, —OCH_2CH_3, —$OCH_2CH(CH_3)_2$, —$OCHF_2$, —CH_2OCH_3, —$CH_2OCH_2CH_3$, —$OCH_2CH_2OC(O)CH_3$, —NH_2, —NH(CH_2CH_3), —NH(CH_2CF_3), —NH($CH_2C(CH_3)_2OH$), —$NHCH_2$(phenyl), —$NHS(O)_2$(cyclopropyl), cyclopropyl, morpholinyl, dioxothiomorpholinyl, or methylpiperazinyl.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein each R_2 is independently halo, —CN, C_{1-3} alkyl, —CD_3, C_{1-2} fluoroalkyl, C_{1-2} cyanoalkyl, C_{1-3} hydroxyalkyl, —$O(CH_2)_{1-2}$OH, —$(CH_2)_{0-4}$O(C_{1-4} alkyl), C_{1-3} fluoroalkoxy, —$O(CH_2)_1$ and R_1, R_3, R_4, R_5, R_x, R_y, m, n, and p are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which $_2$OC(O)(C_{1-3} alkyl), —NR_yR_y, —NR_y(C_{1-3} fluoroalkyl), —NR_y(C_{1-4} hydroxyalkyl), —NR_xCH_2(phenyl), —$NR_xS(O)_2$(C_{3-6} cycloalkyl), C_{3-6} cycloalkyl, morpholinyl, dioxothiomorpholinyl, or methylpiperazinyl; and R_1, R_3, R_4, R_5, R_x, R_y, m, n, and p are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which each R_2 is independently F, Cl, —CN, —OH, C_{1-3} alkyl, —CD_3, C_{1-2} fluoroalkyl, C_{1-2} cyanoalkyl, C_{1-3} hydroxyalkyl, —$O(CH_2)_{1-2}$OH, —O(C_{1-4} alkyl), C_{1-2} fluoroalkoxy, —$(CH_2)_{1-4}$O(C_{1-3} alkyl), —$O(CH_2)_{1-2}$ OC(O)(C_{1-3} alkyl), —NR_yR_y, —NR_y(C_{1-3} fluoroalkyl), —NR_y(C_{1-4} hydroxyalkyl), —NR_xCH_2(phenyl), —$NR_xS(O)_2$(C_{3-6} cycloalkyl), C_{3-6} cycloalkyl, morpholinyl, dioxothiomorpholinyl, or methylpiperazinyl. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_2 is F, Cl, —CN, C_{1-2} alkyl, —CD_3, —CF_3, —CH_2OH, —$C(CH_3)_2OH$, —OCH_3, —CH_2OCH_3, —OCH_2CH_3, cyclopropyl, or morpholinyl; and R_1, R_3, R_4, R_5, m, n, and p are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which each R_2 is independently —CH_3 or —OCH_3. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is -L_1-A; and R_1, R_2, R_4, R_5, L_1, and A are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which L_1 is a bond, —$(CR_xR_x)_{1-2}$—, —$(CR_xR_x)_{1-2}CR_x$(OH)—, —$(CR_xR_x)_{1-2}O$—, —$CR_xR_xC(O)$—, —$(CR_xR_x)_2NR_x$$(CR_xR_x)_{0-1}$—, —$CR_xR_xC(O)NR_x(CR_xR_x)_{0-4}$—, —C(O)$(CR_xR_x)_{0-3}$—, —C(O)$(CR_xR_x)_{0-2}NR_xCR_xR_x)_{0-2}$—, —C(O)$(CR_xR_x)_{0-2}N$($C_{1-2}$ hydroxyalkyl)$(CR_xR_x)_{0-2}$—, —C(O)$(CR_xR_x)_{1-2}C(O)NR_x$—, —C(O)$(CR_xR_x)_{0-2}NR_x(CR_x$$R_x)_{1-2}CR_x$(OH)—, —$(CR_xR_x)_{0-2}C(O)NR_x(CR_xR_x)_{1-2}CR_x$(OH)—, —$(CR_xR_x)_{0-2}C(O)N$($C_{1-2}$ hydroxyalkyl)$(CR_x$$R_x)_{1-2}$—, —C(O)$(CR_xR_x)_{0-1}O$—, —C(O)$(CR_xR_x)_{1-2}NHS(O)_2$—, —$C(O)CR_x(NH_2)CR_xR_x$—, —C(O)C(O)$(CR_x$$R_x)_{0-2}$—, —C(O)$NR_x(CR_xR_x)_{1-2}$—, or —$S(O)_2$—. Also included are compounds in which L_1 is a bond, —CR_xR_x, —$CR_xR_xC(O)$—, —$CR_xR_xC(O)NR_x$—, or —C(O)$(CR_x$$R_x)_{0-2}$—. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is -L_1-A; L_1 is a bond, —CR_xR_x, —$CR_xR_xC(O)$—, —$CR_xR_xC(O)NR_x$—, or —C(O)$(CR_x$$R_x)_{0-2}$—; A is a ring selected from azetidinyl, C_{3-6} cycloalkyl, dioxotetrahydrothiopyranyl, dioxidothiadiazinanyl, dioxidothiomorpholinyl, furanyl, imidazolyl, isoquinolinyl, morpholinyl, oxazolyl, 2-oxa-6-azaspiro[3.3]heptanyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazinyl, pyrazolyl, pyridinyl, pyrrolidinyl, pyrrolyl, quinolinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrazolyl, thiadiazolyl, thiazolyl, and triazolyl, each substituted wtih -L_2-R_a and zero to 4 R_b; and R_1, R_2, R_4, R_5, R_x, L_2, R_a m, n, and p are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which L_2 is a bond or

—CR_xR_x—; and R_a is (a) H, —CN, —OH, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, —$(CH_2)_{1-2}O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-3}NHC(O)O(C_{1-4}$ alkyl), —$(CR_xR_x)_{1-3}NH_2$, —$(CR_xR_x)_{1-3}NR_x(C_{1-4}$ alkyl), —$O(C_{1-2}$ fluoroalkyl), —$S(O)_2NR_xR_x$, —$NHS(O)_2(C_{1-3}$ alkyl), —NR_xR_x, —$NR_x(C_{1-4}$ alkyl), —$(CR_xR_x)_{1-2}C(O)OH$, —C(O)OH, —C(O)(C_{1-3} alkyl), —$C(O)O(C_{1-3}$ alkyl), —$C(O)NR_x(C_{1-2}$ alkyl), —$C(O)N(C_{1-3}$ alkyl)$_2$, —$C(O)NR_xCH_2C(O)NR_xR_x$, or —$C(O)NR_xCH_2CH_2NHC(O)(C_{1-3}$ alkyl); (b) C_{3-6} cycloalkyl or —$C(O)NH(C_{3-6}$ cycloalkyl), wherein each cycloalkyl is substituted with zero to 2 substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, and —$C(O)O(C_{1-3}$ alkyl); or (c) A_1, —CH_2A_1, —$C(O)A_1$, or —$C(O)NHA_1$, wherein A_1 is furanyl, imidazolyl, indolyl, isoxazolyl, octahydropyrrolo[3,4-c]pyrrolyl, oxazolyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolidinyl, pyrrolyl, tetrahydrofuranyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophenyl, or triazolyl, each substituted with zero to three substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, —$C(O)(C_{1-2}$ alkyl), —$C(O)O(C_{1-3}$ alkyl), —NR_xR_x, phenyl, trifluoromethyl-phenyl, —CH_2(bromophenyl), and —CH_2CH_2(pyrrolidinyl). Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is H, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} cyanoalkyl, C_{1-6} hydroxyalkyl, C_{1-3} hydroxy-fluoroalkyl, —$CR_xR_xCR_x(OH)CR_x{=}CR_xR_x$, —$C{=}N(NR_xR_x)$, —$(CR_xR_x)_{1-4}O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-4}O(CR_xR_x)_{1-3}O(C_{1-3}$ alkyl), —$CH_2CH(OH)CH_2O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-3}S(C_{1-3}$ alkyl), —$(CH_2)_{1-3}C(O)OC(CH_3)_3$, —$(CR_xR_x)_{0-3}NR_xR_y$, —$(CR_xR_x)_{0-3}NR_x(C_{1-4}$ hydroxyalkyl), —$CH_2CH(OH)CH_2NR_xR_y$, —C(O)H, —$C(O)(C_{1-6}$ alkyl), —$C(O)(C_{1-4}$ hydroxyalkyl), —$C(O)(C_{1-3}$ fluoroalkyl), —$C(O)(C_{1-3}$ chloroalkyl), —$C(O)(C_{1-3}$ cyanoalkyl), —$(CR_xR_x)_{0-3}C(O)OH$, —$C(O)(CH_2)_{0-2}O(C_{1-4}$ alkyl), —$C(O)(CR_xR_x)_{0-2}O(CR_xR_x)_{1-2}O(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-2}O(CR_xR_x)_{1-2}NR_yR_y$, —$C(O)CR_xR_xS(O)_2(C_{1-3}$ alkyl), —$C(O)CR_xR_xNR_xS(O)_2(C_{1-3}$ alkyl), —$C(O)CR_xR_xOC(O)(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-3}NR_yR_y$, —$C(O)(CR_xR_x)_{0-1}NR_x(C_{1-3}$ cyanoalkyl), —$C(O)(CR_xR_x)_{0-2}NR_y(C_{1-6}$ hydroxyalkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(C_{1-3}$ fluoroalkyl), —$C(O)(CR_xR_x)_{0-1}NR_x(C_{1-5}$ hydroxy-fluoroalkyl), —$C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}O(C_{1-3}$ hydroxyalkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-2}$ alkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{1-2}O(C_{1-2}$ alkyl)), —$C(O)(CR_xR_x)_{0-2}N((CR_xR_x)_{1-2}O(C_{1-2}$ alkyl))$_2$, —$C(O)(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{1-3}NR_xR_x$, —$C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xR_x$, —$C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xC(O)NR_xR_x$, —$C(O)(CR_xR_x)_{0-3}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-3}N((CH_2)_{0-1}C(O)(C_{1-3}$ alkyl))$_2$, —$C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ cyanoalkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(CH_2)_{1-2}C(O)NR_yR_y$, —$C(O)(CR_xR_x)_{1-3}C(O)NR_yR_y$, —$C(O)(CR_xR_x)_{1-3}S(O)_2NR_yR_y$, —$C(O)(CR_xR_x)_{0-2}NR_x(CHR_y(CH_2OH))$, —$(CR_xR_x)_{1-2}C(O)NR_yR_y$, —$CH(CN)C(O)NR_yR_y$, —$(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ fluoroalkyl), —$(CR_xR_x)_{1-2}C(O)NR_y(C_{1-4}$ hydroxyalkyl), —$(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ cyanoalkyl), —$(CR_xR_x)_{1-2}C(O)NR_x(CH_2)_{1-2}O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-2}C(O)NR_xCH(C_{1-4}$ alkyl)(C_{1-3} hydroxyalkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}C(O)NR_xR_x$, —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(C_{1-3}$ alkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(O)_2OH$, —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-3}$ alkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-3}NR_xR_x$, —$(CH_2)_{1-2}C(O)N(CH_2CH_3)(CH_2)_{1-3}NR_xR_x$, —$(CR_xR_x)_{0-3}S(O)_2(C_{1-4}$ alkyl), —$(CH_2)_{0-2}S(O)_2(C_{1-3}$ fluoroalkyl), —$(CR_xR_x)_{0-2}S(O)_2NR_yR_y$, —$(CR_xR_x)_{0-2}NR_xS(O)_2(C_{1-3}$ alkyl), —C(O)C(O)OH, —$C(O)C(O)NR_yR_y$, or —$C(O)C(O)NR_y(CR_xR_x)_{1-2}NR_yR_y$; and R_1, R_2, R_4, R_5, R_x, R_y, m, n, and p are defined in the first aspect or the second aspect. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is H, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} cyanoalkyl, C_{1-5} hydroxyalkyl, —$C{=}N(NR_xR_x)$, —$(CR_xR_x)_{1-2}O(C_{1-2}$ alkyl), —$(CR_xR_x)_{1-4}O(CR_xR_x)_{1-3}O(C_{1-3}$ alkyl), —$CH_2CH(OH)CH_2O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-3}S(C_{1-3}$ alkyl), —$(CH_2)_{1-3}C(O)OC(CH_3)_3$, —$(CR_xR_x)_{0-3}NR_xR_y$, —$(CR_xR_x)_{0-3}NR_x(C_{1-4}$ hydroxyalkyl), —$CH_2CH(OH)CH_2NR_xR_y$, —$C(O)(C_{1-6}$ alkyl), —$C(O)(C_{1-4}$ hydroxyalkyl), —$C(O)(C_{1-3}$ fluoroalkyl), —$C(O)(C_{1-3}$ chloroalkyl), —$C(O)(C_{1-3}$ cyanoalkyl), —$(CR_xR_x)_{0-3}C(O)OH$, —$C(O)(CH_2)_{0-2}O(C_{1-4}$ alkyl), —$C(O)(CR_xR_x)_{0-2}O(CR_xR_x)_{1-2}O(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-2}O(CH_2)_{1-2}HR_yR_y$, —$C(O)CR_xR_xS(O)_2(C_{1-2}$ alkyl), —$C(O)CR_xR_xNR_xS(O)_2(C_{1-2}$ alkyl), —$C(O)CR_xR_xOC(O)(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-2}NR_yR_y$, —$C(O)(CR_xR_x)_{0-2}NR_x(C_{1-2}$ cyanoalkyl), —$C(O)(CR_xR_x)_{0-2}NR_y(C_{1-6}$ hydroxyalkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(C_{1-3}$ fluoroalkyl), —$C(O)(CR_xR_x)_{0-1}NR_x(C_{1-5}$ hydroxy-fluoroalkyl), —$C(O)(CR_xR_x)_{0-1}NR_x((CR_xR_x)_{1-2}O(C_{1-2}$ alkyl)), —$C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}O(C_{1-3}$ hydroxyalkyl), —$C(O)(CR_xR_x)_{0-1}NR_xCH_2)_{1-2}NR_xC(O)(C_{1-2}$ alkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{1-2}O(C_{1-2}$ alkyl)), —$C(O)(CR_xR_x)_{0-1}NR_x(CR_xR_x)_{1-3}NR_xR_x$, —$C(O)CR_xNH_2)(CR_xR_x)_{1-4}NR_xR_x$, —$C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xC(O)NR_xR_x$, —$C(O)(CR_xR_x)_{0-3}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ cyanoalkyl), —$C(O)(CR_xR_x)_{0-2}NR_xCH_2)_{1-2}C(O)NR_yR_y$, —$C(O)(CR_xR_x)_{0-2}NR_x(CHR_y(CH_2OH))$, —$(CR_xR_x)_{1-2}C(O)NR_yR_y$, —$(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ fluoroalkyl), —$(CR_xR_x)_{1-2}C(O)NR_y(C_{1-4}$ hydroxyalkyl), —$(CR_xR_x)_{1-2}C(O)NR_x(C_{1-3}$ cyanoalkyl), —$CH(CN)C(O)NR_xR_y$, —$(CR_xR_x)_{1-2}C(O)NR_x(CH_2)_{1-2}O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-2}C(O)NR_xCH(C_{1-4}$ alkyl)(C_{1-3} hydroxyalkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}C(O)NR_xR_x$, —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(C_{1-3}$ alkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(O)_2OH$, —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-3}$ alkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-3}NR_xR_x$, —$(CH_2)_{1-2}C(O)N(CH_2CH_3)(CH_2)_{1-3}NR_xR_x$, —$(CR_xR_x)_{0-3}S(O)_2(C_{1-4}$ alkyl), —$(CH_2)_{0-2}S(O)_2(C_{1-3}$ fluoroalkyl), —$(CH_2)_{1-2}S(O)_2NR_yR_y$, —C(O)C(O)OH, —$C(O)C(O)NR_yR_y$, or —$C(O)C(O)NR_y(CR_xR_x)_{1-2}NR_yR_y$; and R_1, R_2, R_4, R_5, m, n, and p are defined in the first aspect or the second aspect. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is —$C(O)CH_2$(2-oxa-6-azaspiro[3.3]heptanyl), —$C(O)CH_2$(piperazinonyl), —$C(O)CH_2$(piperazinyl), —$C(O)CH_2$(piperidinyl), —$C(O)CH_2$(pyrimidinyl), —$C(O)CH_2$(pyrrolidinyl), —$C(O)CH_2$(tetrahydropyranyl), —$C(O)CH_2$(tetrazolyl), —$C(O)CH_2$(thiazolyl), —$C(O)CH_2CH_2$(azepanyl), —$C(O)CH_2CH_2$(azetidinyl), —$C(O)CH_2CH_2$(dioxothiomorpholinyl), —$C(O)CH_2CH_2$(morpholinyl), —$C(O)CH_2CH_2$(piperidinonyl), —$C(O)CH_2CH_2$(piperidinyl), —$C(O)CH_2CH_2$(pyrrolidinonyl), —$C(O)CH_2CH_2$(pyrrolidinyl), —$C(O)CH_2CH(CH_3)$(oxetanyl), —C(O)NH(piperidinyl), —C(O)NH(pyrrolidinyl, —$C(O)CH_2NH$(cyclopropyl), —$C(O)CH_2NH$(cyclobutyl), —$C(O)CH_2NH$(cyclohexyl), —$C(O)CH_2NH$(oxetanyl), —$C(O)CH_2N(CH_3)$(cyclopropyl), —$C(O)CH_2N(CH_3)$(cyclohexyl), —$C(O)CH_2CH_2NH$(cyclopentyl), —$C(O)CH_2CH_2NH$(cyclohexyl), —$C(O)CH_2CH_2N(CH_3)$(cyclohexyl), —$C(O)CH_2N(CH_2CH_2OH)$(cyclopropyl), —$C(O)CH_2CH_2N(CH_2CH_2OH)$(cyclopropyl), —$C(O)CH_2CH_2NH(CH_2$(cyclopropyl)), —$C(O)CH_2CH_2NH(CH_2$(tetrahydrofuranyl)), —$C(O)CH_2NH(CH_2$(cyclopropyl)), —$C(O)CH_2NH(CH_2$(cyclo-

hexyl)), —C(O)CH_2NH(CH_2(tetrahydrofuranyl)), —C(O)NH(CH_2(piperidinyl)), —C(O)NH(CH_2(pyrrolidinyl)), —C(O)NH(CH_2CH_2(morpholinyl)), —C(O)NH(CH_2CH_2(piperazinyl)), —C(O)NH(CH_2CH_2(piperidinyl)), —C(O)NH(CH_2CH_2(pyrrolidinyl)), —C(O)O(azetidinyl), —C(O)O(piperidinyl), —C(O)O(pyrrolidinyl), —C(O)OCH_2(azetidinyl), —C(O)OCH_2(piperidinyl), —C(O)OCH_2(pyrrolidinyl), —C(O)OCH_2CH_2(dioxothiomoropholinyl), —C(O)OCH_2CH_2(imidazolyl), —C(O)OCH_2CH_2(morpholinyl), —C(O)OCH_2CH_2(piperazinyl), —C(O)OCH_2CH_2(piperidinyl), —C(O)OCH_2CH_2(pyrrolidinyl), CH_2(cyclopropyl), CH_2(dioxotetrahydrothiopyranyl), —CH_2(imidazolyl), —CH_2(isoxazolyl), —CH_2(morpholinyl), —CH_2(oxadiazolyl), —CH_2(oxazolyl), —CH_2(oxetanyl), —CH_2(phenyl), —CH_2(pyrazinyl), —CH_2(pyrazolyl), —CH_2(pyridazinyl), —CH_2(pyrimidinyl), —CH_2(tetrazolyl), —CH_2(thiadiazolyl), —CH_2(thiazolyl), —CH_2(triazolonyl), —CH_2(triazolyl), —$CH(CH_3)$(pyrazolyl), —$CH(CH_3)$(pyridazinyl), —$CH(CH_3)$(pyrimidinyl), —CH_2CH_2(dioxoisothiazolidinyl), —CH(CN)(oxetanyl), —$CH(CH_3)CH_2S(O)_2$(morpholinyl), —$CH(CH_3)CH_2S(O)_2$(piperidinyl), —$CH_2C(O)$(morpholinyl), —$CH_2C(O)$(2-oxa-6-azaspiro[3.3]heptanyl), —$CH_2C(O)$(azetidinyl), —$CH_2C(O)$(dioxidothiadiazinanyl), —$CH_2C(O)$(dioxidothiazolidinyl), —$CH_2C(O)$(dioxidothiomorpholinyl), —$CH_2C(O)$(dioxothiomorpholinyl), —$CH_2C(O)$(2-oxa-6-azaspiro[3.3]heptanyl), —$CH_2C(O)$(piperazinonyl), —$CH_2C(O)$(piperazinyl), —$CH_2C(O)$(piperidinyl), —$CH_2C(O)$(pyrrolidinyl), —$CH_2C(O)NHCH(CH_2CH_2OH)$(cyclopropyl), —$CH_2C(O)N(CH_2CH_2OH)$(cyclopropyl), —$CH_2C(O)N(CH_3)$(cyclopropyl), —$CH_2C(O)N(CH_3)$(tetrahydrofuranyl), —$CH_2C(O)N(CH_3)$(tetrahydropyranyl), —$CH_2C(O)N(CH_3)CH_2CH_2$(cyclopentyl), —$CH_2C(O)N(CH_3)CH_2CH_2$(pyrazolyl), —$CH_2C(O)NH$(azetidinyl), —$CH_2C(O)NH($$CH_2$(oxetanyl)), —$CH_2C(O)NH$(cyclobutyl), —$CH_2C(O)NH$(cyclopropyl), —$CH_2C(O)NH$(oxetanyl), —$CH_2C(O)NH$(tetrahydropyranyl), —$CH_2CH_2S(O)_2$(morpholinyl), or —$CH_2CH_2S(O)_2$(phenyl); and R_1, R_2, R_4, R_5, m, n, and p are defined in the first aspect or the second aspect. Also included are compounds in which m is zero and n is zero.

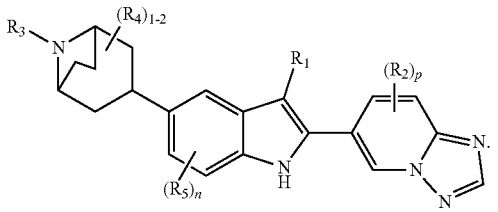
One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is H, C_{1-5} alkyl, C_{2-3} fluoroalkyl, C_{1-3} cyanoalkyl, C_{2-5} hydroxyalkyl, —$CH_2CH_2OCH_3$, —$CH_2N(CH_3)_2$, —$CH_2CH_2NH(CH_3)$, —C═N(NH_2), —C(O)CH_3, —C(O)$CH(CH_2CH_3)_2$, —C(O)CH_2CF_3, —C(O)CH_2CH_2OH, —C(O)$CH(CH_3)OH$, —C(O)$CH_2CH(CH_3)OH$, —C(O)$CH_2C(CH_3)_2OH$, —C(O)CH_2CN, —C(O)CH_2CH_2CN, —C(O)O$C(CH_3)_3$, —C(O)CH_2OCH_3, —C(O)$CH_2CH_2OCH_3$, —C(O)O$CH_2CH_2NH_2$, —C(O)O$CH_2CH_2N(CH_3)_2$, —C(O)O$CH_2CH_2N(CH_2CH_3)_2$, —C(O)$CH_2S(O)_2CH_3$, —C(O)$CH_2CH_2S(O)_2CH_3$, —C(O)$CH_2NHS(O)_2CH_3$, —C(O)NH($CH_2C(CH_3)_3$), —C(O)$CH_2NH(CH_3)$, —C(O)$CH_2NH(CH_2CH_3)$, —C(O)$CH_2NH(CH_2CH_2CH_3)$, —C(O)$CH_2NH(CH(CH_3)_2)$, —C(O)$CH_2NH(CH_2CH(CH_3)_2)$, —C(O)$CH_2NH(C(CH_3)_3)$, —C(O)$CH_2N(CH_3)_2$, —C(O)$CH_2N(CH_3)(CH_2CH_3)$, —C(O)$CH_2N(CH_3)(CH_2CH_2CH_3)$, —C(O)$CH_2N(CH_3)(CH(CH_3)_2)$, —C(O)$CH_2N(CH_3)(CH_2CH(CH_3)_2)$, —C(O)$CH_2N(CH_2CH_3)_2$, —C(O)$CH_2CH_2NH(CH_3)$, —C(O)$CH_2CH_2NH(CH_2CH_3)$, —C(O)$CH_2CH_2NH(CH_2CH_2CH_3)$, —C(O)$CH_2CH_2NH(CH(CH_3)_2)$, —C(O)$CH_2CH_2NH(CH_2C(CH_3)_3)$, —C(O)$CH_2CH_2N(CH_3)_2$, —C(O)$CH_2CH_2N(CH_3)(CH_2CH_3)$, —C(O)$CH_2CH_2N(CH_3)(CH_2CH_2CH_3)$, —C(O)$CH_2CH_2N(CH_3)(CH(CH_3)_2)$, —C(O)$CH(CH_3)NH(CH_3)$, —C(O)$CH_2NH(CH_2CN)$, —C(O)$CH_2N(CH_3)(CH_2CH_2CN)$, —C(O)$CH_2NH(CH_2C(O)NH_2)$, —C(O)$CH_2N(CH_3)(CH_2C(O)N(CH_3)_2)$, —C(O)$CH_2CH_2NH(CH_2C(O)NH_2)$, —C(O)$CH_2CH_2N(CH_3)CH_2C(O)N(CH_3)_2$, —C(O)$CH_2NH(CH_2CH_2OH)$, —C(O)$CH_2N(CH_3)(CH_2CH_2OH)$, —C(O)$CH_2CH_2NH(CH_2CH_2OH)$, —C(O)$CH_2CH_2N(CH_3)(CH_2CH_2OH)$, —C(O)$CH_2NH(CH_2CH_2F)$, —C(O)$CH_2NH(CH_2CF_3)$, —C(O)$CH_2CH_2NH(CH_2CH_2F)$, —C(O)$CH_2NH(CH_2CH_2OCH_3)$, —C(O)$CH_2N(CH_3)(CH_2CH_2OCH_3)$, —C(O)$CH_2CH_2NH(CH_2CH_2OCH_3)$, —C(O)$CH_2CH_2N(CH_3)(CH_2CH_2OCH_3)$, —C(O)$CH_2N(CH_2CH_2OCH_3)_2$, —C(O)$CH_2CH_2CH_2S(O)_2NH_2$, —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)N(CH_3)_2$, —$CH_2C(O)NH(CH_2CH_3)$, —$CH_2C(O)N(CH_3)(CH_2CH_3)$, —$CH_2C(O)N(CH_2CH_3)_2$, —$CH_2C(O)NH(CH_2CH_2CH_3)$, —$CH_2C(O)NH(CH(CH_3)_2)$, —CH(CN)C(O)$N(CH_3)_2$, —$CH_2C(O)NH(CH_2CH_2CF_3)$, —$CH_2C(O)N(CH_3)(CH_2CH_2OH)$, —$CH_2C(O)N(CH_3)(CH_2CH_2OH)$, —$CH_2C(O)N(CH_2CH_3)(CH_2CH_2OH)$, —$CH_2C(O)N(CH_2CH_2CH_3)(CH_2CH_2OH)$, —$CH_2C(O)N(CH_3)(CH_2CH_2CH_2OH)$, —$CH_2C(O)NH(CH_2C(CH_3)_2OH)$, —$CH_2C(O)N(CH_2CH(CH_3)CH_2CH_3)(CH_2CH_2OH)$, —$CH_2C(O)NH(CH_2CH_2CN)$, —$CH_2C(O)N(CH_3)(CH_2CH_2CN)$, $CH_2C(O)N(CH_3)(CH_2CH_2OCH_3)$, —CH$(CH_3)CH_2S(O)_2(CH_2CH_2CH_2CH_3)$, —$CH_2CH_2S(O)_2NH_2$, —$CH_2CH_2S(O)_2NH(CH_3)$, —$CH_2CH_2S(O)_2N(CH_3)_2$, —$CH(CH_3)CH_2S(O)_2N(CH_2CH_3)_2$, —$CH_2CH_2NHS(O)_2CH_3$, —$CH_2CH_2N(CH_3)S(O)_2CH_3$, —$CH_2C(O)NH(CH_2CH_2SCH_3)$, —C(O)NH($CH_2CH_2NH_2$), —C(O)N$(CH_3)CH_2CH_2NH_2$, —C(O)NH($CH_2CH_2N(CH_3)_2$), —C(O)NH($CH_2CH_2CH_2NH_2$), —$CH_2CH_2S(O)_2CH_3$, —$CH_2CH_2CH_2S(O)_2CH_3$, or —$CH(CH_3)CH_2S(O)_2CH_3$; and R_1, R_2, R_4, R_5, m, n, and p are defined in the first aspect or the second aspect. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein each R_4 is independently F, —OH, C_{1-2} alkyl, or —OCH_3; or two R_4 attached to the same carbon atom form ═O; and R_1, R_2, R_3, R_5, m, n and p are defined in the first aspect. Included in this embodiment are compounds in which each R_4 is independently F, —CH_3, or —OCH_3. Also included are compounds in which n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein each R_5 is independently F, Cl, —CN, —CH_3, —CF_3, or —OCH_3; and R_1, R_2, R_3, R_4, m, n and p are defined in the first aspect. Included in this embodiment are compounds in which each R_5 is independently F, —CN, —CH_3, or —CF_3. Also included are compounds in which m is zero. Further, included are compounds in which m is zero and n is 1.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein m is 2, 3, or 4; two R_4, each attached to a different carbon atom adjacent to the nitrogen atom in the piperidinyl ring, can form a —CH_2CH_2— bridge; and R_1, R_2, R_3, R_5, m, n, and p are defined in the first aspect. The compounds of this embodiment have the structure of Formula (Ia):

(Ia)



Included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; each R_2 is —CH_3; R_3 is —CH_2CN, —$CH_2C(O)N(CH_3)_2$, or —$CH_2CH_2S(O)_2CH_3$; m is 2; n is zero, and p is zero, 1, or 2. Also included in this embodiment are compounds selected from 2-(3-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-8-azabicyclo[3.2.1]octan-8-yl)acetonitrile (981);

2-(3-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-8-azabicyclo[3.2.1]octan-8-yl)-N,N-dimethylacetamide (982-983); and

6-(3-isopropyl-5-(8-(2-(methylsulfonyl)ethyl)-8-azabicyclo[3.2.1]octan-3-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (984-985).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein: R_1 is H, Cl, —CN, C_{1-4} alkyl, or C_{1-2} fluoroalkyl; each R_2 is independently F, Cl, —CN, —OH, C_{1-3} alkyl, —CD_3, C_{1-2} fluoroalkyl, C_{1-2} cyanoalkyl, C_{1-3} hydroxyalkyl, C_{1-3} aminoalkyl, —$O(CH_2)_{1-2}OH$, —$O(C_{1-4}$ alkyl), C_{1-2} fluoroalkoxy, —$(CH_2)_{1-4}O(C_{1-3}$ alkyl), —$O(CH_2)_{1-2}OC(O)(C_{1-3}$ alkyl), —$O(CH_2)_{1-2}NR_xR_x$, —$C(O)O(C_{1-3}$ alkyl), —$C(O)NR_yR_y$, —NR_yR_y, —$NR_y(C_{1-3}$ fluoroalkyl), —$NR_y(C_{1-4}$ hydroxyalkyl), —NR_xCH_2(phenyl), —$NR_xS(O)_2(C_{3-6}$ cycloalkyl), —$NR_xC(O)(C_{1-3}$ alkyl), —$NR_x(CH_2$-cyclopropyl), C_{3-6} cycloalkyl, morpholinyl, dioxothiomorpholinyl, methylpiperidinyl, methylpiperazinyl, amino-oxadiazolyl, imidazolyl, triazolyl, or —C(O)(thiazolyl); R_3 is: (a) -L_1-A; or (b) H, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-3} cyanoalkyl, C_{1-5} hydroxyalkyl, —C═N(NR_xR_x), —$(CR_xR_x)_{1-2}O(C_{1-2}$ alkyl), —$(CR_xR_x)_{1-4}O(CR_xR_x)_{1-3}O(C_{1-3}$ alkyl), —$CH_2CH(OH)CH_2O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-3}S(C_{1-3}$ alkyl), —$(CH_2)_{1-3}C(O)OC(CH_3)_3$, —$(CR_xR_x)_{0-3}NR_xR_y$, —$(CR_xR_x)_{0-3}NR_xC_{1-4}$ hydroxyalkyl), —$CH_2CH(OH)CH_2NR_xR_y$, —C(O)(C_{1-6} alkyl), —C(O)(C_{1-4} hydroxyalkyl), —C(O)(C_{1-3} fluoroalkyl), —C(O)(C_{1-3} chloroalkyl), —C(O)(C_{1-3} cyanoalkyl), —$(CR_xR_x)_{0-3}C(O)OH$, —$C(O)(CH_2)_{0-2}O(C_{1-4}$ alkyl), —$C(O)(CR_xR_x)_{0-2}O(CR_xR_x)_{1-2}O(C_{1-3}$ alkyl), —$C(O)(CH_2)_{0-2}O(CH_2)_{1-2}HR_yR_y$, —$C(O)CR_xR_xS(O)_2(C_{1-2}$ alkyl), —$C(O)CR_xR_xNR_xS(O)_2(C_2$ alkyl), —$C(O)CR_xR_xOC(O)(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-2}NR_yR_y$, —$C(O)(CR_xR_x)_{0-2}NR_x(C_{1-2}$ cyanoalkyl), —$C(O)(CR_xR_x)_{0-2}NR_y(C_{1-6}$ hydroxyalkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(C_{1-3}$ fluoroalkyl), —$C(O)(CR_xR_x)_{0-1}NR_x(C_{1-5}$ hydroxy-fluoroalkyl), —$C(O)(CR_xR_x)_{0-1}NR_x((CR_xR_x)_{1-2}O(C_{1-2}$ alkyl)), —$C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}O(C_{1-3}$ hydroxyalkyl), —$C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-2}$ alkyl), —$C(O)(CR_xR_x)_{0-2}NR_x(CR_xR_x)_{1-2}O(C_{1-2}$ alkyl)), —$C(O)(CR_xR_x)_{0-1}NR_x(CR_xR_x)_{1-3}NR_xR_x$, —C(O)$CR_x(NH_2)(CR_xR_x)_{1-4}NR_xR_x$, —$C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xC(O)NR_xR_x$, —$C(O)(CR_xR_x)_{0-3}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ alkyl), —$C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ cyanoalkyl), —$C(O)(CR_xR_x)_{0-2}NR_xCH_2)_{1-2}C(O)NR_yR_y$, —$C(O)(CR_xR_x)_{0-2}NR_x(CHR_y(CH_2OH))$, —$(CR_xR_x)_{1-2}C(O)NR_yR_y$, —$(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ fluoroalkyl), —$(CR_xR_x)_{1-2}C(O)NR_y(C_{1-4}$ hydroxyalkyl), —$(CR_xR_x)_{1-2}C(O)NR_x(C_{1-3}$ cyanoalkyl), —$CH(CN)C(O)NR_xR_y$, —$(CR_xR_x)_{1-2}C(O)NR_x(CH_2)_{1-2}O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-2}C(O)NR_xCH(C_{1-4}$ alkyl)(C_{1-3} hydroxyalkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}C(O)NR_xR_x$, —$(CH_2)_{1-2}S(O)_2NR_x(CH_2)_{1-2}S(C_{1-2}$ alkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(O)_2OH$, —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-3}$ alkyl), —$(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-3}NR_xR_x$, —$(CH_2)_{1-2}C(O)N(CH_2CH_3)(CH_2)_{1-3}NR_xR_x$, —$(CR_xR_x)_{1-3}S(O)_2(C_{1-4}$ alkyl), —$(CH_2)_{0-2}S(O)_2(C_{1-3}$ fluoroalkyl), —$(CH_2)_{1-2}S(O)_2NR_yR_y$, —C(O)C(O)OH, —C(O)C(O)$NR_yR_y$, or —C(O)C(O)$NR_y(CR_xR_x)_{1-2}NR_yR_y$; L_1 is a bond, —CR_xR_x—, —$CR_xR_xC(O)$—, —$CR_xR_xC(O)NR_x$—, or —$C(O)(CR_xR_x)_{0-2}$—; A is a ring selected from azetidinyl, C_{3-6} cycloalkyl, dioxotetrahydrothiopyranyl, dioxidothiadiazinanyl, dioxidothiomorpholinyl, furanyl, imidazolyl, isoquinolinyl, morpholinyl, oxazolyl, 2-oxa-6-azaspiro[3.3]heptanyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazinyl, pyrazolyl, pyridinyl, pyrrolidinyl, pyrrolyl, quinolinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrazolyl, thiadiazolyl, thiazolyl, and triazolyl, each substituted with -L_2-R_a and zero to 4 R_b; L_2 is a bond or —CR_xR_x—; R_a is: (a) H, —CN, —OH, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, —$(CH_2)_{1-2}O(C_{1-3}$ alkyl), —$(CR_xR_x)_{1-3}NHC(O)O(C_{1-4}$ alkyl), —$(CR_xR_x)_{1-3}NH_2$, —$(CR_xR_x)_{1-3}NR_x(C_{1-4}$ alkyl), —$O(C_{1-2}$ fluoroalkyl), —$S(O)_2NR_xR_x$, —$NHS(O)_2(C_{1-3}$ alkyl), —NR_xR_x, —$NR_x(C_{1-4}$ alkyl), —$(CR_xR_x)_{1-2}C(O)OH$, —C(O)OH, —C(O)(C_{1-3} alkyl), —C(O)O(C_{1-3} alkyl), —$C(O)NR_x(C_{1-2}$ alkyl), —$C(O)N(C_{1-3}$ alkyl)$_2$, —$C(O)NR_xCH_2C(O)NR_xR_x$, or —$C(O)NR_xCH_2CH_2NHC(O)(C_{1-3}$ alkyl); (b) C_{3-6} cycloalkyl or —C(O)NH(C_{3-6} cycloalkyl), wherein each cycloalkyl is substituted with zero to 2 substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, and —C(O)O(C_{1-3} alkyl); or (c) A_1, —CH_2A_1, —C(O)A_1, or —C(O)NHA_1, wherein A_1 is furanyl, imidazolyl, indolyl, isoxazolyl, octahydropyrrolo[3,4-c]pyrrolyl, oxazolyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolidinyl, pyrrolyl, tetrahydrofuranyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophenyl, or triazolyl, each substituted with zero to three substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, —C(O)(C_{1-2} alkyl), —C(O)O(C_{1-3} alkyl), —NR_xR_x, phenyl, trifluoromethyl-phenyl, —CH_2(bromophenyl), and —CH_2CH_2(pyrrolidinyl); each R_4 is independently F, —OH, C_{1-2} alkyl, or —OCH_3; or two R_4 attached to the same carbon atom form ═O; R_5 is F, Cl, —CN, C_{1-2} alkyl, or —OCH_3; each R_b is independently —CH_3 or —CF_3; each R_x is independently H or —CH_3; each R_y is independently H or C_{1-5} alkyl; m is zero, 1, or 2; n is zero or 1; and p is zero, 1, or 2.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein: R_1 is —$CH(CH_3)_2$; each R_2 is independently —CH_3, —OCH_3, or —CH_2OCH_3; R_3 is H, —$CH(CH_3)_2$, —$CH(CH_3)_2$, —$CH_2CH(CH_3)_2$, —CH_2CN, —CH_2CH_2CN, —$CH_2CH_2CH_2CN$, —$CH_2C(CH_3)_2OH$, —$C(O)CH_3$, —$C(O)CH(CH_2CH_3)_2$, —$C(O)CH_2OCH_3$, —$C(O)CH_2CH_2OCH_3$, —$C(O)CH_2CH(CH_3)OH$, —$C(O)CH_2CN$, —$C(O)CH_2CH_2CN$, —$C(O)CH(CH_3)NH(CH_3)$, —$C(O)CH_2NH(CH_3)$, —$C(O)CH_2N(CH_3)_2$, —$C(O)CH_2NHCH_2CH_2CH_3$, —$C(O)CH_2NHCH(CH_3)_2$, —$C(O)CH_2NHC(CH_3)_3$, —$C(O)CH_2N(CH_3)CH(CH_3)_2$, —$C(O)CH_2NHCH_2CH_2OCH_3$, —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)N(CH_3)CH_2CH_3$, —$CH_2C(O)NHCH_2CH_2CH_3$, —$CH_2C(O)NH(CH(CH_3)_2)$, —$CH_2C(O)N(CH_3)_2$, —$CH_2C(O)N(CH_2CH_3)_2$, —$CH_2CH_2S(O)_2CH_3$, —$CH_2CH_2S(O)_2NH_2$, —$CH_2C(O)NH$(cyclobutyl), —$CH_2C(O)NH$(cyclopropyl), —$CH_2C(O)NH$(methyloxetanyl), —$CH_2C(O)N(CH_3)$(cyclopropyl), oxetanyl, tetrahydropyranyl, dioxotetrahydrothiopyranyl, —CH_2(oxazolyl), —CH_2(pyrazolyl), —CH_2(tetrazolyl), —CH_2(triazolyl), —CH_2(methyltriazolyl), —$CH_2C(O)$(2-oxa-6-azaspiro[3.3]heptanyl), —$CH_2C(O)$(azetidinyl), —$CH_2C(O)$(dioxidothiadiazinanyl), —$CH_2C(O)$(dioxidothiomorpholinyl), —$CH_2C(O)$(morpholinyl), —$CH_2C(O)$(methoxyethylpiperazinyl), —$CH_2C(O)$(piperidinyl), —$CH_2C(O)$(hydroxypiperidinyl), —$CH_2C(O)$(pyrrolidinyl), —$CH_2C(O)$(hydroxypyrrolidinyl), —C(O)(azetidinyl), —C(O)(methylcyclopropyl), —C(O)(methyloxetanyl), or —$C(O)CH_2$(morpholinyl); m is zero; n is zero; and p is zero, 1 or 2.

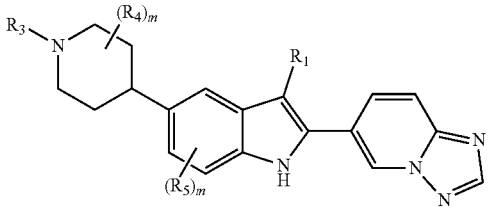
One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_1 is H, Cl, —CN, C_{1-4} alkyl, C_{1-2} fluoroalkyl, C_{1-2} hydroxy-fluoroalkyl, C_{3-6} cycloalkyl, —CH_2(C_{3-6} cycloalkyl), —C(O)O(C_{1-2} alkyl), or tetrahydropyranyl; and R_2, R_3, R_4, R_5, m, n, and p are defined in the first aspect. Included in this embodiment are compounds in which R_1 is H, Cl, —CN, C_{1-4} alkyl, or C_{1-2} fluoroalkyl. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein each R_2 is independently F, Cl, —CN, —OH, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, C_{1-3} aminoalkyl, —$(CH_2)_{0-2}$O(C_{1-2} alkyl), C_{1-3} fluoroalkoxy, or C_{3-6} cycloalkyl; and R_1, R_3, R_4, R_5, m, n, and p are defined in the first aspect. Included in this embodiment are compounds in which each R_2 is independently F, —CN, —OH, C_{1-2} alkyl, or —$(CH_2)_{0-1}$O(C_{1-2} alkyl). Also included in this embodiment are compounds in which each R_2 is independently —CH_3, —OCH_3, or —CH_2OCH_3. Also included are compounds in which m is zero and n is zero.

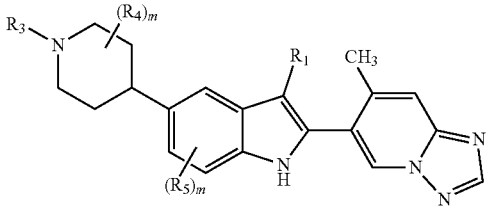
One embodiment provides a compound of Formula (I) or a salt thereof, wherein each R_2 is independently F, —CN, —OH, C_{1-2} alkyl, or $(CH_2)_{0-1}O(C_{1-2}$ alkyl); p is zero, 1 or 2; and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect. Included in this embodiment are compounds in which each R_2 is independently —CH_3, —OCH_3, or —CH_2OCH_3. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein the compound has one of the following structures:

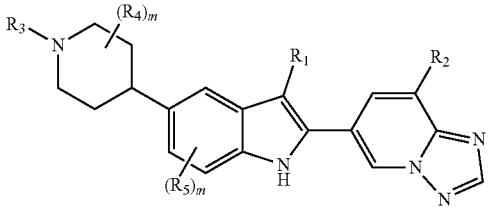
(I-1)



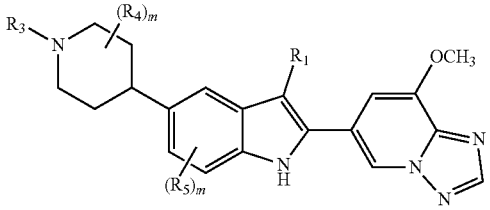
(I-2)



(I-3)

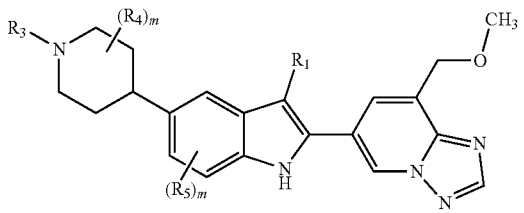


(I-4)

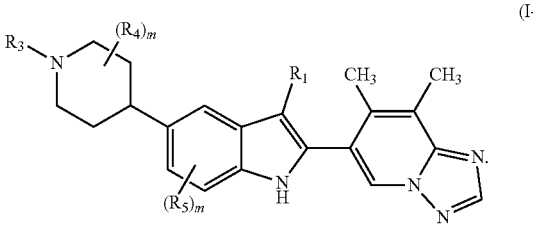


-continued

(I-5)



(I-6)



Included in this embodiment are compounds in which R_1 is H, Cl, —CN, C_{1-4} alkyl, or C_{1-2} fluoroalkyl. Also included in this embodiment are compounds in which R_1 is —CH$(CH_3)_2$. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is -L_1-A; and R_1, R_2, R_4, R_5, L_1, A, m, n, and p are defined in the first aspect. Included in this embodiment are compounds in which L_1 is a bond, —CR_xR_x—, —CR_xR_xC(O), —CR_xR_xC(O)NR_x—, or —C(O)($CR_xR_x)_{0-2}$—; A is a ring selected from azetidinyl, C_{3-6} cycloalkyl, dioxotetrahydrothiopyranyl, dioxidothiazinanyl, dioxidothiomorpholinyl, furanyl, imidazolyl, isoquinolinyl, morpholinyl, oxazolyl, 2-oxa-6-azaspiro[3.3]heptanyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazinyl, pyrazolyl, pyridinyl, pyrrolidinyl, pyrrolyl, quinolinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrazolyl, thiadiazolyl, thiazolyl, and triazolyl, each substituted with -L_2-R_a and zero to 4 R_b; L_2 is a bond or —CR_xR_x—; R_a is (a) H, —CN, —OH, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, —$(CH_2)_{1-2}$O(C_{1-3} alkyl), —$(CR_xR_x)_{1-3}$NHC(O)O(C_{1-4} alkyl), —$(CR_xR_x)_{1-3}NH_2$, —$(CR_xR_x)_{1-3}NR_x$(C_{1-4} alkyl), —O(C_{1-2} fluoroalkyl), —$S(O)_2NR_xR_x$, —$NHS(O)_2$(C_{1-3} alkyl), —NR_xR_x, —NR_x(C_{1-4} alkyl), —$(CR_xR_x)_{1-2}$C(O)OH, —C(O)OH, —C(O)(C_{1-3} alkyl), —C(O)O(C_{1-3} alkyl), —C(O)NR_x(C_{1-2} alkyl), —C(O)N(C_{1-3} alkyl)$_2$, —C(O)NR_xCH_2C(O)NR_xR_x, or —C(O)$NR_xCH_2CH_2NHC$(O)(C_{1-3} alkyl); (b) C_{3-6} cycloalkyl or —C(O)NH(C_{3-6} cycloalkyl), wherein each cycloalkyl is substituted with zero to 2 substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, and —C(O)O(C_{1-3} alkyl); or (c) A_1, —CH_2A_1, —C(O)A_1, or —C(O)NHA_1, wherein A_1 is furanyl, imidazolyl, indolyl, isoxazolyl, octahydropyrrolo[3,4-c]pyrrolyl, oxazolyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolidinyl, pyrrolyl, tetrahydrofuranyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophenyl, or triazolyl, each substituted with zero to three substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, —C(O)(C_{1-2} alkyl), —C(O)O(C_{1-3} alkyl), —NR_xR_x, phenyl, trifluoromethyl-phenyl, —CH_2(bromophenyl), and —CH_2CH_2(pyrrolidinyl); each R_b is independently —CH_3 or —CF_3; and each R_x is independently H or —CH_3. Included in this embodiment are compounds in which R_3 is —CH_2C(O)NH(cyclobutyl), —CH_2C(O)NH(cyclopropyl), —CH_2C(O)NH(methyloxetanyl), —CH_2C(O)N(CH_3)(cyclopropyl), oxetanyl, tet-

rahydropyranyl, dioxotetrahydrothiopyranyl, —CH_2(oxazolyl), —CH_2(pyrazolyl), —CH_2(tetrazolyl), —CH_2(triazolyl), —CH_2(methyltriazolyl), —$CH_2C(O)$(2-oxa-6-azaspiro[3.3]heptanyl), —$CH_2C(O)$(azetidinyl), —$CH_2C(O)$(dioxidothiadiazinanyl), —$CH_2C(O)$(dioxidothiomorpholinyl), —$CH_2C(O)$(morpholinyl), —$CH_2C(O)$(methoxyethylpiperazinyl), —$CH_2C(O)$(piperidinyl), —$CH_2C(O)$(hydroxypiperidinyl), —$CH_2C(O)$(pyrrolidinyl), —$CH_2C(O)$(hydroxypyrrolidinyl), —$C(O)$(azetidinyl), —$C(O)$(methylcyclopropyl), —$C(O)$(methyloxetanyl), or —$C(O)CH_2$(morpholinyl). Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is H, C_{1-6} alkyl, C_{1-3} cyanoalkyl, C_{1-4} hydroxyalkyl, $—(CR_xR_x)_{1-4}O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-4}O(CR_xR_x)_{1-30}(C_{1-3}$ alkyl), $—CH_2CH(OH)CH_2O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-3}S(C_{1-3}$ alkyl), $—(CH_2)_{1-3}C(O)OC(CH_3)_3$, $—(CR_xR_x)_{0-3}NR_xR_y$, $—(CR_xR_x)_{0-3}NR_x(C_{1-4}$ hydroxyalkyl), $—CH_2CH(OH)CH_2NR_xR_y$, $—C(O)(C_{1-6}$ alkyl), $—C(O)(C_{1-3}$ hydroxyalkyl), $—C(O)(C_{1-3}$ fluoroalkyl), $—C(O)(C_{1-3}$ chloroalkyl), $—C(O)(C_{1-3}$ cyanoalkyl), $—(CR_xR_x)_{0-3}C(O)OH$, $—C(O)(CH_2)_{1-2}O(C_{1-2}$ alkyl), $—C(O)(CR_xR_x)_{0-2}O(CR_xR_x)_{1-2}O(C_{1-3}$ alkyl), $—C(O)CR_xR_xS(O)_2(C_{1-3}$ alkyl), $—C(O)CR_xR_xNR_xS(O)_2(C_{1-3}$ alkyl), $—C(O)CR_xR_xOC(O)(C_{1-3}$ alkyl), $—C(O)(CR_xR_x)_{0-3}NR_yR_y$, $—C(O)(CR_xR_x)_{0-1}NR_x(C_3$ cyanoalkyl), $—C(O)(CR_xR_x)_{0-2}NR_y(C_{1-6}$ hydroxyalkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(C_{1-3}$ fluoroalkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(C_{1-5}$ hydroxy-fluoroalkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}O(C_{1-3}$ hydroxyalkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-2}$ alkyl), $—C(O)(CR_xR_x)_{0-1}NR_x((CR_xR_x)_{1-2}O(C_{1-2}$ alkyl)), $—C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xR_x$, $—C(O)CR_x(NH_2)(CR_xR_x)_{1-4}NR_xC(O)NR_xR_x$, $—C(O)(CR_xR_x)_{0-3}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ alkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{0-1}C(O)(C_{1-3}$ cyanoalkyl), $—C(O)(CR_xR_x)_{0-1}NR_x(CH_2)_{1-2}C(O)NR_yR_y$, $—C(O)(CR_xR_x)_{0-1}NR_x(CHR_y(CH_2OH))$, $—(CR_xR_x)_{1-2}C(O)NR_yR_y$, $—(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ fluoroalkyl), $—(CR_xR_x)_{1-2}C(O)NR_y(C_{1-4}$ hydroxyalkyl), $—(CR_xR_x)_{1-2}C(O)NR_y(C_{1-3}$ cyanoalkyl), $—(CR_xR_x)_{1-2}C(O)NR_x(CH_2)_{1-2}O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-2}C(O)NR_xCH(C_{1-4}$ alkyl)$(C_{1-3}$ hydroxyalkyl), $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}C(O)NR_xR_x$, $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}S(O)_2OH$, $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-2}NR_xC(O)(C_{1-3}$ alkyl), $—(CH_2)_{1-2}C(O)NR_x(CH_2)_{1-3}NR_xR_x$, $—(CH_2)_{1-2}C(O)N(CH_2CH_3)(CH_2)_{1-3}NR_xR_x$, $—(CH_2)_{1-2}S(O)_2(C_{1-4}$ alkyl), $—(CH_2)_{0-2}S(O)_2(C_{1-3}$ fluoroalkyl), $—(CH_2)_{1-2}S(O)_2NR_xR_x$, $—C(O)C(O)OH$, $—C(O)C(O)NR_yR_y$, or $—C(O)C(O)NR_y(CR_xR_x)_{1-2}NR_yR_y$; and R_1, R_2, R_4, R_5, R_x, R_y, m, n, and p are defined in the first aspect. Included in this embodiment are compounds in which R_3 is H, $—CH(CH_3)_2$, $—CH(CH_3)_2$, $—CH_2CH(CH_3)_2$, —CH_2CN, $—CH_2CH_2CN$, $—CH_2CH_2CH_2CN$, $—CH_2C(CH_3)_2OH$, $—C(O)CH_3$, $—C(O)CH(CH_2CH_3)_2$, $—C(O)CH_2OCH_3$, $—C(O)CH_2CH_2OCH_3$, $—C(O)CH_2CH(CH_3)OH$, $—C(O)CH_2CN$, $—C(O)CH_2CH_2CN$, $—C(O)CH(CH_3)NH(CH_3)$, $—C(O)CH_2NH(CH_3)$, $—C(O)CH_2N(CH_3)_2$, $—C(O)CH_2NHCH_2CH_2CH_3$, $—C(O)CH_2NHCH(CH_3)_2$, $—C(O)CH_2NHC(CH_3)_3$, $—C(O)CH_2N(CH_3)CH(CH_3)_2$, $—C(O)CH_2NHCH_2CH_2OCH_3$, $—CH_2C(O)NH_2$, $—CH_2C(O)NH(CH_3)$, $—CH_2C(O)N(CH_3)CH_2CH_3$, $—CH_2C(O)NHCH_2CH_2CH_3$, $—CH_2C(O)NH(CH(CH_3)_2)$, $—CH_2C(O)N(CH_3)_2$, $—CH_2C(O)N(CH_2CH_3)_2$, $—CH_2CH_2S(O)_2CH_3$, or $—CH_2CH_2S(O)_2NH_2$. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is H, $—CH(CH_3)_2$, $—CH(CH_3)_2$, $—CH_2CH(CH_3)_2$, —CH_2CN, $—CH_2CH_2CN$, $—CH_2CH_2CH_2CN$, $—CH_2C(CH_3)_2OH$, $—C(O)CH_3$, $—C(O)CH(CH_2CH_3)_2$, $—C(O)CH_2OCH_3$, $—C(O)CH_2CH_2OCH_3$, $—C(O)CH_2CH(CH_3)OH$, $—C(O)CH_2CN$, $—C(O)CH_2CH_2CN$, $—C(O)CH(CH_3)NH(CH_3)$, $—C(O)CH_2NH(CH_3)$, $—C(O)CH_2N(CH_3)_2$, $—C(O)CH_2NHCH_2CH_2CH_3$, $—C(O)CH_2NHCH(CH_3)_2$, $—C(O)CH_2NHC(CH_3)_3$, $—C(O)CH_2N(CH_3)CH(CH_3)_2$, $—C(O)CH_2NHCH_2CH_2OCH_3$, $—CH_2C(O)NH_2$, $—CH_2C(O)NH(CH_3)$, $—CH_2C(O)N(CH_3)CH_2CH_3$, $—CH_2C(O)NHCH_2CH_2CH_3$, $—CH_2C(O)NH(CH(CH_3)_2)$, $—CH_2C(O)N(CH_3)_2$, $—CH_2C(O)N(CH_2CH_3)_2$, $—CH_2CH_2S(O)_2CH_3$, or $—CH_2CH_2S(O)_2NH_2$. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_3 is H, $—CH(CH_3)_2$, $—CH(CH_3)_2$, $—CH_2CH(CH_3)_2$, —CH_2CN, $—CH_2CH_2CN$, $—CH_2CH_2CH_2CN$, $—CH_2C(CH_3)_2OH$, $—C(O)CH_3$, $—C(O)CH(CH_2CH_3)_2$, $—C(O)CH_2OCH_3$, $—C(O)CH_2CH_2OCH_3$, $—C(O)CH_2CH(CH_3)OH$, $—C(O)CH_2CN$, $—C(O)CH_2CH_2CN$, $—C(O)CH(CH_3)NH(CH_3)$, $—C(O)CH_2NH(CH_3)$, $—C(O)CH_2N(CH_3)_2$, $—C(O)CH_2NHCH_2CH_2CH_3$, $—C(O)CH_2NHCH(CH_3)_2$, $—C(O)CH_2NHC(CH_3)_3$, $—C(O)CH_2N(CH_3)CH(CH_3)_2$, $—C(O)CH_2NHCH_2CH_2OCH_3$, $—CH_2C(O)NH_2$, $—CH_2C(O)NH(CH_3)$, $—CH_2C(O)N(CH_3)CH_2CH_3$, $—CH_2C(O)NHCH_2CH_2CH_3$, $—CH_2C(O)NH(CH(CH_3)_2)$, $—CH_2C(O)N(CH_3)_2$, $—CH_2C(O)N(CH_2CH_3)_2$, $—CH_2CH_2S(O)_2CH_3$, $—CH_2CH_2S(O)_2NH_2$, $—CH_2C(O)NH$(cyclobutyl), $—CH_2C(O)NH$(cyclopropyl), $—CH_2C(O)NH$(methyloxetanyl), $—CH_2C(O)N(CH_3)$(cyclopropyl), oxetanyl, tetrahydropyranyl, dioxotetrahydrothiopyranyl, —CH_2(oxazolyl), —CH_2(pyrazolyl), —CH_2(tetrazolyl), —CH_2(triazolyl), —CH_2(methyltriazolyl), —$CH_2C(O)$(2-oxa-6-azaspiro[3.3]heptanyl), —$CH_2C(O)$(azetidinyl), —$CH_2C(O)$(dioxidothiadiazinanyl), —$CH_2C(O)$(dioxidothiomorpholinyl), —$CH_2C(O)$(morpholinyl), —$CH_2C(O)$(methoxyethylpiperazinyl), —$CH_2C(O)$(piperidinyl), —$CH_2C(O)$(hydroxypiperidinyl), —$CH_2C(O)$(pyrrolidinyl), —$CH_2C(O)$(hydroxypyrrolidinyl), —$C(O)$(azetidinyl), —$C(O)$(methylcyclopropyl), —$C(O)$(methyloxetanyl), or —$C(O)CH_2$(morpholinyl); and R_1, R_2, R_4, R_5, m, n, and p are defined in the first aspect. Included in this embodiment are compounds in which each R_2 is independently F, —CN, —OH, C_{1-2} alkyl, or $—(CH_2)_{0-1}O(C_{1-2}$ alkyl); p is zero, 1 or 2. Included in this embodiment are compounds in which each R_2 is independently $—CH_3$, $—OCH_3$, or $—CH_2OCH_3$. Also included are compounds in which m is zero and n is zero.

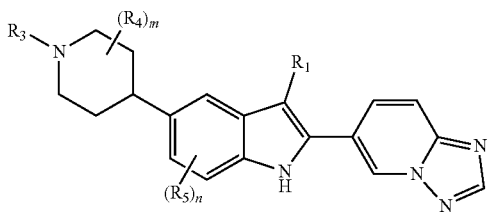
One embodiment provides a compound of Formula (I) or a salt thereof, wherein m is zero, 1, or 2; and R_1, R_2, R_3, R_4, R_5, n, and p are defined in the first aspect. Included in this embodiment are compounds in which m is zero or 1. Also included in this embodiment are compounds in which m is zero. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein n is zero or 1; and R_1, R_2, R_3, R_4, R_5, m, and p are defined in the first aspect. Included in this embodiment are compounds in which n is zero. Also included are compounds in which m is zero. Also included are compounds in which m is zero and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein m is zero, 1, or 2; n is zero or 1; and p is zero, 1, or 2; and R_1, R_2, R_3, R_4, and R_5 are defined in the first aspect. Included in this embodiment are compounds in which m is zero or 1; n is zero; and p is zero, 1, or 2. Also included are compounds in which m is zero; n is zero; and p is zero, 1, or 2.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-1):

(I-1)



and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —$CHCH_3$ or —$CH(CH_3)_2$. Included in this embodiment are compounds in which R_3 is H, —CH_3, —$CH(CH_3)_2$, —CH_2CHF_2, —CH_2CH_2OH, —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)N(CH_3)_2$, —$CH_2C(CH_3)_2OH$, —$C(O)CH_2S(O)_2CH_3$, —$C(O)CH_2NH(CH_3)$, —$C(O)CH_2N(CH_3)_2$, —$C(O)CH_2CH(CH_3)OH$, or -L_1-A; L_1 is —CH_2—, —C(O)—, or —$C(O)CH_2CH(CH_3)$—; and A is isoxazolyl, oxazolyl, oxetanyl, pyrazolyl, pyrimidinyl, pyrrolidinonyl, tetrahydrofuranyl, tetrahydropyranyl, thiazolyl, or triazolyl, each substituted wtih -L_2-R_a and zero to 2 R_b; L_2 is a bond; R_a is H, C_{1-3} alkyl, —OCH_3, or —CH_2(cyclopropyl); and each R_b is —CH_3. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (1);

1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (47);

1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (51); (S)-1-(4-(2-([1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (53); 6-(3-ethyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (121);

2-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (164);

2-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (240);

1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (241);

2-(4-(2-([1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (242);

6-(3-isopropyl-5-(1-methylpiperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (350);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (351);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (352);

6-(3-isopropyl-5-(1-((l-methyl-1H-1,2,4-triazol-3-yl) methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (353);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (354);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (355);

2-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-ol (356);

6-(3-isopropyl-5-(1-(oxetan-3-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (358);

6-(3-isopropyl-5-(1-((2-methoxypyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)[1,2,4]triazolo[1,5-a]pyridine (359);

2-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)acetamide (360);

3-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)-5-methylisoxazole (361);

4-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)-2-isopropylthiazole (362);

6-(3-isopropyl-5-(1-((1-propyl-1H-pyrazol-4-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (363);

6-(5-(1-((3,5-dimethyl-1H-pyrazol-4-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a] pyridine (364);

6-(5-(1-((1H-1,2,3-triazol-4-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (365);

6-(5-(1-((1-(cyclopropylmethyl)-1H-pyrazol-3-yl)methyl) piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (366);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (367);

6-(3-isopropyl-5-(1-((5-methoxy-1,3-dimethyl-1H-pyrazol-4-yl)methyl)pi p eri din-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (368);

5-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)-2,4-dimethylthiazole (369);

4-((4-(2-([1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)-3,5-dimethylisoxazole (370);

6-(5-(1-((1,3-dimethyl-1H-pyrazol-4-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a] pyridine (371);

4-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)-2,5-dimethyloxazole (372);

6-(5-(1-((1,3-dimethyl-1H-pyrazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a] pyridine (373);

2-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)thiazole (374);

6-(3-isopropyl-5-(1-((1-isopropyl-1H-pyrazol-4-yl) methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (375);

6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-4-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (376);

5-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)methyl)thiazole (377);

4-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)-2-methyloxazole (378);

6-(5-(1-((1H-pyrazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (379);

6-(3-isopropyl-5-(1-((3-methyl-1H-pyrazol-4-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (380);

6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (381);

6-(5-(1-((1-ethyl-1H-pyrazol-3-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (382);

2-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)methyl)-5-methylthiazole (383);

4-((4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)oxazole (384);

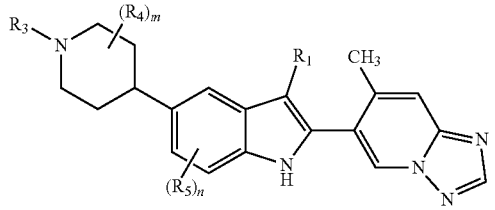
6-(3-isopropyl-5-(1-isopropylpiperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (536);

4-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carbonyl)-1-methylpyrrolidin-2-one (601);

1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylsulfonyl)ethan-1-one

(619); or 1-(4-(2-([1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(oxetan-3-yl) butan-1-one (713).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-2):



(I-2)

and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$. Included in this embodiment are compounds in which R_3 is H, C_{1-3} cyanoalkyl, —$CH_2C(CH_3)_2OH$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)N(CH_3)_2$, —$CH_2C(O)NH(CH_2CH_3)$, —$CH_2C(O)NH(CH(CH_3)_2)$, —$CH_2C(O)N(CH_3)(CH_2CH_3)$, —$CH_2C(O)N(CH_2CH_3)_2$, —$CH_2C(O)N(CH_3)(CH_2CH_2OH)$, —$CH_2CH_2S(O)_2CH_3$, —$CH(CH_3)CH_2S(O)_2CH_3$, —$CH_2CH_2S(O)_2NH_2$, —$CH_2CH_2S(O)_2NH(CH_3)$, —$CH_2CH_2S(O)_2N(CH_3)_2$, —$CH_2CH_2NHS(O)_2CH_3$, —$C(O)CH_2CN$, or -$L_1$-A; L_1 is —CH_2—, —$CH_2C(O)$—, —$CH_2C(O)NH$—, or —$C(O)CH_2CH_2$—; and A is cyclopropyl, dioxotetrahydrothiophenyl, dioxotetrahydrothiopyranyl, isoxazolyl, morpholinyl, oxadiazolyl, oxazolyl, oxetanyl, piperidinyl, pyrazinyl, pyrazolyl, pyridazinyl, pyrimidinyl, pyrrolidinyl, tetrahydropyranyl, thiazolyl, or triazolyl, each substituted wtih -L_2-R_a and zero to 1 R_b; L_2 is a bond; R_a is H, —CH_3, —CN, or —OCH_3; and R_b is —OCH_3. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (3); 3-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-3-oxopropanenitrile (49);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethane-1-sulfonamide (180);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetonitrile (181);

1-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (182);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethane-1-sulfonamide (183);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylethane-1-sulfonamide (184);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylethane-1-sulfonamide (185);

1-((4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl) cyclopropane-1-carbonitrile (186);

1-((4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)cyclopropane-1-carbonitrile (187);

3-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) propanenitrile (188);

N-(2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethyl)methanesulfonamide (189);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (190);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (191);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (441);

6-(3-isopropyl-5-(1-((2-methoxypyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (442);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl[1,2,4]triazolo[1,5-a]pyridine (443);

6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (444);

6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (445);

2-((4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methypoxazole (446);

6-(3-isopropyl-5-(1-((4-methyl-4H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4] triazolo[1,5-a]pyridine (447);

6-(5-(1-((1H-pyrazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7-methyl[1,2,4]triazolo[1,5-a]pyridine (448);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4] triazolo[1,5-a]pyridine (449);

5-((4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)thiazole (450);

6-(5-(1-((1H-1,2,3-triazol-5-yl) methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a] pyridine (451);

6-(3-isopropyl-5-(1-(pyrimidin-5-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (452);

3-((4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)-5-methylisoxazole (453);

6-(3-isopropyl-5-(1-(pyrimidin-2-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (454);

4-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (455);

6-(5-(1-((4,6-dimethoxypyrimidin-2-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo [1,5-a]pyridine (456);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4] triazolo[1,5-a]pyridine (457);

2-((4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methyl)-1,3,4-oxadiazole (458);

6-(5-(1-((1H-1,2,4-triazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a] pyridine (459);

3-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) tetrahydrothiophene 1,1-dioxide (460);

6-(3-isopropyl-5-(1-(pyridazin-3-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine ((461);

3-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)butanenitrile (462);

6-(3-isopropyl-5-(1-((2-methylpyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (463);

6-(3-isopropyl-5-(1-(1-(methylsulfonyl)propan-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a] pyridine (464);

6-(3-isopropyl-5-(1-((2-methylpyrimidin-4-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (465);

6-(3-isopropyl-5-(1-((5-methylpyrazin-2-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a] pyridine (466);

6-(3-isopropyl-5-(1-(pyrazin-2-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (467);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one (802);

N-isopropyl-2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (803);

N-ethyl-2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (804);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(piperidin-1-yl)ethan-1-one (805);

N-cyclopropyl-2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl) acetamide (806);

N-ethyl-2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (807);

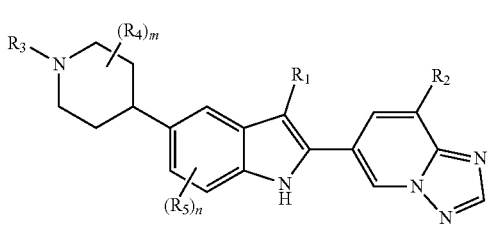
N,N-diethyl-2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (808);

2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-1-morpholinoethan-1-one (809);

N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(7-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (810); or

1-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-3-morpholinopropan-1-one (885).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-3):



(I-3)

R_2 is —CH_3 or —CD_3; and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —$CHCH_3$, —$CH(CH_3)_2$, or —CH_2CHF_2. Included in this embodiment are compounds in which R_3 is H, C_{3-5} alkyl, C_{2-3} fluoroalkyl, C_{2-5} hydroxyalkyl, C_{1-3} cyanoalkyl, —$CH_2C(CH_3)_2OH$, —$CH_2CH_2OCH_3$, —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)NH(CH_2CH_2CH_3)$, —$CH_2C(O)NH(CH(CH_3)_2)$, —$CH_2C(O)N(CH_3)_2$, —$CH_2C(O)N(CH_3)CH_2CH_3$, —$CH_2C(O)N(CH_2CH_3)_2$, —$CH(CN)C(O)N(CH_3)_2$, —$CH_2C(O)N(CH_3)(CH_2CH_2OH)$, —$CH_2C(O)N(CH_2CH_3)(CH_2CH_2OH)$, —$CH_2C(O)N(CH_2CH_2CH_3)(CH_2CH_2OH)$, —$CH_2C(O)N(CH_3)(CH_2CH_2CH_2OH)$, —$CH_2C(O)N(CH_3)(CH_2C(CH_3)_2OH)$, —$CH_2C(O)N(CH_2CH_2OH)(CH_2CH(CH_3)CH_2CH_3)$, —$CH_2C(O)NH(CH_2CH_2SCH_3)$, —$CH_2CH_2S(O)_2CH_3$, —$CH_2CH_2CH_2S(O)_2CH_3$, —$CH(CH_3)CH_2S(O)_2CH_3$, —$CH(CH_3)CH_2S(O)_2(CH_2CH_2CH_2CH_3)$, —$CH_2CH_2S(O)_2NH_2$, —$CH_2CH_2S(O)_2NH(CH_3)$, —$CH_2CH_2S(O)_2N(CH_3)_2$, —$CH(CH_3)CH_2S(O)_2N(CH_2CH_3)_2$, —$CH_2CH_2NHS(O)_2CH_3$, —C═$N(NH_2)$, —$C(O)CH_3$, —$C(O)CH(CH_2CH_3)_2$, —$C(O)CH_2CH_2CN$, —$C(O)CH_2CH(CH_3)OH$, —$C(O)CH_2OCH_3$, —$C(O)CH_2CH_2OCH_3$, —$C(O)CH_2NH(CH_3)$, —$C(O)CH_2NH(CH_2CH_2CH_3)$, —$C(O)CH_2NHCH(CH_3)_2$, —$C(O)CH_2NHC(CH_3)_3$, —$C(O)CH_2N(CH_3)_2$, —$C(O)CH(CH_3)NH(CH_3)$, —$C(O)CH_2N(CH_3)CH(CH_3)_2$, —$C(O)CH_2N(CH_3)(CH_2CH_2OH)$, —$C(O)CH_2NH(CH_2CH_2OCH_3)$, —$C(O)CH_2S(O)_2CH_3$, —$C(O)CH_2CH_2S(O)_2CH_3$, —$C(O)CH_2NHS(O)_2CH_3$, or -$L_1$-A; L_1 is —CH_2—, —$CH_2C(O)$—, —$CH_2C(O)N(CH_2CH_2OH)$—, —$CH_2C(O)N(CH_3)$—, —$CH_2C(O)N(CH_3)CH_2CH_2$—, —$CH_2C(O)NH$—, $CH_2CH_2S(O)_2$—, —C(O)—, —$C(O)CH_2$—, —$C(O)CH_2CH_2$—, —$C(O)CH_2CH_2N(CH_2CH_2OH)$—, —$C(O)CH_2N(CH_2CH_2OH)$—, —$C(O)CH_2NH$—, —$CH(CH_3)$—, or —$CH(CH_3)CH_2S(O)_2$—; and A is 2-oxa-6-azaspiro[3.3]heptanyl, azetidinyl, C_{3-6} cycloalkyl, di oxidothiadiazinanyl, dioxidothiazolidinyl, dioxidothiomorpholinyl, dioxotetrahydrothiophenyl, dioxotetrahydrothiopyranyl, dioxothiomorpholinyl, imidazolyl, isoxazolyl, morpholinyl, oxa-azaspiro[3.3]heptanyl, oxadiazolyl, oxazolyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazinyl, pyrazolyl, pyridazinyl, pyrimidinyl, pyrrolidinonyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrazolyl, thiadiazolyl, thiazolyl, or triazolyl, each substituted wtih -L_2-R_a and zero to 2 R_b; L_2 is a bond; R_a is H, F, —CH_3, —CN, —OH, —OCH_3, —CH_2OH, —CH_2CH_2OH, —$CH_2CH_2OCH_3$, —$C(O)CH_3$, —$C(O)OCH_2CH_3$, —$C(O)OC(CH_3)_3$, —$NHC(O)OC(CH_3)_3$, —$S(O)_2CH_3$, cyclopropyl, or pyrazinyl; and each R_b is independently F, —OH, —CH_3, or —OCH_3. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero, and n is zero. Additionally, included in this embodiment are compounds in which R_2 is —CH_3.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine hydrochloride (2);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl acetamide (7);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetonitrile (8);

3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propanenitrile (9);

6-(5-(1-butylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (10);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (11);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (12);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo [1,5-a]pyridine (26);

6-(3-isopropyl-5-(1-isopropylpiperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (27);

6-(3-isopropyl-5-(1-propylpiperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (28);

6-(5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (29);

6-(5-(1-((1H-pyrazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (30);

4-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)oxazole (31);

6-(5-(1-((1H-1,2,3-triazol-4-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (32);

6-(5-(1-((4H-1,2,4-triazol-3-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (33);

6-(5-(1-((1H-tetrazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (34);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (35);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (36);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) tetrahydro-2H-thiopyran 1,1-dioxide (37);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (46);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (48);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-(methylamino) ethan-1-one (50);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methoxyethan-1-one (52);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-4-oxobutanenitrile (54);

(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone (55);

(S)-azetidin-2-yl(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methanone (56);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (57);

(S)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) propan-1-one (58);

(R)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)propan-1-one (59);

(S)-3-hydroxy-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) butan-1-one (60);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-3-methoxypropan-1-one (61);

(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(3-methyloxetan-3-yl) methanone (64);

2-ethyl-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)butan-1-one (65);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-morpholino-ethan-1-one (68);

2-(tert-butylamino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (69);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(isopropylamino)ethan-1-one (70);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-((2-methoxyethyl)amino) ethan-1-one (71);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(propylamino) ethan-1-one (72);

2-(isopropyl(methyl)amino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (73);

1-(1,1-dioxidothiomorpholino)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (74);

N-cyclopropyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetamide (75);

N-ethyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methyl-acetamide (76);

(S)-1-(3-hydroxypiperidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl) ethan-1-one (77);

N-cyclobutyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (78);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(2-oxa-6-azaspiro[3.3]heptan-6-yl)ethan-1-one (79);

N,N-diethyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (80);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-propylacetamide (81);

(R)-1-(3-hydroxypiperidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (82);

(S)-1-(3-hydroxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (83);

(R)-1-(3-hydroxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (84);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(4-(2-methoxyethyl)piperazin-1-yl)ethan-1-one (85);

1-(azetidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (86);

N-isopropyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetamide (87);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-morpholinoethan-1-one (88);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(piperidin-1-yl) ethan-1-one (89);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one (90);

1-(1,1-dioxidothiomorpholino)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl) ethan-1-one (91);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(3-methyloxetan-3-yl)acetamide (92);

N-cyclopropyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (93);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-(trideuteromethyl)-[1,2,4]triazolo[1,5-a]pyridine (117);

6-(3-ethyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo [1,5-a]pyridine (158);

6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (161);

6-(5-(1-isopentylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (165);

6-(3-isopropyl-5-(1-(2-methoxyethyl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (166);

4-((2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethyl)sulfonyl)morpholine (167);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethane-1-sulfonamide (168);

2-cyano-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (169);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propanenitrile (170);

1-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl) cyclopropane-1-carbonitrile (171-172);

6-(3-isopropyl-5-(1-(2-(phenylsulfonyl)ethyl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (173);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylethane-1-sulfonamide (174);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylethane-1-sulfonamide (175);

N-(2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethyl)methanesulfonamide (176);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (177);

6-(3-isopropyl-5-(1-(3-(methylsulfonyl)propyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (178);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)-[1,4'-bipiperidin]-1'-yl)ethan-1-one (179);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carbonyl)-1-methylpyrrolidin-2-one (243);

2-(4-(3-ethyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (337);

2-(4-(3-ethyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (338);

6-(3-ethyl-5-(1-(2-(methylsulfonyl) ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (339);

2-(4-(3-ethyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (340);

6-(3-ethyl-5-(1-(2-methoxyethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (341);

1-(4-(3-ethyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (342);

2-(4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (343);

2-(4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (344);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trideuteromethyl)-[1,2,4]triazolo[1,5-a]pyridine (357);

6-(5-(1-(2,2-difluoroethyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (385);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4] triazolo[1,5-a]pyridine (386);

6-(3-isopropyl-5-(1-((2-methoxypyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (387);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-ol (388);

6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-5-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (389);

3-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methyl)-1,2,4-oxadiazole (390);

3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propan-1-ol (391);

6-(3-isopropyl-5-(1-((4-methyl-4H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4] triazolo[1,5-a]pyridine (392);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (393);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (394);

3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydrothiophene 1,1-dioxide (395);

6-(3-isopropyl-5-(1-(pyrimidin-2-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (396);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) butan-1-ol (397);

6-(5-(1-(2,6-difluorobenzyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (398);

6-(5-(1-((3,5-dimethyl-112-pyrazol-4-yl)methyl) piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (399);

(3,5-difluoro-4-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methyl)phenyl)methanol (400);

3,5-difluoro-4-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methyl)benzonitrile (401);

6-(3-isopropyl-5-(1-(pyrimidin-5-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (402);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)cyclohexan-1-ol (403);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-5-yl) methyl)pip eridin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (404);

6-(5-(1-((1,3-dimethyl-1H-pyrazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (405);

4-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)thiazole (406);

4-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methyl)-5-methylthiazole (407);

2-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)thiazole (408);

6-(3-isopropyl-5-(1-((3-methyl-1H-pyrazol-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (409);

6-(5-(1-((1,5-dimethyl-1H-pyrazol-3-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (410);

4-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)-1,2,3-thiadiazole (411);

6-(3-isopropyl-5-(1-(pyridazin-3-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (412);

(2-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)pyrimidin-5-yl)methanol (413);

6-(3-isopropyl-5-(1-((2-methylpyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (414);

6-(3-isopropyl-5-(1-((2-methylpyrimi din-4-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (415);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-methylcyclopentane-1-carbonitrile (416-417);

6-(3-isopropyl-5-(1-(1-(6-methylpyridazin-3-yl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (418);

6-(3-isopropyl-5-(1-(1-(1-methyl-1H-pyrazol-4-ypethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (419);

6-(5-(1-(1-(1H-pyrazol-5-yl)ethyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (420);

6-(3-isopropyl-5-(1-(1-(pyrimidin-2-yl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (421);

6-(3-isopropyl-5-(1-(1-(methylsulfonyl)propan-2-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (422);

3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)butanenitrile (423);

6-(3-isopropyl-5-(1-((5-methylpyrazin-2-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (424);

6-(3-isopropyl-5-(1-(tetrahydro-2H-thiopyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (425);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(1H-tetrazol-5-yl)ethan-1-one (426);

N,N-diethyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propane-1-sulfonamide (427);

6-(5-(1-(1-(butylsulfonyl)propan-2-yl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (428);

6-(3-isopropyl-5-(1-(pyrazin-2-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (429);

4-((2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propyl)sulfonyl)morpholine (430);

6-(3-isopropyl-5-(1-(1-(piperidin-1-ylsulfonyl)propan-2-yl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (431);

3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)pentane-1,5-diol (432);

6-(3-isopropyl-5-(1-((2-methyl-2H-tetrazol-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (433);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (434);

3-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)-5-methylisoxazole (435);

5-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methyl)thiazole (436);

6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (437);

6-(5-(1-((4,6-dimethoxypyrimidin-2-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo [1,5-a]pyridine (438);

5-cyclopropyl-2-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methypoxazole (439);

2-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methyl)oxazole (440);

6-(3-isopropyl-5-(1-(3,3,3-trifluoropropyl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (537);

tert-butyl (3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)cyclobutyl)carbamate (538);

ethyl 3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)cyclobutane-1-carboxylate (539);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (540-541);

6-(3-ethyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (596);

6-(3-(2,2-difluoroethyl)-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (597);

2-(4,4-difluoropiperidin-1-yl)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (602);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(pyrazin-2-yl) ethan-1-one (603);

(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(1-(pyrazin-2-yl)cyclopropyl)methanone (604);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(2-methyl-2H-tetrazol-5-yl)ethan-1-one (605);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylsulfonyl)ethan-1-one (606);

N-(2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-oxoethyl) methanesulfonami de (607);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-(methylsulfonyl)propan-1-one (608);

6-(3-isopropyl-5-(1-((2-methyl-1H-imidazol-4-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo [1,5-a]pyridine (620);

(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(2,2,3,3-tetramethylcyclopropyl)methanone (621);

((2S,4R)-4-hydroxypyrrolidin-2-yl)(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (622);

((2S,3R)-3-hydroxypyrrolidin-2-yl)(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (623);

((2S,4S)-4-hydroxypyrrolidin-2-yl)(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (624);

((2R,4R)-4-hydroxypyrrolidin-2-yl)(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (625);

(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)((2S,4R)-4-methoxypyrrolidin-2-yl)methanone (626);

((2S,4R)-4-fluoropyrrolidin-2-yl)(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (627);

1-((2S,4R)-4-hydroxy-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carbonyl)pyrrolidin-1-yl)ethan-1-one (628);

2-(dimethylamino)-1-(4-(3-ethyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (703);

1-(4-(3-ethyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (704);

(R)-1-(4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (705);

1-(4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-(methylamino)ethan-1-one (706);

(S)-1-(4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (707);

1-(4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-(dimethylamino)ethan-1-one (712);

2-((2-hydroxyethyl)(methyl)amino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl) ethan-1-one (714);

2-(cycl opropyl (2-hydroxyethyl)amino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (715);

2-(3,3-difluoropyrrolidin-1-yl)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (716);

2-(1,1-dioxidothiomorpholino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (717);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-((1-methylcyclopropyl)amino)ethan-1-one (768);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(piperidin-1-yl) ethan-1-one (769);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(pyrrolidin-1-yl)ethan-1-one (770);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(2-oxa-6-azaspiro [3.3]heptan-6-yl)ethan-1-one (771);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(4-(2-methoxyethyl)piperazin-1-yl)ethan-1-one (772);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-(4-methoxypiperidin-1-yl)ethan-1-one (773);

(S)-2-(3-hydroxypyrrolidin-1-yl)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (774);

(S)-2-(3-hydroxypiperidin-1-yl)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (775);

(R)-2-(3-hydroxypyrrolidin-1-yl)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (776);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(3-(methylsulfonyl) azetidin-1-yl)ethan-1-one (782);

1-(1,1-dioxidothiazolidin-3-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (783-784);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-(2-(methylthio)ethyl)acetamide (785);

1-((2R,4R)-2-(hydroxymethyl)-4-methoxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (786);

N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (787);

N-ethyl-N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (788);

N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-propylacetamide (789);

(R)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (790);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)acetamide (791);

N-(3-hydroxypropyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (792);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl-N-(tetrahydrofuran-3-yl)acetamide (793);

N-(2-(1-hydroxycycl op entyl)ethyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (794);

(R)-1-(3-(hydroxymethyl) morpholino)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (795);

N-(2-hydroxy-2-methylpropyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (796);

(S)-1-(3-(hydroxymethyl)morpholino)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (797);

(S)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl-N-(tetrahydrofuran-3-yl)acetamide (798);

1-((2R,4R)-2-(hydroxymethyl)-4-methylpyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (799);

N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(2-methylbutyl)acetamide (800);

N-cyclopropyl-N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetamide (801);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-morpholinopropan-1-one (882);

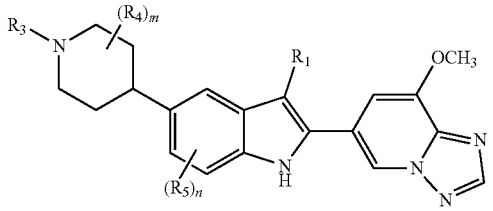
3-(cyclopropyl(2-hydroxyethyl)(methyl)-14-azaneyl)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propan-1-one (883);

3-(1,1-dioxidothiomorpholino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)propan-1-one (884); or

4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboximidamide (994).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-4):

(I-4)



and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —$CHCH_3$, —$CH(CH_3)_2$, or —CH_2CHF_2. Included in this embodiment are compounds in which R_3 is H, —$CH_2CH(CH_3)_2$, —CH_2CN, —$CH_2C(CH_3)_2OH$, —$CH_2CH_2OCH_3$, —$CH_2CH_2NH(CH_3)$, —$CH_2CH_2S(O)_2CH_3$, —$CH(CH_3)CH_2S(O)_2CH_3$, —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)N(CH_3)_2$, —$CH_2C(O)NH(CH_2C(CH_3)_2OH)$, —$CH_2C(O)N(CH_3)(CH_2CH_3)$, —$C(O)CH_2S(O)_2CH_3$, —$C(O)CH_2OCH_3$, —$C(O)CH_2NH(CH_3)$, —$C(O)CH_2NH(CH_2CH_2OCH_3)$, —$C(O)CH_2N(CH_3)_2$, —$C(O)CH_2CH_2OCH_3$, —$C(O)CH_2CH_2N(CH_3)_2$, —$C(O)CH_2CH_2CH_2S(O)_2NH_2$, —$C(O)CH_2C(CH_3)_2OH$, or -$L_1$-A; L_1 is —CH_2, —C(O)—, —C(O)CH_2—, —$C(O)CH_2CH_2$—, —$C(O)CH_2NH$—, —$CH_2C(O)$—, or —$CH_2C(O)NH$—; and A is azetidinyl, cyclobutyl, dioxanyl, dioxotetrahydrothiopyranyl, dioxothiomorpholinyl, morpholinyl, oxetanyl, piperazinonyl, pyrrolidinonyl, pyrrolidinyl, tetrahydrofuranyl, or tetrahydropyranyl, each substituted wtih -L_2R_a and zero to 1 R_b; L_2 is a bond; R_a is H, F, C_{1-2} alkyl, —CN, —OH, —OCH_3, —$C(O)CH_3$, or —$C(O)OC(CH_3)_3$; and R_b is F or —CH_3. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (5);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetonitrile (21);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (22);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (23);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (24);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (25);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (44);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)pi p eri din-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a] pyridine (45);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (62);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methoxyethan-1-one (63);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (67);

6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo [1,5-a]pyridine (156);

6-(3-ethyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (157);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (263);

6-(3-isopropyl-5-(1-(1-(methylsulfonyl)propan-2-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (264);

6-(3-isopropyl-5-(1-(1-(methylsulfonyl)propan-2-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (265);

6-(3-isopropyl-5-(1-(2-methoxyethyl) piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (266);

2-(4-(3-(2,2-difluoroethyl)-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (329);

2-(4-(3-(2,2-difluoroethyl)-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (330);

2-(4-(3-ethyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (331);

6-(3-ethyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (332);

2-(4-(3-ethyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetamide (333);

1-(4-(3-ethyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (334);

2-(4-(3-ethyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (335);

6-(3-ethyl-5-(1-(2-methoxyethyl) piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (336);

1-(4-(3-(2,2-difluoroethyl)-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (349);

4-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (561);

6-(5-(1-(2,2-dimethyltetrahydro-2H-pyran-4-yl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo [1,5-a]pyridine (562-564);

(R)-3-((4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) methyl)morpholine (565);

6-(3-isopropyl-5-(1-((3-methyloxetan-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (566);

3-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)cyclobutane-1-carbonitrile (567);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (568-569);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylethan-1-amine (570);

6-(3-(2,2-difluoroethyl)-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (598);

6-(3-ethyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (600);

(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(tetrahydrofuran-2-yl)methanone (663);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-methoxypropan-1-one (664);

4-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-4-oxobutane-1-sulfonamide (665);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(tetrahydro-2H-pyran-4-yl) ethan-1-one (666);

3-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propan-1-one (667);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-(methylsulfonyl)ethan-1-one (668);

3-hydroxy-1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-methylbutan-1-one (669);

(S)-1-(2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidine-1-carbonyl) pyrrolidin-1-yl)ethan-1-one (670);

1-(3-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-oxopropyl) pyrrolidin-2-one (671);

(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)(1-methylpyrrolidin-3-yl)methanone (672);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-morpholinoethan-1-one (673);

((2S,4R)-4-hydroxypyrrolidin-2-yl)(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)methanone (674);

(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)((2S,4R)-4-methoxypyrrolidin-2-yl)methanone (675);

(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(1-methylpyrrolidin-3-yl) methanone (676);

4-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carbonyl)-1-methylpyrrolidin-2-one (677);

4-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carbonyl)-1-methylpyrrolidin-2-one (678);

(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(1-methylpyrrolidin-3-yl)methanone (679);

2-(dimethylamino)-1-(4-(3-ethyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (701);

1-(4-(3-ethyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (702);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-((2-methoxyethyl)amino)ethan-1-one (780);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-((3-methyl oxetan-3-yl)amino)ethan-1-one (781);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-(3-methyloxetan-3-yl) acetamide (854);

tert-butyl 3-(2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamido) azetidine-1-carboxylate (855);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(4-methyltetrahydro-2H-pyran-4-yl)acetamide (856);

N-(2-hydroxy-2-methylpropyl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetamide (857);

1-(1,1-dioxidothiomorpholino)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (858);

N-ethyl-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (859);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(1-methylcyclobutyl)acetamide (860);

N-((3-ethyloxetan-3-yl)methyl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetamide (861);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-((3-methyloxetan-3-yl)methyl)acetamide (862);

(R)-1-(3-hydroxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (863);

1-(3-fluoroazetidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (864);

1-(3,3-difluoroazetidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (865);

4-(2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetyl)piperazin-2-one (866);

1-(3-hydroxyazetidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (867);

(R)-1-(3-fluoropyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (868);

1-((2S,6R)-2,6-dimethyl morpholino)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (869);

1-(azetidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (870);

(R)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(3-methylmorpholino)ethan-1-one (871);

1-(3,3-difluoropyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (872);

1-(2,5-dimethylpyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (873);

(S)-1-(3-hydroxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (874);

(S)-1-(3-fluoropyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (875);

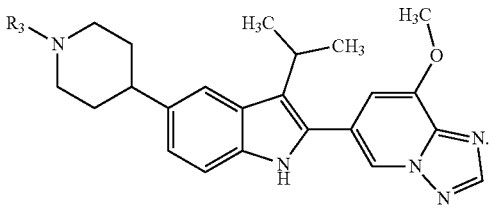
2-(4-(4-fluoro-3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (991);

6-(4-fluoro-5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (992);

or 6-(5-(1-(2,2-dimethyl-1,3-dioxan-5-yl) piperidin-4-yl)-4-fluoro-3-isopropyl-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (993).

One embodiment provides a compound of Formula (I-4) or a salt thereof, wherein R_1 is —$CH(CH_3)_2$; m is zero; n is zero, and R_3 is defined in the first aspect or the second aspect. Compounds of this embodiment have the structure of Formula (I-4a)

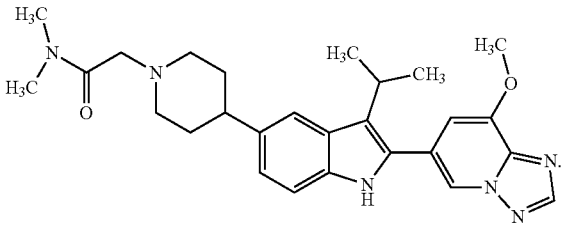
(I-4a)



Included in this embodiment are compounds in which R_3 is —$(CR_xR_x)_{1-2}C(O)NR_yR_y$ wherein each R_x is independently H or —CH_3; and each R_x is independently H or —CH_3. Also included in this embodiment are compounds in which R_3 is —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, or —$CH_2C(O)N(CH_3)_2$.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is:

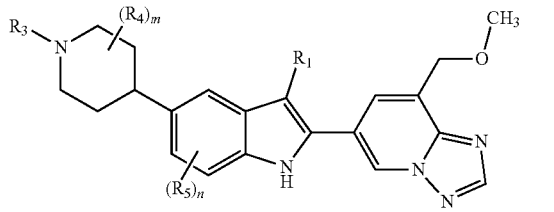
(25)



Included in this embodiment is 2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (25). Also included in this embodiment is one or more salts of 2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-5):

(I-5)



and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$. Included in this embodiment are compounds in which R_3 is H, —CH_2CN, —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)NH(CH_2CH_3)$, —$CH_2C(O)NH(CH_2CH_2CN)$, —$CH_2C(O)NH(CH_2CH_2CF_3)$, —$CH_2C(O)NH(CH(CH_3)_2)$, —$CH_2C(O)N(CH_3)CH_2CH_2OCH_3$, —$CH_2C(O)N(CH_3)CH_2CH_2CN$, —$CH_2C(O)N(CH_3)CH_2CH_2CH_2OH$, —$CH_2CH_2S(O)_2NH_2$, —$CH_2CH_2S(O)_2CH_3$, —$CH_2C(O)NHCH(CH_2CH_2OH)$(cyclopropyl), or -$L_1$-A; L_1 is —CH_2—, —CH_2CH_2—, —$CH_2C(O)$—, —$CH_2C(O)N(CH_3)$—, or —$CH_2C(O)N(CH_3)CH_2CH_2$—; A is azetidinyl, dioxidothiadiazinanyl, dioxoisothiazolidinyl, dioxothiomorpholinyl, morpholinyl, oxetanyl, piperidinyl, pyrazolyl, pyrimidinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydropyranyl, or triazolyl, each substituted wtih -L_2R_a and zero to 1 R_b; L_2 is a bond; R_a is H, F, —CH_3, —CN, —CH_2OH, or —$S(O)_2CH_3$; and R_b is F, —CH_3, —CF_3, or —OCH_3. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (6);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (198);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetamide (199);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxy methyl)-[1,2,4]triazolo[1,5-a]pyridine (200);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetonitrile (201);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (202);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethane-1-sulfonamide (203);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (470);

6-(3-isopropyl-5-(1-((2-methylpyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (471);

6-(3-isopropyl-5-(1-((3-methyl oxetan-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (472);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (473);

2-(2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethyl) isothiazolidine 1,1-dioxide (474);

N-(2-cyanoethyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (811);

(S)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (812);

1-(1,1-di oxido-1,2,4-thi adiazinan-4-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (813);

N-(3-hydroxypropyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (814);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl-N-(tetrahydro-2H-pyran-4-yl)acetamide (815);

N-ethyl-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetamide (816);

N,N-diethyl-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (817);

N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (818);

N-ethyl-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (819);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(2-methoxyethyl)-N-methylacetamide (820);

N-isopropyl-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (821);

1-((2R,4R)-2-(hydroxymethyl)-4-methoxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (822);

(S)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl-N-(tetrahydrofuran-3-yl)acetamide (823);

1-((2R,4R)-2-(hydroxymethyl)-4-(trifluoromethyppyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (824);

N-ethyl-N-(2-hydroxyethyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (825);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(3-(methylsulfonyl)azetidin-1-yl)ethan-1-one (826);

1-(1,1-dioxidothiomorpholino)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (827);

N-(2-hydroxy-2-methylpropyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (828);

(R)-1-(3-(hydroxymethyl)morpholino)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (829);

1-(4,4-difluoropiperidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (830);

1-(3,3-dimethyl azetidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (831);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(3,3,3-trifluoropropyl)acetamide (832);

1-(3,3-difluoropyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (833);

N-(1-cyclopropyl-3-hydroxypropyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (834);

(R)-1-(2-(hydroxymethyl)pyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (835);

N-(2-(1H-pyrazol-4-yl) ethyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl acetamide (836);

1-((2R,4R)-2-(hydroxymethyl)-4-methylpyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (837);

1-(2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetyl) azetidine-3-carbonitrile (838);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl-N-(tetrahydrofuran-3-yl)acetamide (839);

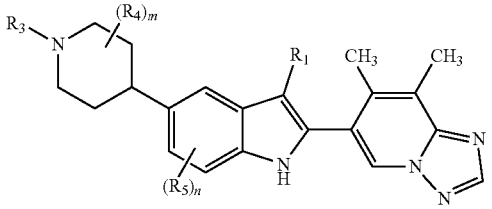
1-(3,3-difluoroazetidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (840);

1-((2S,4S)-2-(hydroxymethyl)-4-(trifluoromethyl)pyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (841); or

N-(2-cyanoethyl)-2-(4-(3-isopropyl-2-(8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (842).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-6):

(I-6)



and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is $—CH(CH_3)_2$ or $—CH_2CHF_2$. Included in this embodiment are compounds in which R_3 is H, C_{1-5} alkyl, C_{1-2} cyanoalkyl, $—CH_2CH_2CF_3$, $—CH_2C(CH_3)_2OH$, $—CH_2CH_3$, $—CH_2CH_2OCH_3$, $—CH_2N(CH_3)_2$, $—CH_2C(O)NH_2$, $—CH_2C(O)NH(CH_3)$, $—CH_2C(O)N(CH_3)_2$, $—CH_2C(O)N(CH_3)(CH_2CH_2OH)$, $—CH_2CH_2S(O)_2CH_3$, $—CH_2CH_2S(O)_2NH_2$, $—CH_2CH_2S(O)_2N(CH_3)_2$, $—CH_2CH_2NHS(O)_2CH_3$, $—CH_2CH_2N(CH_3)S(O)_2CH_3$, $—C(O)OCH_2CH_2NH_2$, $—C(O)OCH_2CH_2N(CH_3)_2$, $—C(O)OCH_2CH_2N(CH_2CH_3)_2$, $—C(O)OC(CH_3)_3$, $—C(O)NHCH_2C(CH_3)_3$, $—C(O)NH(CH_2CH_2NH_2)$, $—C(O)NH(CH_2CH_2N(CH_3)_2)$, $—C(O)NH(CH_2CH_2CH_2NH_2)$, $—C(O)N(CH_3)CH_2CH_2NH_2$, $—C(O)CH_2NHCH(CH_3)_2$, $—C(O)CH_2NHC(CH_3)_3$, $—C(O)CH_2NH(CH_3)$, $—C(O)CH_2NH(CH_2CN)$, $—C(O)CH_2NH(CH_2CH_3)$, $—C(O)CH_2NH(CH_2CH_2OH)$, $—C(O)CH_2NH(CH_2CH_2OCH_3)$, $—C(O)CH_2NH(CH_2CH_2F)$, $—C(O)CH_2NH(CH_2CH_2CH_3)$, $—C(O)CH_2NH(CH_2CH(CH_3)_2)$, $—C(O)CH_2NH(CH_2CF_3)$, $—C(O)CH_2NH(CH_2C(O)NH_2)$, $—C(O)CH_2N(CH_3)CH_2CH_3$, $—C(O)CH_2N(CH_3)CH_2CH_2CN$, $—C(O)CH_2N(CH_3)CH_2CH_2CH_3$, $—C(O)CH_2N(CH_3)CH_2CH(CH_3)_2$, $—C(O)CH_2N(CH_3)CH_2C(O)N(CH_3)_2$, $—C(O)CH_2N(CH_3)CH(CH_3)_2$, $—C(O)CH_2N(CH_3)_2$, $—C(O)CH_2N(CH_3)(CH_2CH_2OH)$, $—C(O)CH_2N(CH_3)(CH_2CH_2OCH_3)$, $—C(O)CH_2N(CH_2CH_3)_2$, $—C(O)CH_2N(CH_2CH_2OCH_3)_2$, $—C(O)CH_2CH_2NH(CH_3)$, $—C(O)CH_2CH_2NH(CH_2CH_3)$, $—C(O)CH_2CH_2NH(CH_2CH_2OH)$, $—C(O)CH_2CH_2NH(CH_2CH_2OCH_3)$, $—C(O)CH_2CH_2NH(CH_2CH_2F)$, $—C(O)CH_2CH_2NH(CH_2CH_2CH_3)$, $—C(O)CH_2CH_2NH(CH_2C(O)NH_2)$, $—C(O)CH_2CH_2NH(CH_2C(CH_3)_3)$, $—C(O)CH_2CH_2NH(CH(CH_3)_2)$, $—C(O)CH_2CH_2N(CH_3)CH_2CH_2OH$, $—C(O)CH_2CH_2N(CH_3)CH_2CH_2OCH_3$, $—C(O)CH_2CH_2N(CH_3)CH_2C(O)N(CH_3)_2$, $—C(O)CH_2CH_2N(CH_3)(CH_2CH_3)$, $—C(O)CH_2CH_2N(CH_3)(CH_2CH_2CH_3)$, $—C(O)CH_2CH_2N(CH_3)(CH(CH_3)_2)$, or $-L_1$-A; L_1 is $—CH_2—$, $—CH_2CH_2—$, —CH(CN)—, —C(O)—, $—C(O)CH_2—$, $—C(O)CH_2CH_2—$, $—C(O)CH_2NH—$, $—C(O)CH_2N(CH_3)—$, $—C(O)CH_2CH_2NH—$, $—C(O)CH_2CH_2N(CH_3)—$, $—C(O)CH_2NHCH_2—$, $—C(O)CH_2CH_2NHCH_2—$, $—CH_2C(O)—$, $—CH_2C(O)NH—$, —C(O)NH—, $—C(O)NHCH_2—$, $—C(O)NHCH_2CH_2—$, —C(O)O—, $—C(O)OCH_2—$, or $—C(O)OCH_2CH_2—$; and A is azepanyl, azetidinyl, cyclobutyl, cyclohexyl, cyclopentyl, cyclopropyl, dioxoisothiazolidinyl, di oxotetrahydrothiopyranyl, dioxothiomorpholinyl, imidazolyl, morpholinyl, octahydropyrrolo[3,4-b]pyridinyl, oxa-azaspiro[3.3]heptan-6-yl, oxetanyl, piperazinonyl, piperazinyl, piperidinonyl, piperidinyl, pyridinyl, pyrimidinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydropyranyl, triazolonyl, or triazolyl; azetidinyl, cyclobutyl, dioxanyl, dioxotetrahydrothiopyranyl, dioxothiomorpholinyl, morpholinyl, oxetanyl, piperazinonyl, pyrrolidinonyl, pyrrolidinyl, tetrahydrofuranyl, or tetrahydropyranyl, each substituted wtih $-L_2R_a$ and zero to 1 R_b; L_2 is a bond; R_a is H, F, C_{1-3} alkyl, C_{1-2} hydroxyalkyl, $—CH_2OCH_3$, $—CH_2CH_2OCH_3$, —OH, $—OCH_3$, $—NH_2$, $—C(O)CH_3$, $—C(O)CH(CH_2CH_3)_2$, $—C(O)NH_2$, $—C(O)N(CH_2CH_3)_2$, $—C(O)OC(CH_3)_3$, $—S(O)_2CH_3$, or pyridinyl; and R_b is F or $—CH_3$. Also included in this embodiment are compounds in which R_1 is $—CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridine (4);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetonitrile (13);

3-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)propanenitrile (14);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) acetamide (15);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (16);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (17);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (18);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethane-1-sulfonamide (19);

4-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (20);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (38);

6-(5-(1-((1H-1,2,3-triazol-5-yl)methyl) piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (39);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (40);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (41);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (42);

6-(3-isopropyl-5-(1-((l-methyl-1H-1,2,4-triazol-3-yl) methyl) piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (43);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (66);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (110);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (124);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (125);

N-(2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethyl) methanesulfonamide (204);

N-(2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethyl)-N-methylmethanesulfonamide (205);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylethane-1-sulfonamide (206);

2-(2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethypisothiazolidine 1,1-dioxide (475);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(3-methyloxetan-3-yl)acetonitrile (476);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-morpholinoethan-1-one (477);

6-(5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (478);

6-(5-(1-isopentylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (479);

6-(5-(1-ethylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (480);

6-(3-isopropyl-5-(1-propylpiperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridine (481);

6-(5-(1-ethylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (482);

5-((4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methyl)-2,4-dihydro-3H-1,2,4-triazol-3-one (483);

6-(3-isopropyl-5-(1-(3,3,3-trifluoropropyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine(484);

6-(3-isopropyl-5-(1-methylpiperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (485);

6-(3-isopropyl-5-(1-(2-methoxyethyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (486);

tert-butyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (609);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-morpholinopropan-1-one (610);

2-(bis(2-methoxyethyl)amino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (718);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(3-hydroxypyrrolidin-1-yl)ethan-1-one (719);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(2,6-dimethylmorpholino)ethan-1-one (720);

1 (1 (2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-oxoethyl)piperidin-3-yl)-2-ethylbutan-1-one (721);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(2-(methoxymethyl) pyrrolidin-1-yl)ethan-1-one (722);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(isobutyl(methyl)amino)ethan-1-one (723);

1-(2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-oxoethyl)piperidine-4-carboxamide (724);

4-(2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-oxoethyl)piperazin-2-one (725);

3-((2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-oxoethyl)(methyl)amino)propanenitrile (726);

2-(cyclopentylamino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (727);

2-(cyclohexylamino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (728);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-((4-hydroxycyclohexyl)amino)ethan-1-one (729);

2-((cyclohexylmethyl)amino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (730);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(((tetrahydrofuran-2-yl)methyl)amino)ethan-1-one (731);

2-(tert-butylamino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (732);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(neopentylamino)ethan-1-one (733);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(propylamino) ethan-1-one (734);

(R)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(3-hydroxypyrrolidin-1-yl)ethan-1-one (735);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(3-hydroxypyrrolidin-1-yl)ethan-1-one (736);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(isopropylamino)ethan-1-one (737);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(3-fluoropyrrolidin-1-yl)ethan-1-one (738);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-((2-fluoroethyl)amino)ethan-1-one (739);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(ethylamino) ethan-1-one (740);

2-(4,4-difluoropiperidin-1-yl)-1-(4-(2-(7,8-dimethyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (741);

2-(cyclopropylamino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (742);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-((2-methoxyethyl)amino)ethan-1-one (743);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(piperidin-1-yl)ethan-1-one (744);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(pyrrolidin-1-yl) ethan-1-one (745);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(isobutylamino)ethan-1-one (746);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(3,3-dimethylpiperidin-1-yl)ethan-1-one (747);

2-((2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-oxoethyl)amino)acetamide (748);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(2-(hydroxymethyl)pyrrolidin-1-yl)ethan-1-one (749);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(4-methoxypiperidin-1-yl)ethan-1-one (750);

2-(cyclohexyl(methyl)amino)-1-(4-(2-(7,8-dimethyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (751);

2-((2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-oxoethyl)amino)acetonitrile (752);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methyl amino) ethan-1-one (753);

2-(azepan-1-yl)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl) ethan-1-one (754);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(4-hydroxypiperidin-1-yl)ethan-1-one (755);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-((2-hydroxyethyl)(methyl)amino) ethan-1-one (756);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-((2-hydroxyethyl) amino)ethan-1-one (757);

2-((cyclopropylmethyl)amino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (758);

2-((2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-oxoethyl)(methyl)amino)-N,N-dimethylacetamide (759);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-((2-methoxyethyl)(methyl)amino)ethan-1-one (760);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-((2,2,2-trifluoroethyl)amino)ethan-1-one (761);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methyl (propyl)amino)ethan-1-one (762);

2-(diethylamino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (763);

2-(cycl ° butyl amino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (764);

2-(azetidin-1-yl)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (765);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(ethyl(methyl) amino)ethan-1-one (766);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(isopropyl (methyl)amino)ethan-1-one (767);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-1-morpholino-ethan-1-one (843);

1-(azetidin-1-yl)-2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (844);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-1-(3-(methylsulfonyl)azetidin-1-yl)ethan-1-one (845);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-(3-methyloxetan-3-yl)acetamide (846);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-1-(1,1-dioxidothiomorpholino)ethan-1-one (847);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N-(2-hydroxyethyl)-N-methylacetamide (848);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-1-(2-oxa-6-azaspiro [3.3]heptan-6-yl)ethan-1-one (849);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-((4-hydroxycyclohexyl)amino)propan-1-one (886);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-(((tetrahydrofuran-2-yl)methyl)amino)propan-1-one (887);

(R)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(3-fluoropyrrolidin-1-yl)propan-1-one (888);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-((2-hydroxyethypamino)propan-1-one (889);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(propylamino) propan-1-one (890);

2-((3-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-oxopropyl)amino)acetamide (891);

3-((cyclopropylmethyl)amino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)propan-1-one (892);

3-(azetidin-1-yl)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl) propan-1-one (893);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(ethyl(methyl) amino)propan-1-one (894);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(methyl(propyl)amino)propan-1-one (895);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(isopropyl (methyl)amino)propan-1-one (896);

2-((3-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-oxopropyl)(methyl)amino)-N,N-dimethylacetamide (897);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-((2-methoxyethyl)(methyl)amino)propan-1-one (898);

(R)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-(3-hydroxypyrrolidin-1-yl)propan-1-one (899);

3-(4,4-difluoropiperidin-1-yl)-1-(4-(2-(7,8-dimethyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl) propan-1-one (900);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-((2-methoxyethyl)amino)propan-1-one (901);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(i sopropyl amino)propan-1-one (902);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(ethylamino) propan-1-one (903);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(piperidin-1-yl)propan-1-one (904);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(methylamino) propan-1-one (905);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(2,6-dimethylmorpholino)propan-1-one (906);

1-(3-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-oxopropyl)-N,N-diethylpiperidine-3-carboxamide (907);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(3,3-dimethylpiperidin-1-yl)propan-1-one (908);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-(4-hydroxypiperidin-1-yl)propan-1-one (909);

3-(azepan-1-yl)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) propan-1-one (910);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-(2-(methoxymethyl)pyrrolidin-1-yl)propan-1-one (911);

1-(3-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-oxopropyl)piperidine-4-carboxamide (912);

4-(3-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-oxopropyl) piperazin-2-one (913);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-((2-hydroxyethyl)(methyl)amino)propan-1-one (914);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(4-methoxypiperidin-1-yl)propan-1-one (915);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(pyrrolidin-1-yl)propan-1-one (916);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-(2-(hydroxymethyl)pyrrolidin-1-yl)propan-1-one (917);

3-(cycl ° butyl amino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)propan-1-one (918);

3-(cyclopentylamino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)propan-1-one (919);

3-(cycl ohexyl amino)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)propan-1-one (920);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(3-fluoropyrrolidin-1-yl)propan-1-one (921);

(S)-1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-(3-hydroxypyrrolidin-1-yl)propan-1-one (922);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(3-hydroxypyrrolidin-1-yl)propan-1-one (923);

3-(cyclohexyl(methyl)amino)-1-(4-(2-(7,8-dimethyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)propan-1-one (924);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-((2-fluoroethyl)amino)propan-1-one (925);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-(neopentylamino)propan-1-one (926);

azetidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (927);

2-aminoethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (928);

(R)-pyrrolidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (929);

piperidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (930);

(S)-pyrrolidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (931);

piperidin-3-ylmethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (932);

(S)-pyrrolidin-2-ylmethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (933);

3-aminopropyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (934);

piperidin-4-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (935);

piperidin-4-ylmethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (936);

pyrrolidin-2-ylmethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (937-938);

(R)-pyrrolidin-3-ylmethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (939);

pyrrolidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (940);

azetidin-3-ylmethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (941);

(S)-(1-methylpyrrolidin-2-yl) methyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (942);

2-(dimethylamino)ethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (943);

2-(1H-imidazol-1-yl)ethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (944);

1-isopropylpyrrolidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (945);

2-(1,1-dioxidothiomorpholino)ethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (946);

2-(piperidin-1-yl)ethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (947);

2-(pyrrolidin-1-yl)ethyl
4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (948);

2-(diethylamino)ethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (949);

(1-(2-methoxyethyl)pyrrolidin-3-yl)methyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (950);

2-(4-methylpiperazin-1-yl)ethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (951);

2-morpholinoethyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (952);

(R)-(1-methylpyrrolidin-2-yl)methyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (953);

1-methylpyrrolidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (954);

1-(2-methoxyethyl)azetidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (955);

1-propylazetidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (956);

(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(4-methylpiperazin-1-yl)methanone (957);

(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(4-(2-hydroxyethyl)piperazin-1-yl)methanone (958);

N-(3-aminopropyl)-4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxamide (959);

(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)methanone ((960);

(R)-4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(pyrrolidin-3-yl)piperidine-1-carboxamide (961);

N-(2-aminoethyl)-4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxamide (962);

4-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carbonyl)-1-methylpiperazin-2-one (963);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(piperidin-3-yl)piperidine-1-carboxamide (964);

(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(4-propylpiperazin-1-yl)methanone (965);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(piperidin-2-ylmethyl) piperidine-1-carboxamide (966);

(3-aminoazetidin-1-yl)(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)methanone (967);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(pyrrolidin-3-yl) piperidine-1-carboxamide (968);

(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(4-(pyridin-4-yl) piperazin-1-yl)methanone (969);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(piperidin-4-ylmethyl)piperidine-1-carboxamide (970);

(S)-4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(pyrrolidin-3-yl)piperidine-1-carboxamide (971);

N-(2-aminoethyl)-4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-methylpiperidine-1-carboxamide (972);

(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(4-isopropylpiperazin-1-yl) methanone (973);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(2-(pyrrolidin-1-yl)ethyl)piperidine-1-carboxamide (974);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-((1-(2-methoxyethyl) pyrrolidin-2-yl)methyl)piperidine-1-carboxamide (975);

4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(2-(4-methylpip erazin-1-yl) ethyl) piperidine-1-carboxamide (976);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-((1-methylpyrrolidin-2-yl) methyl)piperidine-1-carboxamide (977);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(2-(dimethylamino)ethyl)piperidine-1-carboxamide (978);

4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(2-morpholinoethyl)piperidine-1-carboxamide (979);

4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-N-(2-(piperidin-1-yl)ethyl)piperidine-1-carboxamide (980);

6-(3-isopropyl-5-(1-(pyridin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (986);

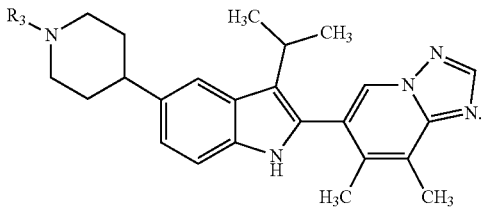
1-(6-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)pyridin-3-yl)-N,N-dimethylmethanamine (987);

1-(2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)pyridin-4-yl)-N,N-dimethylmethanamine (988); or

6-(3-isopropyl-5-(1-(pyrimidin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (989).

One embodiment provides a compound of Formula (I-6) or a salt thereof, wherein R_1 is —$CH(CH_3)_2$; m is zero; n is zero, and R_3 is defined in the first aspect or the second aspect. Compounds of this embodiment have the structure of Formula (I-6a)

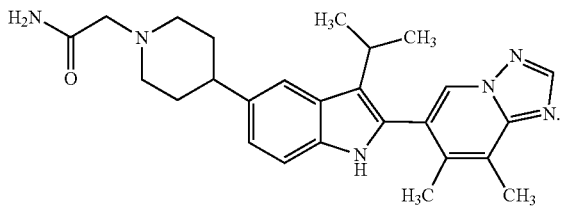
(I-6a)



Included in this embodiment are compounds in which R_3 is —$(CR_xR_x)_{1-2}C(O)NR_yR_y$, wherein each R_x is independently H or —CH_3; and each R_x is independently H or —CH_3. Also included in this embodiment are compounds in which R_3 is —$CH_2C(O)NH_2$, —$CH_2C(O)NH(CH_3)$, or —$CH_2C(O)N(CH_3)_2$.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from:

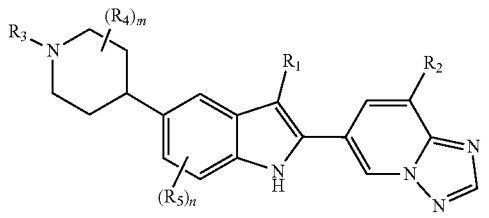
(15)



Included in this embodiment is 2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl) acetamide (15). Also included in this embodiment is one or more salts of 2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) acetamide (15).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-7):

(I-7)



wherein R_2 is F, Cl, —CN, —NH_2, —CH_2CH_3, —$CH(CH_3)_2$, —CF_3, C_{1-3} hydroxyalkyl, —CH_2CN, —$CH_2OCH_2CH_3$, —OCH_2F, —OCH_2CH_3, —$OCH_2CH(CH_3)_2$, —OCH_2CH_2OH, —$OCH_2CH_2OC(O)CH_3$, —$NH(CH_2CH_3)$, —$NH(CH_2CF_3)$, —$NH(CH_2C(CH_3)_2OH)$, —$NHCH_2$(phenyl), —$NHS(O)_2$(cyclopropyl), cyclopropyl, morpholinyl, methyl-piperazinyl, or dioxothiomorpholinyl; and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$. Included in this embodiment are compounds in which R_3 is H, C_{3-4} alkyl, C_{1-2} cyanoalkyl, —$CH_2C(CH_3)_2OH$, —$CH_2C(O)N(CH_3)_2$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)NH_2$, —$CH_2CH_2NHS(O)_2CH_3$, —$CH_2CH_2S(O)_2CH_3$, —$CH_2CH_2S(O)_2NH_2$, —$C(O)CH_2CF_3$, —$C(O)CH_2CH_2OH$, —$C(O)CH(CH_3)OH$, —$C(O)CH_2CH(CH_3)OH$, —$C(O)CH_2C(CH_3)_2OH$, —$C(O)CH_2OCH_3$, —$C(O)CH_2CH_2OCH_3$, —$C(O)CH_2NH(CH_3)$, —$C(O)CH_2N(CH_3)_2$, —$C(O)CH_2N(CH_3)(CH_2CH_3)$, —$C(O)CH_2N(CH_3)CH(CH_3)_2$, —$C(O)CH_2CH_2N(CH_3)_2$, or -$L_1$-A; L_1 is —CH_2—, —CH_2CH_2—, —C(O)—, —$C(O)CH_2$—, —$C(O)CH_2CH_2$—, —$C(O)CH_2N(CH_3)$—, —$CH_2C(O)$—; and A is cyclopropyl, dioxoisothiazolidinyl, dioxotetrahydrothiopyranyl, morpholinyl, oxetanyl, piperidinyl, pyrazinyl, pyrazolyl, pyrimidinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrazolyl, thiadiazolyl, thiazolyl, or triazolyl, each substituted with -L_2R_a; L_2 is a bond; and R_a is H, —CN, —CH_3, —CF_3, or —OCH_3. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from

8-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (94);

8-isopropyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (95);

8-(ethoxymethyl)-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (99);

2-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (100);

1-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-ol (103);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile (111);

8-fluoro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine(112);

(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (113);

2-((6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)oxy)ethan-1-ol (114);

2-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo [1,5-a]pyridin-8-yl)ethan-1-01 (115);

2-((6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)oxy)ethyl acetate (116);

8-chloro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (118);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (128);

8-ethoxy-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (132);

8-isobutoxy-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (136);

4-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) morpholine (143);

N-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo [1,5-a]pyridin-8-amine (144);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-N-(2,2,2-trifluoroethyl)-[1,2,4]triazolo[1,5-a]pyridin-8-amine (145);

1-((6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)amino)-2-methylpropan-2-ol (146);

N-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) cyclopropanesulfonamide (147);

4-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)thiomorpholine 1,1-dioxide (148);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-(4-methylpiperazin-1-yl)-[1,2,4]triazolo[1,5-a]pyridine (149);

8-cyclopropyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (151);

N-benzyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-amine (159);

8-(difluoromethoxy)-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (160);

2-(4-(2-(8-(ethoxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (163);

2-(4-(2-(8-fluoro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (193);

8-fluoro-6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (194);

2-(4-(2-(8-fluoro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetonitrile (195);

2-(4-(2-(8-fluoro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)acetamide (196);

2-(4-(2-(8-fluoro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (197);

3 (4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl) propanenitrile (211);

2 (4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) acetonitrile (212);

2 (4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl) acetamide (213);

2-(6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) propan-2-ol (214);

N-(2-(4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ethyl)methanesulfonamide (215);

2 (4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (216);

2 (4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (217);

2 (4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ethane-1-sulfonamide (218);

N-(2-(4-(2-(8 cyano-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)ethyl)methanesulfonamide (220);

6-(5-(1-(2-hydroxy-2-methylpropyl) piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile (221);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carb onitril e (222);

6-(5-(1-(cyanomethyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile (223);

2-(4-(2-(8-cyano-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (224);

2 (4-(2-(8 (1 hydroxyethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (225);

2-(4-(2-(8-(cyanomethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (228);

2 (4-(2-(8 (1 hydroxyethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetonitrile (229);

2-(4-(2-(8-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (231);

2-(4-(2-(8-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl -1H-indol-5-yl)piperidin-1-yl)acetonitrile (232);

(6-(3-isopropyl-5-(1-(2-(methyl sul fonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) methanol (233);

2-(4-(2-(8-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl -1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (234);

3-(4-(2-(8-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)oxetane-3-carbonitrile (235);

2 (4-(2-(8 (2 hydroxyethoxy)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (236);

2-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (250);

2-(4-(3-isopropyl-2-(8-(tri fluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (251);

1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (252);

2-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetonitrile (253);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoro methyl)-[1,2,4]triazolo[1,5-a]pyridine (254);

2-(4-(2-(8-ethoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (268);

2-(4-(2-(8-ethoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (269);

1-(4-(2-(8-ethoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (270);

2-(4-(2-(8-isobutoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (278);

2-(4-(2-(8-isobutoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (279);

2-(4-(2-(8-chloro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (280);

2-(4-(2-(8-chloro-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (281);

1-(4-(2-(8-chloro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (282);

2-(4-(3-isopropyl-2-(8-morpholino-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (291);

2-(4-(3-isopropyl-2-(8-morpholino-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (292);

2-(4-(2-(8-ethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (293); 2-(4-(2-(8-ethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (294);

2-(4-(3-isopropyl-2-(8-isopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (295);

2-(4-(3-isopropyl-2-(8-isopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (296);

2-(4-(2-(8-(ethylamino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (297);

2-(4-(3-isopropyl-2-(8-((2,2,2-trifluoroethyl)amino)-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (298);

2-(4-(3-isopropyl-2-(8-((2,2,2-trifluoroethyl)amino)-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (299);

2-(4-(2-(8-((2-hydroxy-2-methylpropyl) amino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (300);

2-(4-(2-(8-((2-hydroxy-2-methylpropyl)amino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (301);

2-(4-(2-(8-(cyclopropanesulfonamido)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (307);

2-(4-(2-(8-(1,1-dioxidothiomorpholino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (308);

2-(4-(2-(8-(1,1-dioxidothiomorpholino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (309);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-(4-methyl piperazin-1-yl)-[1,2,4]triazolo[1,5-a]pyridine (310);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-(4-methyl piperazin-1-yl)-[1,2,4]triazolo[1,5-a]pyridine (311);

2-(4-(2-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (319);

2-(4-(2-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (320);

8-cyclopropyl-6-(3-isopropyl-5-(1-(2-(methylsulfonyl) ethyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (321);

1-(4-(2-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (322);

2-(4-(2-(8-(difluoromethoxy)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (347);

2-(4-(2-(8-(benzylamino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (348);

8-fluoro-6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo [1,5-a]pyridine (468);

8-fluoro-6-(3-isopropyl-5-(1-(oxetan-3-yl)pip eri di n-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (469);

2-(6-(3-isopropyl-5-(1-((2-methylpyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (490);

2-(6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-3-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (491);

2-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (492);

2-(6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (493);

2-(6-(3-isopropyl-5-(1-(pyrimi din-2-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (494);

2-(6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (495);

4-(4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) tetrahydro-2H-thiopyran 1,1-dioxide (496);

2-(6-(5-(1-((1H-1,2,3-triazol-4-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (497);

2 (2-(4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl) ethyl)isothiazolidine 1,1-dioxide (498);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile (500);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile (501);

1-(6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-ol (502);

1-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-ol (503);

2-(6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)acetonitrile (506);

(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (510);

(6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1, 5-a]pyridin-8-yl)methanol (511);

(6-(3-isopropyl-5-(1-((2-methylpyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (512);

(6-(5-(1-((1H-1,2,3-triazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (513);

4-(4-(2-(8-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (514);

(6-(3-isopropyl-5-(1-((2-methoxypyrimi din-5-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (515);

(6-(3-isopropyl-5-(1-((1-methyl-1H-pyrazol-3-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (516);

(6-(3-isopropyl-5-(1-(pyrimidin-5-ylmethyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) methanol (517);

(6-(5-(1-((1,2,3-thiadiazol-4-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (518);

(6-(3-isopropyl-5-(1-((2-methylpyrimidin-4-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (519);

(6-(3-isopropyl-5-(1-(pyrimidin-2-ylmethyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (520);

(6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) methanol (521);

(6-(3-isopropyl-5-(1-((2-methyl-2H-tetrazol-5-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (522);

(6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1, 5-a]pyridin-8-yl)methanol (523);

(6-(3-isopropyl-5-(1-((5-methylpyrazin-2-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (524);

2-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-ol (525);

2-(6-(3-isopropyl-5-(1-((2-methylpyrimidin-5-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-01 (526);

2-(6-(3-isopropyl-5-(1-((l-methyl-1H-1,2,3-triazol-4-yl) methyl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1, 5-a]pyridin-8-yl)ethan-1-ol (527);

2-((6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) oxy)ethyl acetate (528);

2-((6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)oxy)ethan-1-ol (529-530);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (549);

4-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1, 5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (550);

6-(3-isopropyl-5-(1-isopropylpiperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (551);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1, 5-a]pyridine (552);

6-(5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (553);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1, 5-a]pyridine (554);

6-(3-isopropyl-5-(1-((3-methyloxetan-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (555);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a] pyridine (556-557);

8-ethoxy-6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (571);

8-ethoxy-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (572);

4-(4-(2-(8-ethoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (573);

4-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl) morpholine (581);

8-ethyl-6-(5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (582);

8-ethyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (583);

6-(5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-isopropyl-[1,2,4]triazolo[1,5-a]pyridine (584);

8-isopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (585);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-N-(2,2,2-trifluoroethyl)-[1,2,4]triazolo[1,5-a]pyridin-8-amine (586);

N-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)cyclopropanesulfonamide (590);

4-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)thiomorpholine 1,1-dioxide (591);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(4-methylpiperazin-1-yl)-[1,2,4]triazolo[1,5-a] pyridine (592);

8-cyclopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (593);

2-(dimethylamino)-1-(4-(2-(8-fluoro-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (640);

1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1, 5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (641);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (642);

1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1, 5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methoxyethan-1-one (643);

1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1, 5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-(piperidin-1-yl)propan-1-one (644);

(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)(tetrahydrofuran-2-yl)methanone (645);

1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-methoxypropan-1-one (646);

3-hydroxy-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propan-1-one (647);

3,3,3-trifluoro-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propan-1-one (648);

3-(dimethylamino)-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)propan-1-one (649);

1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(2-methylthiazol-4-yl)ethan-1-one (650);

3-hydroxy-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-methylbutan-1-one (651);

2-hydroxy-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)propan-1-one (652);

(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(1-(trifluoromethyl)cyclopropyl) methanone (653);

(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)(oxetan-3-yl) methanone (654);

1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-morpholinoethan-1-one (655);

2-(dimethylamino)-1-(4-(2-(8-ethoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (680);

1-(4-(2-(8-ethoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (681);

2-(dimethylamino)-1-(4-(2-(8-isobutoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (684);

(S)-1-(4-(2-(8-chloro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (685);

1-(4-(2-(8-chloro-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino) ethan-1-one (686);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-morpholino-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (690);

2-(dimethylamino)-1-(4-(2-(8-(1,1-dioxidothiomorpholino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (691);

1-(4-(2-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (696);

1-(4-(2-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (697);

2-(i sopropyl(methyl)amino)-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (777);

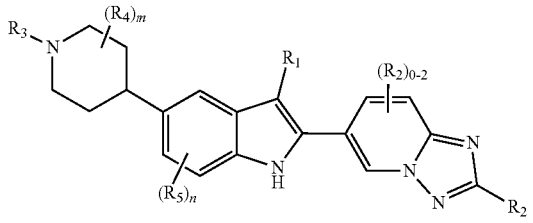
2-(ethyl(methyl)amino)-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (778);

2-(cyclopropyl(methyl)amino)-1-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (779);

2 (4-(2-(8 (2 hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-1-morpholinoethan-1-one (850); and 2-(4-(2-(8-amino-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (990).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-8):

(I-8)



wherein each R_2 is independently F, Cl, —NH_2, $C_{1\text{-}2}$ alkyl, —CF_3, —OCH_3, —OCH_2CH_3, —$OCHF_2$, cyclopropyl, or morpholinyl; and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —CH_2CH_3, —$CH(CH_3)_2$, or —CH_2CHF_2. Included in this embodiment are compounds in which R_3 is H, —$CH(CH_3)_2$, —$CH_2CH(CH_3)_2$, —$CH_2C(CH_3)_2OH$, —$CH_2C(O)NH(CH_3)$, —$CH_2C(O)N(CH_3)_2$, —$C(O)CH_2CH(CH_3)OH$, —$C(O)CH_2C(CH_3)_2OH$, —$C(O)CH_2NH(CH_3)$, —$C(O)CH_2N(CH_3)_2$, or -L_1-A; L_1 is —CH_2—, —C(O)—, or —$CH_2C(O)$—; and A is dioxotetrahydrothiopyranyl, dioxothiomorpholinyl, imidazolyl, morpholinyl, oxetanyl, pyrazolyl, pyrrolidinyl, tetrahydrofuranyl, or tetrahydropyranyl, each substituted wtih -L_2R_a and zero to 1 R_b; L_2 is a bond; R_a is H, —OH, —CH_3, or —$C(O)OC(CH_3)_3$; and R_b is —OH. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from

8-chloro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (96);

8-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (97);

6-(3-ethyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-2-amine (109);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (120);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (122);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (124);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (125);

8-fluoro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (126);

7-fluoro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (127);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (133);

8-(difluoromethoxy)-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (134);

8-ethoxy-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (135);

8-chloro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (138);

8-cyclopropyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (141);

6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (142);

4-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl) morpholine (150);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (153);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (154);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (155);

6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (162);

2-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methyl acetamide (237);

2-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (238);

1-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (239);

2-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (244);

2-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (245);

1-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (246);

2-(4-(2-(2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (247);

2-(4-(2-(2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (248);

1-(4-(2-(2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (249);

2-(4-(3-(2,2-difluoroethyl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (255);

2-(4-(3-(2,2-difluoroethyl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (256);

2-(4-(2-(2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (257);

2-(4-(2-(2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (258);

2-(4-(3-isopropyl-2-(2-methyl-8-(trifluoromethyl)-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (259);

2-(4-(2-(8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (260);

2-(4-(2-(8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (261);

1-(4-(2-(8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-methylpropan-2-ol (262);

2-(4-(3-isopropyl-2-(8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (271);

2-(4-(3-isopropyl-2-(8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (272);

1-(4-(3-isopropyl-2-(8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (273);

2-(4-(2-(8-(difluoromethoxy)-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (274);

2-(4-(2-(8-(difluoromethoxy)-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (275);

2-(4-(2-(8-ethoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (276);

2-(4-(2-(8-ethoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (277);

2-(4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (283);

1-(4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (284);

2-(4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (285);

2-(4-(3-isopropyl-2-(8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (312);

2-(4-(3-isopropyl-2-(8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (313);

1-(4-(3-isopropyl-2-(8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (314);

2-(4-(3-isopropyl-2-(2-methyl-8-morpholino-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (315);

2-(4-(3-isopropyl-2-(2-methyl-8-morpholino-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (316);

2-(4-(3-isopropyl-2-(8-methoxy-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (317);

2-(4-(3-isopropyl-2-(8-methoxy-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (318);

2-(4-(2-(8-cyclopropyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (323);

1-(4-(2-(8-cyclopropyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indo 1-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (324);

2-(4-(2-(8-cyclopropyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indo 1-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (325);

2-(4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (345);

2-(4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (346);

2-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylethan-1-amine (531);

6-(3-isopropyl-5-(1-((2-methyl-1H-imidazol-4-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo [1,5-a]pyridine (532);

6-(3-isopropyl-5-(1-isopropylpiperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (533);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo [1,5-a]pyridine (534);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl[1,2,4]triazolo[1,5-a]pyridine (535);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (542);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine (543);

6-(5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (544);

4-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) tetrahydro-2H-thiopyran 1,1-dioxide (545);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl) piperidin-4-yl)-1H-indol-2-yl)-2,7-dimethyl-[1,2,4]triazolo[1,5-a] pyridine (546);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (547);

4-(4-(2-(2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (548);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (558);

6-(3-isopropyl-5-(1-isopropylpiperidin-4-yl)-1H-indol-2-yl)-2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (559);

6-(3-isopropyl-5-(1-((l-methyl-1H-pyraz ol-4-yl)methyl) piperidin-4-yl)-1H-indol-2-yl)-2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (560);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (574);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (575-576);

8-ethyl-6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (577);

8-ethyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (578);

8-cyclopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (594);

6-(3-isopropyl-5-(1-isopropylpiperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridine (599);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(2-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (612);

(R)-3-hydroxy-1-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) butan-1-one (613);

3-hydroxy-1-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-methylbutan-1-one (614);

((2S,3R)-3-hydroxypyrrolidin-2-yl)(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (615);

((2S,4R)-4-hydroxypyrrolidin-2-yl)(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (616);

(S)-3-hydroxy-1-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl) butan-1-one (617);

1-(4-(3-isopropyl-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (618);

1-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (629);

1-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (630);

(S)-1-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-hydroxybutan-1-one (631);

1-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-hydroxy-3-methylbutan-1-one (632);

(R)-1-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-3-hydroxybutan-1-one (633);

tert-butyl (2S,3R)-2-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carbonyl)-3-hydroxypyrrolidine-1-carboxylate (634);

(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)((2S,3R)-3-hydroxypyrrolidin-2-yl)methanone (635);

(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) ((2S,4R)-4-hydroxypyrrolidin-2-yl)methanone (636);

(S)-1-(4-(2-(2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (637);

1-(4-(2-(2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(dimethylamino)ethan-1-one (638);

1-(4-(2-(2,7-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methyl amino)ethan-1-one (639);

1-(4-(3-(2,2-difluoroethyl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-(dimethylamino)ethan-1-one(656);

(R)-1-(4-(3-(2,2-di fluoroethyl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (657);

1-(4-(3-(2,2-difluoroethyl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-3-hydroxy-3-methylbutan-1-one (658);

1-(4-(3-(2,2-difluoroethyl)-2-(2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-(methylamino)ethan-1-one (659);

1-(4-(2-(2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (660);

1-(4-(2-(2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (661);

1-(4-(2-(8-chl oro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(dimethylamino)ethan-1-one (662);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (682);

1-(4-(3-isopropyl-2-(8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (683);

2-(dimethylamino)-1-(4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (687);

1-(4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(methylamino)ethan-1-one (688);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (692);

1-(4-(3-isopropyl-2-(8-methyl-2-(trifluoromethyl)-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (693);

(4-(3-isopropyl-2-(8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) (1-methylpiperidin-4-yl)methanone (694);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methoxy-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (695);

1-(4-(2-(8-cyclopropyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (698);

1-(4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (708);

(S)-1-(4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (709);

1-(4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-hydroxy-3-methylbutan-1-one (710);

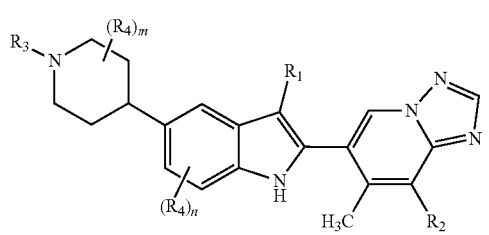
1-(4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (711);

2-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one (851);

2-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-1-morpholinoethan-1-one (852); and

2-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-1-(1,1-dioxidothiomorpholino)ethan-1-one (853).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-9):



(I-9)

wherein R_2 is F, Cl, $—CH_2CH_3$, $—CF_3$, $—OCH_3$, $—CH_2OH$, $—CH_2OCH_3$, or cyclopropyl; and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is $—CH(CH_3)_2$. Included in this embodiment are compounds in which R_3 is H, $—CH(CH_3)_2$, $—CH_2CH(CH_3)_2$, $—CH_2C(CH_3)_2OH$, $—CH_2C(O)NH(CH_3)$, $—CH_2C(O)N(CH_3)_2$, $—C(O)CH_2CH(CH_3)OH$, $—C(O)CH_2C(CH_3)_2OH$, $—C(O)CH_2NH(CH_3)$, $—C(O)CH_2N(CH_3)_2$, or $-L_1$-A; L_1 is $—CH_2—$, $—CH_2C(O)NHCH_2—$, or $—CH_2C(O)—$; and A is azetidinyl, dioxothiomorpholinyl, morpholinyl, oxetanyl, tetrahydropyranyl, or triazolyl, each substituted wtih $-L_2R_a$; L_2 is a bond; R_a is H or $—CH_3$. Also included in this embodiment are compounds in which R_1 is $—CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from tert-butyl

4-(2-(8-ethyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (98);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (101);

8-fluoro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (102);

(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (104);

8-fluoro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (106);

8-fluoro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (107);

8-chloro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (119);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (140);

8-cyclopropyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (152);

2-(4-(3-isopropyl-2-(8-(methoxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (219);

2-(4-(2-(8-(hydroxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (226);

2-(4-(2-(8-(hydroxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) acetonitrile (227);

2-(4-(2-(8-chloro-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (286);

1-(4-(2-(8-chloro-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-methylpropan-2-ol (287);

2-(4-(2-(8-chloro-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (288);

2-(4-(2-(8-chloro-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (289);

8-chloro-6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (290);

2-(4-(2-(8-ethyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (302);

2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (303);

2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (304);

1-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (305);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (306);

2-(4-(2-(8-cyclopropyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (326);

2-(4-(2-(8-cyclopropyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-1-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (327);

1-(4-(2-(8-cyclopropyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (328);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (499);

(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (504);

(6-(5-(1-((1H-1,2,3-triazol-4-yl) methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (505);

8-fluoro-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (507);

8-chloro-6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (579);

8-chloro-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (580);

8-ethyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (587); 6-(3-isopropyl-5-(1-(oxetan-3-yl) piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (588);

6-(3-isopropyl-5-(1-((3-methyloxetan-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (589);

8-cyclopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (595);

1-(4-(2-(8-chloro-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(dimethylamino)ethan-1-one (689);

1-(4-(2-(8-cyclopropyl-7-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (699);

1-(4-(2-(8-cyclopropyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one (700);

2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-((3-methyloxetan-3-yl)methyl)acetamide (876);

2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(3-methyloxetan-3-yl) acetamide (877);

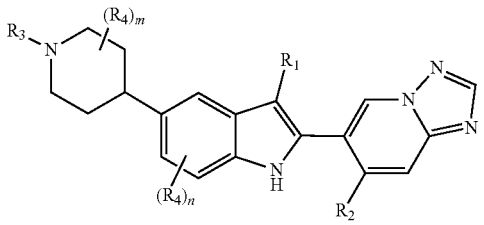
1-(azetidin-1-yl)-2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (878);

N-ethyl-2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (879);

1-(1,1-dioxidothiomorpholino)-2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (880); and 2-(4-(3-isopropyl-2-(8-methoxy-7-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-morpholinoethan-1-one (881).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-10):

(I-10)



wherein R_2 is —CH_3, —OCH_3, or —CH_2OH; and R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$. Included in this embodiment are compounds in which R_3 is H, —CH_2CN, —$CH_2C(O)NH_2$, —$CH_2C(O)N(CH_3)_2$, —CH_2(triazolyl), or oxetanyl. Also included in this embodiment are compounds in which R_1 is —$CH(CH_3)_2$; m is zero; and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from (6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo [1,5-a]pyridin-7-yl)methanol (108);

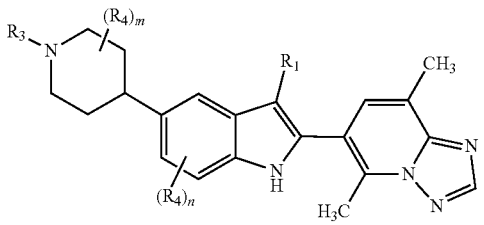
6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methoxy-[1,2,4]triazolo[1,5-a]pyridine (131); 2-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (192);

2-(4-(2-(7-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetonitrile (230);

2-(4-(3-isopropyl-2-(7-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (267); (6-(3-isopropyl-5-(1-(oxetan-3-yl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-7-yl)methanol (508); and (6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-7-yl)methanol (509).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound has the structure of Formula (I-11):

(I-11)



wherein R_1, R_3, R_4, R_5, m, and n are defined in the first aspect or the second aspect. Included in this embodiment are compounds in which R_1 is $—CH(CH_3)_2$. Included in this embodiment are compounds in which R_3 is $—CH_2CN$, $—CH_2C(O)N(CH_3)_2$, $—CH_2CH_2S(O)_2CH_3$, $—CH_2$(methyltriazolyl), $—C(O)CH_2N(CH_3)_2$, dioxotetrahydrothiopyranyl, oxetanyl, or tetrahydropyranyl. Also included in this embodiment are compounds in which R_1 is $—CH(CH_3)_2$; m is zero, and n is zero.

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from

2-(4-(2-(5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (207);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (208);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-5,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine (209);

2-(4-(2-(5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetonitrile (210);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (487);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-5,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine (488);

4-(4-(2-(5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (489);

and 1-(4-(2-(5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (611).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from

2-(6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4] triazolo[1,5-a]pyridin-8-ypacetonitrile (105);

and 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-5-methyl-[1,2,4]triazolo[1,5-a]pyridine (123);

One embodiment provides a compound of Formula (I) or a salt thereof, wherein said compound is selected from

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (1);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine hydrochloride (2);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (3);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (4);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (5);

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (6);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (7);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetonitrile (8);

3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) propanenitrile (9);

6-(5-(1-butylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (10);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (11);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (12);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetonitrile (13);

3-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)propanenitrile (14);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) acetamide (15);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (16);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (17);

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine (18);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)ethane-1-sulfonamide (19);

4-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (20);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetonitrile (21);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetamide (22);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (23);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methylpropan-2-ol (24);

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (25);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (26);

6-(3-isopropyl-5-(1-isopropylpiperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (27);

6-(3-isopropyl-5-(1-propylpiperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (28);

6-(5-(1-isobutylpiperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (29);

6-(5-(1-((1H-pyrazol-5-yl)methyl) piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (30);

4-((4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methyl)oxazole (31);

6-(5-(1-((1H-1,2,3-triazol-4-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a] pyridine (32);

6-(5-(1-((4H-1,2,4-triazol-3-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a] pyridine (33);

6-(5-(1-((1H-tetrazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (34);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (35);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (36);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) tetrahydro-2H-thiopyran 1,1-dioxide (37);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (38);

6-(5-(1-((1H-1,2,3-triazol-5-yl)methyl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (39);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl) piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine (40);

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (41);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,3-triazol-4-yl) methyl) piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (42);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-3-yl) methyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (43);

6-(3-isopropyl-5-(1-(oxetan-3-yl) piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (44);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (45);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (46);

1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-2-(methylamino)ethan-1-one (47);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (48);

3-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-oxopropanenitrile (49);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (50);

1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (51);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methoxyethan-1-one (52);

(S)-1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-3-hydroxybutan-1-one (53);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-4-oxobutanenitrile (54);

(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone (55);

(S)-azetidin-2-yl(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)methanone (56);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (57);

(S)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)propan-1-one (58);

(R)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)propan-1-one (59);

(S)-3-hydroxy-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl) butan-1-one (60);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-3-methoxypropan-1-one (61);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino) ethan-1-one (62);

1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-methoxyethan-1-one (63);

(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)(3-methyloxetan-3-yl) methanone (64);

2-ethyl-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)butan-1-one (65);

1-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(dimethylamino)ethan-1-one (66);

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methoxy-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (67);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-morpholinoethan-1-one (68);

2-(tert-butylamino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (69);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(isopropylamino)ethan-1-one (70);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-((2-methoxyethyl)amino)ethan-1-one (71);

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-2-(propylamino) ethan-1-one (72);

2-(isopropyl (methyl)amino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl) ethan-1-one (73);

1-(1,1-dioxido-1,2,4-thiadiazinan-4-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one (74);

N-cyclopropyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) acetamide (75);

N-ethyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (76);

(S)-1-(3-hydroxypiperidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (77);

N-cyclobutyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (78);

2-(4-3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-1-(2-oxa-6-azaspiro [3.3]heptan-6-yl)ethan-1-one (79);

N,N-diethyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetamide (80);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-propylacetamide (81);

(R)-1-(3-hydroxypiperidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (82);

(S)-1-(3-hydroxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (83);

(R)-1-(3-hydroxypyrrolidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (84);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-1-(4-(2-methoxyethyl) piperazin-1-yl)ethan-1-one (85);

1-(azetidin-1-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl) ethan-1-one (86);

N-isopropyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetamide (87);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-morpholino-ethan-1-one (88);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-1-(piperidin-1-yl)ethan-1-one (89);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-(pyrrolidin-1-yl)ethan-1-one (90);

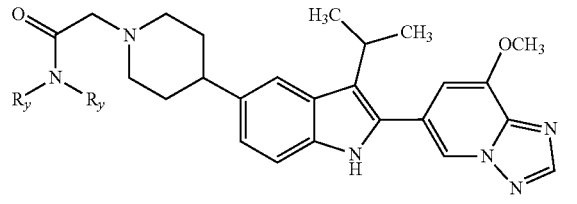
1-(1,1-dioxidothiomorpholino)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one (91);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-(3-methyl-oxetan-3-yl) acetamide (92);

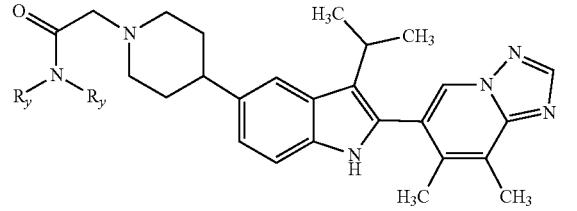
and N-cyclopropyl-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4] triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide (93).

One embodiment provides a compound of Formula (I) or a salt thereof, wherein R_1 is $—CH(CH_3)_2$; each R_2 is independently $—CH_3$ or $—OCH_3$; R_3 is $—(CR_xR_x)_{1-2}C(O)NR_yR_y$; m is zero, n is zero, p is 1 or 2; each R_x is independently H or $—CH_3$; and each R_y is independently H or $—CH_3$. Included in this embodiment are compounds in which R_3 is $—CH_2C(O)NR_yR_y$. Also included in this embodiment are compounds having the structure of Formula (I-4b) or Formula (I-6b) in which each R_y is H or $—CH_3$:

(I-4b)



(I-6b)



Additionally, included in this embodiment are compounds in which R_3 is $—CH_2C(O)NH_2$ or $—CH_2C(O)N(CH_3)_2$.

The present invention may be embodied in other specific forms without departing from the spirit or essential attributes thereof. The invention encompasses all combinations of the aspects and/or embodiments of the invention noted herein. It is understood that any and all embodiments of the present invention may be taken in conjunction with any other embodiment or embodiments to describe additional embodiments. It is also to be understood that each individual element of the embodiments is meant to be combined with any and all other elements from any embodiment to describe an additional embodiment.

Definitions

The features and advantages of the invention may be more readily understood by those of ordinary skill in the art upon reading the following detailed description. It is to be appreciated that certain features of the invention that are, for clarity reasons, described above and below in the context of separate embodiments, may also be combined to form a single embodiment. Conversely, various features of the invention that are, for brevity reasons, described in the context of a single embodiment, may also be combined so as to form sub-combinations thereof. Embodiments identified herein as exemplary or preferred are intended to be illustrative and not limiting.

Unless specifically stated otherwise herein, references made in the singular may also include the plural. For example, "a" and "an" may refer to either one, or one or more.

As used herein, the phrase "compounds" refers to at least one compound. For example, a compound of Formula (I) includes a compound of Formula (I) and two or more compounds of Formula (I).

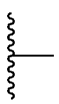
Unless otherwise indicated, any heteroatom with unsatisfied valences is assumed to have hydrogen atoms sufficient to satisfy the valences.

The definitions set forth herein take precedence over definitions set forth in any patent, patent application, and/or patent application publication incorporated herein by reference.

Listed below are definitions of various terms used to describe the present invention. These definitions apply to the terms as they are used throughout the specification (unless they are otherwise limited in specific instances) either individually or as part of a larger group.

Throughout the specification, groups and substituents thereof may be chosen by one skilled in the field to provide stable moieties and compounds.

In accordance with a convention used in the art,



is used in structural formulas herein to depict the bond that is the point of attachment of the moiety or substituent to the core or backbone structure.

The terms "halo" and "halogen," as used herein, refer to F, Cl, Br, and I.

The term "cyano" refers to the group —CN.

The term "amino" refers to the group $—NH_2$.

The term "oxo" refers to the group =O.

The term "alkyl" as used herein, refers to both branched and straight-chain saturated aliphatic hydrocarbon groups containing, for example, from 1 to 12 carbon atoms, from 1 to 6 carbon atoms, and from 1 to 4 carbon atoms. Examples of alkyl groups include, but are not limited to, methyl (Me), ethyl (Et), propyl (e.g., n-propyl and i-propyl), butyl (e.g., n-butyl, i-butyl, sec-butyl, and t-butyl), and pentyl (e.g., n-pentyl, isopentyl, neopentyl), n-hexyl, 2-methylpentyl, 2-ethylbutyl, 3-methylpentyl, and 4-methylpentyl. When numbers appear in a subscript after the symbol "C", the subscript defines with more specificity the number of carbon atoms that a particular group may contain. For example, "C_{1-6} alkyl" denotes straight and branched chain alkyl groups with one to six carbon atoms.

The term "fluoroalkyl" as used herein is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups substituted with one or more fluorine atoms. For example, "C_{1-4} fluoroalkyl" is intended to include C_1, C_2, C_3, and C_4 alkyl groups substituted with one or more fluorine atoms. Representative examples of fluoroalkyl groups include, but are not limited to, —CF_3 and —CH_2CF_3.

The term "chloroalkyl" as used herein is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups substituted with one or more chlorine atoms. For example, "C_{1-4} chloroalkyl" is intended to include C_1, C_2, C_3, and C_4 alkyl groups substituted with one or more chlorine atoms. Representative examples of fluoroalkyl groups include, but are not limited to, —CCl_3 and —CH_2CCl_3.

The term "cyanoalkyl" includes both branched and straight-chain saturated alkyl groups substituted with one or more cyano groups. For example, "cyanoalkyl" includes —CH_2CN, —CH_2CH_2CN, and C_{1-4} cyanoalkyl.

The term "aminoalkyl" includes both branched and straight-chain saturated alkyl groups substituted with one or more amine groups. For example, "aminoalkyl" includes —CH_2NH_2, —$CH_2CH_2NH_2$, and C_{1-4} aminoalkyl.

The term "hydroxyalkyl" includes both branched and straight-chain saturated alkyl groups substituted with one or more hydroxyl groups. For example, "hydroxyalkyl" includes —CH_2OH, —CH_2CH_2OH, and C_{1-4} hydroxyalkyl.

The term "hydroxy-fluoroalkyl" includes both branched and straight-chain saturated alkyl groups substituted with one or more hydroxyl groups and one or more fluorine atoms. For example, "hydroxy-fluoroalkyl" includes —$CHFCH_2OH$, —$CH_2CHFC(CH_3)_2OH$, and C_{1-4} hydroxyfluoroalkyl.

The term "cycloalkyl," as used herein, refers to a group derived from a non-aromatic monocyclic or polycyclic hydrocarbon molecule by removal of one hydrogen atom from a saturated ring carbon atom. Representative examples of cycloalkyl groups include, but are not limited to, cyclopropyl, cyclopentyl, and cyclohexyl. When numbers appear in a subscript after the symbol "C", the subscript defines with more specificity the number of carbon atoms that a particular cycloalkyl group may contain. For example, "C_3-C_6 cycloalkyl" denotes cycloalkyl groups with three to six carbon atoms.

The term "alkoxy," as used herein, refers to an alkyl group attached to the parent molecular moiety through an oxygen atom, for example, methoxy group (—OCH_3). For example, "C_{1-3} alkoxy" denotes alkoxy groups with one to three carbon atoms.

The terms "fluoroalkoxy" and "—O(fluoroalkyl)" represent a fluoroalkyl group as defined above attached through an oxygen linkage (—O—). For example, "C_{1-4} fluoroalkoxy" is intended to include C_1, C_2, C_3, and C_4 fluoroalkoxy groups.

The term "alkoxyalkoxy," as used herein, refers to an alkoxy group attached through its oxygen atom to a carbon atom in a second alkoxy group, which is attached to the parent molecular moiety through an oxygen atom, for example, methoxymethoxy group (—OCH_2OCH_3). For example, "C_{2-4} alkoxyalkoxy" denotes alkoxyalkoxy groups with two to four carbon atoms, such as —OCH_2OCH_3, —$OCH_2CH_2OCH_3$, —$OCH_2OCH_2CH_3$, and —$OCH_2CH_2OCH_2CH_3$.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

The compounds of Formula (I) can be provided as amorphous solids or crystalline solids. Lyophilization can be employed to provide the compounds of Formula (I) as amorphous solids.

It should further be understood that solvates (e.g., hydrates) of the compounds of Formula (I) are also within the scope of the present invention. The term "solvate" means a physical association of a compound of Formula (I) with one or more solvent molecules, whether organic or inorganic. This physical association includes hydrogen bonding. In certain instances the solvate will be capable of isolation, for example when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. "Solvate" encompasses both solution-phase and isolable solvates. Exemplary solvates include hydrates, ethanolates, methanolates, isopropanolates, acetonitrile solvates, and ethyl acetate solvates. Methods of solvation are known in the art.

Various forms of prodrugs are well known in the art and are described in:

a) The Practice of Medicinal Chemistry, Camille G. Wermuth et al., Ch 31, (Academic Press, 1996);

b) Design of Prodrugs, edited by H. Bundgaard, (Elsevier, 1985);

c) A Textbook of Drug Design and Development, P. KrogsgaardLarson and H. Bundgaard, eds. Ch 5, pgs 113-191 (Harwood Academic Publishers, 1991); and

d) Hydrolysis in Drug and Prodrug Metabolism, Bernard Testa and Joachim M. Mayer, (Wiley-VCH, 2003).

In addition, compounds of Formula (I), subsequent to their preparation, can be isolated and purified to obtain a composition containing an amount by weight equal to or greater than 99% of a compound of Formula (I) ("substantially pure"), which is then used or formulated as described herein. Such "substantially pure" compounds of Formula (I) are also contemplated herein as part of the present invention.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent. The present invention is intended to embody stable compounds.

"Therapeutically effective amount" is intended to include an amount of a compound of the present invention alone or an amount of the combination of compounds claimed or an amount of a compound of the present invention in combination with other active ingredients effective to act as an inhibitor to TLR7/8/9, or effective to treat or prevent auto-

immune and/or inflammatory disease states, such as SLE, IBD, multiple sclerosis (MS), and Sjögren's syndrome, and rheumatoid arthritis.

As used herein, "treating" or "treatment" cover the treatment of a disease-state in a mammal, particularly in a human, and include: (a) preventing the disease-state from occurring in a mammal, in particular, when such mammal is predisposed to the disease-state but has not yet been diagnosed as having it; (b) inhibiting the disease-state, i.e., arresting its development; and/or (c) relieving the disease-state, i.e., causing regression of the disease state.

The compounds of the present invention are intended to include all isotopes of atoms occurring in the present compounds. Isotopes include those atoms having the same atomic number but different mass numbers. By way of general example and without limitation, isotopes of hydrogen include deuterium (D) and tritium (T). Isotopes of carbon include ^{13}C and ^{14}C. Isotopically-labeled compounds of the invention can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described herein, using an appropriate isotopically-labeled reagent in place of the non-labeled reagent otherwise employed. For example, methyl (—CH_3) also includes deuterated methyl groups such as —CD_3.

Utility

The human immune system has evolved to defend the body from micro-organisms, viruses, and parasites that can cause infection, disease or death. Complex regulatory mechanisms ensure that the various cellular components of the immune system target the foreign substances or organisms, while not causing permanent or significant damage to the individual. While the initiating events are not well understood at this time, in autoimmune disease states the immune system directs its inflammatory response to target organs in the afflicted individual. Different autoimmune diseases are typically characterized by the predominate or initial target organ or tissues affected; such as the joint in the case of rheumatoid arthritis, the thyroid gland in the case of Hashimoto's thyroiditis, the central nervous system in the case of multiple sclerosis, the pancreas in the case of type I diabetes, and the bowel in the case of inflammatory bowel disease.

The compounds of the invention inhibit signaling through Toll-like receptor 7, or 8, or 9 (TLR7, TLR8, TLR9) or combinations thereof. Accordingly, compounds of Formula (I) have utility in treating conditions associated with the inhibition of signaling through one or more of TLR7, TLR8, or TLR9. Such conditions include TLR7, TLR8, or TLR9 receptor associated diseases in which cytokine levels are modulated as a consequence of intracellular signaling.

As used herein, the terms "treating" or "treatment" encompass the treatment of a disease state in a mammal, particularly in a human, and include: (a) preventing or delaying the occurrence of the disease state in a mammal, in particular, when such mammal is predisposed to the disease state but has not yet been diagnosed as having it; (b) inhibiting the disease state, i.e., arresting its development; and/or (c) achieving a full or partial reduction of the symptoms or disease state, and/or alleviating, ameliorating, lessening, or curing the disease or disorder and/or its symptoms.

In view of their activity as selective inhibitors of TLR7, TLR8, or TLR9, compounds of Formula (I) are useful in treating TLR7, TLR8, or TLR9 family receptor associated diseases, but not limited to, inflammatory diseases such as Crohn's disease, ulcerative colitis, asthma, graft versus host disease, allograft rejection, chronic obstructive pulmonary disease; autoimmune diseases such as Graves' disease, rheumatoid arthritis, systemic lupus erythematosis, lupus nephritis, cutaneous lupus, psoriasis; auto-inflammatory diseases including Cryopyrin-Associated Periodic Syndromes (CAPS), TNF Receptor Associated Periodic Syndrome (TRAPS), Familial Mediterranean Fever (FMF), adult onset stills, systemic onset juvenile idiopathic arthritis, gout, gouty arthritis; metabolic diseases including type 2 diabetes, atherosclerosis, myocardial infarction; destructive bone disorders such as bone resorption disease, osteoarthritis, osteoporosis, multiple myeloma-related bone disorder; proliferative disorders such as acute myelogenous leukemia, chronic myelogenous leukemia; angiogenic disorders such as angiogenic disorders including solid tumors, ocular neovasculization, and infantile haemangiomas; infectious diseases such as sepsis, septic shock, and Shigellosis; neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, cerebral ischemias or neurodegenerative disease caused by traumatic injury, oncologic and viral diseases such as metastatic melanoma, Kaposi's sarcoma, multiple myeloma, and HIV infection and CMV retinitis, AIDS, respectively.

More particularly, the specific conditions or diseases that may be treated with the inventive compounds include, without limitation, pancreatitis (acute or chronic), asthma, allergies, adult respiratory distress syndrome, chronic obstructive pulmonary disease, glomerulonephritis, rheumatoid arthritis, systemic lupus erythematosis, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, graft vs. host disease, inflammatory reaction induced by endotoxin, tuberculosis, atherosclerosis, muscle degeneration, cachexia, psoriatic arthritis, Reiter's syndrome, gout, traumatic arthritis, rubella arthritis, acute synovitis, pancreatic β-cell disease; diseases characterized by massive neutrophil infiltration; rheumatoid spondylitis, gouty arthritis and other arthritic conditions, cerebral malaria, chronic pulmonary inflammatory disease, silicosis, pulmonary sarcoidosis, bone resorption disease, allograft rejections, fever and myalgias due to infection, cachexia secondary to infection, keloid formation, scar tissue formation, ulcerative colitis, pyresis, influenza, osteoporosis, osteoarthritis, acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma, sepsis, septic shock, and Shigellosis; Alzheimer's disease, Parkinson's disease, cerebral ischemias or neurodegenerative disease caused by traumatic injury; angiogenic disorders including solid tumors, ocular neovasculization, and infantile haemangiomas; viral diseases including acute hepatitis infection (including hepatitis A, hepatitis B and hepatitis C), HIV infection and CMV retinitis, AIDS, ARC or malignancy, and herpes; stroke, myocardial ischemia, ischemia in stroke heart attacks, organ hypoxia, vascular hyperplasia, cardiac and renal reperfusion injury, thrombosis, cardiac hypertrophy, thrombin-induced platelet aggregation, endotoxemia and/or toxic shock syndrome, conditions associated with prostaglandin endoperoxidase syndase-2, and pemphigus vulgaris. Included in this embodiment are methods of treatment in which the condition is selected from lupus including lupus nephritis and systemic lupus erythematosus (SLE), Crohn's disease, ulcerative colitis, allograft rejection, rheumatoid arthritis, psoriasis, ankylosing spondylitis, psoriatic arthritis, and pemphigus vulgaris. Also included are methods of treatment in

which the condition is selected from ischemia reperfusion injury, including cerebral ischemia reperfusions injury arising from stroke and cardiac ischemia reperfusion injury arising from myocardial infarction. Another method of treatment is one in which the condition is multiple myeloma.

In one embodiment, the compounds of Formula (I) are useful in treating cancer, including Waldenstrom's Macroglobulinemia (WM), diffuse large B cell lymphoma (DLBCL), chronic lymphocytic leukemia (CLL), cutaneous diffuse large B cell lymphoma, and primary CNS lymphoma.

In addition, the TLR7, TLR8, or TLR9 inhibitors of the present invention inhibit the expression of inducible pro-inflammatory proteins such as prostaglandin endoperoxide synthase-2 (PGHS-2), also referred to as cyclooxygenase-2 (COX-2), IL-1, IL-6, IL-18, chemokines. Accordingly, additional TLR7/8/9 associated conditions include edema, analgesia, fever and pain, such as neuromuscular pain, headache, pain caused by cancer, dental pain and arthritis pain. The inventive compounds also may be used to treat veterinary viral infections, such as lentivirus infections, including, but not limited to equine infectious anemia virus; or retrovirus infections, including feline immunodeficiency virus, bovine immunodeficiency virus, and canine immunodeficiency virus.

The present invention thus provides methods for treating such conditions, comprising administering to a subject in need thereof a therapeutically-effective amount of at least one compound of Formula (I) or a salt thereof. "Therapeutically effective amount" is intended to include an amount of a compound of the present invention that is effective when administered alone or in combination to inhibit autoimmune disease or chronic inflammatory disease.

The methods of treating TLR7, TLR8, or TLR9 associated conditions may comprise administering compounds of Formula (I) alone or in combination with each other and/or other suitable therapeutic agents useful in treating such conditions. Accordingly, "therapeutically effective amount" is also intended to include an amount of the combination of compounds claimed that is effective to inhibit TLR7, TLR8, or TLR9 and/or treat diseases associated with TLR7, TLR8, or TLR9.

Exemplary of such other therapeutic agents include corticosteroids, rolipram, calphostin, cytokine-suppressive anti-inflammatory drugs (CSAIDs), Interleukin-10, glucocorticoids, salicylates, nitric oxide, and other immunosuppressants; nuclear translocation inhibitors, such as deoxyspergualin (DSG); non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, celecoxib and rofecoxib; steroids such as prednisone or dexamethasone; antiviral agents such as abacavir; antiproliferative agents such as methotrexate, leflunomide, FK506 (tacrolimus, PROGRAF®); anti-malarials such as hydroxychloroquine; cytotoxic drugs such as azathiprine and cyclophosphamide; TNF-α inhibitors such as tenidap, anti-TNF antibodies or soluble TNF receptor, and rapamycin (sirolimus or RAPAMUNE®) or derivatives thereof.

The above other therapeutic agents, when employed in combination with the compounds of the present invention, may be used, for example, in those amounts indicated in the Physicians' Desk Reference (PDR) or as otherwise determined by one of ordinary skill in the art. In the methods of the present invention, such other therapeutic agent(s) may be administered prior to, simultaneously with, or following the administration of the inventive compounds. The present invention also provides pharmaceutical compositions capable of treating TLR7/8/9 receptor-associated conditions, including IL-1 family receptor-mediated diseases as described above.

The inventive compositions may contain other therapeutic agents as described above and may be formulated, for example, by employing conventional solid or liquid vehicles or diluents, as well as pharmaceutical additives of a type appropriate to the mode of desired administration (e.g., excipients, binders, preservatives, stabilizers, flavors, etc.) according to techniques such as those well known in the art of pharmaceutical formulation.

Accordingly, the present invention further includes compositions comprising one or more compounds of Formula (I) and a pharmaceutically acceptable carrier.

A "pharmaceutically acceptable carrier" refers to media generally accepted in the art for the delivery of biologically active agents to animals, in particular, mammals. Pharmaceutically acceptable carriers are formulated according to a number of factors well within the purview of those of ordinary skill in the art. These include without limitation the type and nature of the active agent being formulated; the subject to which the agent-containing composition is to be administered; the intended route of administration of the composition; and, the therapeutic indication being targeted. Pharmaceutically acceptable carriers include both aqueous and non-aqueous liquid media, as well as a variety of solid and semi-solid dosage forms. Such carriers can include a number of different ingredients and additives in addition to the active agent, such additional ingredients being included in the formulation for a variety of reasons, e.g., stabilization of the active agent, binders, etc., well known to those of ordinary skill in the art. Descriptions of suitable pharmaceutically acceptable carriers, and factors involved in their selection, are found in a variety of readily available sources such as, for example, Remington's Pharmaceutical Sciences, 17th Edition (1985), which is incorporated herein by reference in its entirety.

Compounds in accordance with Formula (I) can be administered by any means suitable for the condition to be treated, which can depend on the need for site-specific treatment or quantity of Formula (I) compound to be delivered.

Also embraced within this invention is a class of pharmaceutical compositions comprising a compound of Formula (I) and one or more non-toxic, pharmaceutically-acceptable carriers and/or diluents and/or adjuvants (collectively referred to herein as "carrier" materials) and, if desired, other active ingredients. The compounds of Formula (I) may be administered by any suitable route, preferably in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended. The compounds and compositions of the present invention may, for example, be administered orally, mucosally, or parenterally including intravascularly, intravenously, intraperitoneally, subcutaneously, intramuscularly, and intrasternally in dosage unit formulations containing conventional pharmaceutically acceptable carriers, adjuvants, and vehicles. For example, the pharmaceutical carrier may contain a mixture of mannitol or lactose and microcrystalline cellulose. The mixture may contain additional components such as a lubricating agent, e.g. magnesium stearate and a disintegrating agent such as crospovidone. The carrier mixture may be filled into a gelatin capsule or compressed as a tablet. The pharmaceutical composition may be administered as an oral dosage form or an infusion, for example.

For oral administration, the pharmaceutical composition may be in the form of, for example, a tablet, capsule, liquid capsule, suspension, or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a particular amount of the active ingredient. For example, the pharmaceutical composition may be provided as a tablet or capsule comprising an amount of active ingredient in the range of from about 0.1 to 1000 mg, preferably from about 0.25 to 250 mg, and more preferably from about 0.5 to 100 mg. A suitable daily dose for a human or other mammal may vary widely depending on the condition of the patient and other factors, but, can be determined using routine methods.

Any pharmaceutical composition contemplated herein can, for example, be delivered orally via any acceptable and suitable oral preparations. Exemplary oral preparations, include, but are not limited to, for example, tablets, troches, lozenges, aqueous and oily suspensions, dispersible powders or granules, emulsions, hard and soft capsules, liquid capsules, syrups, and elixirs. Pharmaceutical compositions intended for oral administration can be prepared according to any methods known in the art for manufacturing pharmaceutical compositions intended for oral administration. In order to provide pharmaceutically palatable preparations, a pharmaceutical composition in accordance with the invention can contain at least one agent selected from sweetening agents, flavoring agents, coloring agents, demulcents, antioxidants, and preserving agents.

A tablet can, for example, be prepared by admixing at least one compound of Formula (I) with at least one nontoxic pharmaceutically acceptable excipient suitable for the manufacture of tablets. Exemplary excipients include, but are not limited to, for example, inert diluents, such as, for example, calcium carbonate, sodium carbonate, lactose, calcium phosphate, and sodium phosphate; granulating and disintegrating agents, such as, for example, microcrystalline cellulose, sodium crosscarmellose, corn starch, and alginic acid; binding agents, such as, for example, starch, gelatin, polyvinyl-pyrrolidone, and acacia; and lubricating agents, such as, for example, magnesium stearate, stearic acid, and talc. Additionally, a tablet can either be uncoated, or coated by known techniques to either mask the bad taste of an unpleasant tasting drug, or delay disintegration and absorption of the active ingredient in the gastrointestinal tract thereby sustaining the effects of the active ingredient for a longer period. Exemplary water soluble taste masking materials, include, but are not limited to, hydroxypropyl-methylcellulose and hydroxypropyl-cellulose. Exemplary time delay materials, include, but are not limited to, ethyl cellulose and cellulose acetate butyrate.

Hard gelatin capsules can, for example, be prepared by mixing at least one compound of Formula (I) with at least one inert solid diluent, such as, for example, calcium carbonate; calcium phosphate; and kaolin.

Soft gelatin capsules can, for example, be prepared by mixing at least one compound of Formula (I) with at least one water soluble carrier, such as, for example, polyethylene glycol; and at least one oil medium, such as, for example, peanut oil, liquid paraffin, and olive oil.

An aqueous suspension can be prepared, for example, by admixing at least one compound of Formula (I) with at least one excipient suitable for the manufacture of an aqueous suspension. Exemplary excipients suitable for the manufacture of an aqueous suspension, include, but are not limited to, for example, suspending agents, such as, for example, sodium carboxymethylcellulose, methylcellulose, hydroxypropylmethyl-cellulose, sodium alginate, alginic acid, polyvinyl-pyrrolidone, gum tragacanth, and gum acacia; dispersing or wetting agents, such as, for example, a naturally-occurring phosphatide, e.g., lecithin; condensation products of alkylene oxide with fatty acids, such as, for example, polyoxyethylene stearate; condensation products of ethylene oxide with long chain aliphatic alcohols, such as, for example heptadecaethylene-oxycetanol; condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol, such as, for example, polyoxyethylene sorbitol monooleate; and condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, such as, for example, polyethylene sorbitan monooleate. An aqueous suspension can also contain at least one preservative, such as, for example, ethyl and n-propyl p-hydroxybenzoate; at least one coloring agent; at least one flavoring agent; and/or at least one sweetening agent, including but not limited to, for example, sucrose, saccharin, and aspartame.

Oily suspensions can, for example, be prepared by suspending at least one compound of Formula (I) in either a vegetable oil, such as, for example, arachis oil; olive oil; sesame oil; and coconut oil; or in mineral oil, such as, for example, liquid paraffin. An oily suspension can also contain at least one thickening agent, such as, for example, beeswax; hard paraffin; and cetyl alcohol. In order to provide a palatable oily suspension, at least one of the sweetening agents already described hereinabove, and/or at least one flavoring agent can be added to the oily suspension. An oily suspension can further contain at least one preservative, including, but not limited to, for example, an anti-oxidant, such as, for example, butylated hydroxyanisol, and alpha-tocopherol.

Dispersible powders and granules can, for example, be prepared by admixing at least one compound of Formula (I) with at least one dispersing and/or wetting agent; at least one suspending agent; and/or at least one preservative. Suitable dispersing agents, wetting agents, and suspending agents are as already described above. Exemplary preservatives include, but are not limited to, for example, anti-oxidants, e.g., ascorbic acid. In addition, dispersible powders and granules can also contain at least one excipient, including, but not limited to, for example, sweetening agents; flavoring agents; and coloring agents.

An emulsion of at least one compound of Formula (I) thereof can, for example, be prepared as an oil-in-water emulsion. The oily phase of the emulsions comprising compounds of Formula (I) may be constituted from known ingredients in a known manner. The oil phase can be provided by, but is not limited to, for example, a vegetable oil, such as, for example, olive oil and arachis oil; a mineral oil, such as, for example, liquid paraffin; and mixtures thereof. While the phase may comprise merely an emulsifier, it may comprise a mixture of at least one emulsifier with a fat or an oil or with both a fat and an oil. Suitable emulsifying agents include, but are not limited to, for example, naturally-occurring phosphatides, e.g., soy bean lecithin; esters or partial esters derived from fatty acids and hexitol anhydrides, such as, for example, sorbitan monooleate; and condensation products of partial esters with ethylene oxide, such as, for example, polyoxyethylene sorbitan monooleate. Preferably, a hydrophilic emulsifier is included together with a lipophilic emulsifier which acts as a stabilizer. It is also preferred to include both an oil and a fat. Together, the emulsifier(s) with or without stabilizer(s) make-up the so-called emulsifying wax, and the wax together with the oil and fat make up the so-called emulsifying ointment base which forms the oily dispersed phase of the cream formu-

lations. An emulsion can also contain a sweetening agent, a flavoring agent, a preservative, and/or an antioxidant. Emulsifiers and emulsion stabilizers suitable for use in the formulation of the present invention include Tween 60, Span 80, cetostearyl alcohol, myristyl alcohol, glyceryl monostearate, sodium lauryl sulfate, glyceryl distearate alone or with a wax, or other materials well known in the art.

The compounds of Formula (I) can, for example, also be delivered intravenously, subcutaneously, and/or intramuscularly via any pharmaceutically acceptable and suitable injectable form. Exemplary injectable forms include, but are not limited to, for example, sterile aqueous solutions comprising acceptable vehicles and solvents, such as, for example, water, Ringer's solution, and isotonic sodium chloride solution; sterile oil-in-water microemulsions; and aqueous or oleaginous suspensions.

Formulations for parenteral administration may be in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions. These solutions and suspensions may be prepared from sterile powders or granules using one or more of the carriers or diluents mentioned for use in the formulations for oral administration or by using other suitable dispersing or wetting agents and suspending agents. The compounds may be dissolved in water, polyethylene glycol, propylene glycol, ethanol, corn oil, cottonseed oil, peanut oil, sesame oil, benzyl alcohol, sodium chloride, tragacanth gum, and/or various buffers. Other adjuvants and modes of administration are well and widely known in the pharmaceutical art. The active ingredient may also be administered by injection as a composition with suitable carriers including saline, dextrose, or water, or with cyclodextrin (i.e. Captisol), cosolvent solubilization (i.e. propylene glycol) or micellar solubilization (i.e. Tween 80).

The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed, including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

A sterile injectable oil-in-water microemulsion can, for example, be prepared by 1) dissolving at least one compound of Formula (I) in an oily phase, such as, for example, a mixture of soybean oil and lecithin; 2) combining the Formula (I) containing oil phase with a water and glycerol mixture; and 3) processing the combination to form a microemulsion.

A sterile aqueous or oleaginous suspension can be prepared in accordance with methods already known in the art. For example, a sterile aqueous solution or suspension can be prepared with a non-toxic parenterally-acceptable diluent or solvent, such as, for example, 1,3-butane diol; and a sterile oleaginous suspension can be prepared with a sterile non-toxic acceptable solvent or suspending medium, such as, for example, sterile fixed oils, e.g., synthetic mono- or diglycerides; and fatty acids, such as, for example, oleic acid.

Pharmaceutically acceptable carriers, adjuvants, and vehicles that may be used in the pharmaceutical compositions of this invention include, but are not limited to, ion exchangers, alumina, aluminum stearate, lecithin, self-emulsifying drug delivery systems (SEDDS) such as d-alpha-tocopherol polyethyleneglycol 1000 succinate, surfactants used in pharmaceutical dosage forms such as Tweens, polyethoxylated castor oil such as CREMOPHOR surfactant (BASF), or other similar polymeric delivery matrices, serum proteins, such as human serum albumin, buffer substances such as phosphates, 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 carboxymethylcellulose, polyacrylates, waxes, polyethylene-polyoxypropylene-block polymers, polyethylene glycol and wool fat. Cyclodextrins such as alpha-, beta-, and gamma-cyclodextrin, or chemically modified derivatives such as hydroxyalkylcyclodextrins, including 2- and 3-hydroxypropyl-cyclodextrins, or other solubilized derivatives may also be advantageously used to enhance delivery of compounds of the formulae described herein.

The pharmaceutically active compounds of this invention can be processed in accordance with conventional methods of pharmacy to produce medicinal agents for administration to patients, including humans and other mammals. The pharmaceutical compositions may be subjected to conventional pharmaceutical operations such as sterilization and/or may contain conventional adjuvants, such as preservatives, stabilizers, wetting agents, emulsifiers, buffers etc. Tablets and pills can additionally be prepared with enteric coatings. Such compositions may also comprise adjuvants, such as wetting, sweetening, flavoring, and perfuming agents.

The amounts of compounds that are administered and the dosage regimen for treating a disease condition with the compounds and/or compositions of this invention depends on a variety of factors, including the age, weight, sex, the medical condition of the subject, the type of disease, the severity of the disease, the route and frequency of administration, and the particular compound employed. Thus, the dosage regimen may vary widely, but can be determined routinely using standard methods. A daily dose of about 0.001 to 100 mg/kg body weight, preferably between about 0.0025 and about 50 mg/kg body weight and most preferably between about 0.005 to 10 mg/kg body weight, may be appropriate. The daily dose can be administered in one to four doses per day. Other dosing schedules include one dose per week and one dose per two day cycle.

For therapeutic purposes, the active compounds of this invention are ordinarily combined with one or more adjuvants appropriate to the indicated route of administration. If administered orally, the compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanoic acids, cellulose alkyl esters, talc, stearic acid, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulfuric acids, gelatin, acacia gum, sodium alginate, polyvinylpyrrolidone, and/or polyvinyl alcohol, and then tableted or encapsulated for convenient administration. Such capsules or tablets may contain a controlled-release formulation as may be provided in a dispersion of active compound in hydroxypropylmethyl cellulose.

Pharmaceutical compositions of this invention comprise at least one compound of Formula (I) and optionally an additional agent selected from any pharmaceutically acceptable carrier, adjuvant, and vehicle. Alternate compositions of this invention comprise a compound of the Formula (I) described herein, or a prodrug thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle.

The present invention also encompasses an article of manufacture. As used herein, article of manufacture is intended to include, but not be limited to, kits and packages. The article of manufacture of the present invention, comprises: (a) a first container; (b) a pharmaceutical composition located within the first container, wherein the composition, comprises: a first therapeutic agent, comprising: a compound of the present invention or a pharmaceutically acceptable salt form thereof; and (c) a package insert stating that the pharmaceutical composition can be used for the treatment of a cardiovascular and/or inflammatory disorder (as defined previously). In another embodiment, the package insert states that the pharmaceutical composition can be used in combination (as defined previously) with a second therapeutic agent to treat cardiovascular and/or inflammatory disorder. The article of manufacture can further comprise: (d) a second container, wherein components (a) and (b) are located within the second container and component (c) is located within or outside of the second container. Located within the first and second containers means that the respective container holds the item within its boundaries.

The first container is a receptacle used to hold a pharmaceutical composition. This container can be for manufacturing, storing, shipping, and/or individual/bulk selling. First container is intended to cover a bottle, jar, vial, flask, syringe, tube (e.g., for a cream preparation), or any other container used to manufacture, hold, store, or distribute a pharmaceutical product.

The second container is one used to hold the first container and, optionally, the package insert. Examples of the second container include, but are not limited to, boxes (e.g., cardboard or plastic), crates, cartons, bags (e.g., paper or plastic bags), pouches, and sacks. The package insert can be physically attached to the outside of the first container via tape, glue, staple, or another method of attachment, or it can rest inside the second container without any physical means of attachment to the first container. Alternatively, the package insert is located on the outside of the second container. When located on the outside of the second container, it is preferable that the package insert is physically attached via tape, glue, staple, or another method of attachment. Alternatively, it can be adjacent to or touching the outside of the second container without being physically attached.

The package insert is a label, tag, marker, etc. that recites information relating to the pharmaceutical composition located within the first container. The information recited will usually be determined by the regulatory agency governing the area in which the article of manufacture is to be sold (e.g., the United States Food and Drug Administration). In one embodiment, the package insert specifically recites the indications for which the pharmaceutical composition has been approved. The package insert may be made of any material on which a person can read information contained therein or thereon. For example, the package insert is a printable material (e.g., paper, plastic, cardboard, foil, adhesive-backed paper or plastic, etc.) on which the desired information has been formed (e.g., printed or applied).

Methods of Preparation

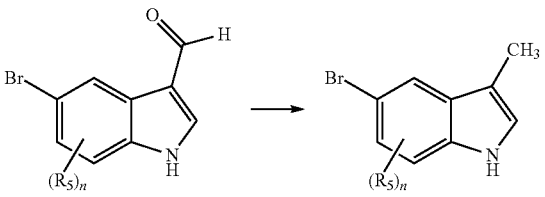
The compounds of the present invention can be prepared in a number of ways well known to one skilled in the art of organic synthesis. The compounds of the present invention can be synthesized using the methods described below, together with synthetic methods known in the art of synthetic organic chemistry, or variations thereon as appreciated by those skilled in the art. Preferred methods include, but are not limited to, those described below. All references cited herein are hereby incorporated in their entirety by reference.

The compounds of this invention may be prepared using the reactions and techniques described in this section. The reactions are performed in solvents appropriate to the reagents and materials employed and are suitable for the transformations being effected. Also, in the description of the synthetic methods described below, it is to be understood that all proposed reaction conditions, including choice of solvent, reaction atmosphere, reaction temperature, duration of the experiment and work up procedures, are chosen to be the conditions standard for that reaction, which should be readily recognized by one skilled in the art. It is understood by one skilled in the art of organic synthesis that the functionality present on various portions of the molecule must be compatible with the reagents and reactions proposed. Such restrictions to the substituents that are compatible with the reaction conditions will be readily apparent to one skilled in the art and alternate methods must then be used. This will sometimes require a judgment to modify the order of the synthetic steps or to select one particular process scheme over another in order to obtain a desired compound of the invention. It will also be recognized that another major consideration in the planning of any synthetic route in this field is the judicious choice of the protecting group used for protection of the reactive functional groups present in the compounds described in this invention. An authoritative account describing the many alternatives to the trained practitioner is Greene and Wuts (Protective Groups In Organic Synthesis, Third Edition, Wiley and Sons, 1999).

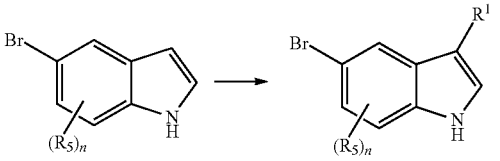
Compounds of Formula (I) may be prepared by reference to the methods illustrated in the following Schemes. As shown therein the end product is a compound having the same structural formula as Formula (I). It will be understood that any compound of Formula (I) may be produced by the schemes by the suitable selection of reagents with appropriate substitution. Solvents, temperatures, pressures, and other reaction conditions may readily be selected by one of ordinary skill in the art. Starting materials are commercially available or readily prepared by one of ordinary skill in the art. Constituents of compounds are as defined herein or elsewhere in the specification.

As shown in Scheme 1, compounds of Formula (I) can be produced, starting with the substituted 5-bromoindoles (2). 2 can be prepared from the 3-formyl indoles (via reduction) or from the 3-H indoles, via alkylation. Transition metal catalyzed cross coupling of 2 and boronate 3 followed by olefin reduction and Boc deprotection affords 4, which can then be coupled with pyridyl boronic acids and deprotected to give 6. Alkylation of 6 leads to the production of the compounds of Formula I.

SCHEME 1

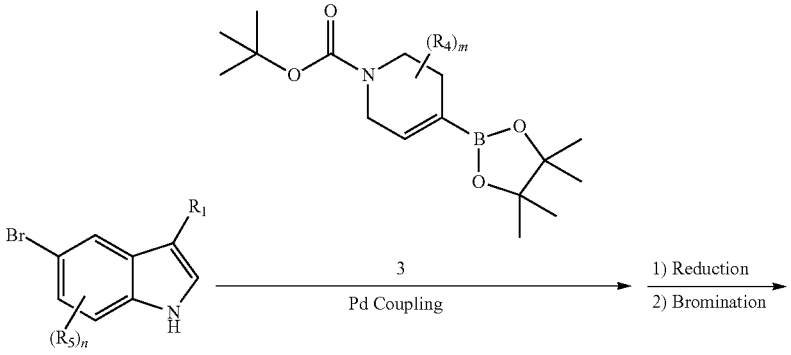


1 2a

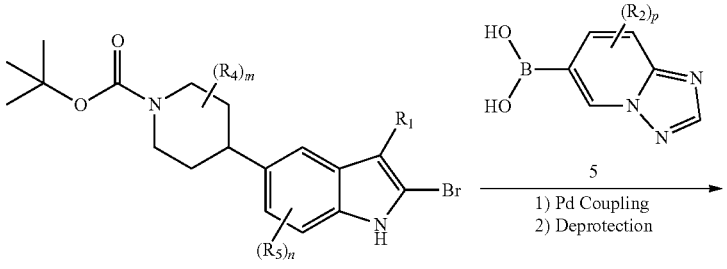


1 2b

R_1 = H, alkyl, fluoroalkyl, cyclopropyl —CH_2(cyclopropyl), —C(O)O(alkyl), or —$C(CF_3)$═CH_2

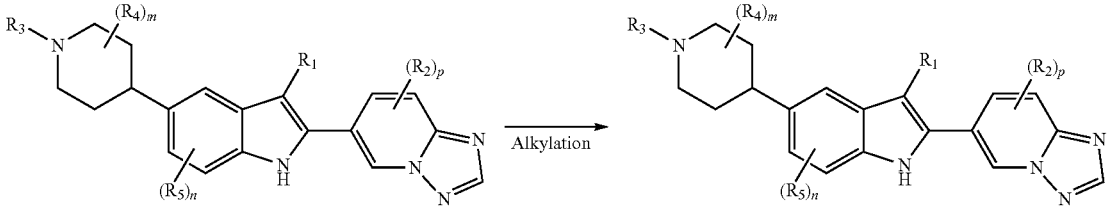


2 3 Pd Coupling 1) Reduction 2) Bromination



4 5 1) Pd Coupling 2) Deprotection

-continued



6 (I)

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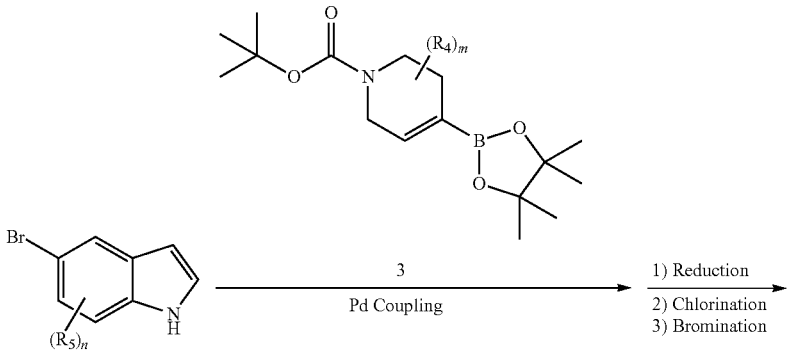
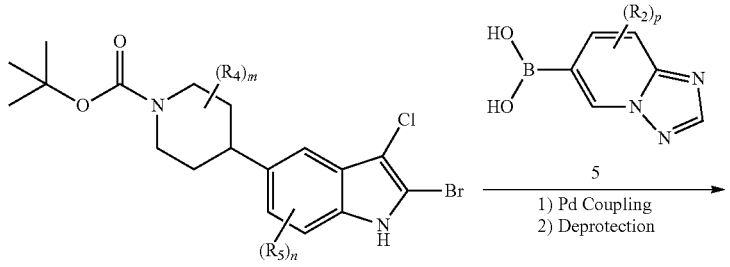
In an alternative preparation, bromoindole 2b can first be coupled with boronate 3 and reduced. Chlorination proceeds selectively on the 3-position, with bromination then providing the di-halogenated compound 7.

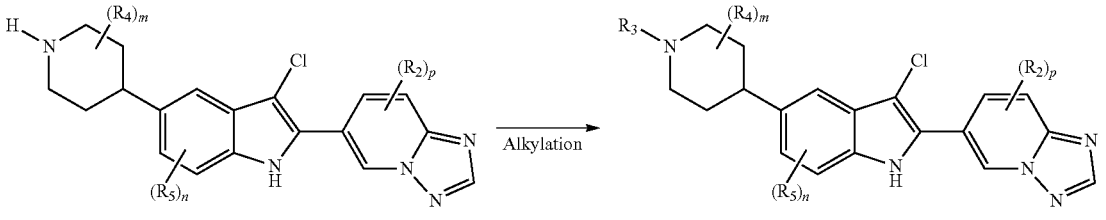
Scheme 2



2b



7



8 9

EXAMPLES

Preparation of compounds of Formula (I), and intermediates used in the preparation of compounds of Formula (I), can be prepared using procedures shown in the following Examples and related procedures. The methods and conditions used in these examples, and the actual compounds prepared in these Examples, are not meant to be limiting, but are meant to demonstrate how the compounds of Formula (I) can be prepared. Starting materials and reagents used in these examples, when not prepared by a procedure described herein, are generally either commercially available, or are reported in the chemical literature, or may be prepared by using procedures described in the chemical literature.

Abbreviations

Ac acetyl
AcOH acetic acid
ACN acetonitrile
AIBN 2,2-azobisiosbutyronitrile
anhyd. anhydrous
aq. aqueous
BH_3DMS boron dimethyl sulfide
Bn benzyl
Bu butyl
Boc tert-butoxycarbonyl
CV Column Volumes
DBU 1,8-diazabicyclo[5.4.0]undec-7-ene
DCE dichloroethane
DCM dichloromethane
DEA diethylamine
DIPEA diisopropylethylamine
DMF dimethylformamide
DMAP dimethylaminopyridine
DMF-DMA N,N-dimethylformamide dimethyl acetal
DMSO dimethylsulfoxide
Et_3N triethylamine
EtOAc ethyl acetate
Et ethyl
EtOH ethanol
Et_2O diethyl ether
H or H_2 hydrogen
h, hr or hrs hour(s)
HATU O-(7-azabenzotriazol-1-yl)-N,N, N', N'-tetramethyl-uronium hexafluorophosphate
hex hexane
i iso
IPA isopropyl alcohol
HOAc acetic acid
HCl hydrochloric acid
HPLC high pressure liquid chromatography
LAH lithium aluminum hydride
LC liquid chromatography
LCMS Liquid Chromatograph-Mass Spectroscopy
M molar
mM millimolar
Me methyl
MeOH methanol
MHz megahertz
min. minute(s)
mins minute(s)
M^{+1} $(M+H)^+$
MOM-C_1 chloromethyl methyl ether
MS mass spectrometry
n or N normal
NB S n-bromosuccinimide
NIS N-iodosuccinimide
nm nanometer
nM nanomolar
NMP N-methylpyrrolidine
Pd/C palladium on carbon
$PdCl_2$(dppf) [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium(II)
$Pd_2(dba)_3$ tris-(dibenzylideneacetone)dipalladium
$Pd(OAc)_2$ palladium acetate
Pet ether petroleum ether
Ph phenyl
Ret Time retention time
sat. saturated
TEA triethylamine
TFA trifluoroacetic acid
THF tetrahydrofuran
TsCl 4-toluenesulfonyl chloride
2nd generation Xphos precatalyst: (Chloro(2-dicyclohexylphosphino-2',4',6'-triisopropyl-1,1'-biphenyl)[2-(2'-amino-1,1'-bi phenyl)]palladium(II)

Analytical and Preparative HPLC conditions:

Method QC-ACN-AA-XB: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7 μm particles; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile:water with 10 mM ammonium acetate; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm.

QC Method:

Method QC-ACN-TFA-XB: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7 μm particles; Mobile Phase A: 5:95 acetonitrile:water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile:water with 0.1% trifluoroacetic acid; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm.

Method A1: L3 Acquity: Column: (LCMS) BEH C18, 2.1×50 mm, 1.7 μm particles;

Mobile Phase: (A) water; (B) acetonitrile; Buffer: 0.05% TFA; Gradient Range: 2%-98% B (0 to 1 min) 98% B (to 1.5 min) 98%-2% B (to 1.6 min); Gradient Time: 1.6 min; Flow Rate: 0.8 mL/min; Analysis Time: 2.2 min; Detection: Detector 1: UV at 254 nm; Detector 2: MS (Est).

Method B1: L2 Aquity(4); Column: (LCMS) BEH C18, 2.1×50 mm, 1.7 μm particles; Mobile Phase: (A) water; (B) acetonitrile; Buffer: 0.05% TFA; Gradient Range: 2%-98% B (0 to 1 min) 98% B (to 1.5 min) 98%-2% B (to 1.5 min); Gradient Time: 1.8 min; Flow Rate: 0.8 mL/min; Analysis Time: 2.2 min; Detection: Detector 1: UV at 254 nm;

Detector 2: MS (Est).

Method C1 SCP: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7 μm particles; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile:water with 10 mM ammonium acetate. Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.11 mL/min; Detection: UV at 220 nm.

Method D1 SCP: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7 μm particles; Mobile Phase A: 5:95 acetonitrile:water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile:water with 0.1% trifluoroacetic acid; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.11 mL/min; Detection: UV at 220 nm.

Method E1 iPAC: Column: Waters Xbridge C18 4.6×50 mm 5 μm particles; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5

acetonitrile:water with 10 mM ammonium acetate. Temperature: 50° C.; Gradient: 0-100% B over 1 minute; Flow: 4 mL/min; Detection: UV at 220 nm.

Method F1 iPAC: Column: Waters Acquity BEH C18 2.1×50 mm 1.7 μm particles; Mobile Phase A: 5:95 acetonitrile:water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile:water with 0.1% trifluoroacetic acid; Temperature: 50° C.; Gradient: 0-100% B over 2.20 minutes; Flow: 0.800 mL/min; Detection: UV at 220 nm.

(A): Column-Ascentis Express C18 (50×2.1 mm 2.7 μm) Mphase A: 10 mM NH_4COOH in water: ACN-(98:02); Mphase B: 10 mM NH_4COOH in water: ACN (02:98), Gradient: 0-100% B over 3 minutes, Flow=1 mL/min.

(B): Waters Acquity BEH C18 (2.1×50 mm) 1.7 μm; Buffer: 5 mM ammonium acetate pH 5 adjusted with HCOOH, Solvent A:Buffer:ACN-(95:5), Solvent B:Buffer:ACN (5:95), Method: % B: 0 min-5%: 1.1 min -95%: 1.7 min-95%, Flow: 0.8 mL/min.

(C): Column-Ascentis Express C18 (50×2.1 mm 2.7 μm) Mobile phase A: 0.1% HCOOH in water; Mobile phase B: ACN. Temperature: 50° C.; Gradient: 0-100% B over 3 minutes; Flow rate: 1.0 mL/min.

(D): Kinetex XB-C18 (75×3 mm) 2.6 μm; Solvent A: 10 mM ammonium formate in water: acetonitrile (98:02); Mobile Phase B: 10 mM ammonium formate in water: acetonitrile (02:98); Temperature: 50° C.; Gradient: 0-100% B over 3 minutes; Flow rate: 1.1 mL/min; Detection: UV at 220 nm.

(E): Column: Ascentis Express C18 (50×2.1)mm, 2.7 μm; Mobile Phase A: 5:95 acetonitrile: water with 10 mM NH_4OAc; Mobile Phase B: 95:5 acetonitrile: water with 10 mM NH_4OAc; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes; Flow: 1.1 mL/min.

(F): Column: Ascentis Express C18(50×2.1)mm, 2.7 μm; Mobile Phase A: 5:95 acetonitrile: water with 0.1% TFA; Mobile Phase B: 95:5 acetonitrile: water with 0.1% TFA; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes; Flow: 1.1 mL/min.

(G): Column: Waters Acquity UPLC BEH C18 (2.1×50 mm), 1.7 μm; Solvent A=100% water with 0.05% TFA; Solvent B=100% acetonitrile with 0.05% TFA; gradient=2-98% B over 1 minute, then a 0.5-minute hold at 98% B; Flow rate: 0.8 mL/min; Detection: UV at 220 nm.

(H): Column: Acentis Express C18 (50×2.1 mm) 1.7 μm, Acentis C8 NH_4COOH 5 min. M, Mobile Phase A: −10 mM ammonium formate: ACN-(98:2), Mobile Phase B: −10 mM ammonium formate: ACN-(2:98), Flow: 1 mL/min.

(I) Column: Sunfire C18 (4.6×150) mm, 3.5 μm; Mobile Phase A: 5:95 acetonitrile: water with 0.05% TFA; Mobile Phase B: 95:5 acetonitrile: water with 0.05% TFA; Temperature: 50° C.; Gradient: 10-100% B over 12 minutes; Flow: 1 mL/min.

(J) Column: Sunfire C18 (4.6×150)mm, 3.5 μm; Mobile Phase A: 5:95 acetonitrile: water with 0.05% TFA; Mobile Phase B: 95:5 acetonitrile: water with 0.05% TFA; Temperature: 50° C.; Gradient: 10-100% B over 25 minutes; Flow: 1 mL/min.

(K): Column: Acquity UPLC BEH C18, 3.0×50 mm, 1.7 μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10 mM ammonium acetate; Method: % B: O min-20%: 1.1 min −90%: 1.7 min-90%; Flow: 0.7 mL/min.

(L): Column: Kinetex XB-C18 (75×3 mm-2.6 μm), Mobile Phase A: 10 mM ammonium formate: ACN-(98:2), Mobile Phase B: 10 mM ammonium formate: ACN-(2:98), Flow: 1 mL/min.

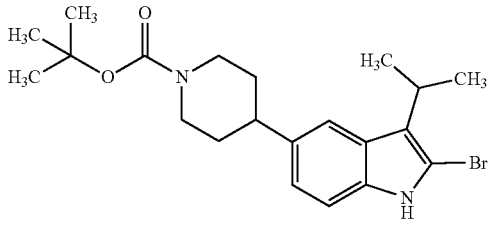
(M): Column: Acquity BEH C18 (3.0×50 mm) 1.7 μm, Mobile phase A: 0.1% TFA in water: Mobile phase B: 0.1% TFA in ACN,% B: 0 min-20%: 1.0 min -90%: 1.6 min 90%, Flow: 0.7 mL/min.

(N) Column:)(Bridge BEH XP C18 (50×2.1)mm, 2.5 μm; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10 mM ammonium acetate; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, Flow: 1.1 mL/min; Detection: UV at 220 nm.

Intermediates

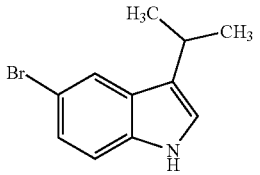
Intermediate T-1: tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(T-1)



Intermediate T-1A: 5-bromo-3-isopropyl-1H-indole

(T-1A)

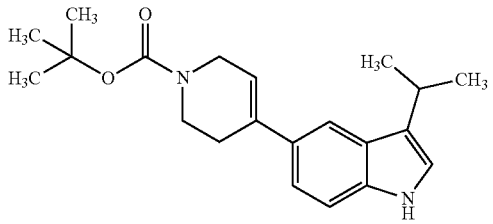


A 250 mL round bottom flask was charged with triethylsilane (8.90 g, 77 mmol), trichloroacetic acid (6.25 g, 38.3 mmol) and toluene (50 mL). The solution was heated to 70° C., then a solution of 5-bromo-1H-indole (5.0 g, 25.5 mmol) and acetone (2.247 mL, 30.6 mmol) in toluene (30 mL) was added drop wise via an addition funnel. The resulting brown solution was heated at 70° C. for 1.5 h. The solution was cooled to 10° C., quenched with 10% sodium bicarbonate and diluted with diethyl ether. The organic layer was separated, dried and concentrated under vacuum to afford crude compound. The crude compound was purified using silica gel chromatography eluting with 5% ethyl acetate in hexanes to afford 5-bromo-3-isopropyl-1H-indole (5.5 g,

23.10 mmol 95% yield) as an oil. LC retention time 1.42 min [D]. MS (E−) m/z: 238.2 (M+H).

Intermediate T-1B: tert-butyl 4-(3-isopropyl-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate

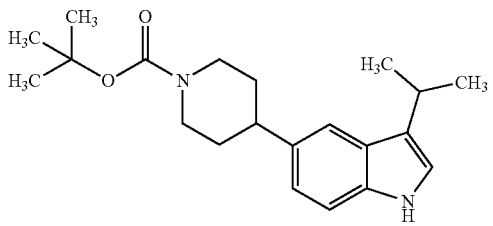
(T-1B)



To a mixture of 5-bromo-3-isopropyl-1H-indole (5.5 g, 23.10 mmol) and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (7.50 g, 24.25 mmol) in a 250 mL round bottom flask were added THF (50 mL) followed by an aqueous solution of potassium phosphate, dibasic (12.07 g, 69.3 mmol, 20 mL). The resulting reaction mixture was degassed for 10 minutes with nitrogen gas, then $PdCl_2(dppf)$-CH_2Cl_2 adduct, (0.472 g, 0.577 mmol) was added. The mixture was degassed again for 5 min. The resulting reaction mixture was heated at 75° C. for 18 hours. The reaction mixture was diluted with ethyl acetate (100 mL), poured into a separate funnel and was washed with water (2×50 mL), brine (50 mL), dried over sodium sulfate, and concentrated to give crude product. The crude material was purified using silica gel chromatography, eluting with 15% ethyl acetate in hexane. The fractions were collected and concentrated to afford tert-butyl 4-(3-isopropyl-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (6.5 g, 83% yield) as an oil. LCMS retention time 1.21 min [B]. MS (E−) m/z: 339 (M−H).

Intermediate T-1C: tert-butyl 4-(3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(T-1C)



To a solution of tert-butyl 4-(3-isopropyl-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (7.9 g, 23.20 mmol) in ethyl acetate (150 mL) under a nitrogen atmosphere, was added palladium on carbon (0.617 g, 0.580 mmol). The vessel was pumped/purged three times with nitrogen gas and then evacuated. Hydrogen gas was introduced via a balloon and the mixture was stirred at room temperature for 5 hours. The suspension was filtered through celite and the filtrate was concentrated to give crude compound. The crude residue was purified by silica gel chromatography, eluting with 15% ethyl acetate in hexane. The combined fractions were collected and concentrated to afford tert-butyl 4-(3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (6.5 g, 82% yield) as a white solid. LCMS retention time 2.48 min [C]. MS (E−) m/z: 341 (M−H).

Intermediate T-1

To a solution of tert-butyl 4-(3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (6.3 g, 18.40 mmol) in DCE (60 mL) was added NBS (3.27 g, 18.40 mmol) dissolved in DCE (50 mL) drop wise via an addition funnel over 10 min at 0° C. The resulting brown solution was stirred at room temperature for 20 min. The reaction was quenched with sodium sulfite solution (15 mL). The volatiles were removed. The residue was taken up in DCM (50 mL) and the aqueous layer was separated. The organic layer was dried over Na_2SO_4 and concentrated to afford crude compound. The crude compound was purified by silica gel chromatography, the compound was eluted in 15% ethyl acetate in Pet ether, the fractions was collected, and concentrated to afford tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (6.4 g, 83% yield) as a white solid. LCMS retention time 2.58 min [H]. MS (E^-) m/z: 367.2 (M−H). ^1H NMR (500 MHz, CHLOROFORM-d) δ 7.84 (br. s., 1H), 7.49 (d, J=0.9 Hz, 1H), 7.22 (d, J=8.4 Hz, 1H), 7.02 (dd, J=8.4, 1.5 Hz, 1H), 4.27 (br. s., 2H), 3.23 (quin, J=7.1 Hz, 1H), 2.84 (br. s., 3H), 1.88 (d, J=13.1 Hz, 2H), 1.50 (s, 9H), 1.43 (d, J=7.2 Hz, 6H), 1.24 (s, 2H).

Alternative Preparation of Intermediate T-1

Intermediate T-1A

A 5-liter 4-neck round bottom flask was charged with triethylsilane (489 mL, 3061 mmol), trichloroacetic acid (250 g, 1530 mmol) and toluene (500 mL). The solution was heated to 70° C. Next, 5-bromo-1H-indole (200 g, 1020 mmol) dissolved in acetone (150 mL, 2040 mmol) and toluene (700 mL) was added dropwise over 30 minutes. After the addition was complete, the resulting solution was heated at 90° C. for 3h. The reaction was then quenched by adding 10% $NaHCO_3$ solution (~2.5 liter) dropwise at 0-10° C. until the pH was basic. The organic layer and the aqueous layer were separated and the aqueous layer was extracted with MTBE (2×1000 mL). The combined organic layers were washed with water and brine solution, dried over Na_2SO_4 and concentrated under vacuum to get a brown color oil. The crude residue was purified by 750 g silica gel chromatography eluting with PE:EtOAc (9:1). The product was eluted at 8% EtOAc in petroleum ether, collected, and concentrated under vacuum at 50° C. A light brown gummy liquid was obtained and hexane (100 mL) was added. The mixture was stirred and cooled to −40° C. to −50° C. After 10 min, a solid was formed which was filtered and washed with a minimal amount cold hexane. The compound was dried under vacuum to afford 5-bromo-3-isopropyl-1H-indole (215 g, 890 mmol, 87% yield) as an off-white solid. LCMS Er: 237.5; HPLC Ret. Time 3.75 min. Method D.

Intermediate T-1B

5-bromo-3-isopropyl-1H-indole (90 g, 378 mmol) and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (140 g, 454 mmol) was dissolved in THF (1200 mL) in a 2 L round-bottomed flask. Tripotassium phosphate (241 g, 1134 mmol) was dissolved in water (300 mL). The aqueous solution was

added to the reaction mixture. The reaction mixture was purged with N_2. Then $PdCl_2(dppf)$-CH_2Cl_2 adduct (7.72 g, 9.45 mmol) was added to the reaction mixture. The reaction mixture was again purged with N_2. The reaction mixture was stirred at 80° C. for 18 h. The reaction mixture was filtered through celite and extracted with EtOAc. The combined organic layers were washed with brine, dried (sodium sulfate), and concentrated to remove the solvent. The crude material was purified by silica gel chromatography. The product was collected by eluting with 30% EtOAc:PE to afford tert-butyl 4-(3-isopropyl-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (125 g, 367 mmol). LCMS MH^-: 341.2; HPLC Ret. Time 2.90 min.; Method: Column: Zorbax SB-18 (50×4.6 mm-5.0 μm); M. phase A: 10 mM NH_4COOH in H_2O: ACN-(98:2); M. phase B: 10 mM NH_4COOH in H_2O: ACN-(2:98); Flow rate: 1.5/min; Gradient: 30% B-100% B over 4 min. UV 220 nm.

Intermediate T-1C

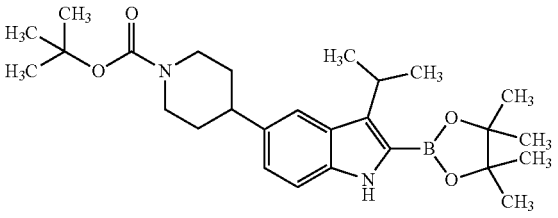
In a 2 L round-bottomed flask, tert-butyl 4-(3-isopropyl-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (125 g, 367 mmol) was dissolved in ethyl acetate (1200 mL). Pd/C (15.63 g, 14.69 mmol) was added and the reaction mixture was degassed under N_2. The reaction mixture was stirred at room temperature for 18 h under H_2. Approximately 80% starting material was converted to product. The reaction mass was filtered through celite and concentrated. The crude material was purified with silica gel chromatography. The product was collected by eluting with 20% EtOAc:PE to afford tert-butyl 4-(3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (105 g, 307 mmol, 84% yield). LCMS MH^-: 343.4; HPLC Ret. Time 2.61 min.; Method: Column: Zorbax SB-18 (50×4.6 mm-5.0 μm); M. phase A: 10 mM NH_4COOH in H_2O: ACN-(98:2); M. phase B: 10 mM NH_4COOH in H_2O: ACN-(2:98); Flow rate: 1.5/min; Gradient: 30% B-100% B over 4 min.; UV 220 nm.

Intermediate T-1

In a 2 L round-bottomed flask tert-butyl 4-(3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (100 g, 292 mmol) was dissolved in 1,2-dichloroethane (1200 mL). NBS (52.0 g, 292 mmol) solution in 1,2-dichloroethane (400 mL) and THF (800 mL) was added dropwise at 0° C. After the addition of NBS solution, the reaction mixture was stirred for 30 min. The reaction mass was quenched with 10% sodium thiosulfate solution at 0° C. and diluted with DCM. The combined organic layers were washed with brine, dried (sodium sulfate), and concentrated. The crude material was purified with silica gel chromatography. The product was collected by eluting with 10% EtOAc:PE. The dibromo product was observed (approximately 5-10%). The material was washed with cooled hexane to remove the dibromo product and afford tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (87 g, 206 mmol, 70.7% yield). LCMS MH^+-56: 365.0; HPLC Ret. Time 4.21 min.; Method: Column: Kinetex XB-C18 (75×3 mm-2.6 μm); M. phase A: 10 mM NH_4COOH in H_2O:ACN-(98:02); M. phase B: 10 mM NH_4COOH in H_2O: ACN-(02:98); Flow rate: 1.0/min; Gradient: 20% B-100% B over 4 min. UV 220 nm.

Intermediate T-2: tert-butyl 4-(3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate

(T-2)



To a mixture of tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (1.0 g, 2.373 mmol), 2-dicyclohexyphosphino-2',6'-dimethoxybiphenyl (0.117 g, 0.285 mmol), and bis(benzonitrile)palladium(II)chloride (0.027 g, 0.071 mmol) in a 50 mL reaction tube was added dioxane (10 mL). The resulting reaction mixture was degassed for 10 min and then pinacolborane (0.456 g, 3.56 mmol) was added followed by the dropwise addition of TEA (0.992 mL, 7.12 mmol). The solution was again degassed for 5 min. The resulting reaction mixture was heated at 85° C. for 3 h. The reaction mixture was concentrated and the crude residue was dissolved in ethyl acetate (100 mL), poured into a separatory funnel and washed thoroughly with water (2×250 mL). The organic layer was dried over Na_2SO_4 and filtered. The filtrate was concentrated under vacuum to afford the crude product. The residue was taken up in DCM (3 mL). The crude material was purified by combiflash system by eluting with 12% EtOAc/Pet ether. Following concentration of the fractions, the product was isolated as a white gummy product (0.75 g, 67.5% yield). LCMS retention time 4.27 min [H]. MS (E−) m/z: 467.3 (M−H). ^1H NMR (400 MHz, CHLOROFORM-d) δ 8.35-8.12 (m, 1H), 7.66-7.59 (m, 1H), 7.11-7.04 (m, 1H), 4.40-4.23 (m, 2H), 3.80-3.63 (m, 1H), 2.99-2.67 (m, 3H), 1.98-1.84 (m, 2H), 1.79-1.64 (m, 2H), 1.54-1.51 (m, 9H), 1.49-1.45 (m, 6H), 1.39-1.35 (m, 12H).

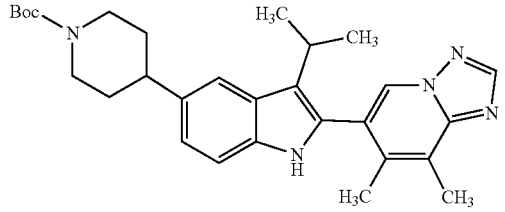
Alternative Preparation of Intermediate T-2

In a 1 L round-bottomed flask, tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (85 g, 202 mmol) was dissolved in dioxane (850 mL). Next, 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (9.11 g, 22.19 mmol) and bis(benzonitrile) palladium chloride (3.87 g, 10.09 mmol) were added. Pinacolborane (387 g, 3026 mmol) was added followed by the addition of TEA (84 mL, 605 mmol). The reaction reaction mixture was purged with nitrogen for 15-20 min. The reaction mixture was stirred at 90° C. for 20h. The reaction mixture was filtered through celite and the reaction was quenched with brine solution. Effervescence was observed. The reaction mixture was extracted with EtOAc, dried (sodium sulfate), and concentrated. The crude material was purified with silica gel chromatography. The product was collected by eluting with 10% EtOAc:PE to afford tert-butyl 4-(3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl) piperidine-1-carboxylate (62.5 g, 133 mmol, 66.1% yield). LCMSEr: 469.4. HPLC Ret. Time 3.04 min.; Method:

Column: Zorbax SB-18 (50×4.6 mm-5.0 μm); M. phase A: 10 mM NH_4COOH in H_2O: ACN-(98:2); M. phase B: 10 mM NH_4COOH in H_2O:ACN-(2:98); Flow rate: 1.5/min; Gradient: 30% B-100% B over 4 min.; UV 220 nm.

Intermediate T-3: Tert-butyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

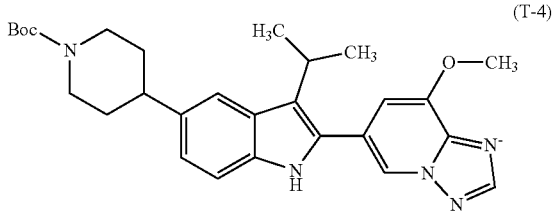
(T-3)



To a mixture of tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (60 g, 142 mmol), bis(benzonitrile)palladium(ii) chloride (1.639 g, 4.27 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (3.51 g, 8.54 mmol) and anhydrous dioxane (407 ml) under N_2 at room temperature were added pinacolborane (62.0 mL, 427 mmol) and triethylamine (59.5 mL, 427 mmol). The mixture was heated at 85° C. for 5 min. The starting material was consumed. After the reaction mixture was cooled to room temperature (a water ice bath was used to fasten the cooling), 2 mL of 2 M K_3PO_4 solution was added. After the generation of bubbles diminished, the remainder of the 2 M potassium phosphate tribasic solution (214 mL, 427 mmol) was added, followed by 6-bromo-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (29.9 g, 132 mmol) and $PdCl_2$(dppf)-CH_2Cl_2 adduct (4.07 g, 4.98 mmol). The reaction mixture was heated at 85° C. for 2h. The reaction went to completion. After the mixture was cooled to room temperature, the organic layer (a suspension) and the aqueous layer was separated. The top organic layer was a suspension. It was concentrated and dissolved in DCM (1.5 L) to give a dark DCM solution and aqueous layer on the top. The water was removed and the DCM extraction was dried over Na_2SO_4, filtered through a Celite pad, washed with DCM and concentrated to give 150 g crude wet mud. The material was purified with silica gel chromatography using a Silica 40 g Gold column. The column was eluted with DCM and ethyl acetate. The product was collected when eluting with 50% ethyl acetate:DCM to afford tert-butyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (56.9 g, 117.0 mmol, 82% yield) as an off-white solid. LCMS MH^+: 488.5. HPLC Ret. Time 1.13 min. Method G. ^1H NMR (499 MHz, CHLOROFORM-d) δ 8.45-8.41 (m, 1H), 8.36-8.33 (m, 1H), 7.90-7.84 (m, 1H), 7.66-7.63 (m, 1H), 7.39-7.34 (m, 1H), 7.17-7.12 (m, 1H), 4.39-4.26 (m, 2H), 3.04-2.94 (m, 1H), 2.92-2.75 (m, 3H), 2.72-2.65 (m, 3H), 2.27-2.21 (m, 3H), 2.00-1.90 (m, 2H), 1.83-1.71 (m, 2H), 1.54-1.51 (m, 9H), 1.42-1.38 (m, 6H).

Intermediate T-4: Tert-butyl 4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

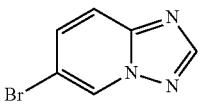
(T-4)



To a mixture of tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (40 g, 95 mmol), bis(benzonitrile)palladium(ii) chloride (1.092 g, 2.85 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (2.338 g, 5.70 mmol) and anhydrous dioxane (271 mL) under N_2 at room temperature, were added pinacolborane (41.3 mL, 285 mmol) and triethylamine (39.7 mL, 285 mmol). The mixture was heated at 85° C. for 10 min. The starting material was consumed. After the reaction mixture was cooled to room temperature, 2-5 mL of 2 M K_3PO_4 aqueous solution was added. After bubbling slowed down, the remainder of the 2 M potassium phosphate tribasic solution (142 mL, 285 mmol) was added, followed by 6-bromo-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (20 g, 88 mmol) and $PdCl_2$(dppf)-CH_2Cl_2 adduct (3.10 g, 3.80 mmol). The mixture was heated at 70° C. for 1.5 h. After completion of the reaction, 81 g of crude product after concentration was purified by silica gel chromatography (3 kg Gold column) eluting with DCM and ethyl acetate. The product was collected at 35% ethyl acetate:DCM to afford tert-butyl 4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidine-1-carboxylate (52.6 g, 107 mmol, 113% yield). LCMS MH^-: 490.1. HPLC Ret. Time 1.08 min. Method G.

Intermediate F-1: 6-bromo-[1,2,4]triazolo[1,5-a]pyridine

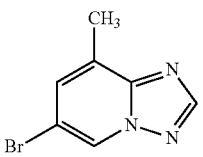
(F-1)



Commercially available reagent: CAS No 356560-80-0

Intermediate F-2: 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine

(F-2)

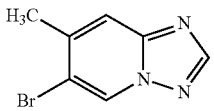


To a stirred solution of 5-bromo-3-methylpyridin-2-amine (1.75 g, 9.36 mmol) in N,N-dimethylformamide (13.04 mL,

168 mmol) was added DMF-DMA (12.53 mL, 94 mmol). The reaction mixture was heated to 130° C. overnight. After cooling to room temperature, the volatiles were removed under reduced pressure to afford a brown oil. To an ice-cooled, stirred solution of the crude product in methanol (100 mL) and pyridine (15 mL) was added hydroxylamine-O-sulfonic acid (1.587 g, 14.03 mmol). The reaction mixture was allowed to warm to room temperature and was stirred overnight. The volatiles were removed under reduced pressure, and the residue was partitioned between aqueous sodium bicarbonate solution and ethyl acetate. The aqueous layer was further extracted with ethyl acetate, and the combined organic layers were washed sequentially with water (10 mL) and saturated aqueous brine solution (10 mL), dried over magnesium sulfate, and concentrated in vacuo to afford 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (1.98 g). LC-MS: M+1=212/214. Rt=0.80 min, [A1]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.20 (s, 1H), 8.48 (s, 1H), 7.67 (s, 1H), 2.55 (s, 3H).

Intermediate F-3: 6-bromo-7-methyl-[1,2,4]triazolo [1,5-a]pyridine

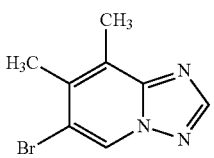
(F-3)



To a 40 mL vial with a pressure relief septum were added 5-bromo-4-methylpyridin-2-amine (5.00 g, 26.7 mmol), DMF (10 mL) and N,N-dimethylformamide dimethyl acetal (11.99 mL, 90 mmol). The vial was heated to 130° C. for 6 hours. The vial was cooled to room temperature, the volatiles were removed under vacuum. The resulting oil was dissolved in MeOH (5 mL) and pyridine (3.24 mL, 40.1 mmol) and cooled to 0° C. Hydroxylamine-O-sulfonic acid (4.53 g, 40.1 mmol) was added over 15 minutes and the mixture was allowed to warm to room temperature overnight. The solution was concentrated under vacuum. The resulting white solid was partitioned between EtOAc and saturated sodium bicarbonate. The organic layer was separated and the bicarbonate layer was extracted with EtOAc (2×50 mL). The combined organics were washed with water (50 mL) and brine (50 mL), dried over magnesium sulfate, filtered and concentrated to afford 6-bromo-7-methyl-[1,2,4]triazolo[1,5-a]pyridine as a white solid. (4.5 g, 21.22 mmol, 79% yield). LC-MS: M+1=212/214, rt=0.70 min., [A1].

Intermediate F-4: 6-bromo-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine

(F-4)



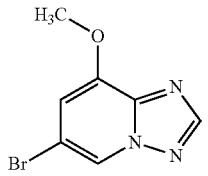
To a 40 mL vial with a pressure relief septum were added 5-bromo-3,4-dimethylpyridin-2-amine (5.00 g, 24.87 mmol), DMF (10 mL) and N,N-dimethylformamide dimethyl acetal (11.15 mL, 83 mmol). The vial was heated to 80° C. for 6 hours. The vial was cooled to room temperature. The volatiles were removed under vacuum and the resulting oil was dissolved in MeOH (5 mL) and pyridine (3.02 mL, 37.3 mmol) and cooled to 0° C. Hydroxylamine-O-sulfonic acid (4.22 g, 37.3 mmol) was added over 15 minutes and the mixture allowed to warm to room temperature overnight. The solution was concentrated under vacuum. The resulting white solid was partitioned between EtOAc and 1.5 M potassium phosphate solution. The organic layer was separated and the aqueous layer was extracted with EtOAc (2×50 mL). The combined organics were washed with water (50 mL) and brine (50 mL), dried over magnesium sulfate, filtered and concentrated to give a white solid. The solid was dissolved in DCM and MeOH and charged to an 80G silica gel column which was eluted with 0-100% ethyl acetate/hexane. Following concentration of the fractions, 6-bromo-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (5.2 g, 23.00 mmol, 92% yield) was collected as a whitish solid. LC-MS: M+1=226/228, rt=0.75 min, [A1]; ^{1}H NMR: ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.68 (s, 1H), 8.26 (s, 1H), 2.68 (s, 3H), 2.50 (s, 3H).

Alternative Preparation of Intermediate F-4

To the suspension of 5-bromo-3,4-dimethylpyridin-2-amine (10 g, 49.7 mmol) in DMF (50 mL) was added 1,1-dimethoxy-N,N-dimethylmethanamine (15.32 mL, 114 mmol). The mixture was stirred at 110° C. for 12 h under N_2. All the starting material amine was converted to intermediate imine (M+1, 256) after 12 h. The reaction mixture was concentrated to remove volatiles under high vacuum rotavap. Solvent DMF still remained in the black reaction mixture. The resulting residue was diluted with MeOH (50 mL) and pyridine (6.03 mL, 74.6 mmol). The mixture was cooled to 0° C. and hydroxylamine-O-sulfonic acid (8.88 g, 74.6 mmol) was added over 15 min. The mixture was stirred at room temperature over 24h. The reaction was completed and the desired product was found after 19 h. The crude reaction mixture was concentrated to remove volatiles. The resulting yellow solid was dissolved in 200 mL EtOAc and quenched with saturated $NaHCO_3$ solution slowly (200 mL) with gas generated during the addition of sodium bicarbonate. The organic layer was separated and the aqueous layer was back-extracted with EtOAc. The combined organic layer was washed with H_2O (30 mL), brine (2×30 mL) and dried over Na_2SO_4. The crude product was purified with silica gel chromatography eluting with EtOAc and hexane to afford 6-bromo-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (8 g, 35.4 mmol, 71.1% yield). LCMS MH^-: 226.08. HPLC Ret. Time 0.71 min. Method G. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.79-8.63 (m, 1H), 8.39-8.10 (m, 1H), 2.81-2.61 (m, 3H), 2.57-2.48 (m, 3H).

Intermediate F-5: 6-bromo-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine

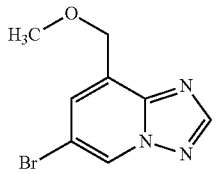
(F-5)



To a stirred solution of 5-bromo-3-methoxypyridin-2-amine (7.5 g, 36.9 mmol) in DMF (15 mL) was added DMF-DMA (15 mL, 112 mmol). The reaction mixture was heated to 130° C. overnight. After cooling to room temperature, the volatiles were removed under reduced pressure to provide a brown oil. To an ice-cooled, stirred solution of the brown oil in methanol (150 mL) and pyridine (20 mL) was added hydroxylamine-O-sulfonic acid (6.27 g, 55.4 mmol). The reaction mixture was allowed to warm to room temperature and was stirred overnight. The volatiles were removed under reduced pressure, and the residue was partitioned between aqueous sodium bicarbonate solution and ethyl acetate. The aqueous layer was further extracted with ethyl acetate, and the combined organic layers were washed sequentially with water (10 mL) and saturated aqueous brine solution (10 mL), dried over sodium sulfate, and concentrated in vacuo to afford crude product. The residue was taken up in DCM (3 mL). The crude was purified by combiflash 3% MeOH: 97% $CHCl_3$. Following concentration of fractions, 6-bromo-8-methoxy-[1,2,4]triazolo[1,5-a] pyridine (5.0 g, 21.93 mmol, 59.4% yield) was collected as a yellow solid. LCMS: M=228.5, R_t=1.06 min., Column: ZORBAX SB C18 (50×4.6 mm, 5.0 μM) Method: 10 mM NH_4COOH in water +ACN; ^1H NMR (400 MHz, DMSO-d6) δ=4.01 (s, 3H), 7.26 (s, 1H), 8.45 (s, 1H), 8.95 (s, 1H).

Intermediate F-6: 6-bromo-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine

(F-6)

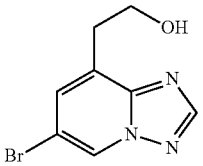


To a 40 mL reaction vial, were added 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (2.000 g, 9.43 mmol), AIBN-(0.155 g, 0.943 mmol), NBS (1.679 g, 9.43 mmol), and CCl_4(15 mL). The vial was sealed and heated to 75° C. overnight. The reaction mixture was cooled to room temperature and concentrated to dryness. The residue was used without purification in the subsequent step.

To a 40 mL vial, were added the above residue, THF (15 mL), MeOH (10 mL), and aqueous NaOH (28.3 mL, 28.3 mmol). The reaction vial was capped and heated to 75° C. for 1 hour. LC-MS showed clean conversion to the product. Water and ethyl acetate was added and the layers were separated. The organics were washed with water, then brine, dried over Na_2SO_4, filtered, and concentrated to give an off-white solid. LC-MS: M+1=242, rt=1.31 min, [A1]. ^1H NMR (400 MHz, DMSO-d_6) δ 9.41-9.28 (m, 1H), 8.52 (s, 1H), 7.78-7.65 (m, 1H), 4.84-4.70 (m, 2H), 3.42 (s, 3H).

Intermediate F-7: 6-2-(2-amino-5-bromo-1,2-dihydropyridin-3-yl)ethanol

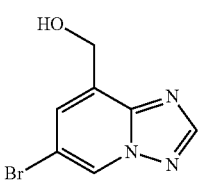
(F-7)



In a 100 mL 2-neck round bottom flask, and under a nitrogen atmosphere, was added 2-(2-aminopyridin-3-yl) acetic acid (0.250 g, 1.622 mmol) and THF (8 mL). At 5° C., LAH was added portion-wise to the solution. The ice bath was removed and the reaction mixture was heated at reflux overnight. After 16 hours, the solvent had evaporated. Diethyl ether was added. Following cooling, the reaction mixture was placed in an ice bath. The LAH was quenched with MeOH, then water. Sodium sulfate was added and the mixture was filtered, and washed with diethyl ether. The filtrate was concentrated and then dissolved in DCM (5 mL) and cooled to 5° C. Next, NBS (0.289 g, 1.622 mmol) in DCM (2 mL) was added. The reaction mixture was warmed to room temperature. The reaction was quenched with 2 mL of a 10% sodium sulfite solution. DCM (20 mL) and water (20 mL) were added and the contents was added to a separatory funnel. The layers were separated. The organics were washed with brine dried over Na_2SO_4, filtered and concentrated to give crude product. LC-MS: M^{+1}=219, R_t=0.49 min, [A1]. This material was carried on similarly as in general procedure for F-2 to afford (6-bromo-[1,2,4] triazolo[1,5-a]pyridin-8-yl)ethanol (0.065 g, 73%). LC-MS: M^{+1}=242/244, R_t=0.65 min, [A1].

Intermediate F-8: (6-bromo-[1,2,4]triazolo[1,5-a] pyridin-8-yl)methanol

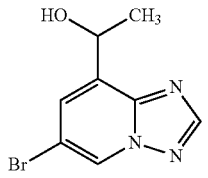
(F-8)



Intermediate F-8 was prepared according to general procedure for F-6 starting from 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine and without methanol in the second step. LC-MS: M^{+1}=228/230, R_t=0.60 min, [A1].

Intermediate F-9: rac-1-(6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-ol

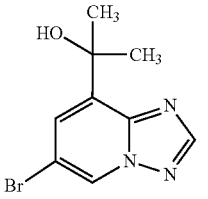
(F-9)



In a 40 mL reaction vial were added 2-amino-5-bromonicotinaldehyde (0.750 g, 3.73 mmol) and under nitrogen gas, THF (10 mL). The mixture was cooled to −20° C. and 3 M methylmagnesium chloride in Et_2O (4.97 mL, 14.92 mmol) was added via syringe over 20 minutes. The reaction mixture was warmed to room temperature and stirred for 3 hours. The reaction mixture was cooled to −20° C. and quenched slowly with saturated ammonium chloride. Water and ethyl acetate were added and the layers were separated. The collected organics were washed with saturated NaCl, dried over Na_2SO_4, filtered and concentrated to dryness to afford rac-1-(2-amino-5-bromopyridin-3-yl)ethanol. This material was carried on similarly as in general procedure for F-1 to afford rac-1-(6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl) ethan-1-ol (0.53 g, 58%). LC-MS: M^{+1}=242/244, R_t=0.58 min, [A1].

Intermediate F-10: 2-(6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol

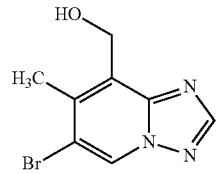
(F-10)



In a 40 mL reaction vial was added methyl 2-amino-5-bromonicotinate (1.240 g, 5.37 mmol) and under a nitrogen atmosphere, THF (10.73 mL). The mixture was cooled to −20° C. and 3 M methylmagnesium chloride in Et_2O (7.16 mL, 21.47 mmol) was added via syringe over 20 minutes. The reaction mixture was warmed to room temperature and stirred for 3 hours. The reaction mixture was cooled to −20° C. and the reaction was quenched slowly with the addition of saturated ammonium chloride. Water and ethyl acetate were added and the layers were separated. The collected organics were washed with saturated NaCl, dried over Na_2SO_4, filtered and concentrated to dryness to afford 2-(2-amino-5-bromopyridin-3-yl) propan-2-ol LC-MS: M^{+1}=231.3/233.0, R_t=0.49 min, [A1]. This material was carried on similarly as in general procedure for F-1 to afford 2-(6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (0.65 g, 59%). LC-MS: M^{+1}=255.6/257.8, R_t=0.85 min, [D1].

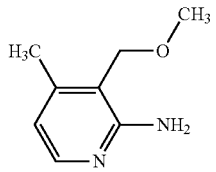
Intermediate F-11: (6-bromo-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol

(F-11)



Intermediate F-11A: (2-amino-4-methylpyridin-3-yl)methanol

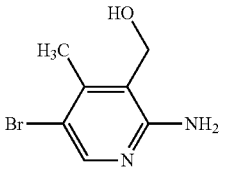
(F-11A)



In a 100 mL Schlenk flask (heat gun dried) was added N-(4-methylpyridin-2-yl) pivalamide (0.300 g, 1.560 mmol). Diethyl ether (5.20 mL) was added and the reaction mixture was cooled to −78° C. Next, 1.7 M tert-butyllithium in pentane (2.019 mL, 3.43 mmol) was added via syringe, drop-wise. The reaction mixture was stirred at −78° C. for 3 hours and then chloromethyl methyl ether (0.142 mL, 1.872 mmol) was introduced. The reaction mixture was warmed to room temperature and stirred overnight. The reaction was quenched with water. Ethyl acetate was added to the mixture. The mixture was poured into a separatory funnel and the layers were separated. The organics were washed with water, then brine, dried over Na_2SO_4, filtered and concentrated. The crude oil was purified on a silica gel using 0-50% ethyl acetate/hexane. Following concentration of the fractions, N-(3-(methoxymethyl)-4-methylpyridin-2-yl)pivalamide was collected as a tan oil. This material was suspended in 4 M aqueous HCl and heated to 110° C. for 48 hours. The reaction mixture was cooled to room temperature, diluted with diethyl ether and the contents poured into a separatory funnel. The layers were separated and the organic layer was discarded. The aqueous layer was basified with 1.5 M potassium phosphate dibasic solution and the suspension was extracted with ethyl acetate (three times extracted). The combined organics were washed with brine, dried over Na_2SO_4, filtered and concentrated to afford (2-amino-4-methylpyridin-3-yl)methanol (0.1 g, 46%). LC-MS: (M^{-1}) not observed on instrument, R_t=0.39 min by UV only, [A1].

Intermediate F-11B: (2-amino-5-bromo-4-methylpyridin-3-yl)methanol

(F-11B)



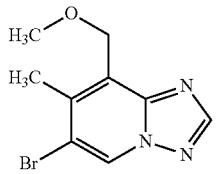
In a 40 mL reaction vial was added (2-amino-4-methylpyridin-3-yl)methanol (0.200 g, 1.448 mmol), DCM, and NBS (0.258 g, 1.448 mmol) as a suspension in 5 mL of DCM. The reaction mixture was stirred for 15 minutes. The reaction was quenched with a 10% sodium sulfite solution (1 mL). The reaction mixture was diluted with water and DCM, and transferred to a separatory funnel. The layers were separated and the organics were washed with brine, dried over Na_2SO_4, filtered and concentrated to afford (2-amino-5-bromo-4-methylpyridin-3-yl)methanol (0.08 g, 26%). LC-MS: M^{+1}=217/219, R_t=0.45 min, [A1].

Intermediate F-11

Intermediate F-11 was prepared from Intermediate F-11B according to the general procedure for F-2 to afford (6-bromo-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl) methanol LC-MS: M^{+1}=242/244, R_t=0.60 min, [A1].

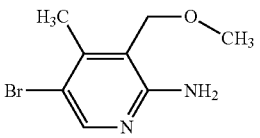
Intermediate F-12: 6-bromo-8-(methoxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine

(F-12)



Intermediate F-12A 6-bromo-8-(methoxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine

(F-12A)



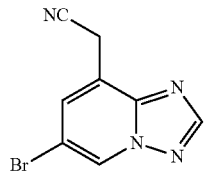
In a 40 mL reaction vial were added N-(3-(methoxymethyl)-4-methylpyridin-2-yl) pivalamide (0.100 g, 0.423 mmol) and 6 N aqueous HCl (2.116 mL, 2.116 mmol). The vial was capped and heated to 80° C. overnight. The mixture was basified with a 1.5 M dibasic potassium phosphate solution. The aqueous layer was extracted with ethyl acetate (2×50 mL). The combined organics were washed with a saturated NaCl solution, dried over Na_2SO_4, filtered and concentrated to afford 3-(methoxymethyl)-4-methylpyridin-2-amine (R_t=0.44 min.) [A1]. This material was suspended in DCM (4 mL). NBS (0.075 g, 0.423 mmol) was dissolved in 1 mL of DCM and added to the reaction mixture dropwise via a pipet over 5 minutes. The reaction was quenched with the addition of 1 mL of a 10% sodium sulfite solution. The organic layer was pipetted off and concentrated. The residue was purified on silica gel using O-10% MeOH/DCM. Following concentration of the fractions, 5-bromo-3-(methoxymethyl)-4-methylpyridin-2-amine was collected as a tan oil. LC-MS: M^{+1}=231/233, R_t=0.53 min. 0.60 min, [D1].

Intermediate F-12

Intermediate F-12 was prepared from Intermediate F-12A according to the general procedure for F-1 to afford 6-bromo-8-(methoxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.03 g, 30%). LC-MS: M^{+1}=256/258, R_t=1.07 min. 0.60 min, [A1].

Intermediate F-13: 2-(6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)acetonitrile

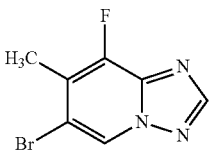
(F-13)



To a 40 mL reaction vial was added (6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl) methanol (0.500 g, 2.193 mmol) followed by the slow addition of $SOCl_2$ (1.600 mL, 21.93 mmol). The reaction mixture was stirred at 50° C. overnight. The reaction mixture was concentrated and placed under vacuum to remove the excess thionyl chloride. Next, acetonitrile, water and KCN-(0.714 g, 10.96 mmol) in water (1 mL) were added. The reaction vessel was sealed and heated to 50° C. overnight. The reaction mixture was diluted with 1.5 M dibasic potassium phosphate solution and ethyl acetate was added. The reaction mixture was poured into a separatory funnel and the layers were separated. The organics were washed with brine, then dried over Na_2SO_4, filtered and concentrated to afford 2-(6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)acetonitrile as a tan solid (0.21 g, 40%). LC-MS: M^{+1}=236/238, R_t=0.60 min, [A1].

Intermediate F-14: 6-bromo-8-fluoro-7-methyl-[1,2,4]triazolo[1,5-a]pyridine

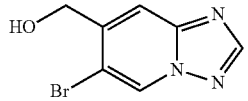
(F-14)



In a 40 mL reaction vial was added 3-fluoro-4-methylpyridin-2-amine (0.250 g, 1.982 mmol) in DCM (5 mL). To this was added a suspension of NBS (0.353 g, 1.982 mmol) in DCM (2 mL). The reaction mixture was stirred for 30 minutes. The reaction was quenched with the addition of 5 mL of a 10% sodium sulfite solution. DCM and water were added and the reaction mixture was poured into a separatory funnel. The layers were separated. The collected organics were washed with brine, dried over Na_2SO_4, filtered and concentrated to afford 5-bromo-3-fluoro-4-methylpyridin-2-amine. This material was carried on similarly as in general procedure for F-2 to afford 6-bromo-8-fluoro-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.45 g, 49%). LC-MS: M^{+1}=230/232, R_t=0.71 min. 0.60 min, [A1].

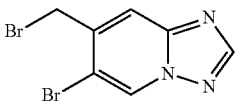
Intermediate F-15: (6-bromo-[1,2,4]triazolo[1,5-a]pyridin-7-yl)methanol

(F-15)



Intermediate F-15A: 6-bromo-7-(bromomethyl)-[1,2,4]triazolo[1,5-a]pyridine

(F-15A)



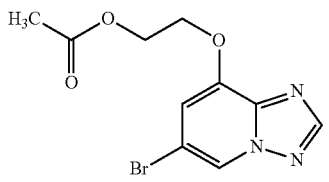
In a 40 mL reaction vial were added 6-bromo-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.670 g, 3.16 mmol), carbon tetrachloride (6.32 mL), NBS (0.562 g, 3.16 mmol) and AIBN-(0.052 g, 0.316 mmol). The reaction vial was capped and heated at 75° C. for 5 hours. The reaction mixture was cooled to room temperature, filtered and the precipitate was washed with CCl_4. The filtrate was concentrated to afford 6-bromo-7-(bromomethyl)-[1,2,4]triazolo [1,5-a]pyridine as a light yellow residue (0.72 g, 78%). LC-MS: M^{+1}=290/292/294, R_t=0.75 min., [A1].

Intermediate F-15

To a 40 mL vial were added 6-bromo-7-(bromomethyl)-[1,2,4]triazolo[1,5-a]pyridine (1.000 g, 3.44 mmol), acetone (11 mL), sodium iodide (0.515 g, 3.44 mmol) and potassium acetate (0.675 g, 6.87 mmol). The reaction mixture was capped and heated to 55° C. for 17 hours. The volatiles were removed under a stream of nitrogen gas and to the residue were added THF (10 mL), 1 mL of water, and sodium hydroxide (2.58 mL, 10.31 mmol). The vial was capped and heated at 65° C. for 8 hours. The mixture was treated with 1 N HCl to approximately pH 7. Ethyl acetate was added and the layers were separated. The organics were washed with brine, dried over Na_2SO_4, filtered and concentrated to afford (6-bromo-[1,2,4]triazolo[1,5-a]pyridin-7-yl)methanol as a whitish solid (0.35 g, 44%). LC-MS: M^{+1}=228/230, R_t=0.54 min., [A1].

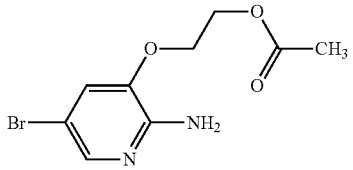
Intermediate F-16: 2-((6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)oxy)ethyl acetate

(F-16)



Intermediate F-16A: 2-((2-amino-5-bromopyridin-3-yl)oxy)ethyl acetate

(F-16A)



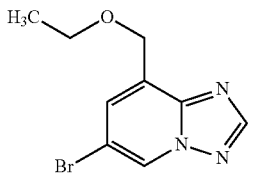
In a 40 mL reaction vial under nitrogen gas, was added 2-amino-5-bromopyridin-3-ol (0.320 g, 1.693 mmol) and DMF (5 mL). The mixture was cooled to 5° C. and NaH (0.102 g, 2.54 mmol) was added. The reaction mixture was stirred at 5° C. for 1 hour. Next, 2-bromoethyl acetate (0.283 mL, 2.54 mmol) was introduced neat via a syringe. The reaction mixture was stirred at 5° C. and slowly warmed to room temperature overnight. The mixture was cooled to 5° C. and carefully diluted with water. Ethyl acetate was added and the mixture was transferred to a separatory funnel. The layers were separated and the organics were washed with brine, dried over sodium sulfate, filtered and concentrated to afford 2-((2-amino-5-bromopyridin-3-yl)oxy)ethyl acetate as a tan oil (0.45 g, 97%). LC-MS: M^{+1}=275/277, rt=0.52 min, [A1].

Intermediate F-16

Intermediate F-16A carried on similarly to general procedure for F-1 to afford 2-((6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)oxy)ethyl acetate as a tan solid. LC-MS: M^{+1}=300/302, R_t=0.69 min, [A1].

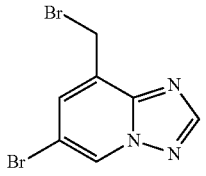
Intermediate F-17: 6-bromo-8-(ethoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine

(F-17)



Intermediate F-17A: 6-bromo-8-(bromomethyl)-[1,2,4]triazolo[1,5-a]pyridine

(F-17-1)



To a 40 mL reaction vial were added 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (2.000 g, 9.43 mmol), AIBN-(0.155 g, 0.943 mmol), NBS (1.679 g, 9.43 mmol), and CCl_4(15 mL). The vial was sealed and heated to 75° C. overnight. The reaction mixture was cooled to room temperature, filtered and the precipitate was washed with CCl_4. The filtrate was concentrated to dryness to afford 6-bromo-8-(bromomethyl)-[1,2,4]triazolo[1,5-a]pyridine, as a light yellow residue (1.9 g, 69%). LC-MS: M^+=290/292/294, R_t=0.73 min., [A1].

Intermediate F-17

To a 40 mL reaction vial were added 6-bromo-8-(bromomethyl)-[1,2,4]triazolo[1,5-a]pyridine (0.300 g, 1.031 mmol), ethanol (3.44 mL), sodium iodide (0.015 g, 0.103 mmol) and potassium acetate (0.051 g, 0.516 mmol). The reaction vial was capped and heated to 55° C. overnight. The reaction mixture was cooled to room temperature and concentrated to dryness. Water and ethyl acetate were added and the mixture was transferred to a separatory funnel. The layers were separated and the organics were washed with water, then brine, dried over Na_2SO_4, filtered, and concentrated to afford 6-bromo-8-(ethoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (0.2 g, 72%). LC-MS: M^{+1}=256/258, R_t=0.79 min, [A1].

The following Fragments were prepared in a fashion similar to the synthetic methods described above.

TABLE 1

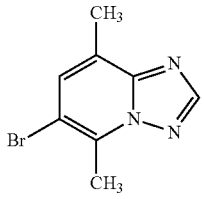
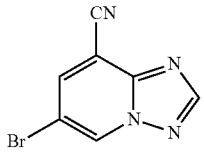
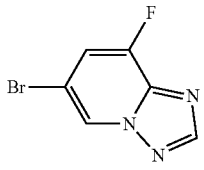
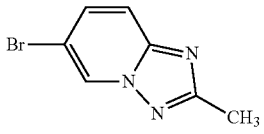
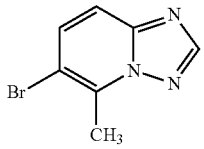
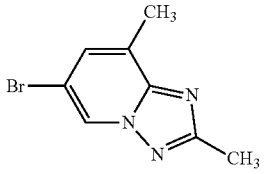
Interm. No.	Starting Material	Structure	LCMS MH^+	Ret Time	HPLC Method
F-18	5-bromo-3,6-dimethyl-pyridin-2-amine		226/228	0.77	[TS1]
F-19	2-amino-5-bromo-nicotinonitrile		222.9	0.60	[TS1]
F-20	5-bromo-3-fluoro-pyridin-2-amine		216/218	0.62	[A1]
F-21	5-bromo-4-methyl pyridin-2-amine		212/214	1.40	D
F-22	5-bromo-6-methyl pyridin-2-amine		212/214	1.47	D
F-23	5-bromo-3-methyl pyridin-2-amine		226/228	1.46	D

TABLE 1-continued

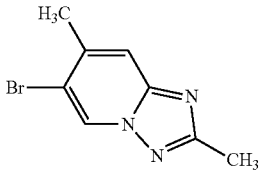
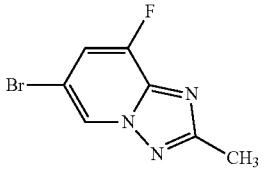
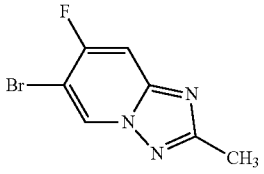
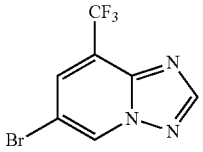
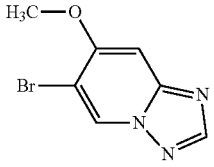
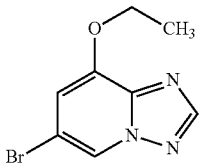
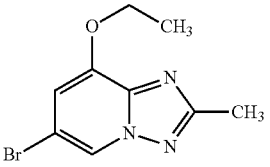
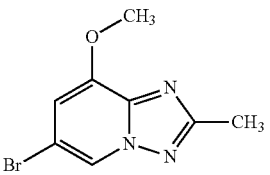
Interm. No.	Starting Material	Structure	LCMS MH^+	Ret Time	HPLC Method
F-24	5-bromo-4-methyl-pyridin-2-amine		226/228	1.45	D
F-25	5-bromo-3-fluoro-pyridin-2-amine		230/232	1.22	D
F-26	5-bromo-4-fluoro-pyridin-2-amine		230/232	1.12	D
F-27	5-bromo-3-(trifluoro-methyl)pyridin-2-amine		266/268	1.73	D
F-28	5-bromo-4-methoxy-pyridin-2-amine		228/230	1.39	D
F-29	5-bromo-3-ethoxy-pyridin-2-amine		242/244	0.99	D
F-30	5-bromo-3-ethoxy-pyridin-2-amine		256/258	1.93	D
F-31	5-bromo-3-methoxy-pyridin-2-amine		242/244	1.55	D

TABLE 1-continued

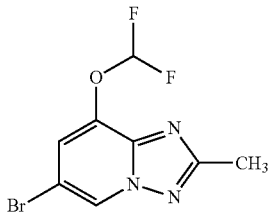
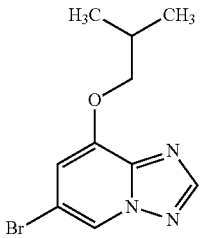
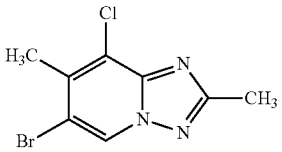
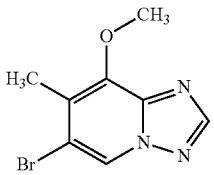
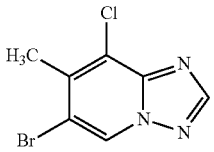
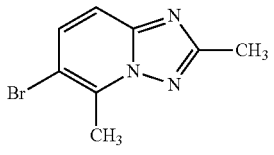
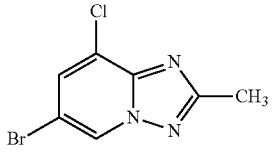
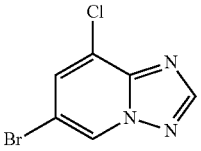
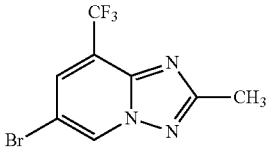
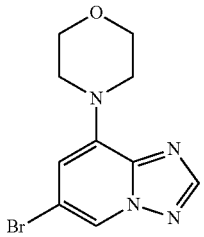
Interm. No.	Starting Material	Structure	LCMS MH^+	Ret Time	HPLC Method
F-32	5-bromo-3-(difluoro-methoxy)pyridin-2-amine		278/280	2.06	D
F-33	5-bromo-4-isobutoxy-pyridin-2-amine		270/272	2.06	D
F-34	5-bromo-3-chloro-4-methylpyridin-2-amine		260/262	1.41	B
F-35	3,5-dibromo-4-methyl-pyridin-2-amine		242/244	1.1	B
F-36	5-bromo-3-chloro-4-methylpyridin-2-amine		246/248	9.9	A
F-37	5-bromo-6-methyl pyridin-2-amine		226/228	0.55	A
F-38	5-bromo-3-chloro-pyridin-2-amine		246/248	0.55	A

TABLE 1-continued

Interm. No.	Starting Material	Structure	LCMS MH^+	Ret Time	HPLC Method
F-39	5-bromo-3-chloro-pyridin-2-amine		232/234	0.48	A
F-40	5-bromo-4-(trifluoro-methyl)pyridin-2-amine		280/282	0.67	K

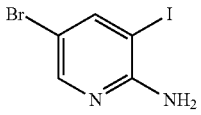
Intermediate F-41: 4-(6-bromo-[1,2,4]triazolo[1,5-a] pyridin-8-yl)morpholine

(F-41)



Intermediate F-41A: 5-bromo-3-iodopyridin-2-amine

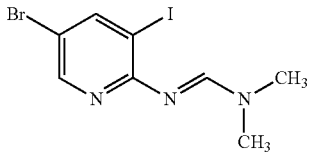
(F-41A)



To a stirred solution of 5-bromopyridin-2-amine (4.0 g, 23.12 mmol), TFA (2.316 mL, 30.1 mmol) in DMF (100 mL) at 0° C. were added portion wise NIS (6.76 g, 30.1 mmol). The reaction mixture was stirred at 50° C. for 16 h. The reaction mixture was quenched with ice cold water and sodium thiosulphate solution (3:1), the product was precipitated by adding the saturated $NaHCO_3$ solution (adjust pH-8), stirred for 10 min at 0° C. The resulting solid compound was collected by filtration to afford 5-bromo-3-iodopyridin-2-amine (5.1 g, 17.06 mmol, 73.8% yield) as a brown solid. MS (E^+) m/z: 298.9 (M). Retention time: 1.16 min. [K].

Intermediate F-42B: (E)-N'-(5-bromo-3-iodopyridin-2-yl)-N,N-dimethylformimidamide

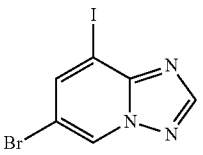
(F-42B)



A solution of DMF-DMA (11.42 mL, 85 mmol) and 5-bromo-3-iodopyridin-2-amine (5.1 g, 17.06 mmol) in DMF (20.0 mL) was stirred at 130° C. for 16 h. The reaction mixture was cooled to room temperature and the volatiles were evaporated. The mixture was dried in high vacuum to afford (E)-N'-(5-bromo-3-iodopyridin-2-yl)-N,N-dimethylformimidamide (6.2 g, 17.51 mmol, 103% yield) as a brown semi-solid. MS (E^+) m/z: 355.8 (M+2H). Retention time: 1.51 min. [K].

Intermediate F-43C: 6-bromo-8-iodo-[1,2,4]triazolo [1,5-a]pyridine

(F-43C)



To a stirred solution of (E)-N'-(5-bromo-3-iodopyridin-2-yl)-N,N-dimethylformimidamide (6.1 g, 17.23 mmol) and pyridine (6.97 mL, 86 mmol) in MeOH (80.0 mL) at 0° C. was added hydroxylamine-O-sulfonic acid (3.89 g, 34.5 mmol). The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was quenched with ice cold water and volatiles were evaporated. The mixture was dried in high vacuum. The residue was dissolved in saturated $NaHCO_3$ solution and extracted with chloroform (2×200 mL) and washed with brine. The organic layer was dried over sodium sulphate and concentrated. The resulting mate-

rial was purified by silica gel chromatography. The compound was eluted with 65% ethyl acetate and petroleum ether to afford 6-bromo-8-iodo-[1,2,4]triazolo[1,5-a]pyridine (1.8 g, 5.56 mmol, 32.2% yield) as a light yellow solid. MS (E^+) m/z: 325.8, Retention time: 1.577 min. [L].

Intermediate F-43

A stirred mixture of 6-bromo-8-iodo-[1,2,4]triazolo[1,5-a]pyridine (0.300 g, 0.926 mmol), morpholine (0.403 g, 4.63 mmol), and $Cs2CO_3$ (0.905 g, 2.78 mmol) in DMF (10.0 mL) was degassed for 5 min. Next, $Pd_2(dba)_3$ (0.085 g, 0.093 mmol) and Xantphos (0.054 g, 0.093 mmol) were added. The reaction mixture was stirred at 120° C. for 2.5 h in a microwave system. The reaction mixture was diluted with ethyl acetate, filtered and washed with excess ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium sulphate and evaporated to afford crude material. The crude material was purified using a 24 g silica gel column, compound was eluted with 35% ethyl acetate and petroleum ether to afford 4-(6-bromo-[1,2,4]triazolo[1,5-a]pyridin-8-yl)morpholine (0.180 g, 0.636 mmol, 68.6% yield) as a light yellow solid. MS (E^+) m/z: 285.0, R_t: 1.60 min. [L].

The following examples were prepared according to the general procedure described above for Intermediate F-43.

TABLE 2

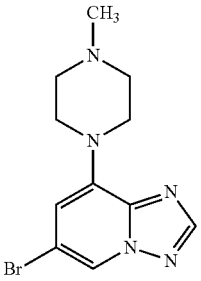
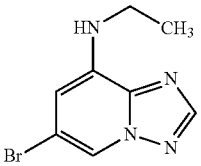
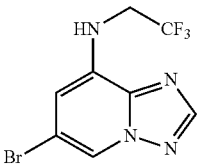
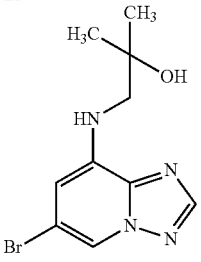
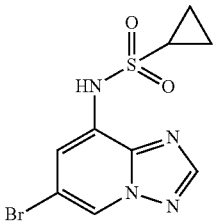
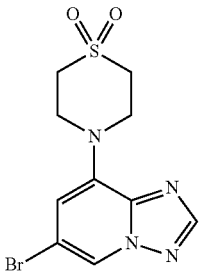
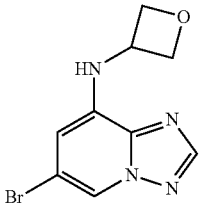
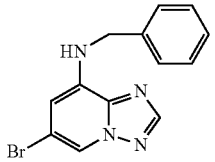
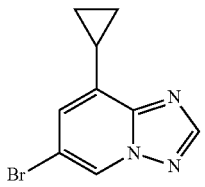
Intermediate No.	Structure	LCMS [M + 2H]	R_t (min)	HPLC Method
F-44		298.0	0.78	K
F-45		243.0	1.05	K
F-46		297.0	1.06	K
F-47		287.0	0.90	K

TABLE 2-continued

Intermediate No.	Structure	LCMS [M + 2H]	R_t (min)	HPLC Method
F-48		319.0	0.76	K
F-49		333.0	0.75	K
F-50		271.0	0.79	K
F-51		305.8	1.350	K

Intermediate F-52: 6-bromo-8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridine

(F-52)

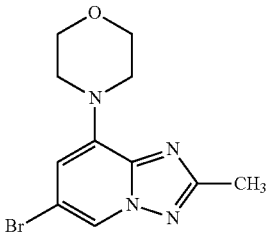


A solution of 6-bromo-8-iodo-[1,2,4]triazolo[1,5-a]pyridine (0.400 g, 1.235 mmol) and cyclopropylboronic acid (0.318 g, 3.70 mmol) in a mixture of toluene (10.0 mL) and water (2.0 mL) was degassed for 5 min. Next, tricyclohexylphosphine (0.069 g, 0.247 mmol), $Pd(OAc)_2$ (0.028 g, 0.123 mmol) and Na_2CO_3 (1.852 mL, 3.70 mmol) were added. The resultant reaction mixture was stirred at 100° C. for 14 h in a sealed tube. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, filtered, and washed with excess ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium

sulphate, and evaporated to afford the crude compound. The crude compound was purified using a 40 g silica column. The compound was eluted with 35% ethyl acetate and pet ether to afford 6-bromo-8-cyclopropyl-[1,2,4]triazolo[1,5-a] pyridine (0.240 g, 1.008 mmol, 82% yield) as a light yellow solid. MS (E^+) m/z: 240.0, R_t: 1.05 min. [M].

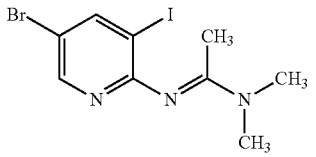
Intermediate F-53: 4-(6-bromo-2-methyl-[1,2,4] triazolo[1,5-a]pyridin-8-yl)morpholine

(F-53)



Intermediate F-53A: (E)-N-(5-bromo-3-iodopyridin-2-yl)-N,N-dimethylacetimidamide

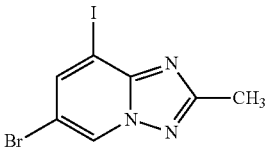
(F-53A)



A solution of 1,1-dimethoxy-N,N-dimethylpropan-2-amine (24.63 g, 167 mmol) and 5-bromo-3-iodopyridin-2-amine (5.0 g, 16.73 mmol) in DMF (20.0 mL) was stirred at 130° C. for 16 h. The reaction mixture was cooled to room temperature. The volatiles were evaporated and the material was dried in high vacuum to afford (E)-N'-(5-bromo-3-iodopyridin-2-yl)-N,N-dimethylacetimidamide (5.8 g, 15.76 mmol, 94% yield) as a brown semi-solid. MS (E^+) m/z: 370.0, R_t: 0.68 min. [M].

Intermediate F-53B: 6-bromo-8-iodo-2-methyl-[1,2, 4]triazolo[1,5-a]pyridine

(F-53B)



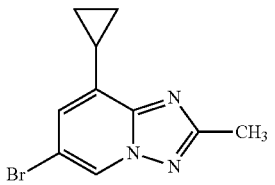
To a stirred solution of (E)-N'-(5-bromo-3-iodopyridin-2-yl)-N,N-dimethylacetimidamide (4.5 g, 12.23 mmol) and pyridine (4.94 mL, 61.1 mmol) in methanol (80.0 mL) at 0° C. was added hydroxylamine-O-sulfonic acid (2.76 g, 24.46 mmol). The reaction mixture was stirred at room temperature for 16 h. The reaction was quenched with ice cold water. The volatiles were evaporated and the resulting material was dried in high vacuum. The residue was dissolved in saturated $NaHCO_3$ solution, extracted with chloroform (2×200 mL) and washed with brine. The organic layer was dried over sodium sulphate and concentrated to afford crude material. The crude material was purified using a 40 g silica column. The compound was eluted with 50% ethyl acetate and pet ether to afford 6-bromo-8-iodo-2-methyl-[1,2,4]triazolo[1, 5-a]pyridine (2.2 g, 6.51 mmol, 53.2% yield) as a light yellow solid. MS (E^+) m/z: 337.9 (M), R_t: 1.04 min. [L].

Intermediate F-53

A stirred mixture of 6-bromo-8-iodo-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.300 g, 0.888 mmol), morpholine (0.232 g, 2.66 mmol), and Cs_2CO_3 (0.723 g, 2.219 mmol) in DMF (10.0 mL) was degassed for 5 min. Next, Xantphos (0.051 g, 0.089 mmol) and $Pd_2(dba)_3$ (0.081 g, 0.089 mmol) were added. The reaction mixture was stirred at 120° C. for 2.5 h in a microwave system. The reaction mixture was diluted with ethyl acetate, filtered and washed with excess ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium sulphate, and evaporated to obtain crude material. The crude material was purified using a 24 g silica column. The compound was eluted with 80% ethyl acetate and pet ether to afford 4-(6-bromo-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl) morpholine (0.180 g, 0.606 mmol, 68.2% yield) as a light yellow solid. MS (E^+) m/z: 298.8, R_t: 1.08 min. [K].

Intermediate F-54: 6-bromo-8-cyclopropyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridine

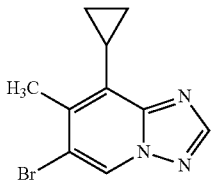
(F-54)



A solution of 6-bromo-8-iodo-2-methyl-[1,2,4]triazolo[1, 5-a]pyridine (0.400 g, 1.184 mmol) and cyclopropylboronic acid (0.305 g, 3.55 mmol) in a mixture of toluene (10.0 mL) and water (2.0 mL) was degassed for 5 min. Next, tricyclohexylphosphine (0.066 g, 0.237 mmol), $Pd(OAc)_2$ (0.027 g, 0.118 mmol) and Na_2CO_3 (1.775 mL, 3.55 mmol) were added. The reaction mixture was stirred at 100° C. for 14 h in a sealed tube. The reaction mixture was cooled to room temperature. The mixture was diluted with ethyl acetate, filtered, and washed with excess ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium sulphate, and evaporated to afford the crude compound. The crude compound was purified using a 24 g silica column. The compound was eluted with 35% ethyl acetate and pet ether to afford 6-bromo-8-cyclopropyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.220 g, 0.873 mmol, 73.7% yield) as a light yellow solid. MS (E^+) m/z: 254.0, R_t: 1.12 min. [K].

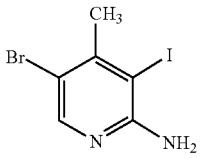
Intermediate F-55: 6-bromo-8-cyclopropyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridine

(F-55)



Intermediate F-55A: 5-bromo-3-iodo-4-methylpyridin-2-amine

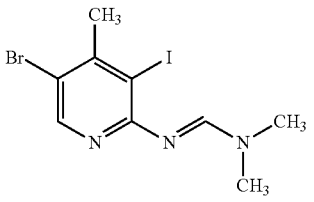
(F-55A)



To a stirred solution of 5-bromo-4-methylpyridin-2-amine (5.0 g, 26.7 mmol), TFA (2.471 mL, 32.1 mmol) in DMF (100 mL) at 0° C. was added portion-wise NIS (9.02 g, 40.1 mmol). The reaction mixture was stirred at 55° C. for 2 h. The reaction was quenched with ice cold water and sodium thiosulphate solution (3:1). The product was precipitated by adding saturated $NaHCO_3$ solution (adjust pH-8) and stirring for 10 min at 0° C. The solid compound was collected by filtration to afford 5-bromo-3-iodo-4-methylpyridin-2-amine (8 g, 25.6 mmol, 96% yield) as a brown solid. MS (E^+) m/z: 314.9, R_t: 0.92 min. [M].

Intermediate F-55B (E)-N'-(5-bromo-3-iodo-4-methylpyridin-2-yl)-N,N-dimethylformimidamide

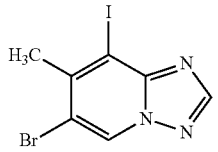
(F-55B)



A solution of DMF-DMA (10.70 mL, 80 mmol) and 5-bromo-3-iodo-4-methylpyridin-2-amine (2.5 g, 7.99 mmol) in DMF (15.0 mL) was stirred at 130° C. for 16 h. The reaction mixture was cooled to room temperature and the volatiles were evaporated. The material was dried in high vacuum to afford crude (E)-N'-(5-bromo-3-iodo-4-methylpyridin-2-yl)-N,N-dimethylformimidamide (2.8 g, 7.61 mmol, 95% yield) as a brown semi-solid. MS (E^+) m/z: 370.1, R_t: 1.59 min. [K].

Intermediate F-55C: 6-bromo-8-iodo-7-methyl-[1,2,4]triazolo[1,5-a]pyridine

(F-55C)



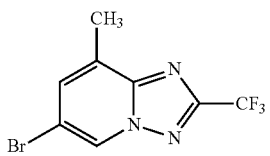
To a stirred solution of (E)-N'-(5-bromo-3-iodo-4-methylpyridin-2-yl)-N,N-dimethyl formimidamide (2.8 g, 7.61 mmol) and pyridine (3.08 mL, 38.0 mmol) in methanol (60.0 mL) at 0° C. was added hydroxylamine-O-sulfonic acid (1.290 g, 11.41 mmol). The reaction mixture was stirred at room temperature for 16 h. The reaction was quenched with ice cold water. The volatiles were evaporated and the mixture was dried in high vacuum. The residue was dissolved in saturated $NaHCO_3$ solution, extracted with chloroform (2×150 mL), and washed with brine. The organic layer was dried over sodium sulphate and concentrated to afford crude product. The crude product was purified by silica gel chromatography. The compound eluted with 65% ethyl acetate and pet ether to afford 6-bromo-8-iodo-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (1.5 g, 4.44 mmol, 58.3% yield) as a light yellow solid. MS (E^+) m/z: 338.2 (M), Retention time: 1.11 min. [K].

Intermediate F-55

A solution of 6-bromo-8-iodo-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.400 g, 1.184 mmol) and cyclopropylboronic acid (0.305 g, 3.55 mmol) in mixture of toluene (15.0 mL) and water (3.0 mL) was degassed for 5 min. Next, tricyclohexylphosphine (0.066 g, 0.237 mmol), $Pd(OAc)_2$ (0.027 g, 0.118 mmol) and Na_2CO_3 (1.775 mL, 3.55 mmol) were added. The reaction mixture was stirred at 100° C. for 14 h in a sealed tube. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, filtered, and washed with excess ethyl acetate. The combined organic layers were washed with water, brine, dried over sodium sulphate, and evaporated to afford crude compound. The crude compound was purified by silica gel chromatography. The compound eluted with 35% ethyl acetate and pet ether to afford 6-bromo-8-cyclopropyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.280 g, 1.111 mmol, 94% yield) as a light yellow solid. MS (E^+) m/z: 254.0, R_t: 2.11 min. [L]

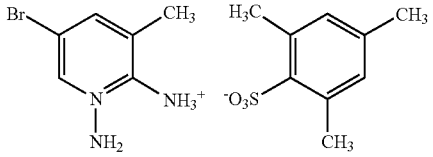
Intermediate F-56: 6-bromo-8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine

(F-56)



Intermediate F-56A: 5-bromo-3-methyl-1λ⁴-pyridine-1,2-diamine 2,4,6-trimethylbenzenesulfonate

(F-56A)



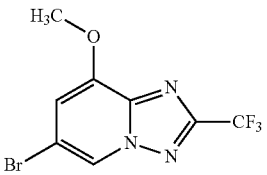
To a stirred solution of ethyl o-mesitylsulfonylacetohydroxamate (3.05 g, 10.69 mmol) in dioxane (20 mL) cooled to 0° C. was added perchloric acid (1.074 g, 10.69 mmol). The mixture was stirred at ambient temperature for 30 min. The reaction mass was quenched with ice cold water, extracted with dichloromethane (100 mL), dried over sodium sulphate, and concentrated to afford crude 1-amino-5-bromo-3-methyl-1λ⁴-pyridin-2-aminium 2,4,6-trimethylbenzenesulfonate. To a stirred solution of 5-bromo-3-methylpyridin-2-amine (2 g, 10.69 mmol) in DCM (10 mL) was added 1-amino-5-bromo-3-methyl-1λ⁴-pyridin-2-aminium 2,4,6-trimethylbenzenesulfonate at 0° C. The reaction mixture was stirred at ambient temperature for 1 h. The reaction mixture was diluted with water (25 mL), extracted with DCM (2×100 mL), dried over sodium sulphate, and concentrated to afford 1,2-diamino-5-bromo-3-methylpyridin-1-ium,2,4,6-trimethylbenzenesulfonate as a white solid (2.1 g, 93%). ^{1}H NMR (300 MHz, CHLOROFORM-d) δ=7.91 (br. s., 1H), 7.63 (d, J=15.9 Hz, 1H), 7.28 (s, 2H), 6.89 (s, 1H), 3.72 (s, 1H), 2.81-2.47 (m, 6H), 2.36-2.02 (m, 6H), 1.23 (t, J=7.0 Hz, 2H).

Intermediate F-56

To a stirred solution of 1,2-diamino-5-bromo-3-methylpyridin-1-ium,2,4,6-trimethylbenzenesulfonate (1 g, 2.141 mmol) in MeOH (25 mL) at 0° C. was added trifluoroacetic anhydride (0.351 mL, 2.486 mmol). The reaction mixture was stirred for 10 min at the same temperature. Next, Et_3N (0.346 mL, 2.486 mmol) was added and the reaction mixture was stirred at ambient temperature for 16 h. The reaction mixture was concentrated. The reaction was quenched with water (25 mL). The reaction mixture was extracted with EtOAc (2×100 mL), dried over sodium sulphate, and concentrated to afford 6-bromo-8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine. The crude mass was purified by silica gel chromatography and eluted in 40% EtOAc in hexane to afford 6-bromo-8-methyl-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (500 mg, 71.8%) as off white solid. LC retention time=1.28 min [K]. MS (E^-) m/z: 280.0 (M+H).

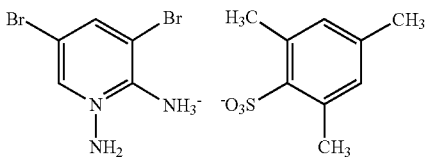
Intermediate F-57: 6-bromo-8-methoxy-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine

(F-57)



Intermediate F-57A: 3,5-dibromo-1λ⁴-pyridine-1,2-diamine 2,4,6-trimethylbenzenesulfonate

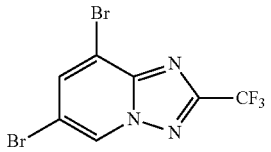
(F-57A)



To a stirred solution of ethyl o-mesitylsulfonylacetohydroxamate (2.266 g, 7.94 mmol) in dioxane (20 mL) cooled to 0° C. was added perchloric acid (1.074 g, 10.69 mmol). The reaction mixture was stirred at ambient temperature for 30 min. The reaction was quenched with ice cold water. The reaction mixture was extracted with dichloromethane (100 mL), dried over sodium sulphate, and concentrated to afford crude 1-amino-3,5-dibromo-1λ⁴-pyridin-2-aminium 2,4,6-trimethylbenzenesulfonate. To a stirred solution of 3,5-dibromopyridin-2-amine (2 g, 7.94 mmol) in DCM (10 mL) was added 1-amino-3,5-dibromo-1λ⁴-pyridin-2-aminium 2,4,6-trimethylbenzenesulfonate at 0° C. The reaction mixture was stirred at ambient temperature for 1 h. The reaction mixture was diluted with water (25 mL), extracted with DCM (2×100 mL), dried over sodium sulphate, and concentrated to afford 1,2-diamino-3,5-dibromopyridin-1-ium, 2,4,6-trimethylbenzenesulfonate as a white solid (2.1 g, 93.5%). ^{1}H NMR (400 MHz, DMSO-d6) δ=7.88 (d, J=2.0 Hz, 1H), 7.70 (d, J=2.0 Hz, 1H), 7.12 (s, 1H), 6.70 (s, 4H), 3.56 (s, 1H), 2.10 (s, 6H).

Intermediate F-57B: 6,8-dibromo-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine

(F-57B)



To a stirred solution of 1,2-diamino-3,5-dibromopyridin-1-ium, 2,4,6-trimethylbenzenesulfonate (1 g, 2.141 mmol) in MeOH (25 mL) cooled to 0° C. was added trifluoroacetic anhydride (0.351 mL, 2.486 mmol). The reaction mixture was stirred for 10 mins. After Et_3N-(0.346 mL, 2.486 mmol) was added, the reaction mixture was stirred at ambient temperature for 16 h. The reaction mixture was concentrated, quenched with water (25 mL), extracted with EtOAc (2×100 mL), dried over sodium sulphate, and concentrated to afford 6,8-dibromo-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine. The crude mass was purified by silica gel chromatography, and eluted with 40% EtOAc in hexane to afford 6,8-dibromo-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (650 mg, 73.8%) as off white solid. LC retention time=1.37 min [K]. MS (E^-) m/z: 344.0 (M+H).

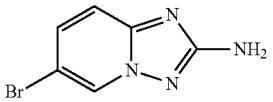
Intermediate F-57

To a solution of 6,8-dibromo-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (350 mg, 1.015 mmol) in acetonitrile

(15 mL) was added sodium methoxide (54.8 mg, 1.015 mmol). The resulting mixture was stirred at 85° C. for 1 h. The reaction mixture was quenched with water (20 mL), extracted with EtOAc (2×50 mL), dried over sodium sulphate, and concentrated to afford 6-bromo-8-methoxy-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine. The crude mass was purified by silica gel chromatography, and was eluted with 50% EtOAc in hexane to afford 6-bromo-8-methoxy-2-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (160 mg, 53.5%) as white solid. LC retention time=1.26 min [K]. MS (E^-) m/z: 294.0 (M−H).

Intermediate F-58: 6-bromo-[1,2,4]triazolo[1,5-a] pyridin-2-amine

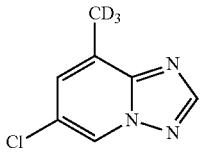
(F-58)



Commercially available reagent: CAS No 356560-80-0.

Intermediate F-59: 6-chloro-8-trideuteromethyl-[1,2, 4]triazolo[1,5-a]pyridine

(F-59)



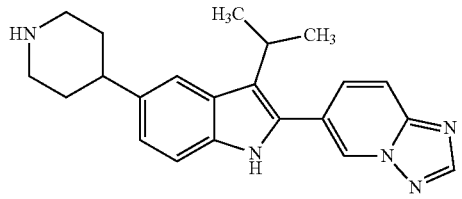
8-bromo-6-chloro-[1,2,4]triazolo[1,5-a]pyridine was prepared following the general procedure for F-2 starting from 3-bromo-5-chloropyridin-2-amine. LC retention time 0.67 min [TS1]. MS (ES^+) m/z: 233.9 (M+H).

A solution of 8-bromo-6-chloro-[1,2,4]triazolo[1,5-a] pyridine (150 mg, 0.645 mmol) in THF (5.0 mL) was degassed with nitrogen gas for 5 minutes. Iron(III) acetylacetonate (22.79 mg, 0.065 mmol) was added. The light yellow solution became red and was degassed again, and then evacuated and backfilled with nitrogen gas three times. Trideuteromethylmagnesium iodide (0.97 mL, 0.97 mmol) was added and the reaction mixture was stirred for 30 minutes at room temperature. Upon completion, the reaction mixture was diluted with dichloromethane (20 mL), ammonium chloride (10 mL) and water (10 mL). The layers were separated, and the aqueous layer was extracted with dichloromethane (2×15 mL). The combined organic layers were dried over sodium sulfate, filtered, and concentrated to afford a crude residue, which was purified using silica gel chromatography eluting with hexanes/ethyl acetate 0-70% to afford 6-chloro-8-trideuteromethyl-[1,2,4]triazolo[1,5-a] pyridine (41 mg, 0.240 mmol, 37.2% yield). LC retention time 0.64 min [TS1]. MS (ES^+) m/z: 171.08 (M+H). ^1H NMR (400 MHz, CHLOROFORM-d) δ 8.50 (d, J=2.0 Hz, 1H), 8.30 (s, 1H), 7.29 (d, J=2.0 Hz, 1H).

Example 1

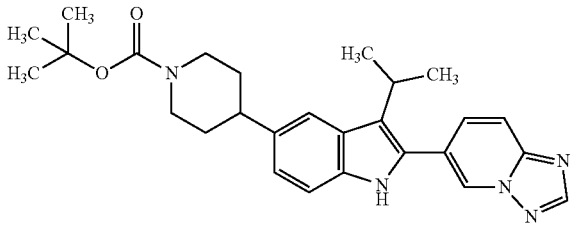
6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1, 2,4]triazolo[1,5-a]pyridine

(1)



Intermediate 1A: tert-butyl 4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(1A)



To a stirred solution of tert-butyl 4-(3-isopropyl-2-(4,4,5, 5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (50 mg, 0.107 mmol), 6-bromo-[1,2, 4]triazolo[1,5-a]pyridine (31.7 mg, 0.160 mmol) in tetrahydrofuran (5 mL), and water (0.5 mL) was added potassium phosphate tribasic (68.0 mg, 0.320 mmol). The solution was degassed with nitrogen for 10 mins. Next, $PdCl_2$(dppf) (7.81 mg, 10.67 μmol) was added and the solution was degassed again for 10 mins. The reaction mixture was heated to 75° C. for 16 h. The reaction progress was monitored by LCMS. The reaction mass was filtered through a celite bed, washed with EtOAc, and concentrated to afford tert-butyl 4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (50 mg, 0.109 mmol). The material was carried on directly into the subsequent step without further purification.

Example 1

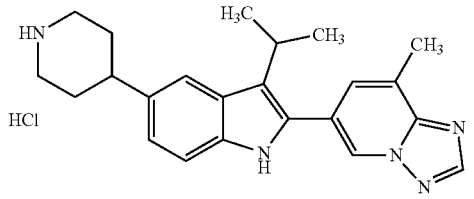
To a stirred solution of tert-butyl 4-(2-([1,2,4]triazolo[1, 5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxy late (50 mg, 0.109 mmol) in DCM (2 mL) was added 1,4-dioxane (4N HCl) (0.2 mL). The reaction mixture was stirred at room temperature for 16 h. The progress of the reaction was monitored by LCMS. The reaction mixture was concentrated and the crude material was purified by preparative LC/MS with the following conditions: Waters Xbridge C18,19×150 mm, 5 μm; Guard Column: Water XBridge C18,19×10 mm, 5 μm; Mobile Phase A: 5:95 acetonitrile:water with 0.1% TFA; Mobile Phase B: 95:5 acetonitrile:water with 0.1% TFA; Gradient: 2-20% B over 25 minutes, followed by a 10 minute hold at 20% B and 5

minute hold at 100% B; Flow:15 mL/min. Fractions containing the product were combined and dried using a Genevac centrifugal evaporator. The yield of the product was 5.4 mg, and its estimated purity by LCMS analysis was 100%. Two analytical LC/MS injections were used to determine the final purity. Injection 1 conditions: Column: Ascentis Express C18(50×2.1)mm, 2.7 μm; Mobile Phase A: 5:95 Acetonitrile:water with 10 mM NH_4OAc; Mobile Phase B: 95:5 Acetonitrile:water with 10 mM NH_4OAc; Temprature: 50° C.; Gradient: 0-100% B over 3 minutes; Flow: 1.1 mL/min. Injection 2 conditions: Column: Ascentis Express C18(50×2.1)mm, 2.7 μm; Mobile Phase A: 5:95 acetonitrile: water with 0.1% TFA; Mobile Phase B: 95: 5 Acetonitrile: water with 0.1% TFA; Temperature: 50° C.; Gradient:0-100% B over 3 minutes; Flow:1.1 mL/min. LCMS MH^+=360 Ret. Time=0.66 min [A1]; Proton NMR was acquired in deuterated DMSO. ^1H NMR (400 MHz, DMSO-d_6) δ=11.24 (s, 1H), 9.01 (d, J=1.0 Hz, 1H), 8.66-8.55 (m, 1H), 8.03-7.96 (m, 1H), 7.79 (dd, J=9.0, 1.5 Hz, 1H), 7.57 (s, 1H), 7.35 (d, J=8.5 Hz, 1H), 7.02 (dd, 1.3 Hz, 1H), 3.41 (d, J=12.0 Hz, 2H), 3.30-3.23 (m, 1H), 3.10-3.00 (m, 2H), 2.96-2.90 (m, 1H), 2.03-1.94 (m, 2H), 1.91-1.84 (m, 2H), 1.45 (d, J=7.0 Hz, 6H).

Example 2

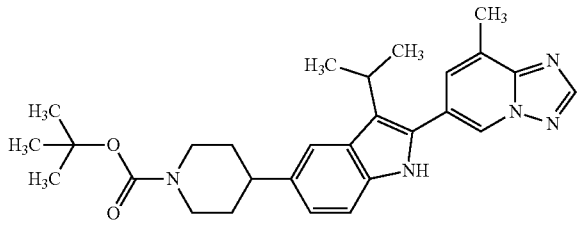
6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine hydrochloride

(2)



Intermediate 2A: tert-butyl 4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

(2A)



The preparation was performed in two batches and combined for workup.

Batch #1: To a mixture of tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (10 g, 23.73 mmol), bis(benzonitrile)palladium(II) chloride (0.182 g, 0.475 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (0.390 g, 0.949 mmol) in dioxane (80 mL) under nitrogen were added pinacolborane (8.61 mL, 59.3 mmol) and triethylamine (6.62 mL, 47.5 mmol). The mixture was heated at 85° C. for 5 min. After cooling down to room temperature, 2 M potassium phosphate tribasic solution (35.6 mL, 71.2 mmol) was added slowly. Next, 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (4.53 g, 21.36 mmol) was added, followed by $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.775 g, 0.949 mmol). The reaction mixture was stirred for 30 min at 65° C.

Batch #2: In a 1 L round bottom flask, pinacolborane (25.8 mL, 178 mmol) and triethylamine (19.85 mL, 142 mmol) were added to a mixture of tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (30 g, 71.2 mmol), bis(benzonitrile) palladium(II) chloride (0.546 g, 1.424 mmol), and 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (1.169 g, 2.85 mmol) in dioxane (240 mL) under nitrogen. The mixture was heated at 85° C. for 5 min. After cooling down to room temperature, 2 M potassium phosphate tribasic solution (107 mL, 214 mmol) was added very slowly first for the first 10 mL. When there were no more bubbles, the remainder of the K_3PO_4 solution was rapidly added, followed by the additions of 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (13.59 g, 64.1 mmol) and $PdCl_2$(dppf)-CH_2Cl_2 adduct (2.326 g, 2.85 mmol). The reaction mixture was stirred for 1 h at 65° C.

The two batches were combined for workup. The aqueous layer was removed and the organic layer was washed with brine, dried over Na_2SO_4, filtered through a Celite pad, and concentrated to give a dark oil (87 g). The material was purified by silica gel chromatography (hexanes/ethyl acetate as eluent) affording 29 grams of the product. LCMS MH^+=430.1 Ret. Time=0.63 min [C1]; ^1H NMR (400 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.80 (d, J=0.7 Hz, 1H), 8.53 (s, 1H), 7.65-7.52 (m, 2H), 7.30 (d, J=8.4 Hz, 1H), 7.02 (dd, J=8.4, 1.5 Hz, 1H), 4.19-4.04 (m, 2H), 3.28-3.19 (m, 1H), 2.96-2.70 (m, 3H), 2.63 (s, 6H), 2.38-2.26 (m, 1H), 1.80 (d, J=12.6 Hz, 2H), 1.56 (qd, J=12.4, 4.0 Hz, 2H), 1.47-1.38 (m, 12H).

Alternative Preparation of Intermediate 2A

To a 500 mL round bottle flask were added tert-butyl 4-(2-bromo-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (11 g, 26.1 mmol), bis(benzonitrile)palladium(II) chloride (0.200 g, 0.522 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (0.429 g, 1.044 mmol) and dioxane (87 mL). Nitrogen was bubbled through the reaction mixture for 5 min. Next, pinacolborane (9.47 ml, 65.3 mmol) and triethylamine (9.10 ml, 65.3 mmol) were added to the reaction mixture. The triethylamine was added in small portions slowly for the first ⅓ and then the rest ⅔ was added quickly. The reaction mixture was heated at 85° C. for 10 min under N_2. The reaction temperature reached 100° C. The reaction mixture was cooled to room temperature with an ice-water bath. Next, 2 M potassium phosphate tribasic solution (39.2 mL, 78 mmol) was added. The first 1/10 was added slowly. When there was no more bubbles, the remainder of the K_3PO_4 solution was added, followed by 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (4.98 g, 23.49 mmol), $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.853 g, 1.044 mmol) washed in with dioxane (10 mL). The mixture was heated at 65° C. for 1 h under N_2. After the mixture was cooled to room temperature, the organic layer and the aqueous layer was separated. EtOAc was used to wash the flask during the transfer. The organic layer was washed with brine, dried over Na_2SO_4, filtered through a Celite pad and concentrated to give 44.4 g crude oil. It was purified with silica gel

chromatography using a 1.5 kg silica column. The column was eluted with hexane and ethyl acetate. The product was eluted at 60% ethyl acetate:hexane to afford tert-butyl 4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (9.27 g, 19.58 mmol, 75% yield) as a lighted tinted foam. LCMS 474.3; HPLC Ret. Time 1.15 min. Method G. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.61-8.54 (m, 1H), 8.43-8.38 (m, 1H), 7.96-7.88 (m, 1H), 7.70-7.64 (m, 1H), 7.48-7.44 (m, 1H), 7.40-7.35 (m, 1H), 7.17-7.09 (m, 1H), 4.40-4.23 (m, 2H), 3.40-3.26 (m, 1H), 2.75 (s, 6H), 1.98-1.89 (m, 2H), 1.85-1.67 (m, 2H), 1.53 (m, 12H), 1.52-1.49 (s, 3H).

Example 2

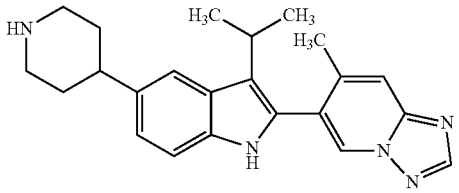
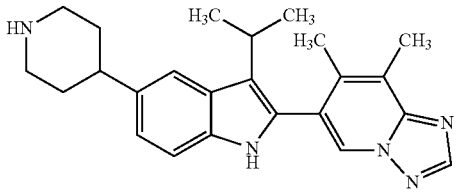
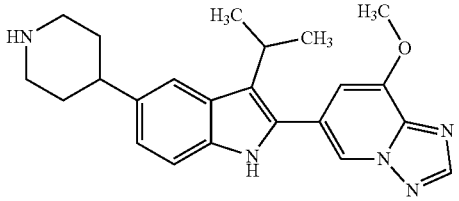
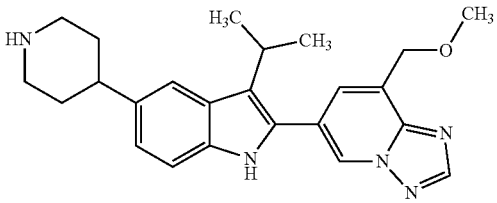
To a stirred solution of tert-butyl 4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidine-1-carboxylate (29 g, 61.2 mmol) in DCM (102 mL), was added 4 M HCl in dioxane (77 mL, 306 mmol) through a syringe. The temperature was observed to increased several degrees. The solution turned into a suspension during the addition, then a clear solution, then a heavy suspension again. MeOH (306 mL) was added to give a clear solution. LCMS showed the reaction was close to completion after 2.5 hr at room temperature. The reaction mixture was concentrated under reduced pressure with a water bath (T=45° C.) and then diluted with diethyl ether (200 mL). The product was collected by filtration to afford 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine dihydrochloride. LC-MS: M+1=374, rt=0.80 min., [A1]; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.10 (s, 1H), 8.80 (d, J=0.7 Hz, 1H), 8.54 (s, 1H), 7.66-7.50 (m, 2H), 7.30 (d, J=8.3 Hz, 1H), 7.02 (dd, 1.5 Hz, 1H), 4.09 (q, J=5.3 Hz, 1H), 3.38-3.23 (m, 6H), 3.18 (d, J=5.3 Hz, 2H), 3.06 (d, J=11.5 Hz, 1H), 2.74-2.59 (m, 4H), 1.75 (d, J=10.0 Hz, 2H), 1.68-1.52 (m, 2H), 1.51-1.37 (m, 6H).

Alternative Preparation of Example 2

To a stirred solution of tert-butyl 4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidine-1-carboxylate (7.45 g, 15.73 mmol) in DCM (40 mL) was added 4 M HCl in dioxane (35.4 mL, 142 mmol) through a syringe at room temperature. The solution turned to a suspension during the addition, then a clear solution, then a heavy suspension again. MeOH (100 mL) was added to give a clear solution. The reaction was complete in 2 h. The reaction mixture was concentrated under reduced pressure and then diluted with diethyl ether (200 mL). The desired product HCl salt was collected by filtration to afford 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine hydrochloride (6.4 g, 15.64 mmol, 99.4% yield) as a yellow. LCMS MH$^+$: 374.1; HPLC Ret. Time 0.64 min. Method G.

The following examples were prepared according to the general procedures disclosed in Examples 1 and 2.

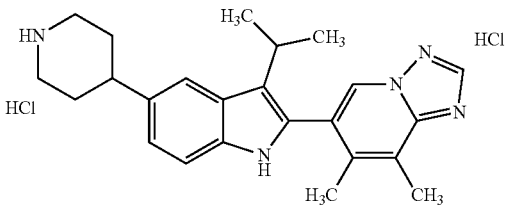
TABLE 3

Ex. No.	Structure	Interm.	LCMS [M + H]	Rt (min)	Method
3		F-3	374.3	1.07	QC-ACN-TFA-XB
4		F-4	388.3	1.26	QC-ACN-AA-XB
5		F-5	390.3	1.02	Method E
6		F-6	404.3	1.21	QC-ACN-AA-XB

Example 4

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine dihydrochloride

(4)

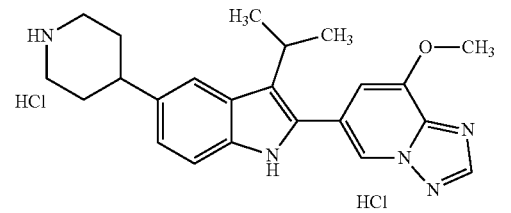


To a stirred suspension of tert-butyl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (37.8 g, 78 mmol) in DCM (97 ml) and MeOH (291 ml) was added 4 M HCl in dioxane (97 mL, 388 mmol) at room temperature to give a clear solution. After a few hours, the reaction mixture became a white suspension. The reaction was complete after 4 h. The reaction mixture was concentrated under reduced pressure and then diluted with diethyl ether (250 mL). The product bis-HCl salt was collected by filtration to afford 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine, 2 HCl (34.66 g, 75 mmol, 97% yield) as an off-white solid. LCMS MH^+: 388.3; HPLC Ret. Time 1.26 min. Method QC-ACN-AA-XB. ^1H NMR (500 MHz, DMSO-d_6) δ 11.08-10.95 (m, 1H), 8.77-8.67 (m, 1H), 8.55-8.41 (m, 1H), 7.64-7.48 (m, 1H), 7.39-7.27 (m, 1H), 7.05-6.94 (m, 1H), 3.47-3.34 (m, 1H), 3.11-2.99 (m, 2H), 2.98-2.82 (m, 2H), 2.61-2.57 (m, 3H), 2.56-2.54 (m, 1H), 2.18-2.13 (m, 3H), 2.03-1.83 (m, 4H), 1.39-1.26 (m, 6H).

Example 5

6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine dihydrochloride

(5)

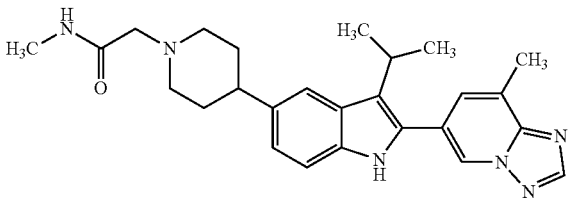


To a stirred suspension of tert-butyl 4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidine-1-carboxylate (46.5 g, 95 mmol) in DCM (47.5 mL) and MeOH (190 mL), was added 4M HCl in dioxane (119 mL, 475 mmol) at room temperature. After 1 h, the clear solution became a white suspension. MeOH (50 mL) was added and the suspension was stirred for another hour. The reaction mixture was concentrated under reduced pressure and then diluted with diethyl ether (300 mL). The desired product HCl salt was collected by filtration and dried for two days to afford 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine dihydrochloride (33.6 g, 72.7 mmol, 76% yield) as an off-white solid. LCMS MH_+: 390.1. HPLC Ret. Time 0.64 min. Method G.

Example 7

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N-methylacetamide

(7)



Triethylamine (9.70 mL, 69.6 mmol) and 2-chloro-N-methylacetamide (2.246 g, 20.88 mmol) were added to a solution of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (2.6 g, 6.96 mmol) in THF (50 mL). The reaction mixture was stirred at room temperature for 12 h. The reaction mass was concentrated under vacuum and the residue obtained was quenched with 150 mL ice cold water resulting in the formation of a precipitate. The solids were collected by vacuum filtration and air dried. The collected solids were further dried under vacuum for 15 h to afford 2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-N-methylacetamide (1.5 g) as an off-white solid. ^1H NMR (400 MHz, DMSO-d_6) δ1.42 (d, J=7.20 Hz, 6H), 1.69-1.72 (m, 4H), 1.75-1.81 (m, 1H), 2.78-2.82 (m, 6H), 2.85-2.88 (m, 4H), 3.25-3.31 (m, 2H), 7.05 (dd, J=1.60, 8.40 Hz, 1H), 7.31 (d, J=8.40 Hz, 1H), 7.59 (d, J=10.00 Hz, 2H), 7.72-7.73 (m, 1H), 8.54 (s, 1H), 8.81 (s, 1H), 11.12 (s, 1H). LCMS for molecular formula $C_{26}H_{32}N_6O$ was 444.264; found 445 (M^-). Waters Xbridge C18,19×150 mm, 5 μm; Guard Column: Water XBridge C18,19×10 mm, 5 μm; Mobile Phase A:5:95 Acetonitrile:water with 10 mM NH_4OAc; Mobile Phase B: 95:5 Acetonitrile:water with 10 mM NH_4OAc; Gradient:10-50% B over 25 minutes, followed by a 10 minute hold at 50% B and 5 minute hold at 100% B; Flow: 15 mL/min. RT Min: 1.91, Wave length: 220 nm. HPLC:)(Bridge Phenyl (4.6×150)mm, 3.5 μm SC/749 Buffer: 0.05% TFA in water pH 2.5 Mobile Phase A: Buffer: ACN-(95:5) Mobile Phase B:ACN: Buffer (95:5) FLOW:1 mL\min TIME B % 0 10, 12 100, 15 100. Retention Time: 6.19 minutes.

The following examples were prepared according to the general procedures disclosed in Example 7.

TABLE 4

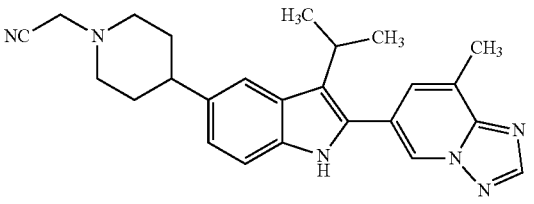
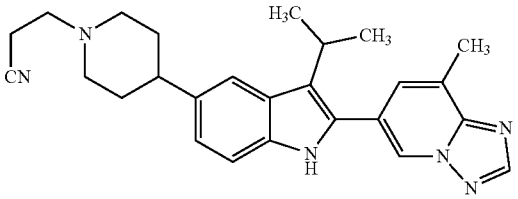
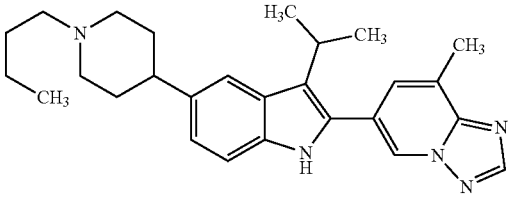
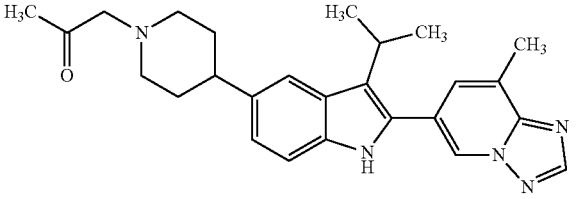
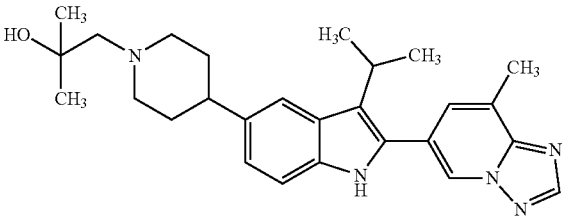
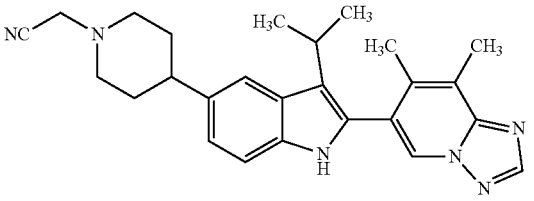
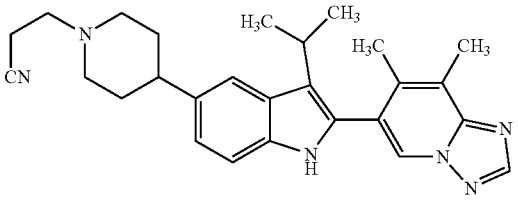
Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
8		413.3	1.28	QC-ACN-TFA-XB
9		427.2	1.82	QC-ACN-AA-XB
10		430	1.57	QC-ACN-AA-XB
11		431.4	1.24	QC-ACN-AA-XB
12		446.3	1.707	Method E
13		427.3	1.46	QC-ACN-TFA-XB
14		441.3	1.27	QC-ACN-TFA-XB

TABLE 4-continued

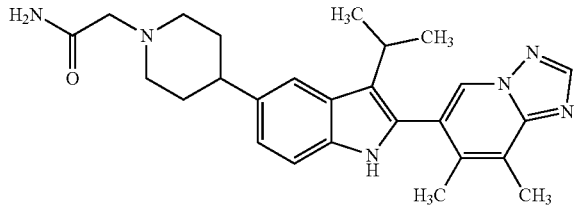
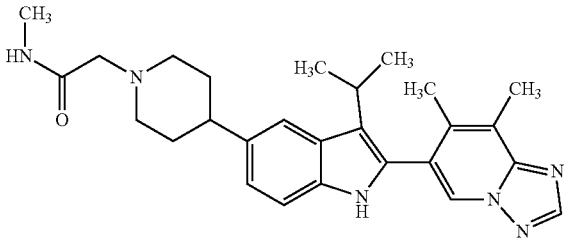
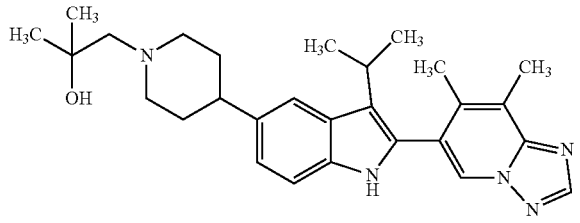
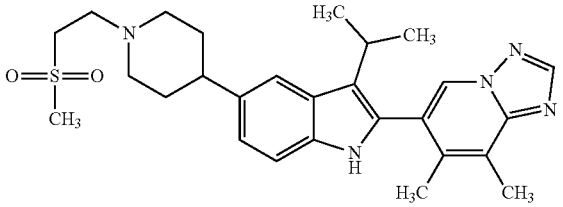
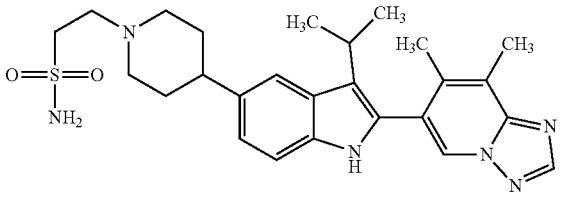
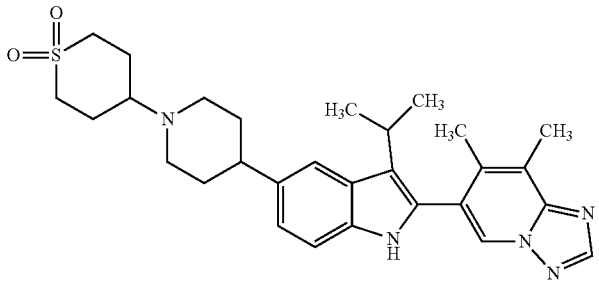
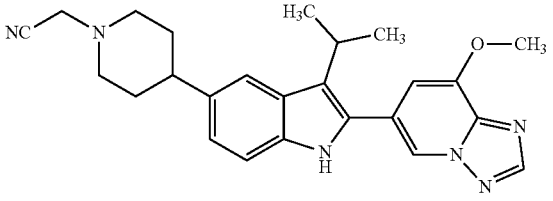
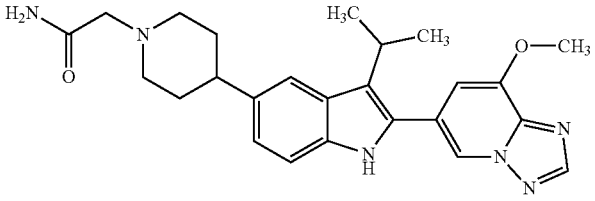
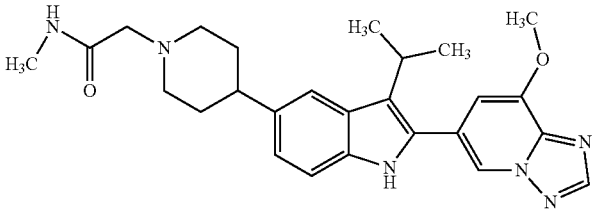
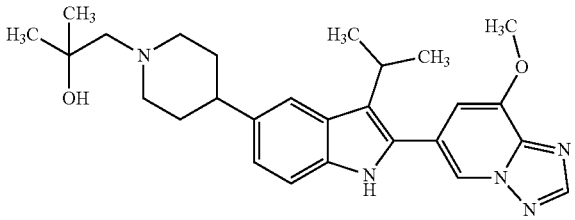
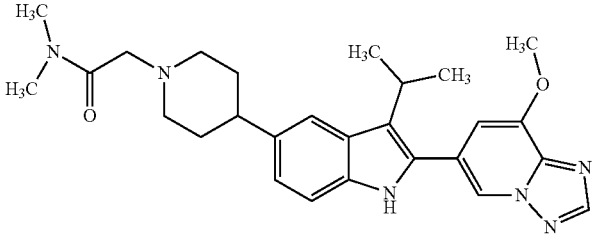
Ex. No.	Structure	LCMS MH+	R_t (min)	Method
15		445	1.19	QC-ACN-TFA-XB
16		459.5	1.71	QC-ACN-AA-XB
17		460	1.7	QC-ACN-AA-XB
18		494.3	1.71	QC-ACN-AA-XB
19		495.2	1.62	QC-ACN-AA-XB
20		520.5	1.31	QC-ACN-TFA-XB

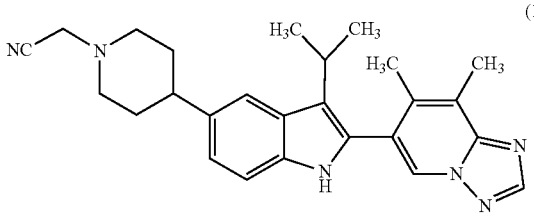
TABLE 4-continued

Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
21		429.2	1.94	Method E
22		447.2	1.64	Method E
23		461.2	1.73	Method E
24		462.4	1.40	Method E
25		475.4	1.37	Method E

Example 13

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetonitrile

(13)

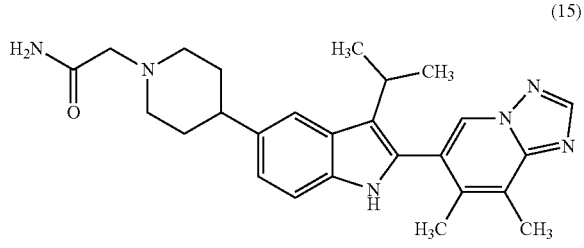


To a 1 dram vial were added 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine hydrochloride (0.050 g, 0.118 mmol), NMP, and DBU (0.025 ml, 0.164 mmol). The material went into solution and 2-bromoacetonitrile (0.014 g, 0.118 mmol) was added. The reaction vial was capped. The reaction mixture was stirred overnight at room temperature. The sample was diluted with solvent (90:10:0.1 CH_3CN:water:TFA), filtered, and purified with preparative HLPC. The crude material was purified via preparative LC/MS with the following conditions: Column:)(Bridge C18, 19×200 mm, 5 μm particles; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile:water with 10 mM ammonium acetate; Gradient: 30-70% B over 20 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the desired product were combined and dried via centrifugal evaporation to afford 2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)acetonitrile (16.8 mg, 0.039 mmol, 32.7% yield). LCMS MH^+: 427.1. HPLC Ret. Time 1.30 min. Method QC-ACN-TFA-XB. ^1H NMR (500 MHz, DMSO-d_6) δ 8.77-8.69 (m, 1H), 8.50-8.35 (m, 1H), 7.61-7.51 (m, 1H), 7.33-7.23 (m, 1H), 7.08-6.93 (m, 1H), 3.44-3.34 (m, 1H), 2.98-2.83 (m, 3H), 2.63-2.56 (m, 4H), 2.56-2.53 (m, 2H), 2.39-2.28 (m, 2H), 2.21-2.12 (m, 3H), 1.90-1.69 (m, 4H), 1.37-1.26 (m, 6H).

Example 15

2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)acetamide

(15)

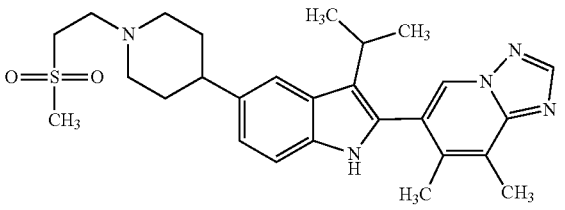


To a reaction flask were added 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine, 2 HCl (47.66 g, 104 mmol), DCE (220 mL), DBU (62.4 mL, 414 mmol), and 2-bromoacetamide (17.14 g, 124 mmol). The reaction flask was capped. The reaction mixture was stirred overnight at room temperature. The reaction mixture was concentrated, diluted with water, and stirred for 30 minutes then filtered. The solid was recrystallized using ethanol to afford 2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl) acetamide (42.3 g, 93 mmol, 90% yield) as a white solid. LCMS MH^+: 445. HPLC Ret. Time 1.20 min. Method QC-ACN-TFA-XB. ^1H NMR (400 MHz, DMSO-d_6) δ 10.97-10.86 (m, 1H), 8.78-8.69 (m, 1H), 8.54-8.40 (m, 1H), 7.64-7.49 (m, 1H), 7.30-7.21 (m, 2H), 7.17-7.09 (m, 1H), 7.06-6.93 (m, 1H), 2.99-2.82 (m, 5H), 2.62-2.54 (m, 4H), 2.24-2.12 (m, 5H), 1.92-1.72 (m, 4H), 1.37-1.29 (m, 6H).

Example 18

6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridine

(18)



Preparation 1:

To a 40 ml vial was added 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (0.800 g, 2.064 mmol), DCM (5 mL) and DBU (0.622 mL, 4.13 mmol). The material went into solution and 2-bromoacetamide (0.299 g, 2.168 mmol) was added. The reaction vial was capped. The reaction mixture was stirred overnight at room temperature. The reaction mixture was diluted with water and extracted with DCM. The organics were washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was dissolved in minimal DCM and purified by silica gel chromatography, eluting with 0-10% MeOH/DCM. Following concentration of the fractions, the product was collected as a white solid (0.6 g). To this was added 40 mL of a 10% MeOH/ethyl acetate solution and the suspension was taken to a boil. The solids were filtered off and rinsed with hot MeOH/ethyl acetate (1:10). The filtrate was reheated and capped to recrystallize. After 3 days, the white solid was filtered off and washed with ethyl acetate, then ether, and dried on the vacuum pump overnight to afford 2-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)acetamide (480 mg, 1.07 mmol, 51.8% yield). MS (M^{+1}) m/z: 445.3 (MH^+). LC retention time 0.69 min [G]. ^1H NMR (400 MHz, DMSO-d_6) δ 11.00-10.85 (m, 1H), 8.79-8.69 (m, 1H), 8.53-8.43 (m, 1H), 7.60-7.49 (m, 1H), 7.32-7.21 (m, 2H), 7.18-7.11 (m, 1H), 7.06-6.99 (m, 1H), 3.00-2.83 (m, 5H), 2.63-2.55 (m, 4H), 2.24-2.12 (m, 5H), 1.92-1.72 (m, 4H), 1.40-1.24 (m, 6H).

Preparation 2:

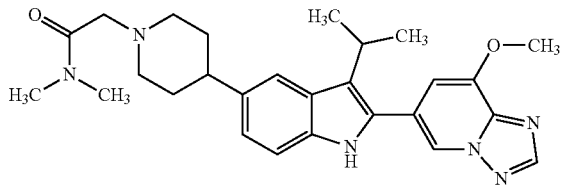
To a reaction vial were added 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridine, 2 HCl (40 g, 87 mmol), DCE (280 mL), and DBU

(45.8 mL, 304 mmol). The material went into solution and 1-bromo-2-(methylsulfonyl) ethane (18.46 g, 99 mmol) was added. The reaction mixture was stirred overnight at room temperature under N_2. The sample was concentrated, diluted with water, stirred for 30 minutes, and then filtered. The solid was recrystallized using EtOH to afford 6-(3-isopropyl-5-(1-(2-(methylsulfonyl)ethyl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (40 g, 81 mmol, 93% yield) as a white solid. LCMS MH^+: 494.3; HPLC Ret. Time 1.70 min. Method QC-ACN-AA-XB. ^1H NMR (400 MHz, CHLOROFORM-d) δ 8.45-8.38 (m, 1H), 8.37-8.30 (m, 1H), 8.18-8.12 (m, 1H), 7.69-7.62 (m, 1H), 7.43-7.35 (m, 1H), 7.19-7.12 (m, 1H), 3.29-3.20 (m, 2H), 3.16-3.07 (m, 5H), 3.02-2.92 (m, 3H), 2.74-2.67 (m, 1H), 2.66-2.60 (m, 3H), 2.31-2.22 (m, 2H), 2.21-2.17 (m, 3H), 2.07-1.79 (m, 4H), 1.42-1.35 (m, 6H).

Example 25

2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide

(25)



Preparation 1:

To a solution of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (0.05 g, 0.128 mmol) in THF (2 mL) and DMF (1 mL) solvent mixture were added 2-chloro-N,N-dimethylacetamide (0.023 g, 0.193 mmol) and TEA (0.179 mL, 1.284 mmol) at room temperature. The reaction mixture was stirred at room temperature for 24 h. The reaction mixture was concentrated under vacuum. To the solid material was added water (5 mL) and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4, filtered and concentrated under vacuum. The crude material was purified via preparative LC/MS with the following conditions: Column: Water XBridge C18, 19×150 mm, 5 μm particles; Mobile Phase A: 10 mM ammonium acetate; Mobile Phase B: methanol; Gradient: 10-50% B over 30 minutes, then a 5-minute hold at 100% B; Flow: 15 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperid in-1-yl)-N,N-dimethylacetamide (14.2 mg, 0.03 mmol, 23.31% yield). MS (M^-) m/z: 475.4 (Mift). LC retention time 1.38 min [A]. ^1H NMR (400 MHz, DMSO-d_6) δ 11.38 (s, 1H), 8.83-8.75 (m, 2H), 7.83 (s, 1H), 7.57 (d, J=8.3 Hz, 1H), 7.41 (d, J=1.2 Hz, 1H), 7.30 (dd, J=8.4, 1.6 Hz, 1H), 4.34 (s, 3H), 3.43 (d, J=5.9 Hz, 3H), 3.34 (s, 4H), 3.22 (d, J=11.0 Hz, 4H), 3.09 (s, 3H), 2.79 (d, J=1.7 Hz, 3H), 2.48-2.38 (m, 2H), 2.15 (s, 5H), 2.08-1.95 (m, 4H), 1.72 (d, J=7.1 Hz, 6H).

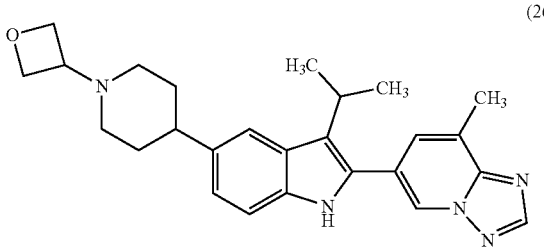
Preparation 2:

To a solution of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine, HCl (30.6 g, 71.8 mmol) in a DMF (700 mL) solvent mixture were added 2-chloro-N,N-dimethylacetamide (9.62 mL, 93 mmol) and TEA (50.1 mL, 359 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The starting material was converted to product. Next, water (2 L) was added to the above solution, the upper layer and the lower layer were extracted with ethyl acetate. The combination of the organic layers was washed with brine, dried and concentrated to give a solid, which was purified by recrystallization fromethanol to afford 2-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (28.3 g, 59.3 mmol, 83% yield). LCMS MiEr: 475.2. HPLC Ret. Time 0.66 min. Method G. C: 68.28%, H: 7.19%, N: 17.63%.

Example 26

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo [1,5-a]pyridine

(26)



To a solution of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine hydrochloride (24.5 g, 59.8 mmol) in DCM (610 mL) were added triethylamine (24.19 g, 239 mmol), oxetan-3-one (17.23 g, 239 mmol), acetic acid (7.18 g, 120 mmol), and sodium triacetoxyborohydride (50.7 g, 239 mmol). The solution was stirred at room temperature. After 5 min, LCMS showed 20% conversion; and after overnight, HPLC showed no starting material. The solvent was removed under vacuum. The residue was dissolved in 500 mL ethyl acetate and washed with saturated $NaHCO_3$ solution (4×300 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by recrystallization from a mixture of EtOH/water(20/80), dried to afford 6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo [1,5-a]pyridine (24.6 g, 57.0 mmol, 95% yield) as a white solid. LCMS Mft=430.1 Ret. Time=0.63 min; Column: BEH C18 2.1×50 mm 1.7 μm Via1:3:1; HPLC Ret. Time 7.86 min. Waters XSelect CSH C18 2.5 μM 4.6 μM×7.5 mm. Solvent A: H_2O w/0.1% TFA. Solvent B ACN w/0.1% TFA. Gradient Complex Start % B 10% 16 min 45% B 20 min 90% 24 min 90% 25 min 10% Stop time 25 min Flow Rate 1.5 mL/min. ^1H NMR (500 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.75 (s, 1H), 8.51 (s, 1H), 7.56 (d, J=16.5 Hz, 2H), 7.30 (d, J=8.4 Hz, 1H), 7.03 (d, J=8.3 Hz, 1H), 4.64-4.33 (m, 4H), 4.72-4.27 (m, 4H), 3.65 (br. s., 2H), 3.47-3.12 (m, 2H), 2.79 (d, J=10.4 Hz, 2H), 2.61 (s, 3H), 1.99-1.59 (m, 7H), 1.41 (d, J=6.8 Hz, 6H).

Alternative Preparation of Example 26

To a solution of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine hydrochloride (24.5 g, 59.8 mmol) in DCM (610 ml) were added triethylamine (24.19 g, 239 mmol), oxetan-3-one (17.23 g,

239 mmol), acetic acid (7.18 g, 120 mmol) and sodium triacetoxyborohydride (50.7 g, 239 mmol). The solution was stirred at room temperature, after 5 min the reaction progressed 20%. The reaction went to completion overnight. The solvent was removed under reduced pressure. The residue was dissolved in 500 mL ethyl acetate and washed with saturated $NaHCO_3$ solution (300 mL×4), dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude product. The crude material was purified to remove Pd in the treatment described below and recrystallized from a mixture of EtOH/water (20/80) and dried to afford 6-(3-isopropyl-5-(1-(oxetan-3-yl) piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (24.6 g, 57.0 mmol, 95% yield) as a solid. LCMS MH^+: 430.1; HPLC Ret. Time 0.63 min. Method G; ^1H NMR (400 MHz, DMSO-d_6) δ 11.18-11.05 (m, 1H), 8.88-8.76 (m, 1H), 8.58-8.47 (m, 1H), 7.64-7.54 (m, 2H), 7.34-7.26 (m, 1H), 7.09-6.96 (m, 1H), 4.61-4.53 (m, 2H), 4.51-4.42 (m, 2H), 3.48-3.37 (m, 1H), 3.31-3.20 (m, 1H), 2.86-2.78 (m, 2H), 2.68-2.63 (m, 3H), 2.63-2.55 (m, 1H), 1.96-1.68 (m, 6H), 1.49-1.38 (m, 6H).

Pd Removal Procedure: The sample was treated to remove Pd using the following steps: 1. The crude sample was dissolved in 500 mL THF and treated with SiliaMetS@DMT (40 g, from SiliCycle). The solution was stirred overnight at room temperature under N_2. 2. After filtration, the solvent was removed and the residue was dissolved in AcOEt and washed with brine and dried. 3. After concentration, the residue was recrystallized from EtOH-water (20/80) to afford the product.

The following examples were prepared according to the general procedure of Examples 26.

TABLE 5

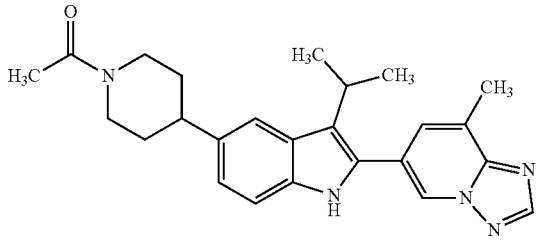
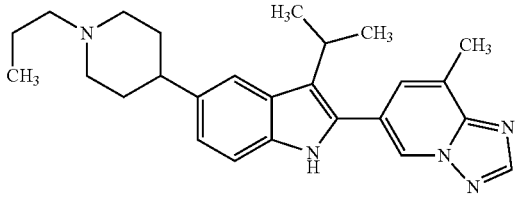
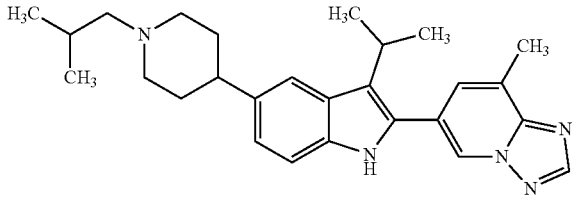
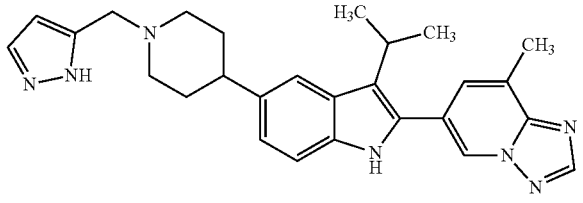
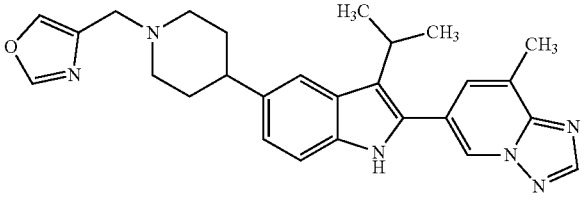
Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
27		416.4	2.39	Method F
28		416	1.43	QC-ACN-AA-XB
29		430.1	1.7	QC-ACN-AA-XB
30		454.2	1.29	QC-ACN-TFA-XB
31		455.3	1.54	QC-ACN-AA-XB

TABLE 5-continued

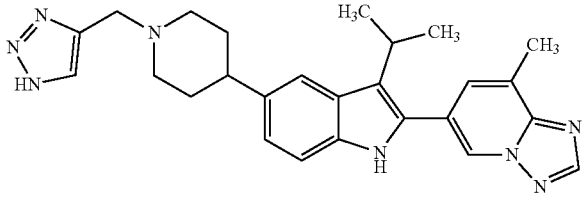
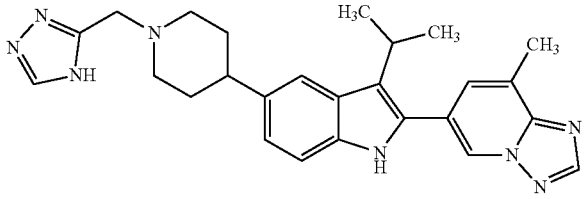
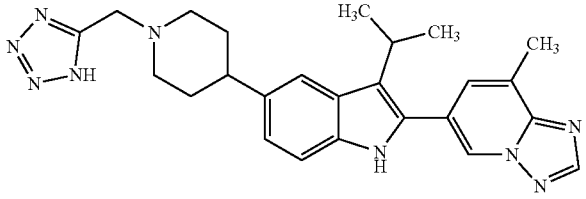
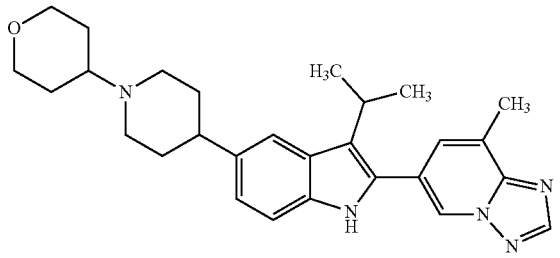
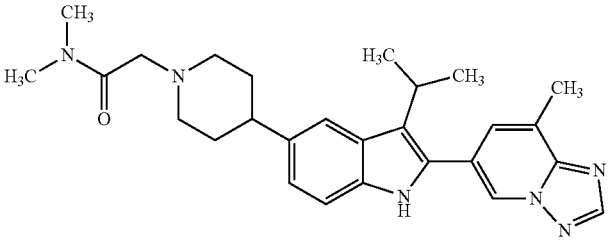
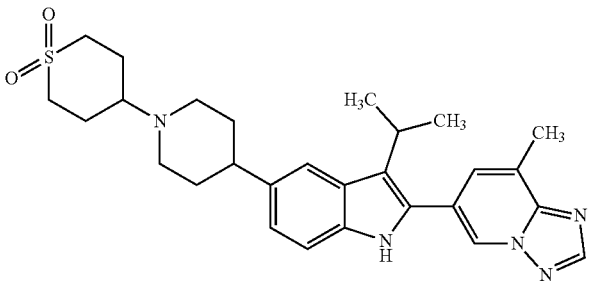
Ex. No.	Structure	LCMS MH+	R_t (min)	Method
32		455.2	1.22	QC-ACN-TFA-XB
33		455.4	1.11	QC-ACN-TFA-XB
34		455.9	1.13	QC-ACN-AA-XB
35		458.4	1.33	QC-ACN-AA-XB
36		459.3	1.37	Method A
37		506.3	1.43	QC-ACN-AA-XB

TABLE 5-continued

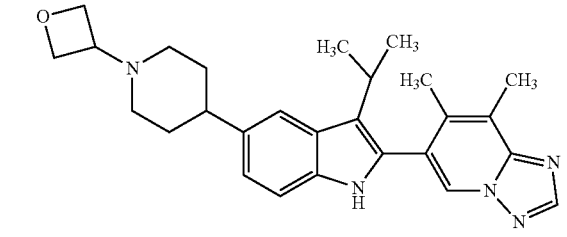
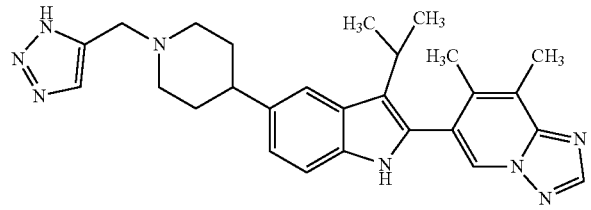
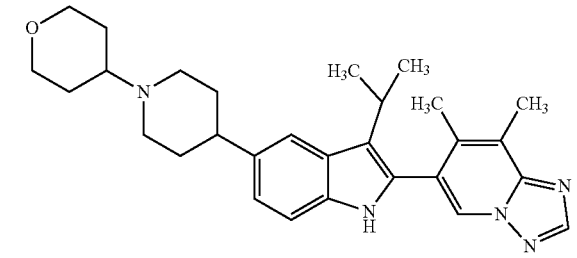
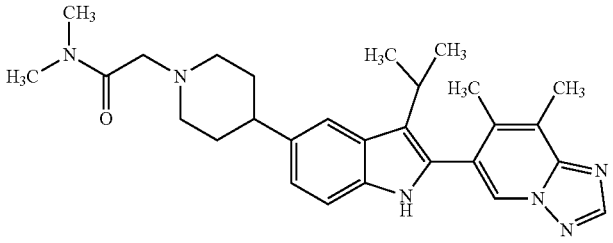
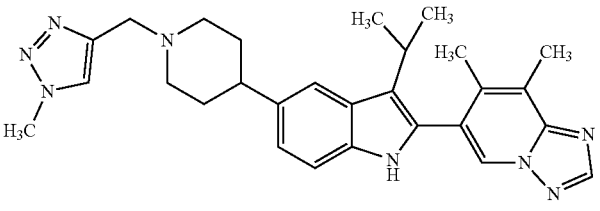
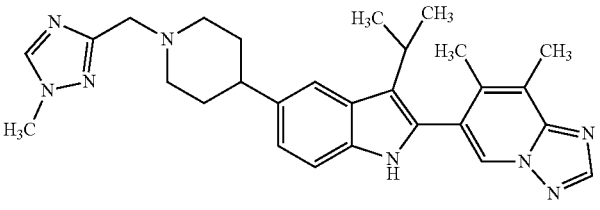
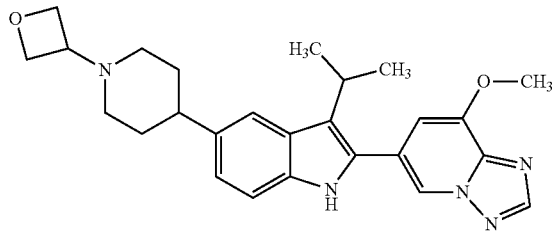
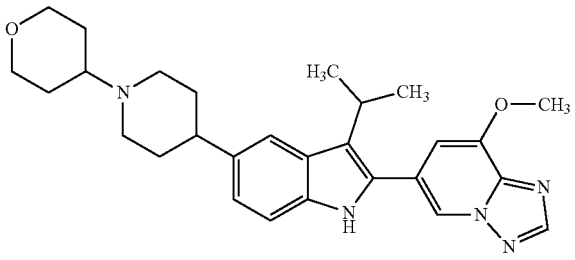
Ex. No.	Structure	LCMS MH+	R_t (min)	Method
38		444.3	1.24	QC-ACN-TFA-XB
39		469.2	1.46	QC-ACN-AA-XB
40		471.9	1.47	QC-ACN-AA-XB
41		473.4	1.41	QC-ACN-AA-XB
42		483	1.52	QC-ACN-AA-XB
43		483	1.68	QC-ACN-AA-XB

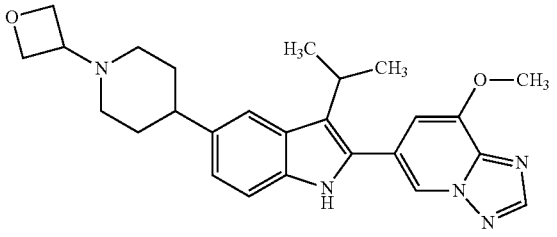
TABLE 5-continued

Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
44		446.2	1.91	Method E
45		474.4	1.31	Method E

Example 44

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine

(44)

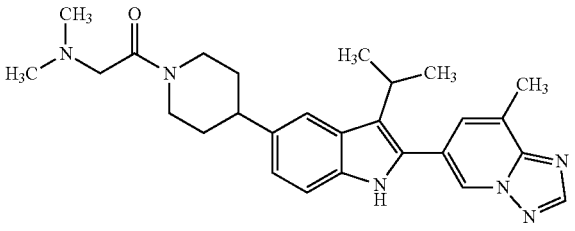


To a solution of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine dihydrochloride (39.7 g, 86 mmol) in DCM (859 ml) was added triethylamine (34.8 g, 343 mmol), oxetan-3-one (24.75 g, 343 mmol), acetic acid (10.31 g, 172 mmol) and sodium triacetoxyborohydride (72.8 g, 343 mmol). The solution was stirred at room temperature. After 9h, the starting material was no longer detected. The solvent was removed by rotavapor. The residue was dissolved in 1500 mL ethyl acetate and washed with saturated $NaHCO_3$ solution (500 mL×4), dried over Na_2SO_4, and concentrated under reduced pressure to give residue. The residue was purified by recrystallization from a mixture of EtOH/water(60/40) two times, dried to give 6-(3-isopropyl-5-(1-(oxetan-3-yl) piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (32.3 g, 72.2 mmol, 84% yield) as a white solid. LCMS MH^+: 446.1. HPLC Ret. Time 0.63 min. Method G. ^1H NMR (400 MHz, CHLOROFORM-d) δ 8.42-8.31 (m, 2H), 8.20-8.10 (m, 1H), 7.77-7.67 (m, 1H), 7.44-7.36 (m, 1H), 7.31-7.26 (m, 1H), 7.21-7.12 (m, 1H), 6.95-6.85 (m, 1H), 4.80-4.63 (m, 4H), 4.12-4.03 (m, 3H), 3.62-3.51 (m, 1H), 3.42-3.25 (m, 1H), 3.02-2.87 (m, 2H), 2.73-2.58 (m, 1H), 2.10-1.85 (m, 6H), 1.55-1.44 (m, 6H).

Example 46

2-(dimethylamino)-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)ethan-1-one

(46)



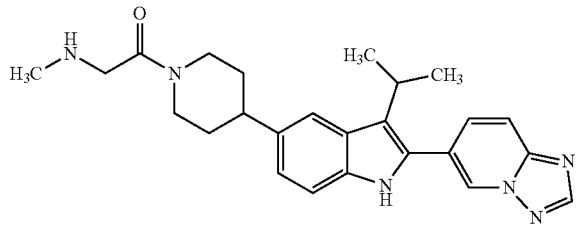
To a solution of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (75 mg, 0.201 mmol) in DMF (1 mL) were added TEA (0.140 mL, 1.004 mmol), 2-(dimethylamino)acetic acid (20.71 mg, 0.201 mmol), and HATU (76 mg, 0.201 mmol). The reaction mixture was stirred at room temperature for 12 h. The reaction mass was diluted with methanol (2 mL) and passed through a syringe pad to filter away inorganics, and then purified by reverse phase preparative chromatography. The crude material was purified via preparative LC/MS with the following conditions: Column: Water XBridge C18, 19×150 mm, 5-μm particles; Mobile Phase A: 10-mM ammonium acetate; Mobile Phase B: acetonitrile; Gradient: 20-60% B over 30 minutes, then a 5-minute hold at 100% B; Flow: 15 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation. The yield of the product was 11.7 mg, and its estimated purity by LCMS analysis was 96%. Two analytical LC/MS injections were used to determine the final purity. Injection 1 conditions:

Column: Ascentis Express C18(50×2.1)mm, 2.7 μm; Mobile Phase A: 5:95 Acetonitrile:water with 10 mM NH_4OAc; Mobile Phase B: 95:5 Acetonitrile:water with 10 mM NH_4OAc; Temperature: 50° C.; Gradient:0-100% B over 3 minutes; Flow: 1.1 mL/min. Injection 2 conditions: Column: Ascentis Express C18 (50×2.1) mm, 2.7 μm; Mobile Phase A: 5:95 Acetonitrile:water with 0.1% TFA; Mobile Phase B: 95:5 acetonitrile:water with 0.1% TFA; Temperature: 50° C.; Gradient:0-100% B over 3 minutes; Flow:1.1 mL/min. ^{1}H-NMR (400 MHz, DMSO-d_6): δ 1.12 (d, J=6.00 Hz, 3H), 1.44 (d, J=6.80 Hz, 6H), 1.69-1.72 (m, 2H), 1.75-1.81 (m, 2H), 2.32-2.34 (m, 1H), 2.50 (s, 3H), 2.62-2.71 (m, 4H), 2.80-2.94 (m, 1H), 3.25-3.32 (m, 2H), 3.54-3.58 (m, 2H), 4.00-4.07 (m, 1H), 4.60 (d, J=11.20 Hz, 1H), 7.04 (dd, J=1.20, 8.40 Hz, 1H), 7.30 (d, J=8.40 Hz, 1H), 7.58 (d, J=8.80 Hz, 1H), 8.53 (s, 1H), 8.80 (s, 1H), 11.11 (s, 1H). LCMS for molecular formula $C_{26}H_{32}N_6O$ was 444.264, found 445 (M^+). Waters Xbridge C18, 19×150 mm, 5 μm; Guard Column: Water XBridge C18,19×10 mm, 5 μm; Mobile Phase A:5:95 Acetonitrile:water with 10 mM NH_4OAc; Mobile Phase B: 95:5 acetonitrile:water with 10 mM NH_4OAc; Gradient:10-50% B over 25 minutes, followed by a 10 minute hold at 50% B and 5 minute hold at 100% B; Flow: 15 mL/min. R_t Min: 1.91, Wave length: 220 nm.

Example 47

1-(4-(2-([1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-2-(methylamino)ethan-1-one

(47)



To a 1 dram vial were added 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (0.035 g, 0.091 mmol), CH_3CN, TEA (0.038 mL, 0.273 mmol), and HATU (0.036 g, 0.091 mmol). The material went into solution and 2-((tert-butoxycarbonyl)(methyl)amino)acetic acid (0.034 g, 0.182 mmol) was added. The reaction vial was capped and allowed to stir overnight at room temperature. After 18 hrs LC-MS showed product had formed. The samples were diluted with ethyl acetate and washed with water. The combined organics were washed with brine, dried over Na_2SO_4 filtered, and concentrated. To this was added 1 mL of DCM and 1 mL of 4 M HCl in dioxane. The reaction mixture was stirred for 30 minutes at room temperature, concentrated, diluted with Solvent B (90:10:0.1 CH_3CN: Water:TFA, filtered and purified by preparative reverse phase chromatography. The crude material was purified via preparative LC/MS with the following conditions: Column: XBridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 10-50% B over 20 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation. The yield of the product was 7.4 mg, and its estimated purity by LCMS analysis was 96%. Two analytical LC/MS injections were used to determine the final purity. Injection 1 conditions: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7-μm particles; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile:water with 10 mM ammonium acetate; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm. Injection 2 conditions: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile:water with 0.1% trifluoroacetic acid; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm. Proton NMR was acquired in deuterated DMSO. LC-MS: M+1=431, rt=1.127 min., [D1]. Proton NMR was acquired in deuterated DMSO. ^{1}H NMR (500 MHz, DMSO-d6) δ 11.19 (s, 1H), 8.97 (s, 1H), 8.58 (s, 1H), 7.98 (d, J=9.2 Hz, 1H), 7.79 (d, J=10.4 Hz, 1H), 7.56 (s, 1H), 7.33 (d, J=8.3 Hz, 1H), 7.03 (d, J=8.8 Hz, 1H), 4.55 (d, J=13.0 Hz, 1H), 3.88 (d, J=13.2 Hz, 1H), 3.58 (s, 1H), 3.33-3.21 (m, 1H), 3.16-3.06 (m, 1H), 2.88 (d, J=7.5 Hz, 2H), 2.77-2.63 (m, 2H), 2.38 (s, 5H), 1.73-1.59 (m, 2H), 1.43 (d, J=7.0 Hz, 6H).

The following examples were prepared according to the general methods disclosed in Examples 46 or 47.

TABLE 6

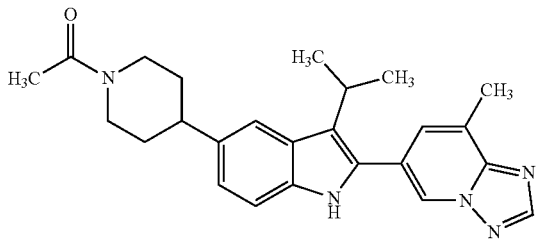
Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
48		415.9	1.62	QC-ACN-AA-XB

TABLE 6-continued

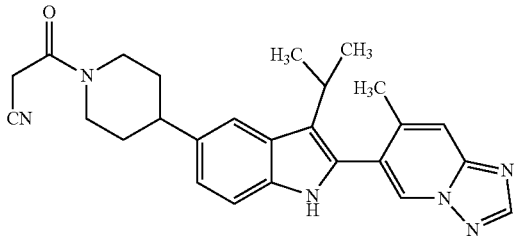
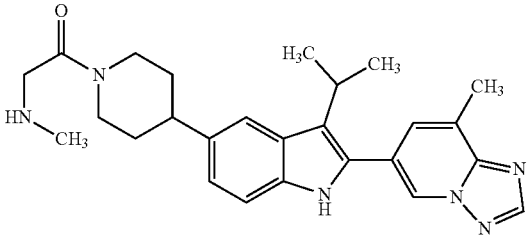
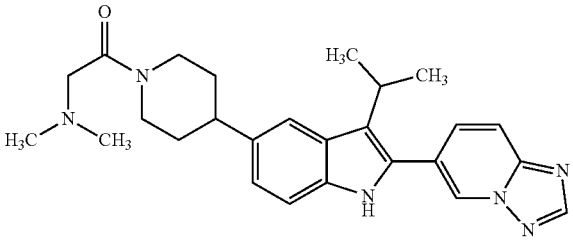
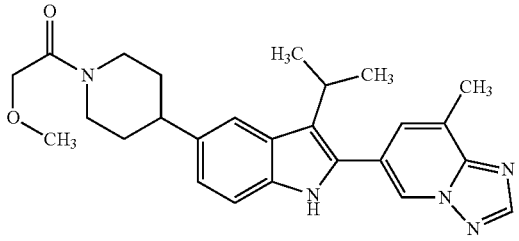
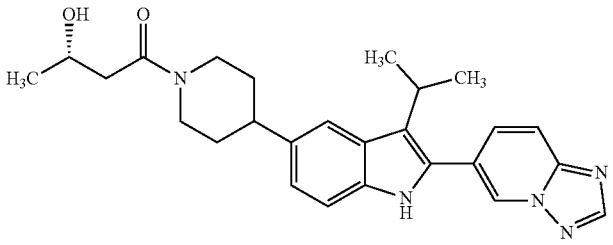
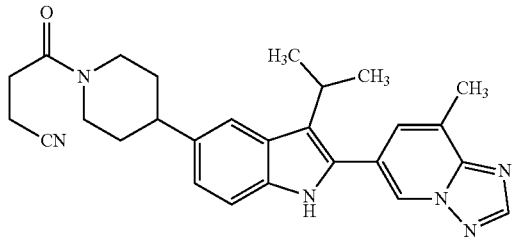
Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
49		441.3	1.46	QC-ACN-TFA-XB
50		445.3	1.47	Method A
51		445.1	1.21	QC-ACN-AA-XB
52		446.4	1.57	Method E
53		446.2	1.70	Method E
54		455.3	1.74	QC-ACN-AA-XB

TABLE 6-continued

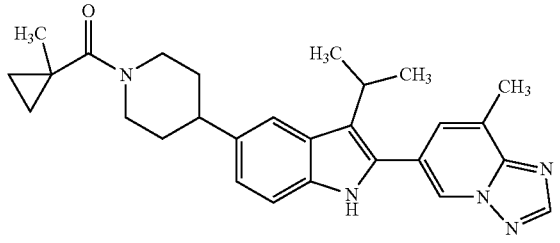
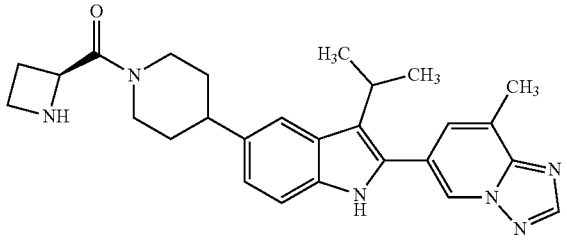
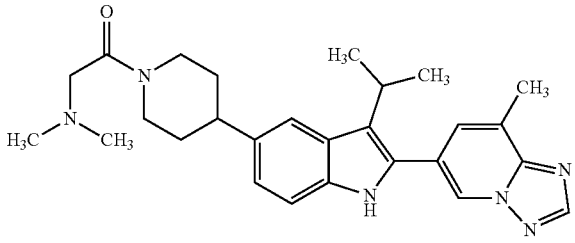
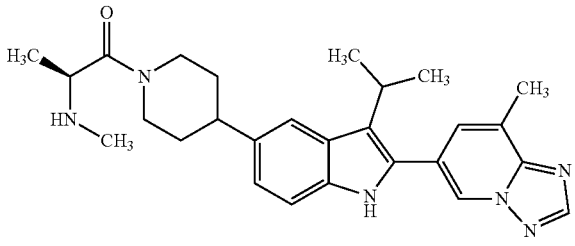
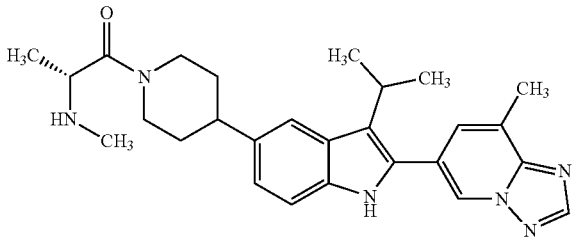
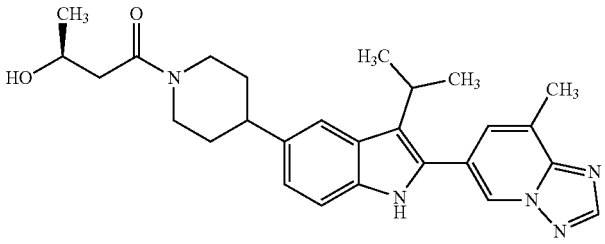
Ex. No.	Structure	LCMS MH+	R_t (min)	Method
55		456.4	1.85	Method E
56		457.4	1.27	Method F
57		459.5	1.16	QC-ACN-TFA-XB
58		459.4	1.29	Method F
59		459.4	1.29	Method F
60		460.3	1.79	A

TABLE 6-continued

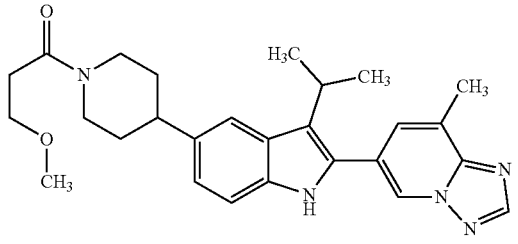
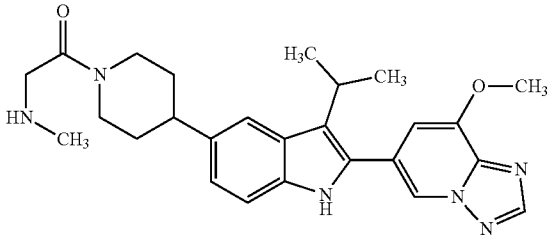
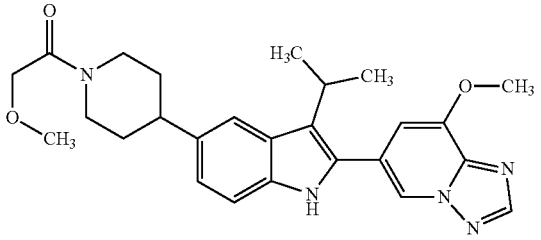
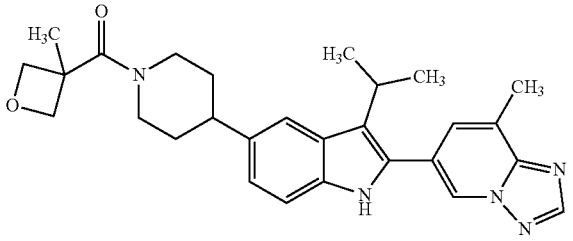
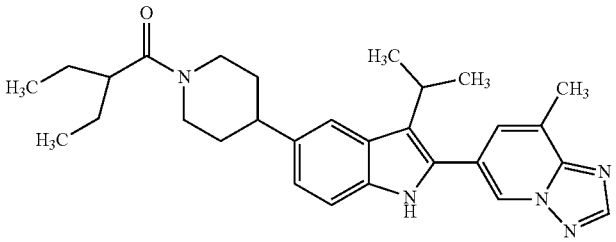
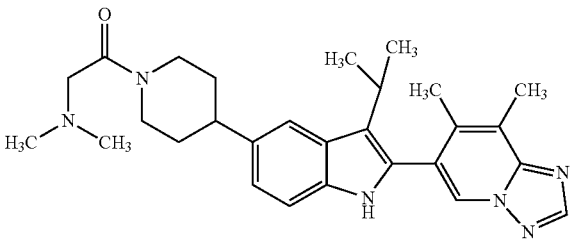
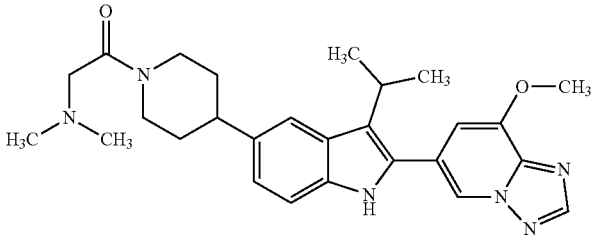
Ex. No.	Structure	LCMS MH+	R_t (min)	Method
61		460.4	1.66	Method F
62		461.3	1.43	Method E
63		462.3	1.52	Method E
64		472.4	1.56	Method E
65		472.4	2.12	Method E
66		473	1.65	QC-ACN-AA-XB

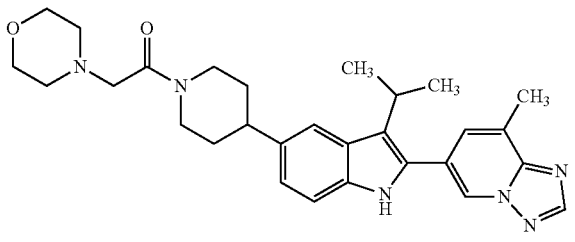
TABLE 6-continued

Ex. No.	Structure	LCMS MH+	Rt (min)	Method
67		475.3	1.50	Method E

Example 68

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)-2-morpholinoethan-1-one

(68)



6-(3-Isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine hydrochloride (0.250 g, 0.610 mmol) was dissolved in NMP (5 mL). Et_3N (0.255 mL, 1.829 mmol) and 2-chloroacetyl chloride (0.073 mL, 0.915 mmol) were added sequentially. The reaction was monitored by LCMS. After stirring for 1.5 hours, the reaction mixture was diluted with NMP and used as a solution in the next step.

2-Chloro-1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethanone (0.035 g, 0.078 mmol) was dissolved in NMP (1 mL). DBU (0.059 mL, 0.389 mmol) and morpholine (0.020 mL, 0.233 mmol) were added sequentially. The reaction was monitored by LCMS. The reaction mixture was stirred overnight. The reaction mixture was diluted with solvent (90:10 ACN: water, 0.1% TFA) and the crude material was purified via preparative LC/MS with the following conditions: Column:) (Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile: water with 0.1% trifluoroacetic acid; Gradient: 10-50% B over 30 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation.

The yield of the product was 37.9 mg, and its estimated purity by LCMS analysis was 100%. Two analytical LC/MS injections were used to determine the final purity. Injection 1 conditions: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7-μm particles; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile:water with 10 mM ammonium acetate; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm. Injection 2 conditions: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7-μm particles; Mobile Phase A: 5:95 acetonitrile:water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile:water with 0.1% trifluoroacetic acid; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm. LC-MS: M+1=501, rt=1.157 min., [D1]. Proton NMR was acquired in deuterated DMSO. ^1H NMR (400 MHz, DMSO-d_6) δ=11.12 (s, 1H), 8.79 (d, J=0.8 Hz, 1H), 8.53 (s, 1H), 7.59 (d, J=6.4 Hz, 2H), 7.29 (d, J=8.4 Hz, 1H), 7.02 (dd, J=8.4, 1.2 Hz, 1H), 4.88-4.82 (m, 2H), 4.52-4.48 (m, 1H), 4.28-4.22 (m, 2H), 4.09-4.04 (m, 1H), 3.28-3.21 (m, 1H), 3.19-3.02 (m, 6H), 2.85-2.76 (m, 1H), 2.68-2.59 (m, 2H), 2.58 (s, 3H), 1.88-1.80 (m, 2H), 1.69-1.50 (m, 2H), 1.43 (d, J=7.2 Hz, 6H).

The following examples were prepared according to the general process disclosed in Example 68.

TABLE 7

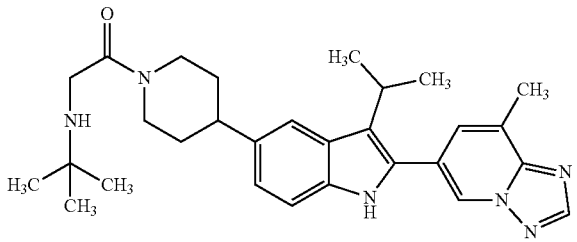
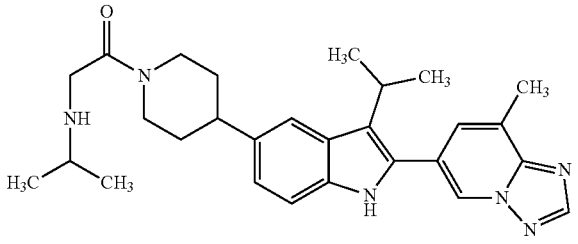
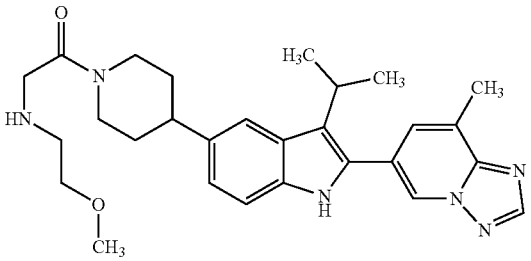
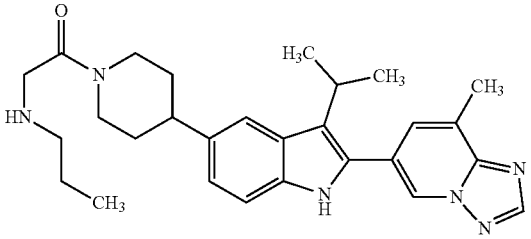
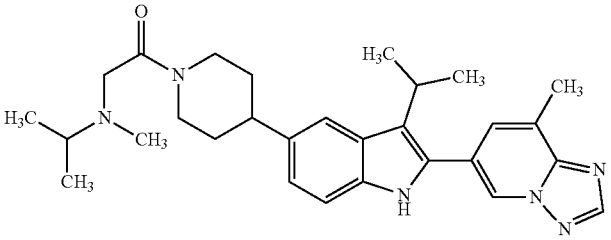
Ex. No.	Structure	LCMS MH+	Rt (min)	Method
69		487.4	1.28	Method F

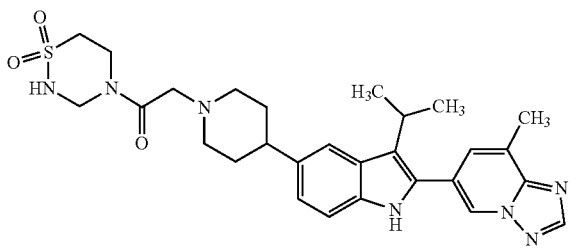
TABLE 7-continued

Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
70		473.4	1.35	Method E
71		489.4	1.40	Method E
72		473.4	1.39	Method E
73		487.4	1.25	Method F

Example 74

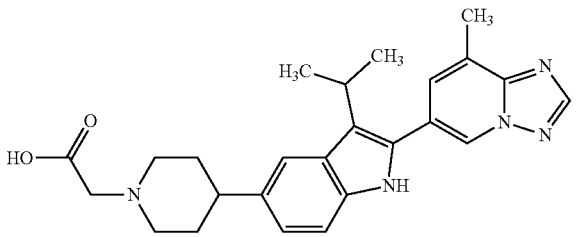
1-(1,1-dioxido-1,2,4-thiadiazinan-4-yl)-2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)ethan-1-one

(74)



Intermediate 74A 2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)acetic acid

(74A)



In a glass vial, 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.580 g, 1.233 mmol) was dissolved in CH_2Cl_2 (8.22 mL) and

N,N-diisopropylethylamine (1.074 mL, 6.16 mmol). Methyl 2-bromoacetate (0.141 mL, 1.479 mmol) was added to the vial, resulting in a clear, bright yellow solution. The reaction mixture was stirred for 1.5 h at room temperature. Excess solvent was evaporated from the reaction mixture under a nitrogen stream. The material was purified by silica gel chromatography using hexane and ethyl acetate as eluents (0%-100% Ethyl acetate gradient). The product fractions were combined and evaporated to dryness. The material was dissolved in 2 mL THF and 2 mL MeOH and treated with 2 mL of 4 M NaOH. Next, 1 mL of water was added and the mixture was stirred at 45° C. overnight. The mixture was diluted with water and acidified to pH=5 with 1 N HCl. Ethyl acetate was added and the layers were separated. The combined organics were washed with dried over Na_2SO_4, filtered and concentrated to afford 2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetic acid.

Example 74

In a 2 dram vial were added 2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidin-1-yl)acetic acid (0.025 g, 0.058 mmol), CH_3CN and TEA (0.024 mL, 0.174 mmol). The sample went into solution and HATU (0.033 g, 0.087 mmol) was added. The reaction vial was capped and allowed to stir overnight at room temperature. The sample was diluted with solvent (90:10:0.1 CH_3CN:water: TFA), filtered and then purified by preparative reverse phase HPLC.

The crude material was purified via preparative LC/MS with the following conditions: Column:)(Bridge Phenyl, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 20-60% B over 20 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation. The yield of the product was 0.8 mg and its estimated purity by LCMS analysis was 99%. Two analytical LC/MS injections were used to determine the final purity. Injection 1 conditions: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7-μm particles; Mobile Phase A: 5:95 acetonitrile:water with 10 mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10 mM ammonium acetate; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm. Injection 2 conditions: Column: Waters Acquity UPLC BEH C18, 2.1×50 mm, 1.7-μm particles; Mobile Phase A: 5:95 acetonitrile:water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile:water with 0.1% trifluoroacetic acid; Temperature: 50° C.; Gradient: 0-100% B over 3 minutes, then a 0.75-minute hold at 100% B; Flow: 1.0 mL/min; Detection: UV at 220 nm. Proton NMR was acquired in deuterated DMSO.

The following examples were prepared according to the general process described in Example 74.

TABLE 8

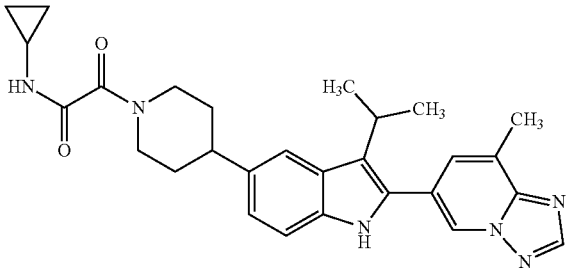
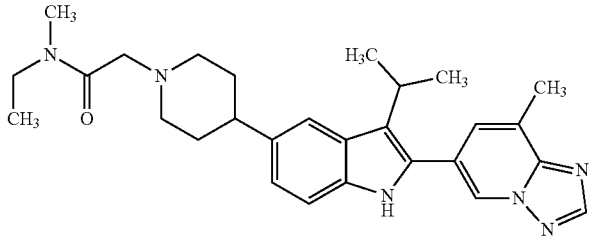
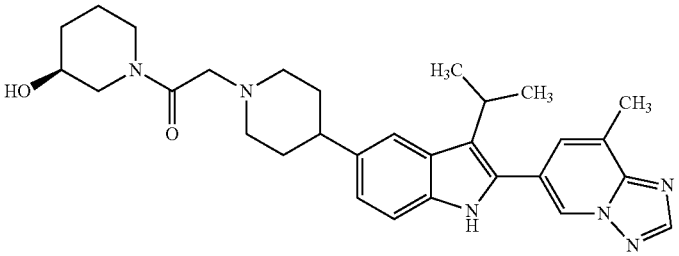
Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
75		471.4	1.72	Method E
76		473.4	1.56	Method E
77		515.4	1.40	Method E

TABLE 8-continued

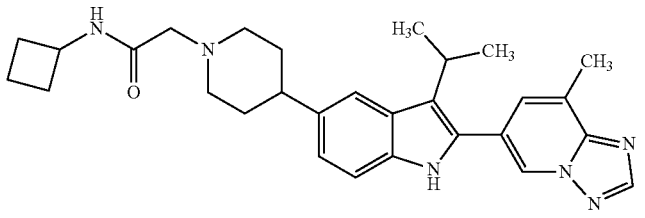
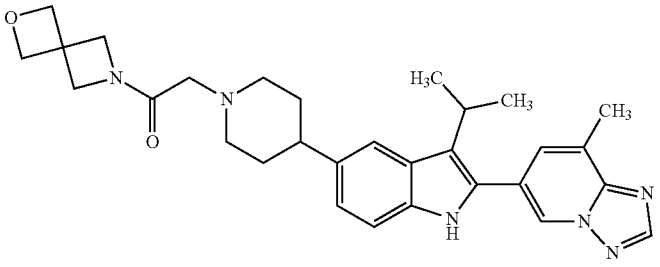
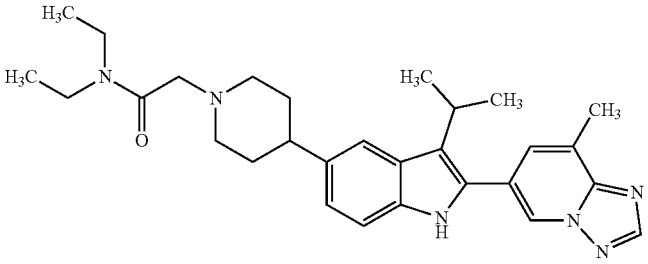
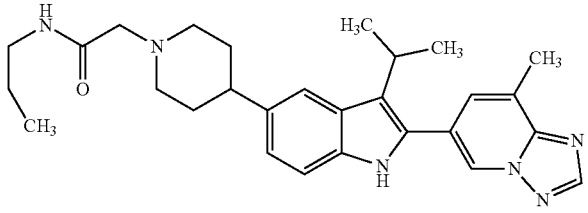
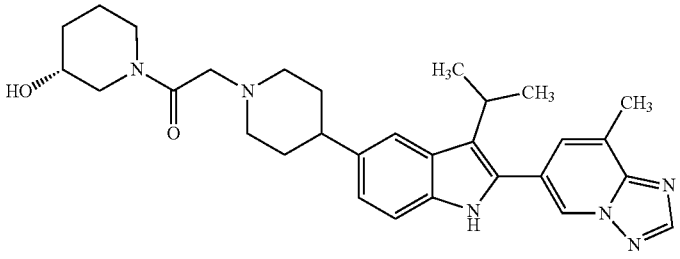
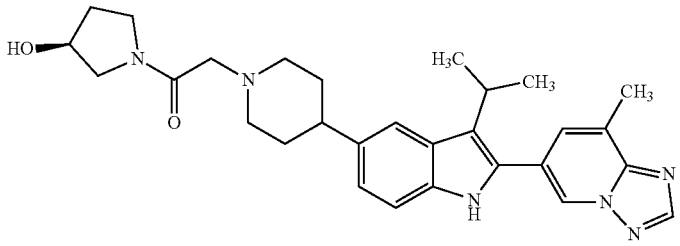
Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
78		485.4	1.25	Method F
79		513.4	1.08	Method F
80		487.4	1.29	Method F
81		473.4	1.83	Method E
82		515.4	1.10	Method F
83		501.4	1.06	Method F

TABLE 8-continued

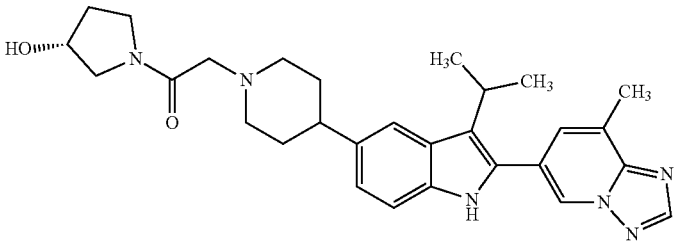
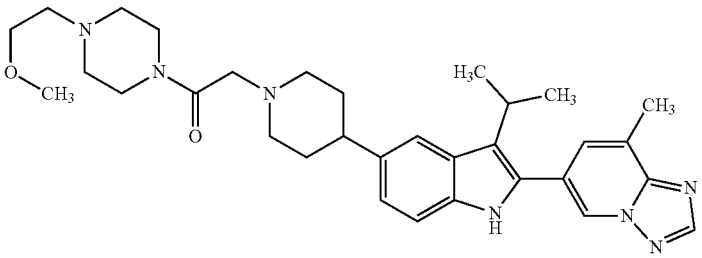
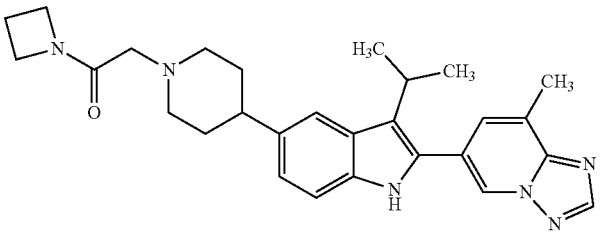
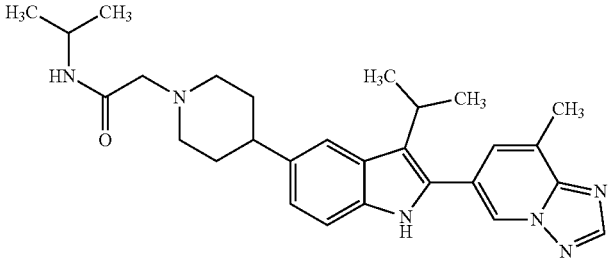
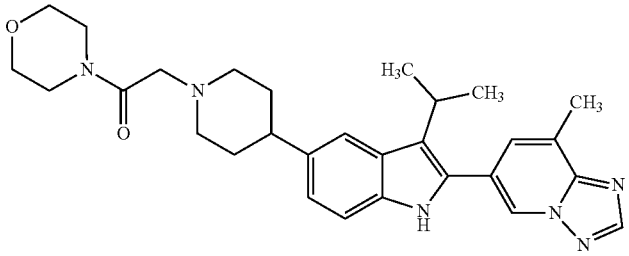
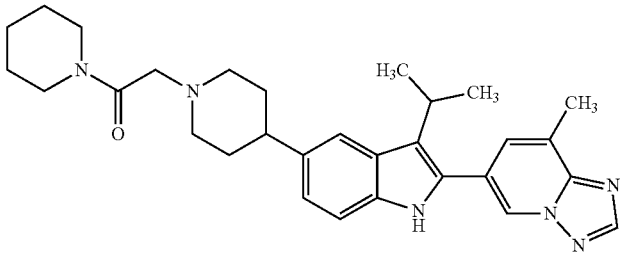
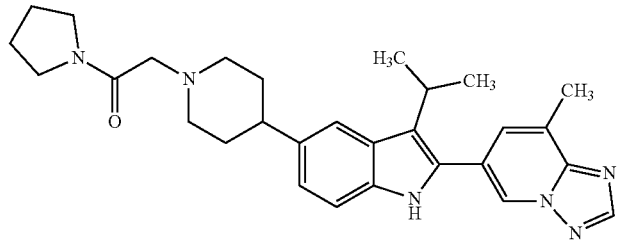
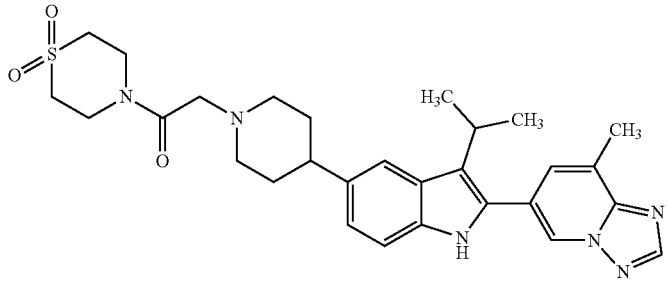
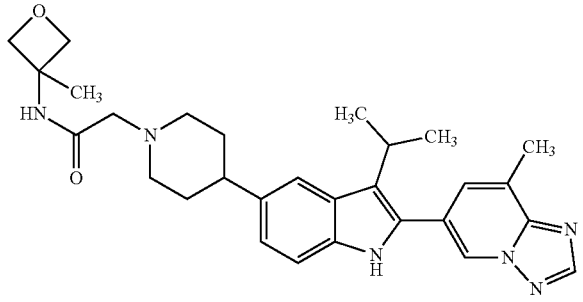
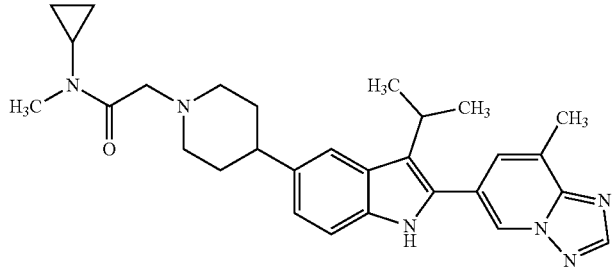
Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
84		501.4	1.05	Method F
85		558.5	0.96	Method F
86		471.4	1.13	Method F
87		473.4	1.23	Method F
88		501.4	1.11	Method F
89		499.4	1.3	Method F

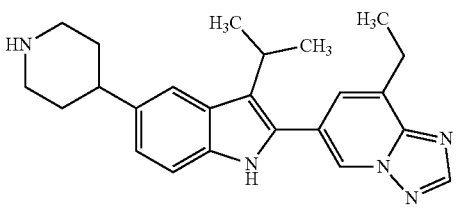
TABLE 8-continued

Ex. No.	Structure	LCMS MH^+	R_t (min)	Method
90		485.4	1.59	Method E
91		549.4	1.52	Method E
92		501.4	1.66	Method E
93		485.4	1.58	Method E

Example 94

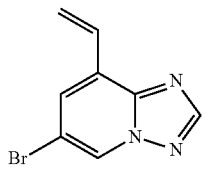
8-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine

(94)



Intermediate 94A: 6-bromo-8-iodo-[1,2,4]triazolo[1,5-a]pyridine

(94A)

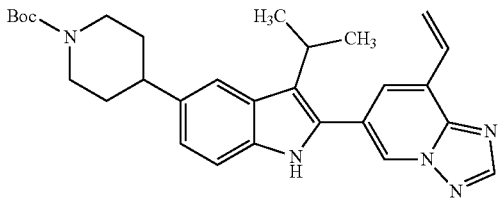


To a stirred solution of 6-bromo-8-iodo-[1,2,4]triazolo[1,5-a]pyridine (100 mg, 0.309 mmol) in EtOH (20 mL) was added vinylboronic acid pinacol ester (62.0 mg, 0.463

mmol). The mixture was degassed for 10 min using N_2. Next, $PdCl_2(dppf)$-CH_2Cl_2 (12.61 mg, 0.015 mmol) and Et_3N (0.129 mL, 0.926 mmol) were added and the reaction mixture was heated to 80° C. for 16 h. The reaction mixture was filtered through pad of celite, washed with EtOAc, and concentrated organic layer to afford 6-bromo-8-vinyl-[1,2,4]triazolo[1,5-a]pyridine (70 mg, 95%). LC retention time 1.0.4 min [K]. MS (E−) m/z: 226 (M+H).

Intermediate 94B: tert-butyl 4-(3-isopropyl-2-(8-vinyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

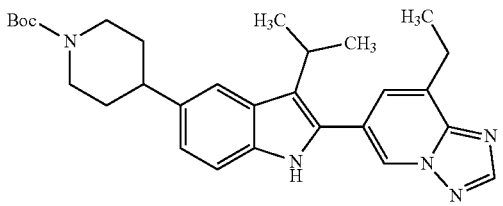
(94B)



To a stirred solution of tert-butyl 4-(3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (300 mg, 0.640 mmol), and 6-bromo-8-vinyl-[1,2,4]triazolo[1,5-a]pyridine (215 mg, 0.961 mmol) in dioxane (15 mL) and water (2 mL) was added potassium phosphate tribasic (408 mg, 1.921 mmol). The mixture was degassed with N_2 for 10 min. Next, $PdCl_2(dppf)$ (46.9 mg, 0.064 mmol) was added the mixture was degassed for 10 min. The reaction mixture was heated 80° C. for 16 h. The reaction mass was filtered through pad of celite, washed with EtOAc, and concentrated to afford tert-butyl 4-(3-isopropyl-2-(8-vinyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidine-1-carboxylate. The crude mass was purified by silica gel chromatography to afford tert-butyl 4-(3-isopropyl-2-(8-vinyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (230 mg, 74%) as white solid. LC retention time 1.74 min [K]. MS (E−) m/z: 486 (M+H).

Intermediate 94C: tert-butyl 4-(2-(8-ethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(94C)



A solution of tert-butyl 4-(3-isopropyl-2-(8-vinyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (180 mg, 0.371 mmol) in ethyl acetate (15 mL) was purged with nitrogen (N_2). Palladium on carbon (39.4 mg, 0.371 mmol)) was added and the mixture was purged with N_2 three times. Hydrogen gas (H_2) was introduced via a balloon to the mixture. The reaction mixture was stirred at room temperature for 5 h. The suspension was filtered through celite, the filtrate was collected and concentrated to afford crude compound. The crude was purified by silica gel chromatography. The compound was eluted in 15% ethyl acetate in hexane, the fractions were collected and concentrated to afford to afford tert-butyl 4-(2-(8-ethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (150 mg, 83% yield) as a white solid. LCMS retention time 1.70 min [K]. MS (E−) m/z: 488 (M+H).

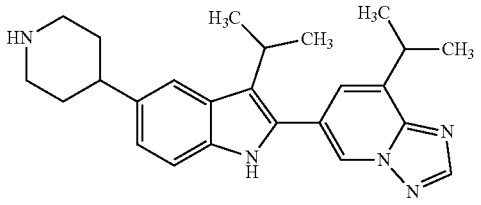
Example 94

To a solution of tert-butyl 4-(2-(8-ethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (140 mg, 0.287 mmol) in DCM (10 mL) was added 4 M HCl in dioxane (3.05 μl, 0.100 mmol at ambient temperature. The mixture was stirred at the same temperature for 1 h. The solution was concentrated to afford crude product. The crude material was purified by prep LCMS with the following conditions: Waters Xbridge C18,19×150 mm, 5 μm; Guard Column: Water XBridge C18,19×10 mm, 5 μm; Mobile Phase A:5:95 methanol:water with 10 mM NH_4OAc; Mobile Phase B: 95:5 methanol:water with 10 mM NH_4OAc; Gradient:15-65% B over 25 minutes, followed by a 10 minute hold at 65% B and 5 minute hold at 100% B; Flow:15 mL/min. Fractions containing the product were combined and dried using a Genevac centrifugal evaporator to provide 8-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (5.4 mg, 8.5%) as a white solid. LC retention time=1.38 min [E]. MS (E^-) m/z: 388 (M+H).

Example 95

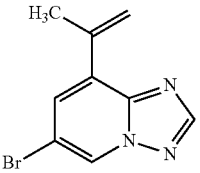
8-isopropyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine

(95)



Intermediate 95A: 6-bromo-8-(prop-1-en-2-yl)-[1,2,4]triazolo[1,5-a]pyridine

(95A)

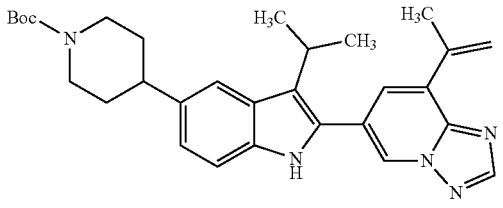


To a stirred solution of 6-bromo-8-iodo-[1,2,4]triazolo[1,5-a]pyridine (300 mg, 0.926 mmol) and 4,4,5,5-tetramethyl-

2-(prop-1-en-2-yl)-1,3,2-dioxaborolane (202 mg, 1.204 mmol) in dioxane (10 mL) and water (0.5 mL) was added potassium phosphate tribasic (590 mg, 2.78 mmol). The reaction mixture was degassed with N_2 for 10 min. Next, $PdCl_2$(dppf) (67.8 mg, 0.093 mmol) was added and the reaction mixture was degassed for 10 min. The reaction mixture was heated to 80° C. for 16 h. The reaction mass was filtered through a pad of celite, washed with EtOAc, and concentrated. The crude mass was purified by silica gel chromatography using 60% EtOAc-hexanes to afford (6-bromo-8-(prop-1-en-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (200 mg, 0.840 mmol, 91% yield) as an off-white solid. LC retention time 1.19 min [K]. MS (E^-) m/z: 240 (M+H).

Intermediate 95B: tert-butyl 4-(3-isopropyl-2-(8-(prop-1-en-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

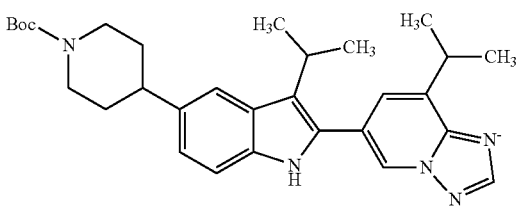
(95B)



To a stirred solution of tert-butyl 4-(3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (300 mg, 0.640 mmol), 6-bromo-8-(prop-1-en-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (229 mg, 0.961 mmol) in dioxane (15 mL), and water (2 mL) was added potassium phosphate tribasic (408 mg, 1.921 mmol) degassed with N_2 for 10 mins, then $PdCl_2$(dppf) (46.9 mg, 0.064 mmol) was added. The reaction mixture was heated 100° C. for 16 h. Reaction mass filtered through celite bed washed with EtOAc and concentrated to afford crude material. This material was purified by silica gel chromatography to afford tert-butyl 4-(3-isopropyl-2-(8-(prop-1-en-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate. The crude mass was purified by ISCO silica column to afford tert-butyl 4-(3-isopropyl-2-(8-(prop-1-en-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (260 mg, 81% yield) as a brown liquid. LC retention time 1.87 min [K]. MS (E−) m/z: 500 (M+H).

Intermediate 95C: tert-butyl 4-(3-isopropyl-2-(8-isopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

(95C)



A solution of tert-butyl 4-(3-isopropyl-2-(8-(prop-1-en-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (180 mg, 0.360 mmol) in ethyl acetate (15 mL), was purged with nitrogen (N_2). Next, palladium on carbon (38.3 mg, 0.360 mmol) was added and the mixture was purged with N_2 three times. Hydrogen gas (H_2) was introduced via a balloon to the mixture. The reaction mixture was stirred at room temperature for 5 h. The suspension was filtered through celite and the filtrate was collected and concentrated to afford the crude compound. The crude material was purified by silica gel chromatography and the compound eluted in 15% ethyl acetate in hexane. The fractions were collected and concentrated to afford tert-butyl 4-(3-isopropyl-2-(8-isopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (160 mg, 89% yield). LCMS retention time 1.81 min [K]. MS (E^-) m/z: 502 (M+H).

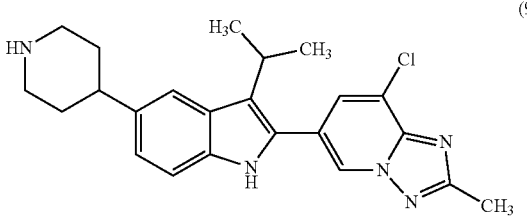
Example 95

To a solution of tert-butyl 4-(3-isopropyl-2-(8-isopropyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (140 mg, 0.279 mmol) in DCM (10 mL) was added 4 M HCl in dioxane (5 mL) at ambient temperature. The mixture was stirred at the same temperature for 1 h. The solution was concentrated to afford crude product. The crude sample was purified by preparative LCMS with the following conditions: Waters Xbridge C18,19×150 mm, 5 Ilm; Guard Column: Water XBridge C18,19×10 mm, 5 μm; Mobile Phase A:5:95 Methanol:water with 10 mM NH_4OAc; Mobile Phase B: 95:5 Methanol:water with 10 mM NH_4OAc; Gradient:15-65% B over 25 minutes, followed by a 10 minute hold at 65% B and 5 minute hold at 100% B; Flow:15 mL/min. Fractions containing the product were combined and dried using a Genevac centrifugal evaporator to provide 8-isopropyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (1.5 mg, 1.3%) as a white solid. LC retention time=1.49 min [E]. MS (E^-) m/z: 402 (M+H).

Example 96

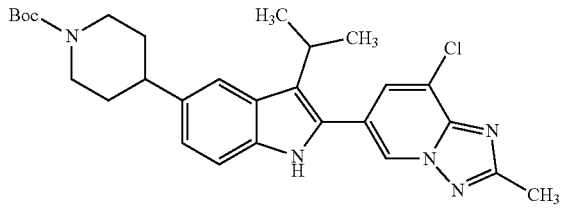
8-chloro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine

(96)



Intermediate 96A: tert-butyl 4-(2-(8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(96A)



A solution of tert-butyl 4-(3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (2.0 g, 4.27 mmol), 6-bromo-8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (1.158 g, 4.70 mmol) and potassium phosphate, tribasic (2.231 g, 12.81 mmol) in dioxane (60 mL) and water (4 mL) was degassed with N_2 for 10 min. Next, $PdCl_2(dppf)$-CH_2Cl_2 adduct (0.174 g, 0.213 mmol) was added and the mixture was degassed for 5 min. The resulting reaction mixture was heated at 90° C. for 12 h. The reaction mixture was concentrated. The residue was dissolved in ethyl acetate and the solution was washed with water. The organic layer was collected, dried over Na_2SO_4 and concentrated to afford crude compound. The residue was taken up in DCM (1 mL) and recrystallized with pet ether (3×10 mL). The brown solid formed was filtered and dried to afford tert-butyl 4-(2-(8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (1.4 g, 2.76 mmol, 64.5%) as a pale yellow solid. LCMS retention time 3.74 min [D]. MS (E^-) m/z: 508.3 (M+H).

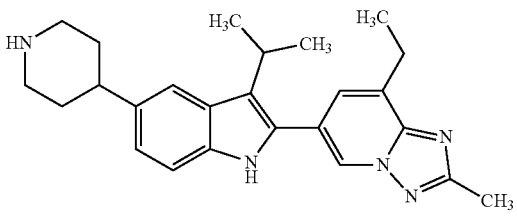
Example 96

To a stirred solution of tert-butyl 4-(2-(8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (250 mg, 0.492 mmol) in CH_2Cl_2 (2 mL) was added TFA (0.2 mL) at room temperature. The reaction mixture was stirred at the same temperature 2 h. The reaction mass was concentrated to afford crude compound. The crude material was purified via preparative LC/MS with the following conditions: Column: Water XBridge C18, 19×150 mm, 5-μm particles; Mobile Phase A: 0.1% trifluoroacetic acid; Mobile Phase B: acetonitrile; Gradient: 10-35% B over 25 minutes, then a 5-minute hold at 100% B; Flow: 15 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 8-chloro-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.200 g, 99% yield) as a pale solid. LC retention time=2.31 min [E]. MS (E^-) m/z: 409.4 (M+H). ^1H NMR (400 MHz, DMSO-d_6) δ ppm 1.32-1.52 (m, 7H) 1.80-1.96 (m, 3H) 2.07 (s, 1H) 2.28-2.40 (m, 1H) 2.61-2.72 (m, 1H) 2.88-3.04 (m, 2H) 3.17 (d, J=5.02 Hz, 2H) 3.21-3.28 (m, 2H) 4.10 (q, J=5.02 Hz, 1H) 7.02 (dd, J=8.53, 1.51 Hz, 1H) 7.35 (d, J=8.03 Hz, 1H) 7.57 (s, 1H), 8.02 (d, J=1.51 Hz, 1H) 8.77-8.94 (m, 1H) 11.24 (s, 1H).

Example 97

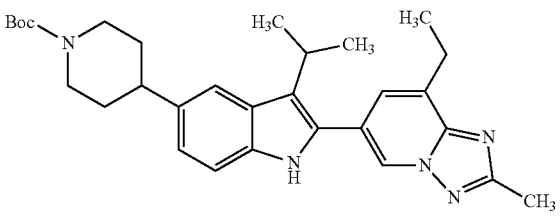
8-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine

(97)



Intermediate 97A: tert-butyl 4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(97A)



A solution of tert-butyl 4-(2-(8-chloro-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (0.1 mg, 0.197 μmol), ethylboronic acid (0.015 mg, 0.197 μmol), and potassium phosphate, dibasic (0.086 mg, 0.492 μmol) in toluene (2 mL) and water (0.5 mL) was degassed with N_2 for 10 min. Next, $Pd(OAc)_2$ (4.42 μg, 0.020 μmol) and tricyclohexylphosphine (2.76 μg, 0.0098 μmol) were added and the reaction mixture was degassed for 5 min. The reaction mixture was heated at 100° C. for 12 h. The reaction mixture was concentrated. The residue was dissolved in ethyl acetate and the solution was washed with water. The organic layer was collected, dried over Na_2SO_4, and concentrated to afford tert-butyl 4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidine-1-carboxylate (80 mg, 1.59 mmol, 81%) as a pale yellow solid. LCMS retention time 3.93 min [D]. MS (E^-) m/z: 502.3 (M+H).

Example 97

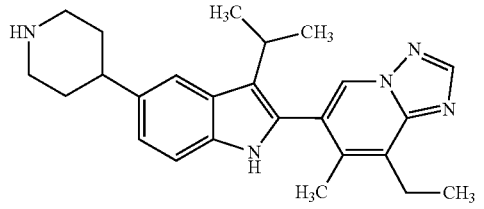
To a solution of tert-butyl 4-(2-(8-ethyl-2-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (0.08 g, 0.159 mmol) in DCM (2 mL) was added 4 M HCl in dioxane (0.399 mL, 1.595 mmol) drop wise. The reaction mixture was stirred at 25° C. for 1 h. The reaction mass was concentrated to afford crude

compound. The crude material was purified via preparative LC/MS with the following conditions: Column: Water XBridge C18, 19×150 mm, 5-μm particles; Mobile Phase A: 10-mM ammonium acetate; Mobile Phase B: acetonitrile; Gradient: 8-38% B over 25 minutes, then a 5-minute hold at 100% B; Flow: 15 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 8-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.0013 g, 2% yield) as a pale solid. LC retention time=1.369 min [D1]. MS (E^-) m/z: 402 (M+H). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 11.17 (s, 1H), 8.69 (s, 1H), 7.54 (d, J=18.6 Hz, 2H), 7.41-7.30 (m, 1H), 7.01 (d, J=9.0 Hz, 1H), 3.19-3.16 (m, 5H), (3.08-2.95 (m, 8H), 2.08 (s, 1H), 1.99 (d, J=13.2 Hz, 6H), 1.87 (d, J=12.2 Hz, 7H), 1.45 (d, J=7.1 Hz, 9H), 1.40-1.34 (m, 3H).

Example 98

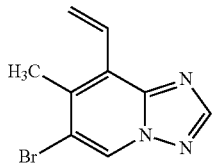
tert-butyl 4-(2-(8-ethyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(98)



Intermediate 98A: 6-bromo-7-methyl-8-vinyl-[1,2,4]triazolo[1,5-a]pyridine

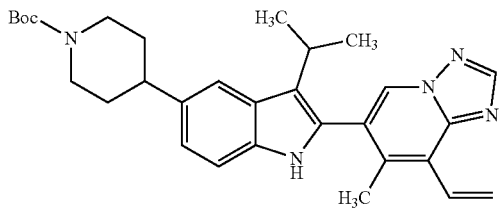
(98A)



A solution of 6-bromo-8-iodo-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.25 g, 0.740 mmol) and potassium vinyltrifluoroborate (0.099 g, 0.740 mmol) in ethanol (5 mL) was degassed with N_2 for 10 min. Next, $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.030 g, 0.037 mmol) was added and the reaction mixture was degassed for 5 min followed by the addition of TEA (0.412 mL, 2.96 mmol). The resulting reaction mixture was heated at 85° C. for 12 h. The reaction mixture was concentrated. The residue was dissolved in ethyl acetate and the solution was washed with water. The organic layer was collected, dried over Na_2SO_4, and concentrated to afford 6-bromo-7-methyl-8-vinyl-[1,2,4]triazolo[1,5-a]pyridine (0.25 g, 0.473 mmol, 63.9% yield) as a yellow solid. LCMS retention time 1.42 min [H]. MS (E^-) m/z: 240.3 (M+2H).

Intermediate 98B: tert-butyl 4-(3-isopropyl-2-(7-methyl-8-vinyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

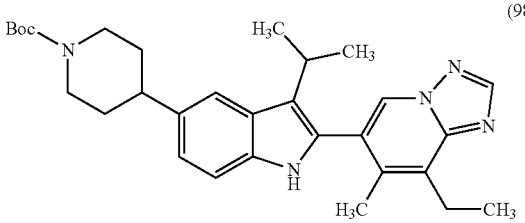
(98B)



A solution of tert-butyl 4-(3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.4 g, 0.854 mmol), 6-bromo-7-methyl-8-vinyl-[1,2,4]triazolo[1,5-a]pyridine (0.224 g, 0.939 mmol), and potassium phosphate tribasic (0.446 g, 2.56 mmol) in dioxane (5 mL) and water (1 mL) was degassed with N_2 for 10 min. Next, $PdCl_2$(dppf)-CH_2Cl_2 adduct (0.035 g, 0.043 mmol) was added and the mixture was again degassed for 5 min. The resulting reaction mixture was heated at 90° C. for 12 h. The reaction mixture was concentrated. The residue was dissolved in ethyl acetate and the solution was washed with water. The organic layer was collected, dried over Na_2SO_4, and concentrated to afford crude compound. The residue was taken up in DCM (1 mL) and recrystallized with pet ether (3×10 mL). The crude material was purified by combiflash 5% MeOH/$CHCl_3$. Concentration of fractions provided tert-butyl 4-(3-isopropyl-2-(7-methyl-8-vinyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.35 g, 0.700 mmol, 82%) as a yellow solid. LCMS retention time 3.11 min [D]. MS (E^-) m/z: 500.3 (M+H).

Intermediate 98C: tert-butyl 4-(2-(8-ethyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(98C)



A solution of tert-butyl 4-(3-isopropyl-2-(7-methyl-8-vinyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.35 g, 0.700 mmol) in methanol (10 mL) was purged with nitrogen (N_2). Next, Pd/C (0.019 g, 0.018 mmol) was added and the mixture was purged with N_2 three times. Hydrogen gas (H_2) was introduced via a balloon to the mixture. The reaction mixture was stirred at room temperature for 5 h. The suspension was filtered through celite bed, the filtrate was collected, and concentrated to afford tert-butyl 4-(2-(8-ethyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidine-1-

carboxylate (250 mg, 0.498 mmol, 72%) as a white solid. LCMS retention time 4.45 min [H]. MS (E^-) m/z: 502.3 (M+H).

Example 98

To a solution of tert-butyl 4-(2-(8-ethyl-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (0.25 g, 0.498 mmol) in DCM (2 mL) was added 4 M HCl in dioxane (0.249 mL, 0.997 mmol) drop wise. The reaction mixture was stirred at 25° C. for 1 h. The crude material was purified via preparative LC/MS with the following conditions: Column: Water XBridge C18, 19×150 mm, 5-μm particles; Mobile Phase A: 10-mM ammonium acetate; Mobile Phase B: methanol; Gradient: 20-60% B over 20 minutes, then a 5-minute hold at 100% B; Flow: 15 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 8-ethyl-6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (180 mg, 90%) as a pale solid. LCMS retention time 1.368 min [E]. MS (E^-) m/z: 402.2 (M+H).

The following examples were prepared according to the general procedures disclosed in Examples 1 and 2.

TABLE 9

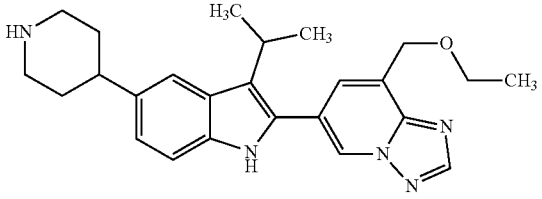
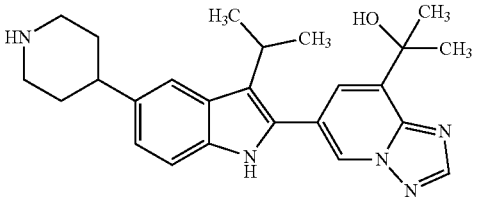
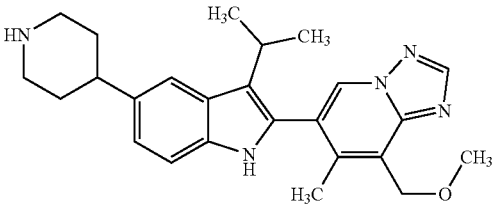
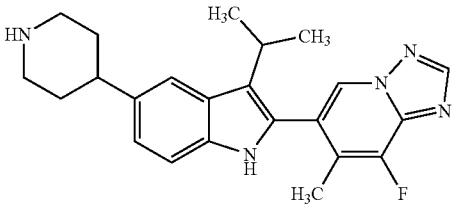
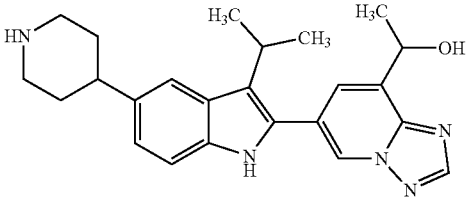
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
99	F-17		418.2	1.33	QC-ACN-AA-XB
100	F-10		417.9	1.18	QC-ACN-AA-XB
101	F-12		418.0	0.65	A1
102	F-14		392.0	1.2	QC-ACN-AA-XB
103	F-9		403.9	1.14	QC-ACN-TFA-XB

TABLE 9-continued

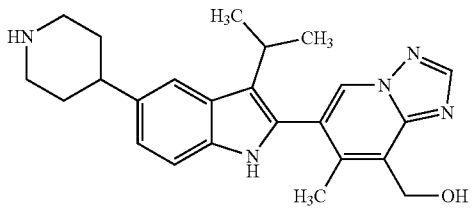
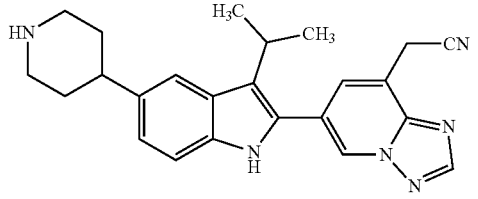
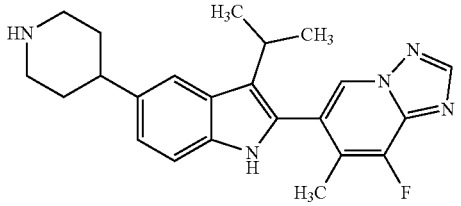
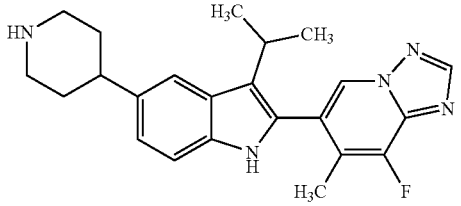
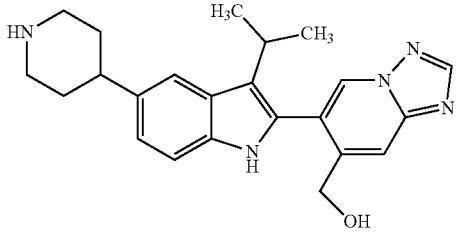
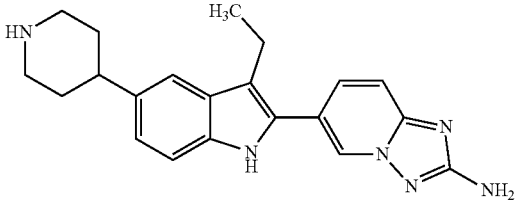
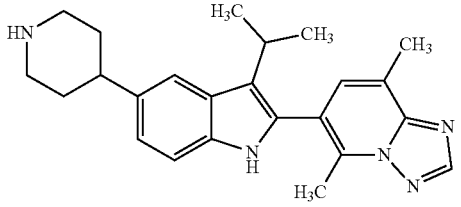
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
104	F-11		404.2	0.99	QC-ACN-AA-XB
105	F-13		399.1	1.21	QC-ACN-AA-XB
106	F-14		392.0	1.2	QC-ACN-TFA-XB
107	F-14		392.0	1.42	QC-ACN-AA-XB
108	F-8		389.9	0.88	QC-ACN-AA-XB
109	F-58		361.3	0.71	QC-ACN-AA-XB
110	F-18		388.2	1.25	QC-ACN-TFA-XB

TABLE 9-continued

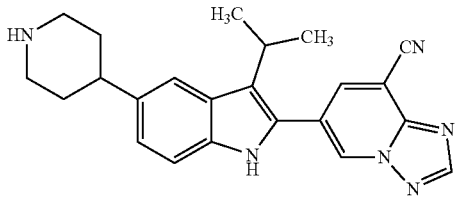
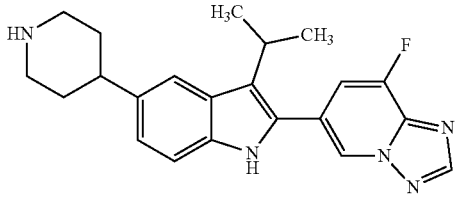
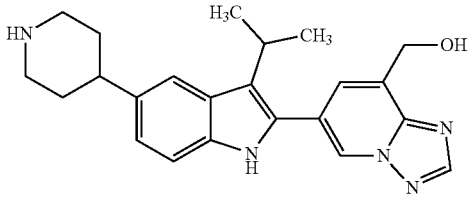
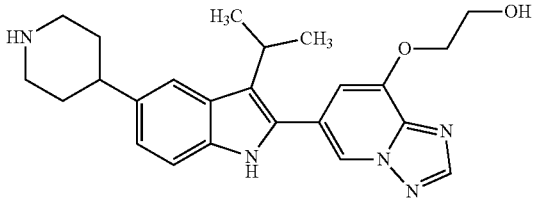
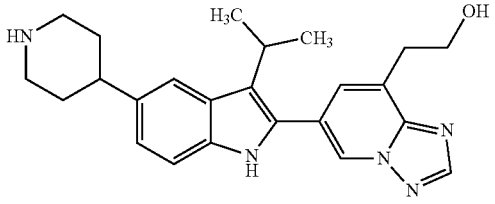
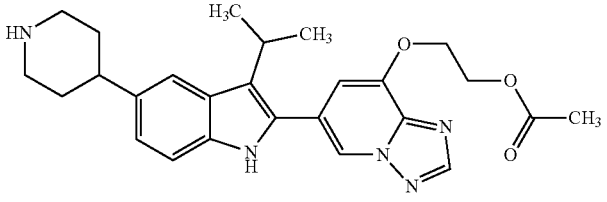
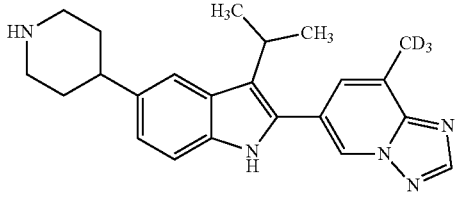
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
111	F-19		385.2	1.19	QC-ACN-TFA-XB
112	F-20		378.0	1.148	QC-ACN-AA-XB
113	F-8		390.2	0.61	A1
114	F16		420.2	0.61	A1
115	F-7		—	0.63	A1
116	F-16		462.2	0.67	A1
117	F-59		377.2	0.66	TS1

TABLE 10

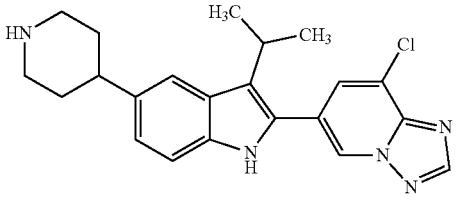
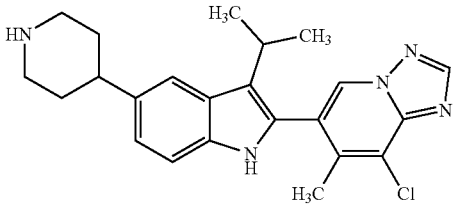
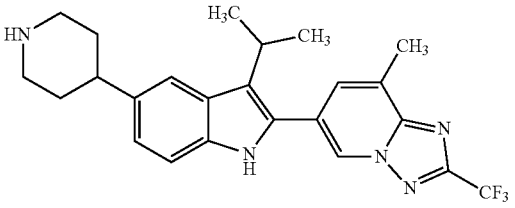
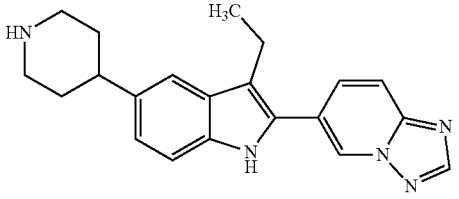
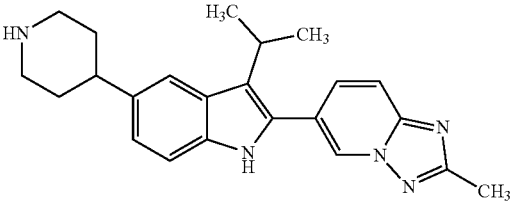
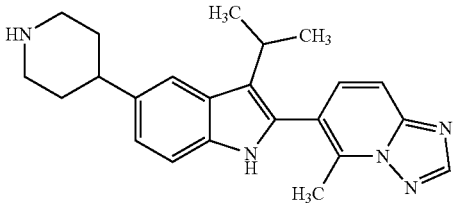
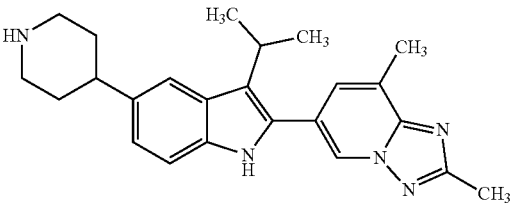
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
118	F-39		395.3	2.01	E
119	F-36		409.1	1.37	E
120	F-40		443.2	1.78	E
121	F-1		346.6	0.81	E
122	F-21		375.3	1.06	E
123	F-22		375.2	1.28	E
124	F-23		389.3	1.22	F

TABLE 10-continued

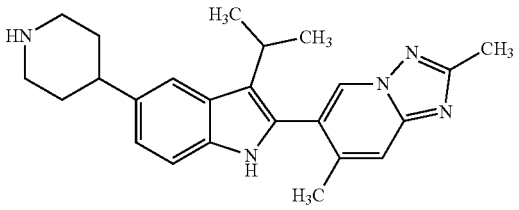
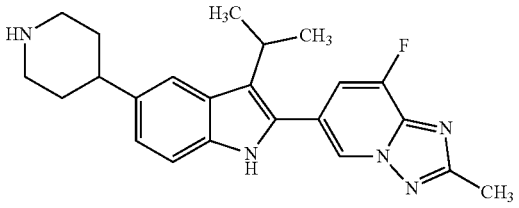
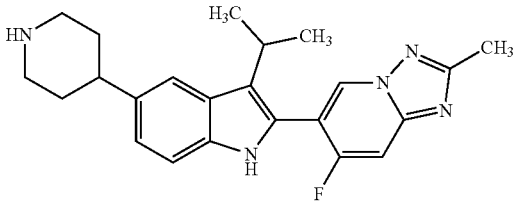
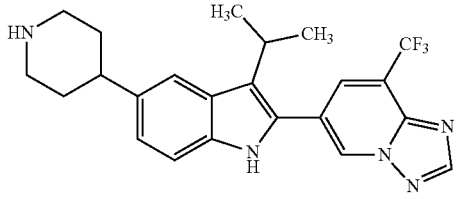
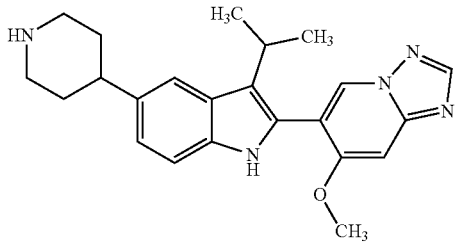
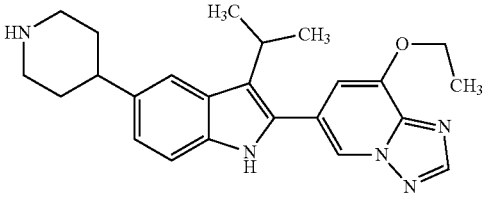
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
125	F-24		389.2	1.30	F
126	F-25		392.3	1.39	F
127	F-26		391.3	1.13	E
128	F-27		428.2	1.46	F
131	F-28		391.3	0.95	E
132	F-29		405.3	1.16	E

TABLE 10-continued

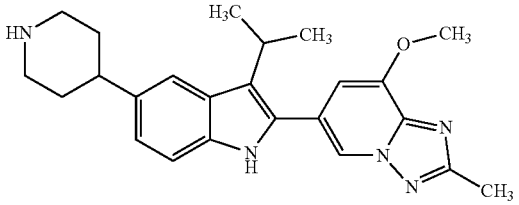
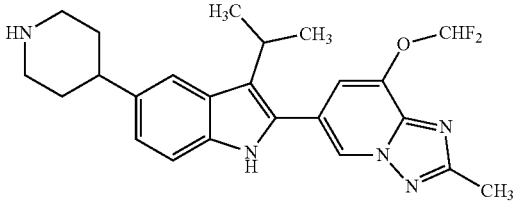
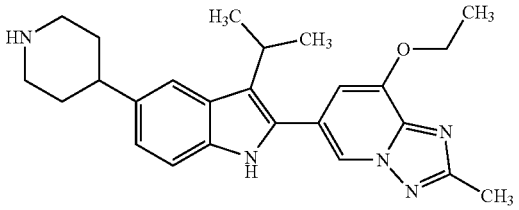
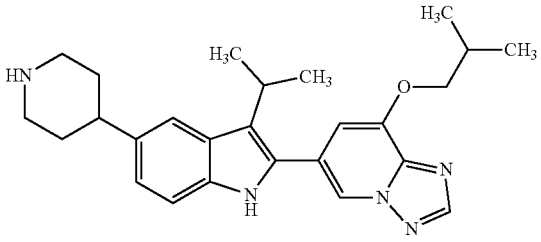
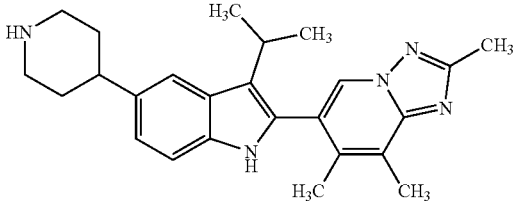
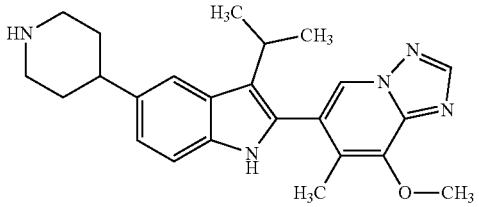
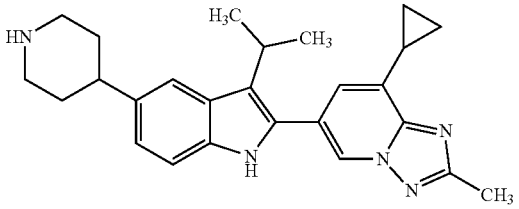
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
133	F-31		405.2	1.37	E
134	F-32		441.2	1.43	E
135	F-30		419.3	1.39	E
136	F-33		433.4	1.41	E
138	F-34		423.2	1.42	E
140	F-35		405.2	1.36	E
141	F-54		415.1	1.40	F

TABLE 10-continued

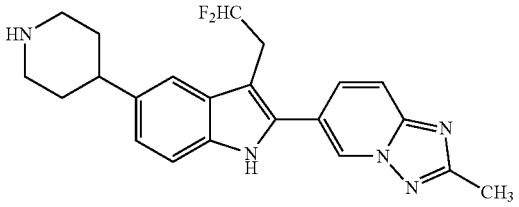
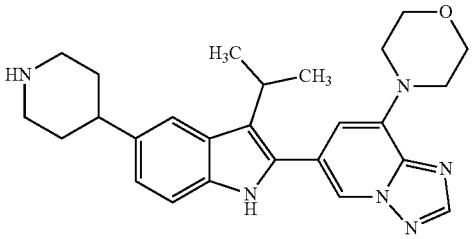
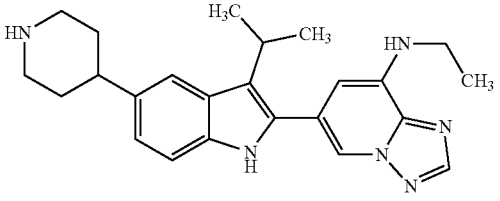
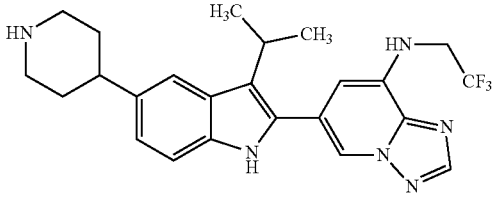
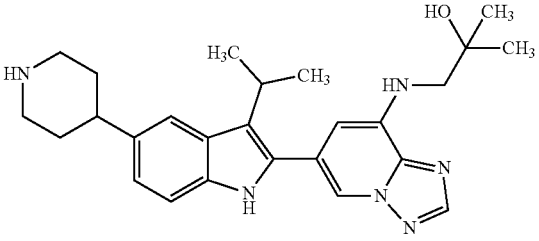
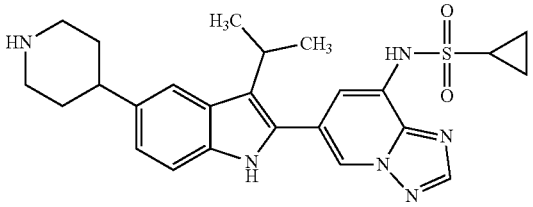
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
142	F-21		396.3	0.88	E
143	F-41		446.3	1.37	E
144	F-45		404.2	1.43	F
145	F-46		458.2	1.49	F
146	F-47		448.3	1.32	F
147	F-48		480.2	1.28	F

TABLE 10-continued

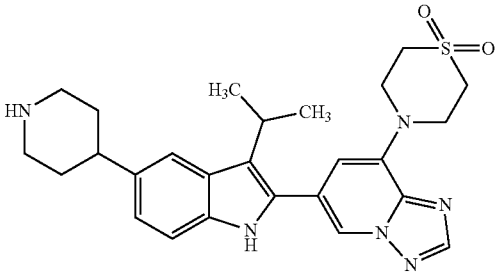
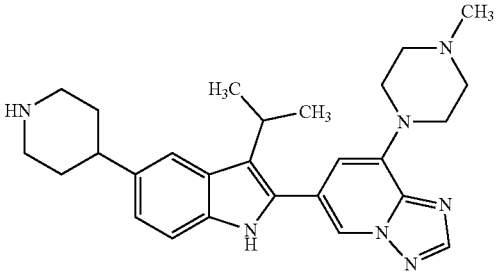
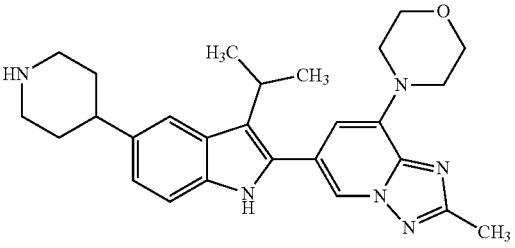
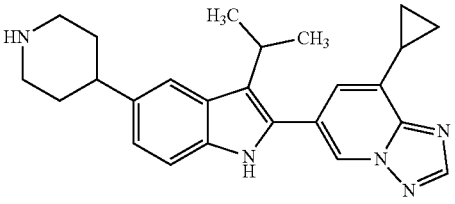
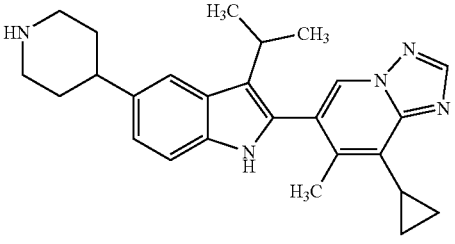
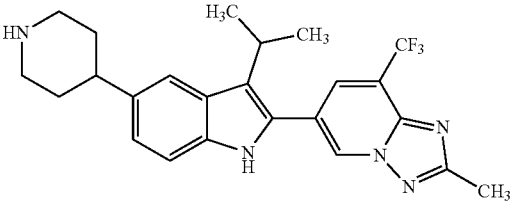
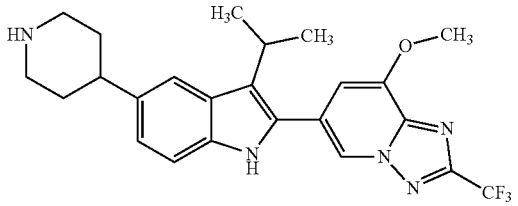
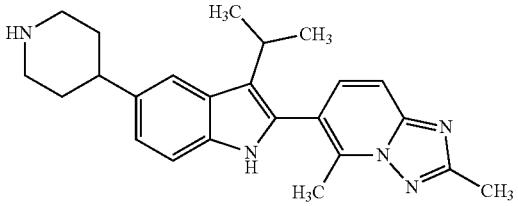
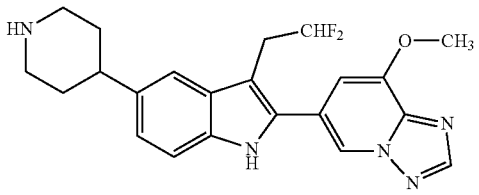
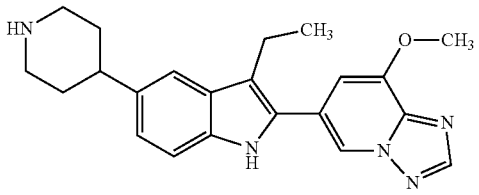
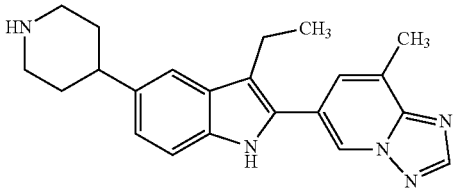
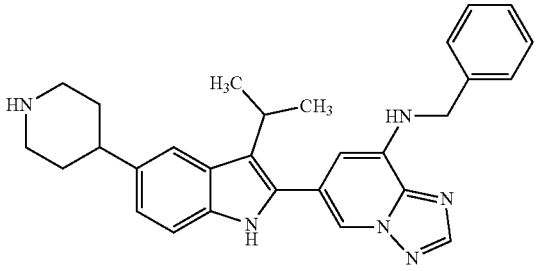
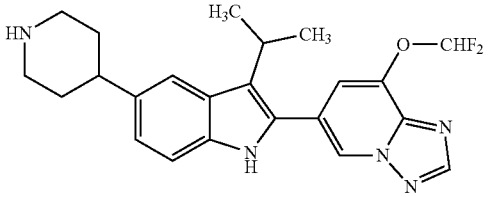
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
148	F-49		493.2	1.28	F
149	F-44		459.3	1.07	F
150	F-41		460.3	1.42	F
151	F-52		401.3	1.21	F
152	F-55		414.2	1.36	F
153	F-40		443.2	1.33	E

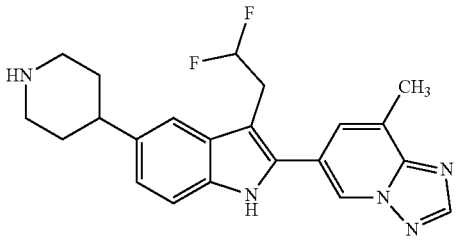
TABLE 10-continued

Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
154	F-57		459.2	1.68	E
155	F-37		389.2	1.15	F
156	F-5		412.2	0.92	E
157	F-5		376.4	1.34	D
158	F-2		360.2	1.40	D
159	F-51		465.3	1.54	N
160			426.2	1.35	N

Example 161

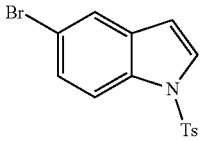
6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine

(161)



Intermediate 161A: 5-bromo-1-tosyl-1H-indole

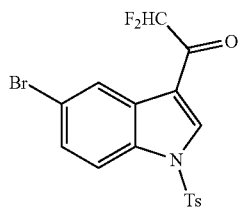
(161A)



To a stirred solution of 5-bromo-1H-indole (5.0 g, 25.5 mmol), TsCl (6.03 g, 31.6 mmol), and tetrabutylammonium hydrogen sulfate (0.63 g, 1.855 mmol) in toluene (100 mL) was added NaOH (50% solution in water, 10.20 g, 255 mmol) dropwise. The reaction mixture was stirred for 16 h at room temperature. The reaction was quenched with water (20 mL). The layers were separated, the aqueous layer was extracted with EtOAc (2×50 mL), the combined organic extracts were dried (Na_2SO_4) and concentrated to yield crude material. The crude material was purified by silica gel chromatography. The compound was eluted in 4% EA in hexanes, the fractions was collected and concentrated to afford 5-bromo-1-tosyl-1H-indole (7.1 g, 20.27 mmol) as a white solid. LC retention time=2.230 min [A]. MS (E) m/z: 393.3 (M−H).

Intermediate 161B: 1-(5-bromo-1-tosyl-1H-indol-3-yl)-2,2-difluoroethan-1-one

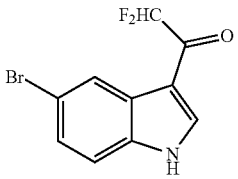
(161B)



To a suspension of $AlCl_3$ (6.85 g, 51.4 mmol) in DCM (50 mL) was added difluoroacetic anhydride (4.47 g, 25.7 mmol). The reaction mixture was stirred for 15 min, then a solution of 5-bromo-1-tosyl-1H-indole (3 g, 8.57 mmol)) in DCM (30 mL) was added. The reaction mixture was stirred for 1 h at ambient temperature. The reaction was quenched with ice-water. The mixture was extracted with DCM (2×50 mL), combined extracts was washed with aqueous $NaHCO_3$, brine, dried over $MgSO_4$, filtered and concentrated to yield crude material. The crude material was purified by silica gel chromatography, the compound was eluted in 10% EtOAc in hexane, the fraction was collected and concentrated to afford 1-(5-bromo-1-tosyl-1H-indol-3-yl)-2,2-difluoroethanone (2.21 g, 4.1 mmol) as a crystalline solid. LC retention time=2.732 min [A]. MS (E^-) m/z: 428.0 (M+H).

Intermediate 161C: 1-(5-bromo-1H-indol-3-yl)-2,2-difluoroethan-1-one

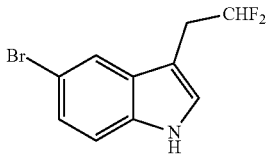
(161C)



To a solution of 1-(5-bromo-1-tosyl-1H-indol-3-yl)-2,2-difluoroethanone (0.2 g, 0.467 mmol) in THF (4 mL) and MeOH (4.00 mL) solvent mixture was added Cs_2CO_3 (0.45 g, 1.381 mmol) at room temperature. The mixture was stirred at room temperature for 12 h. The reaction mixture was concentrated, the residue was diluted with minimum amount of water and undissolved solids were filtered and dried under vacuum to afford 1-(5-bromo-1H-indol-3-yl)-2,2-difluoroethanone (105 mg, 0.244 mmol) as a white solid. LC retention time=2.233 min [A]. MS (E^-) m/z: 276 (M+2H).

Intermediate 161D: 5-bromo-3-(2,2-difluoroethyl)-1H-indole

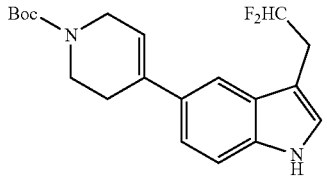
(161D)



To the stirred solution of 1-(5-bromo-1H-indol-3-yl)-2,2-difluoroethanone (0.25 g, 0.912 mmol) in THF (10 mL) was added BH_3DMS (1.368 mL, 2.74 mmol) at 0° C. under nitrogen. The reaction mixture was stirred at 80° C. for 20 h. The reaction was quenched with water (2 mL) at 0° C. The reaction mixture was diluted with ethyl acetate (100 mL), washed with sodium bicarbonate (2×25 mL) and water (2×25 mL), combined organic extracts was dried over anhydrous sodium sulphate, filtered and concentrated to yield crude compound. The crude material was purified on silica gel chromatography, the compound was eluted at 8% ethyl acetate/hexane, the fractions was collected and concentrated to afford 5-bromo-3-(2,2-difluoroethyl)-1H-indole (120 mg, 0.438 mmol) as an oil. LC retention time=2.802 min [D]. MS (E^-) m/z: 260 (M+H).

Intermediate 161E: tert-butyl 4-(3-(2,2-difluoroethyl)-1H-indol-5-yl)-3,6-dihydropyridine-1(2H)-carboxylate

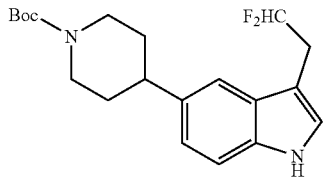
(161E)



Tert-butyl 4-(3-(2,2-difluoroethyl)-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate was prepared according to the general procedure described in Intermediate T-1B using 5-bromo-3-(2,2-difluoroethyl)-1H-indole as the starting intermediate (0.14 g, 80% yield). LC retention time 3.075 min [D]. MS (E^-) m/z: 361.2 (M−H).

Intermediate 161F: tert-butyl 4-(3-(2,2-difluoroethyl)-1H-indol-5-yl)piperidine-1-carboxylate

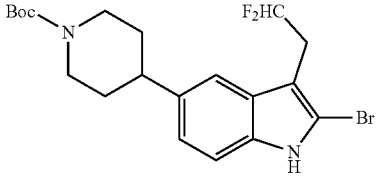
(161F)



Tert-butyl 4-(3-(2,2-difluoroethyl)-1H-indol-5-yl)piperidine-1-carboxylate was prepared according to the general procedure described in Intermediate T-1C using tert-butyl 4-(3-(2,2-difluoroethyl)-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate as the starting intermediate (0.9 g, 88% yield). LC retention time 3.282 min [D]. MS (E^-) m/z: 265.0 (M+H-Boc).

Intermediate 161G: tert-butyl 4-(2-bromo-3-(2,2-difluoroethyl)-1H-indol-5-yl)piperidine-1-carboxylate

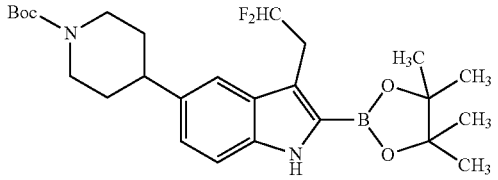
(161G)



Tert-butyl 4-(2-bromo-3-(2,2-difluoroethyl)-1H-indol-5-yl)piperidine-1-carboxylate was prepared according to the general procedure described in Intermediate 194D using tert-butyl 4-(3-(2,2-difluoroethyl)-1H-indol-5-yl)piperidine-1-carboxylate as the starting intermediate (0.3 g, 52% yield). LC retention time 1.10 min [G]. MS (E^-) m/z: 389.0 (M+2H-tBu).

Intermediate 161H: tert-butyl 4-(3-(2,2-difluoroethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)p iperidine-1-carboxylate

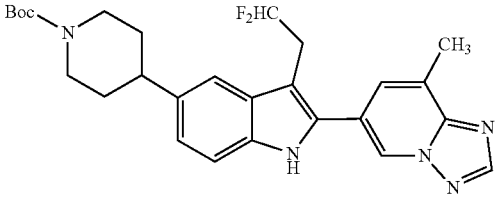
(161H)



A mixture of pinacolborane (1.444 g, 11.28 mmol), tert-butyl 4-(2-bromo-3-(2,2-difluoroethyl)-1H-indol-5-yl)piperidine-1-carboxylate (1.0 g, 2.256 mmol), bis(benzonitrile) palladium(II) chloride (0.086 g, 0.226 mmol), TEA (0.683 g, 6.77 mmol), and 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl (0.092 g, 0.226 mmol) in dioxane (20 mL) was degassed with nitrogen for 10 min. The reaction mixture was stirred at 80° C. for 1 h in a sealed tube. The reaction was quenched with ice cold water. The reaction mixture was diluted with ethyl acetate, filtered and washed with excess ethyl acetate, combined organic layers was washed with water, brine, dried over sodium sulphate and evaporated to afford crude compound. The crude material was purified by silica gel chromatography, the compound was eluted with 25% ethyl acetate in hexane, the fractions were collected and concentrated to afford tert-butyl 4-(3-(2,2-difluoroethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.650 g, 1.325 mmol, 58.8% yield) as an off-white solid. LC retention time 3.282 min [D]. MS (E^-) m/z: 435.4 (M+H-tBu).

Intermediate 161I: tert-butyl 4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

(161I)



A mixture of tert-butyl 4-(3-(2,2-difluoroethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.300, 0.612 mmol), 6-bromo-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.156 g, 0.734 mmol), $PdCl_2(dppf)$-CH_2Cl_2 adduct (0.050 g, 0.061 mmol), and tripotassium phosphate (0.390 g, 1.835 mmol) in a solvent mixture of dioxane (20 mL) and water (2.5 mL) was degassed with nitrogen for 10 min. Next, the resulting slurry was stirred at 95° C. for 3 h in a sealed tube. The reaction mixture was diluted with ethyl acetate, filtered and washed with excess ethyl acetate, combined organic layers were washed with water, brine, dried over sodium sulphate and evaporated to afford crude compound. The crude material was purified by silica gel chromatography, the compound

was eluted with 85% ethyl acetate and pet ether to afford tert-butyl 4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.210 g, 0.424 mmol, 69.3% yield) as a light yellow solid. LC retention time 1.42 min [G]. MS (E^-) m/z: 496.4 (M+H).

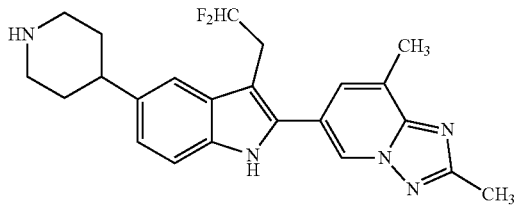
Example 161

To a solution of tert-butyl 4-(3-(2,2-difluoroethyl)-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidine-1-carboxylate (0.210 g, 0.424 mmol) in dioxane (5.0 mL) was added 4 M HCl in dioxane (1.059 mL, 4.24 mmol) at room temperature. The mixture was stirred at the same temperature for 2 h. The volatiles were evaporated and dried under vacuum to afford crude compound. The crude material was triturated with diethyl ether, dried under vacuum to afford 6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.165 g, 0.417 mmol, 98% yield) as a light yellow solid. LCMS retention time 1.021 min [E]. MS (E^-) m/z: 396.2 (M+H).

Example 162

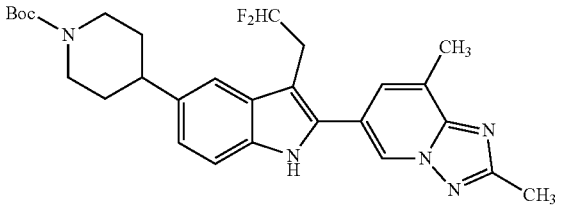
6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine

(162)



Intermediate 162A: tert-butyl 4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate

(162A)



Tert-butyl 4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate was prepared according to the general procedure described for Intermediate 161I using tert-butyl 4-(3-(2,2-difluoroethyl)-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.250 g, 0.510 mmol). LC retention time 3.102 min [D]. MS (E^-) m/z: 510.2 (M+H).

Example 162

6-(3-(2,2-difluoroethyl)-5-(piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine was prepared according to the general procedure described in Example 161 using tert-butyl 4-(3-(2,2-difluoroethyl)-2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboxylate (0.200 g, 0.392 mmol). LC retention time 1.831 min [D]. MS (E^-) m/z: 410.2 (M+H).

The following examples were prepared according to the general procedures disclosed in Example 7.

TABLE 11

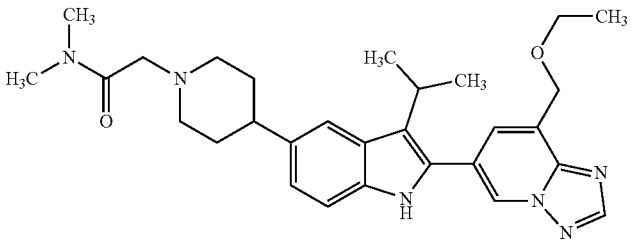
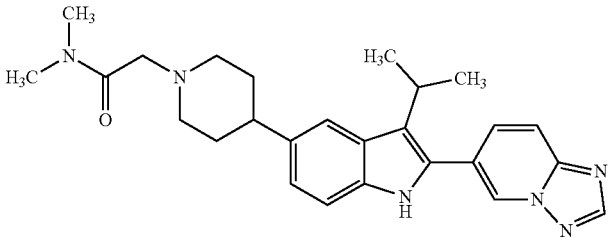
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
163	EX-99		503.2	1.31	QC-ACN-TFA-XB
164	EX-1		445.4	1.31	QC-ACN-AA-XB

TABLE 11-continued

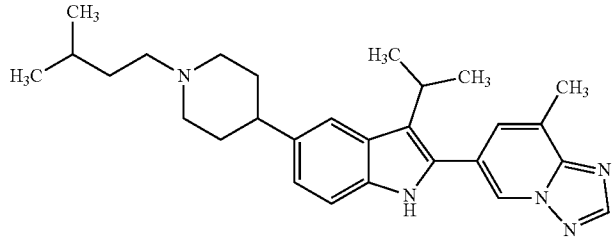
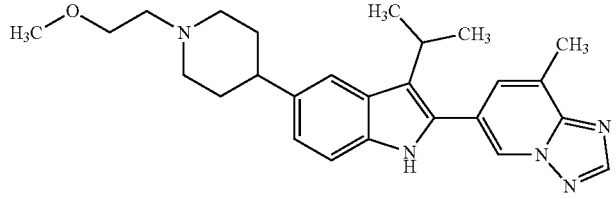
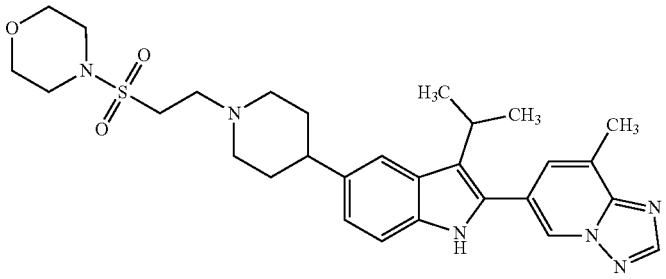
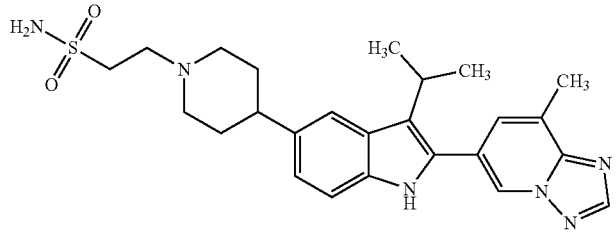
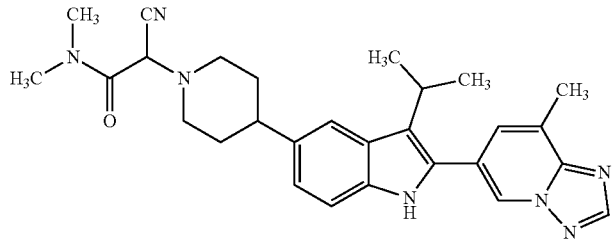
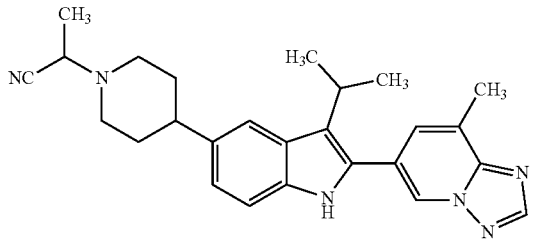
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
165	EX-2		444.4	1.7	QC-ACN-AA-XB
166	EX-2		431.9	1.33	QC-ACN-TFA-XB
167	EX-2		550.9	1.75	QC-ACN-AA-XB
168	EX-2		481.2	1.48	QC-ACN-AA-XB
169	EX-2		484.0	1.85	QC-ACN-AA-XB
170	EX-2		427.1	1.17	QC-ACN-TFA-XB

TABLE 11-continued

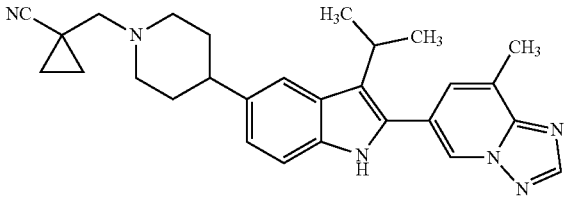
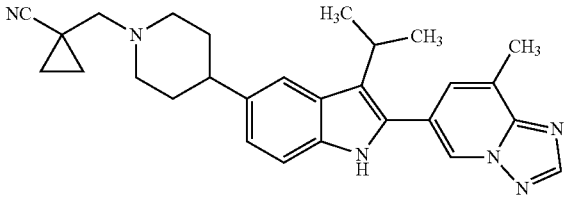
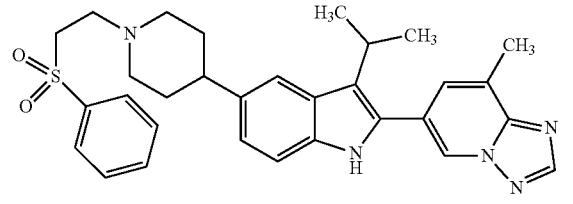
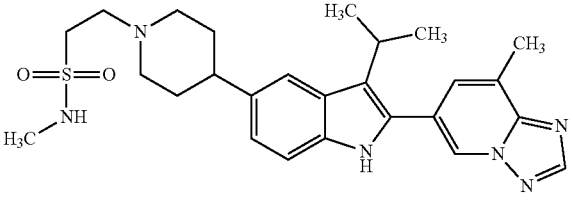
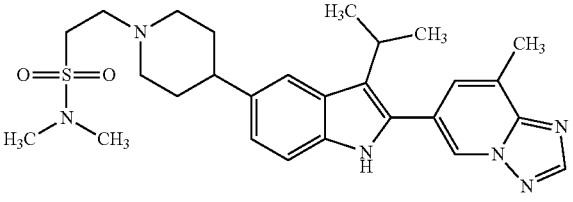
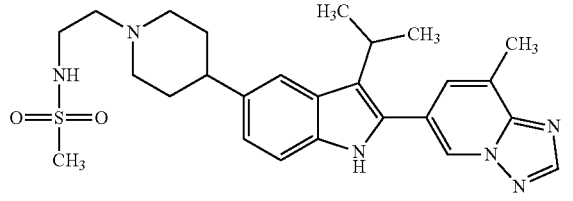
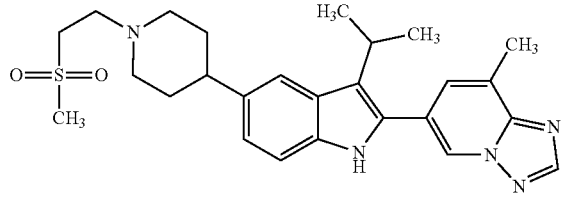
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
171	EX-2		453.0	1.97	QC-ACN-AA-XB
172	EX-2		453.0	2.09	QC-ACN-AA-XB
173	EX-2		542.0	2.16	QC-ACN-AA-XB
174	EX-2		495.1	1.58	QC-ACN-AA-XB
175	EX-2		509.0	1.76	QC-ACN-AA-XB
176	EX-2		495.0	1.34	QC-ACN-TFA-XB
177	EX-2		480.1	1.08	QC-ACN-TFA-XB

TABLE 11-continued

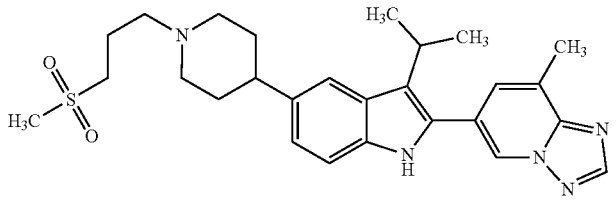
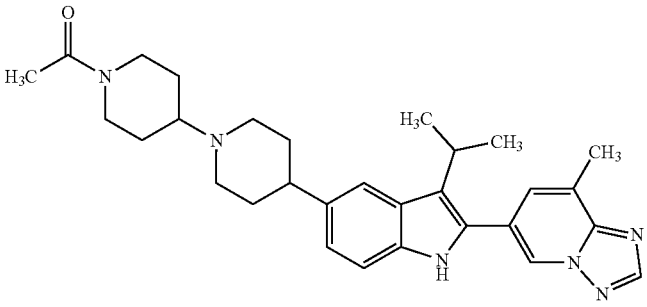
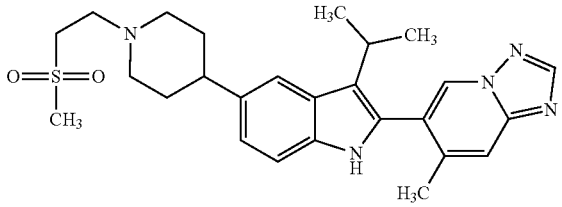
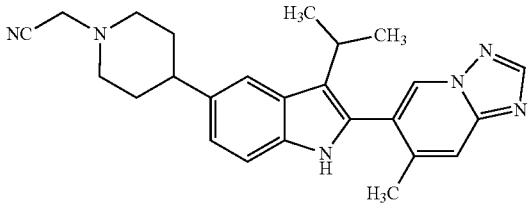
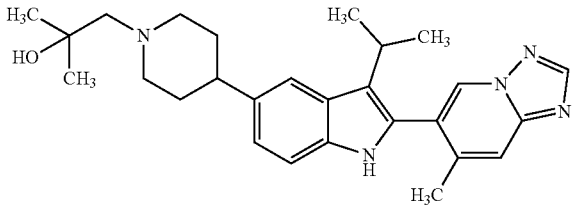
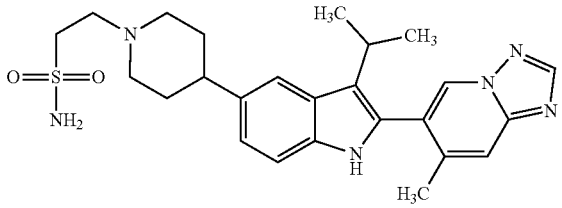
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
178	EX-2		495.1	1.25	QC-ACN-AA-XB
179	EX-2		499.4	1.23	QC-ACN-AA-XB
180	EX-3		480.1	1.56	QC-ACN-AA-XB
181	EX-3		412.9	1.84	QC-ACN-AA-XB
182	EX-3		446.0	1.41	QC-ACN-AA-XB
183	EX-3		481.0	0.98	QC-ACN-TFA-XB

TABLE 11-continued

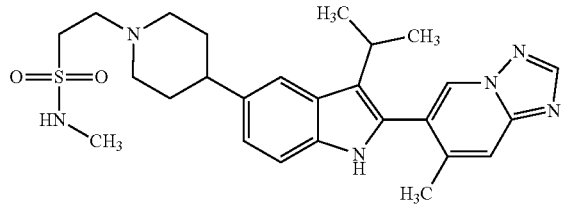
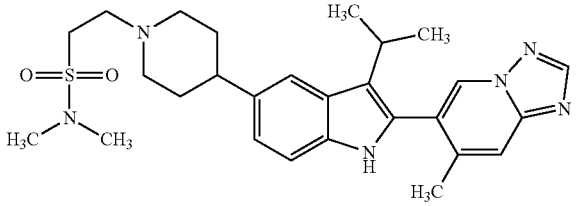
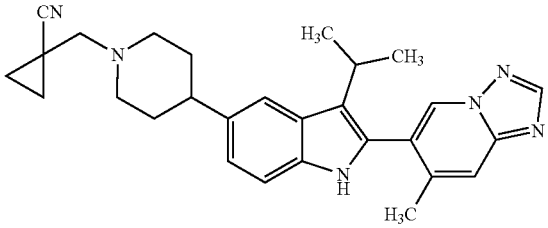
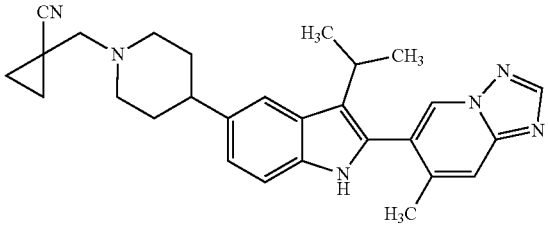
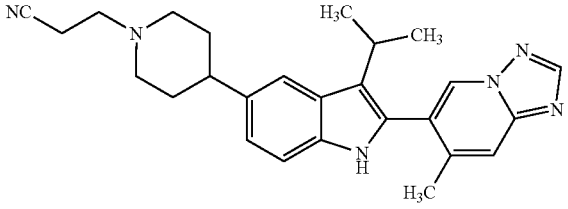
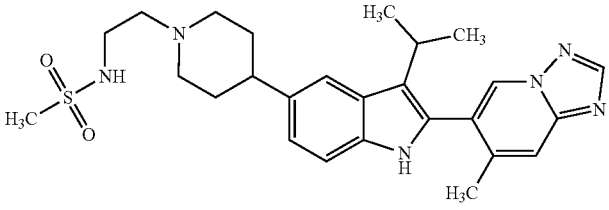
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
184	EX-3		495.0	1.47	QC-ACN-AA-XB
185	EX-3		509.1	1.71	QC-ACN-AA-XB
186	EX-3		453.0	2.19	QC-ACN-AA-XB
187	EX-3		453.3	1.32	QC-ACN-TFA-XB
188	EX-3		427.0	1.73	QC-ACN-AA-XB
189	EX-3		494.9	1.42	QC-ACN-AA-XB

TABLE 11-continued

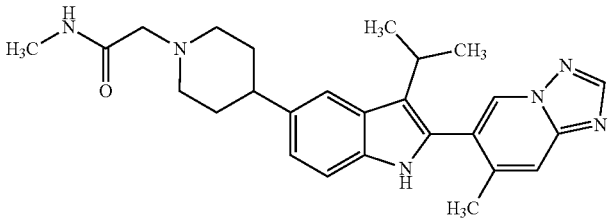
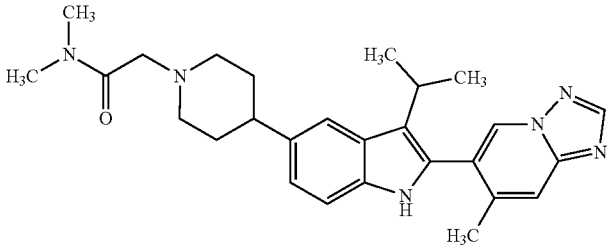
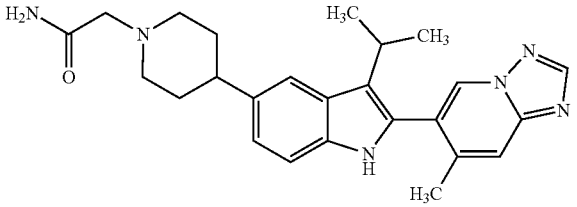
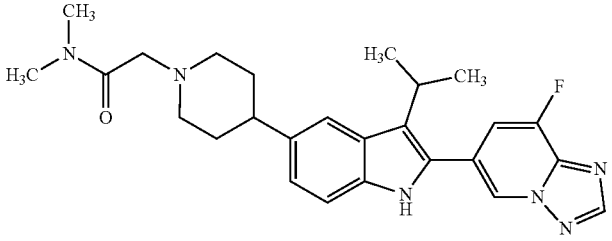
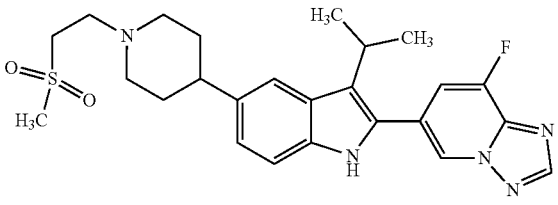
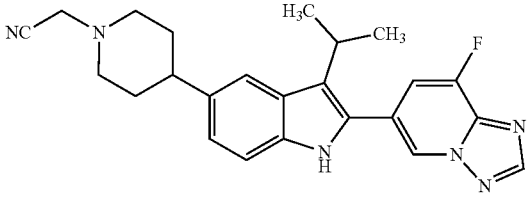
Ex. No.	Template Starting Material	Structure	LCMS MH+	Rt (min)	HPLC Method
190	EX-3		445.4	1.05	QC-ACN-TFA-XB
191	EX-3		459.4	1.33	QC-ACN-AA-XB
192	EX-3		431.1	1.35	QC-ACN-AA-XB
193	EX-112		463.3	1.27	QC-ACN-TFA-XB
194	EX-112		484.0	1.71	QC-ACN-AA-XB
195	EX-112		417.2	1.88	QC-ACN-AA-XB

TABLE 11-continued

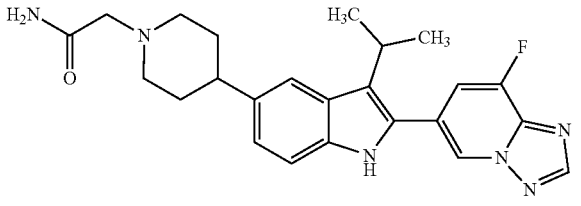
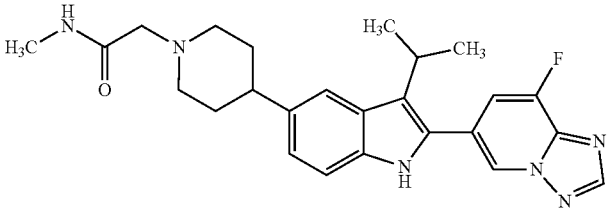
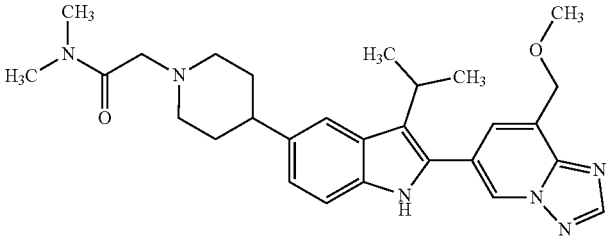
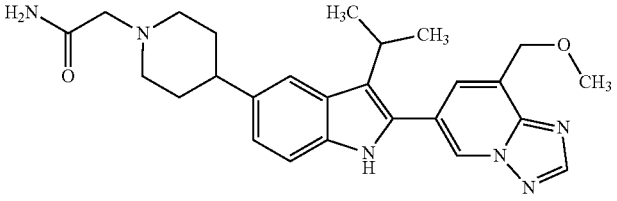
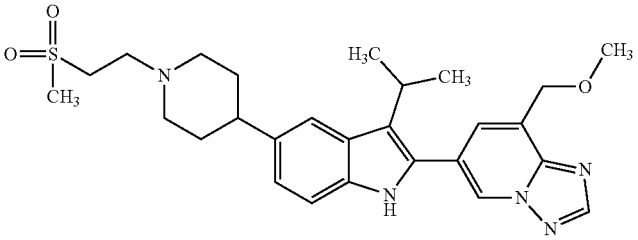
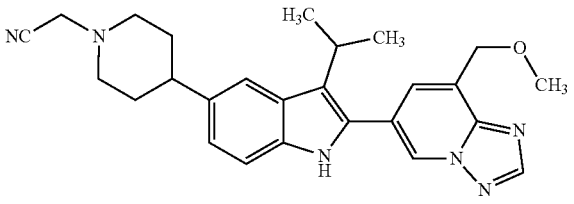
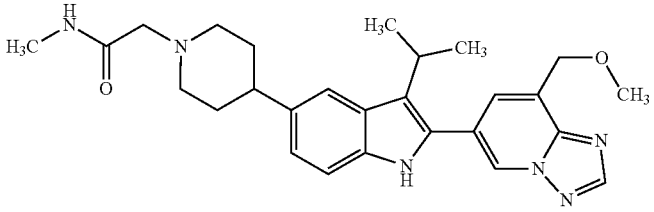
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
196	EX-112		435.1	1.42	QC-ACN-AA-XB
197	EX-112		449.2	1.40	QC-ACN-AA-XB
198	EX-6		489.4	1.44	QC-ACN-AA-XB
199	EX-6		461.1	1.38	QC-ACN-AA-XB
200	EX-6		510.2	1.25	QC-ACN-TFA-XB
201	EX-6		443.0	1.84	QC-ACN-AA-XB
202	EX-6		475.0	1.25	QC-ACN-TFA-XB

TABLE 11-continued

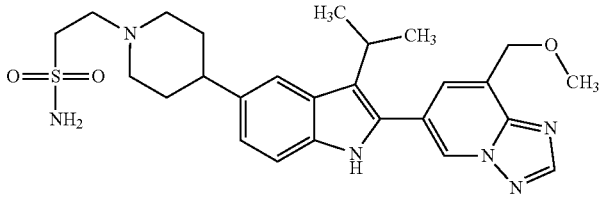
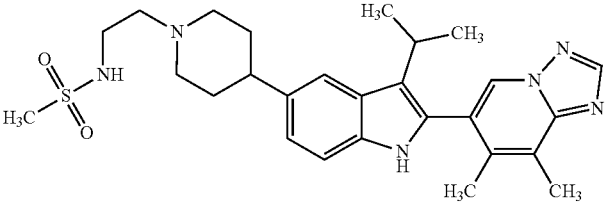
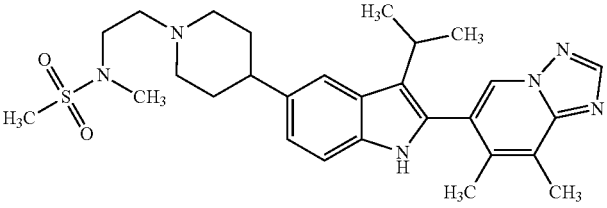
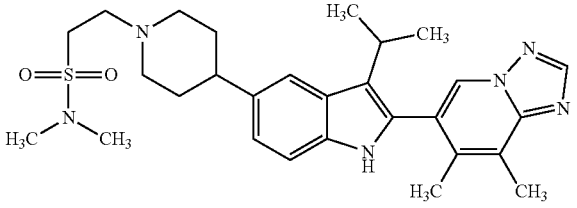
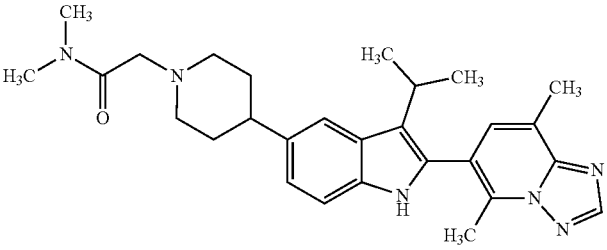
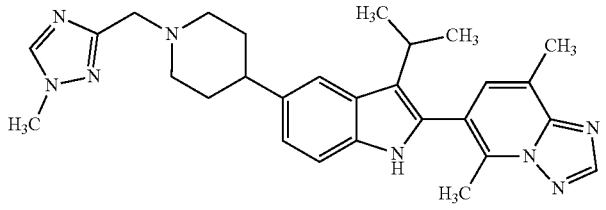
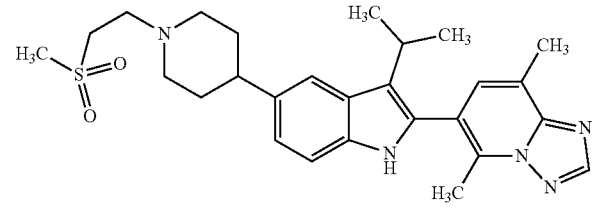
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
203	EX-6		511.3	1.54	QC-ACN-AA-XB
204	EX-4		509.2	1.47	QC-ACN-AA-XB
205	EX-4		523.0	1.73	QC-ACN-AA-XB
206	EX-4		523.0	1.37	QC-ACN-TFA-XB
207	EX-110		473.0	1.35	QC-ACN-TFA-XB
208	EX-110		483.4	1.46	QC-ACN-AA-XB
209	EX-110		494.3	1.65	QC-ACN-AA-XB

TABLE 11-continued

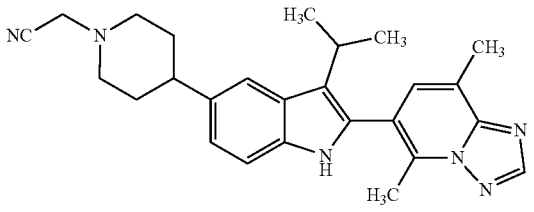
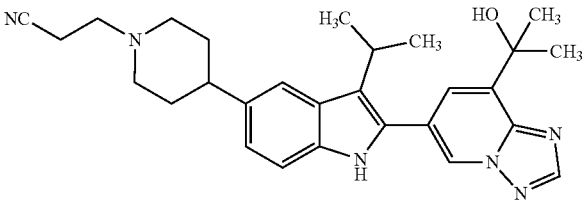
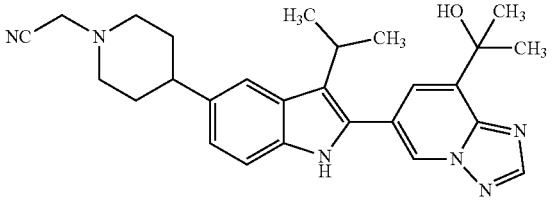
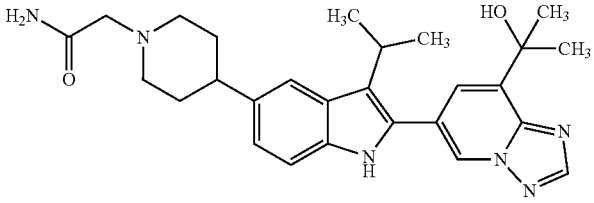
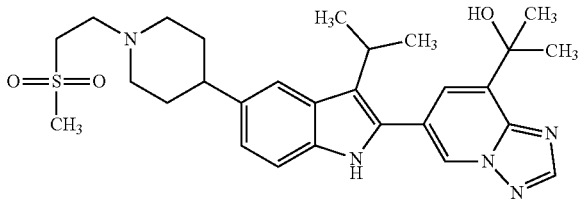
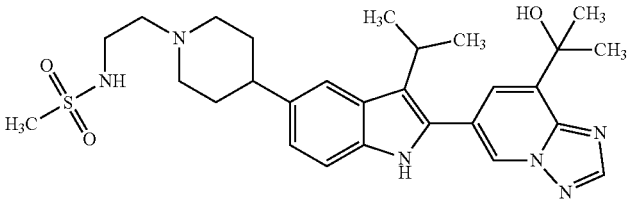
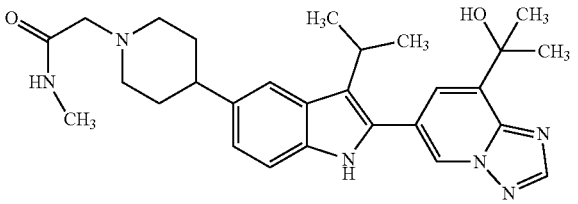
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
210	EX-110		427.35, 427.35		QC-ACN-TFA-XB
211	EX-100		470.9	1.32	QC-ACN-TFA-XB
212	EX-100		457.3	1.33	QC-ACN-TFA-XB
213	EX-100		475.1	1.47	QC-ACN-AA-XB
214	EX-100		524.3	1.63	QC-ACN-AA-XB
215	EX-100		539.0	1.63	QC-ACN-AA-XB
216	EX-100		489.4	1.52	QC-ACN-AA-XB

TABLE 11-continued

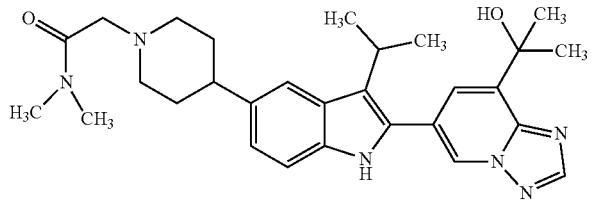
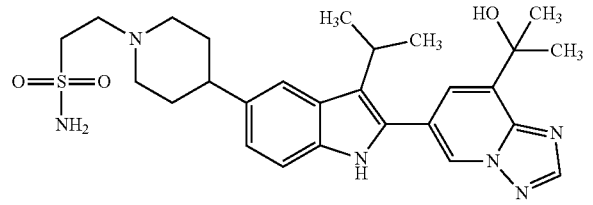
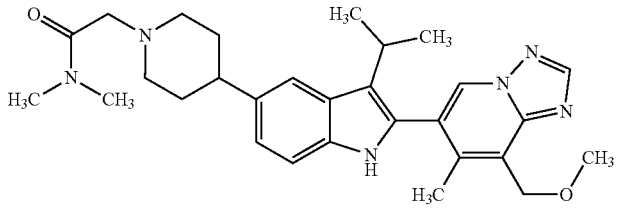
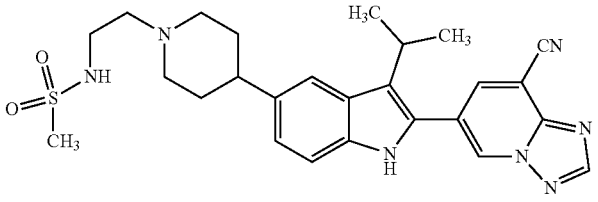
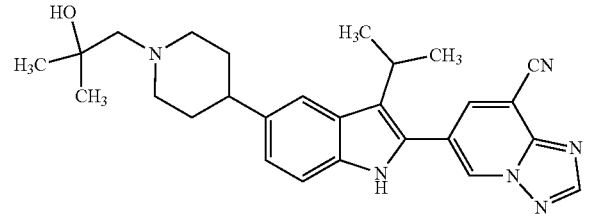
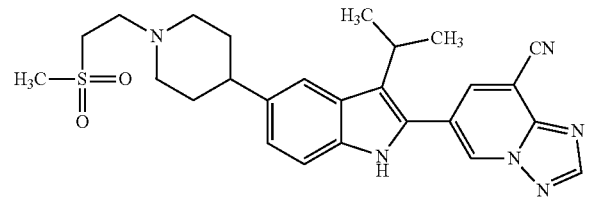
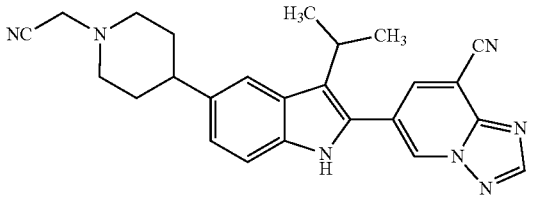
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
217	EX-100		503.1	1.3	QC-ACN-TFA-XB
218	EX-100		525.1	1.15	QC-ACN-TFA-XB
219	EX-101		503.2	1.22	QC-ACN-TFA-XB
220	EX-111		506.2	1.24	QC-ACN-AA-XB
221	EX-111		457.0	1.31	QC-ACN-TFA-XB
222	EX-111		491.2	1.66	QC-ACN-AA-XB
223	EX-111		424.3	1.93	QC-ACN-AA-XB

TABLE 11-continued

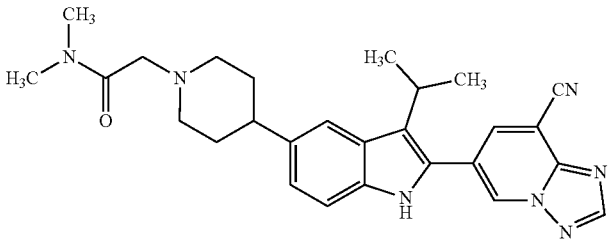
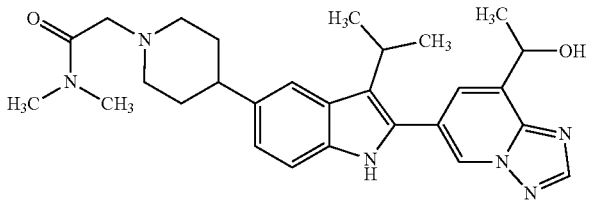
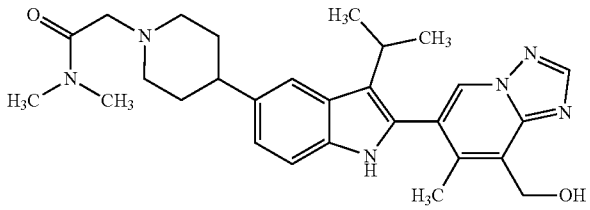
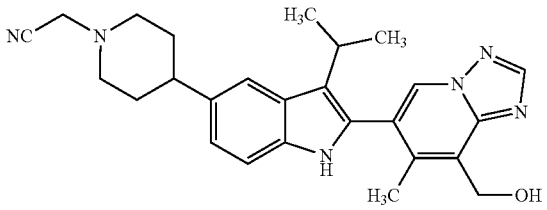
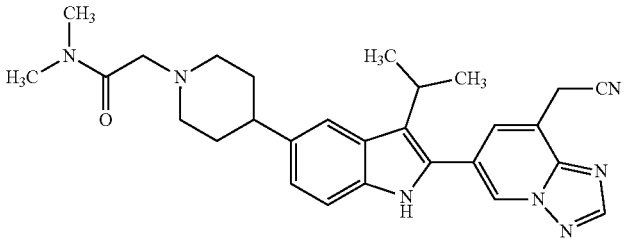
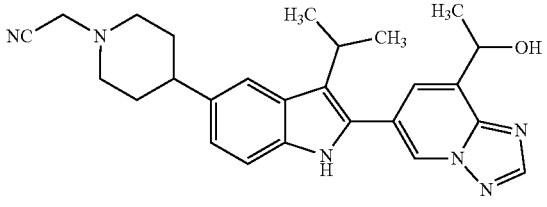
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
224	EX-111		470.0	1.27	QC-ACN-TFA-XB
225	EX-102		489.4	1.1	QC-ACN-TFA-XB
226	EX-104		489.0	1.18	QC-ACN-AA-XB
227	EX-104		442.9	1.21	QC-ACN-TFA-XB
228	EX-105		484.3	1.43	QC-ACN-AA-XB
229	EX-103		443.0	1.27	QC-ACN-TFA-XB

TABLE 11-continued

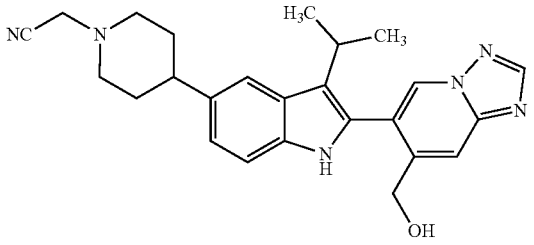
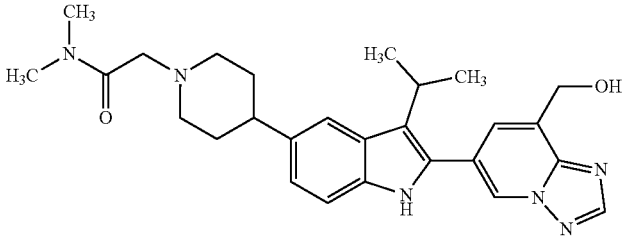
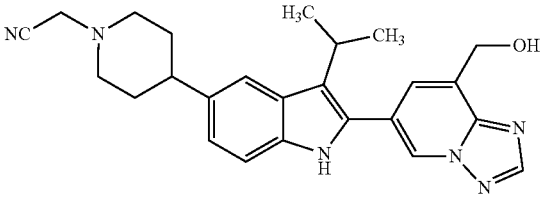
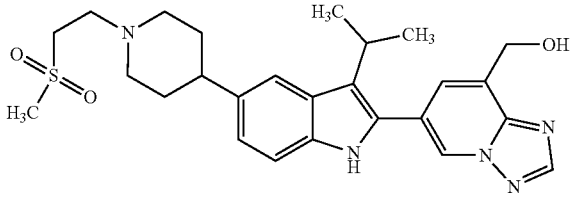
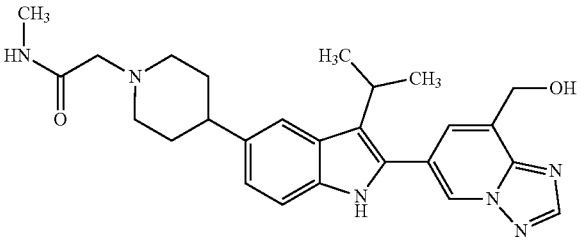
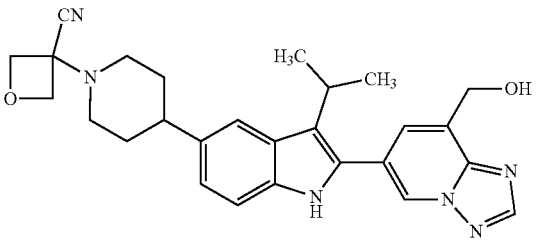
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
230	EX-108		429.1	1.16	QC-ACN-TFA-XB
231	EX-113		475.1	1.0	QC-ACN-TFA-XB
232	EX-113		429.2	1.53	QC-ACN-AA-XB
233	EX-113		496.0	1.12	QC-ACN-TFA-XB
234	EX-113		461.3	0.97	QC-ACN-TFA-XB
235	EX-113		471.1	1.63	QC-ACN-TFA-XB

TABLE 11-continued

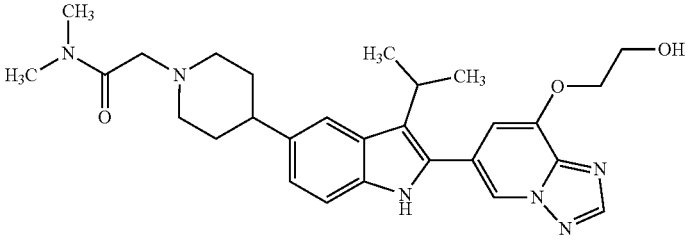
Ex. No.	Template Starting Material	Structure	LCMS MH+	Rt (min)	HPLC Method
236	EX-114		505.2	1.19	QC-ACN-AA-XB

TABLE 12

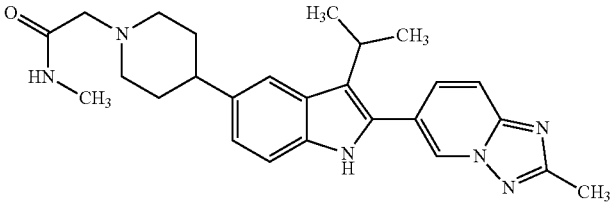
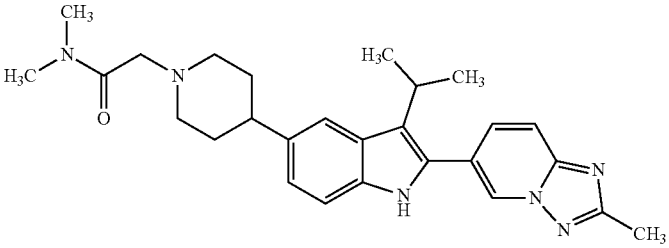
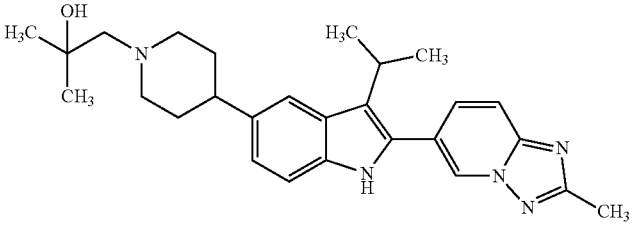
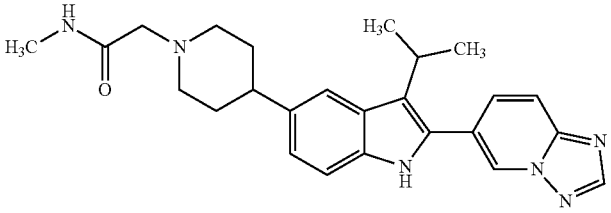
Ex. No.	Template Starting Material	Structure	LCMS MH+	Rt (min)	HPLC Method
237	EX-122		445.3	1.76	E
238	EX-122		459.3	1.62	E
239	EX-122		446.3	1.59	E
240	EX-1		431.2	1.71	E

TABLE 12-continued

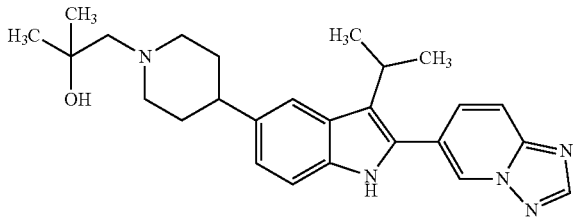
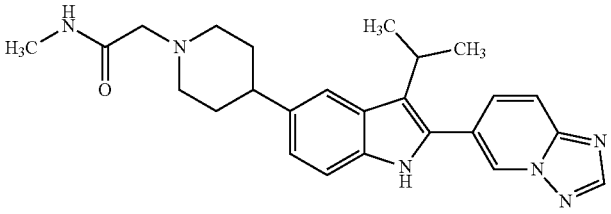
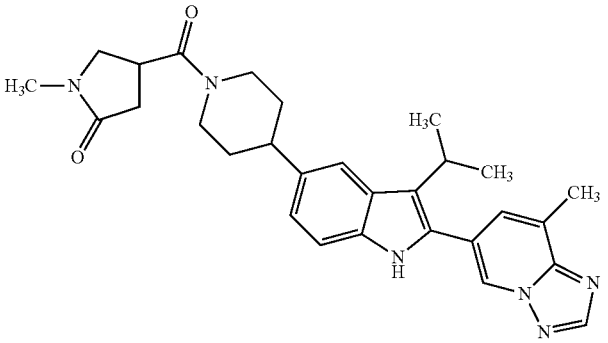
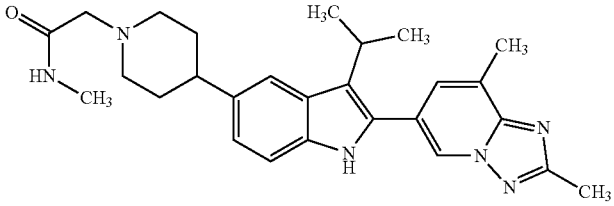
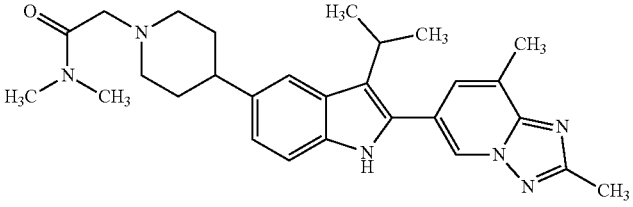
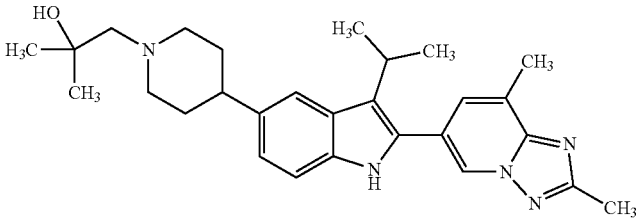
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
241	EX-1		432.3	1.51	E
242	EX-1		431.2	1.75	E
243	EX-2		499.3	2.1	D
244	EX-124		459.3	1.74	E
245	EX-124		473.3	2.09	D
246	EX-124		460	1.74	E

TABLE 12-continued

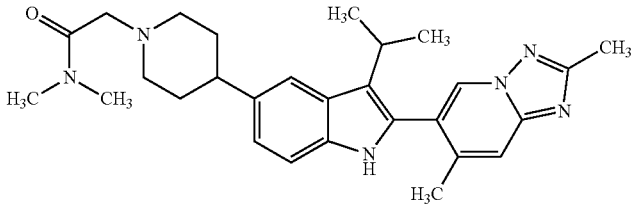
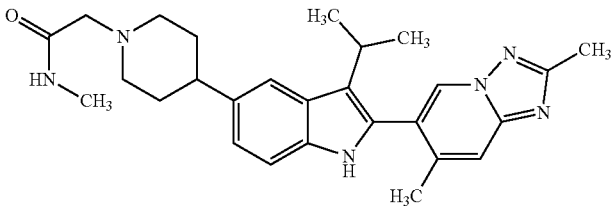
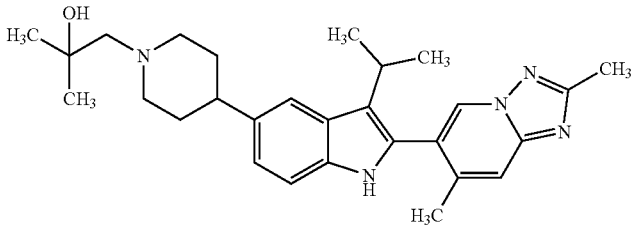
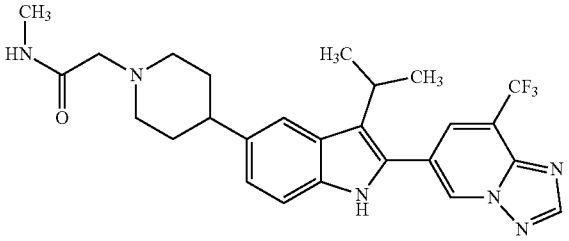
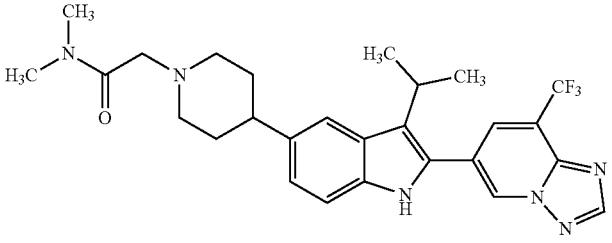
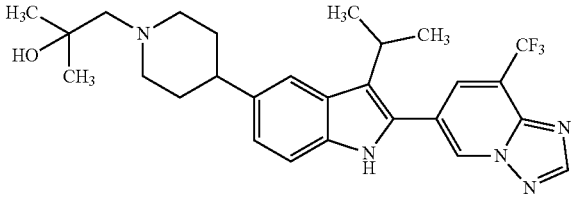
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
247	EX-125		473.3	1.56	E
248	EX-125		459.2	1.72	E
249	EX-125		460	1.66	E
250	EX-128		499.3	2.08	E
251	EX-128		513	1.65	E
252	EX-128		500	1.74	E

TABLE 12-continued

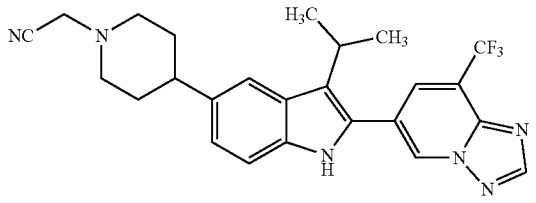
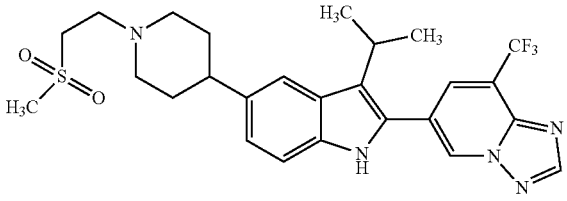
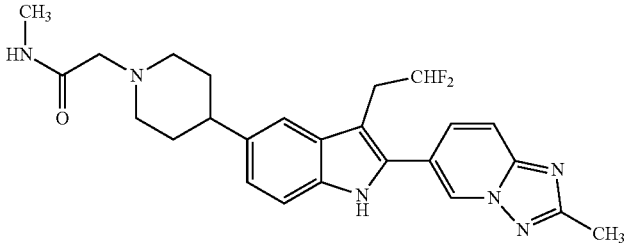
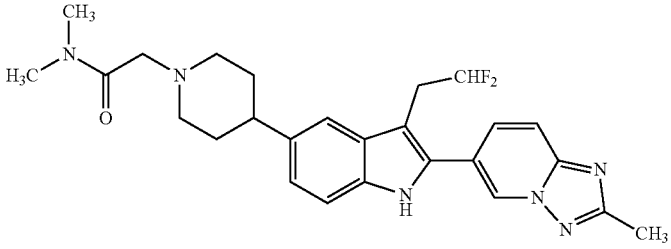
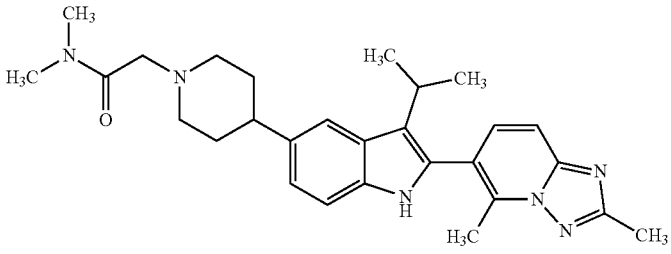
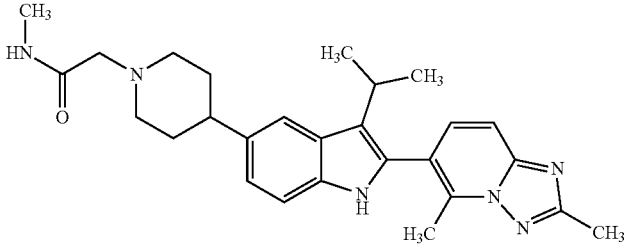
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
253	EX-128		467.2	2.26	E
254	EX-128		534.1	2.07	E
255	EX-142		467.2	1.41	E
256	EX-142		481.2	1.26	E
257	EX-155		473	1.65	E
258	EX-155		459	1.83	E

TABLE 12-continued

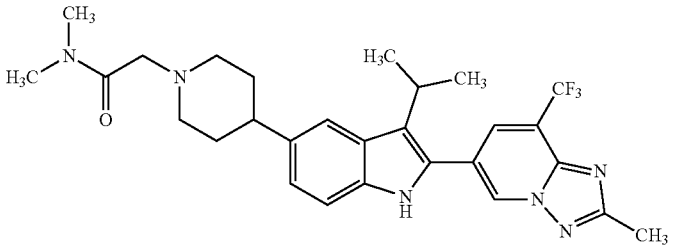
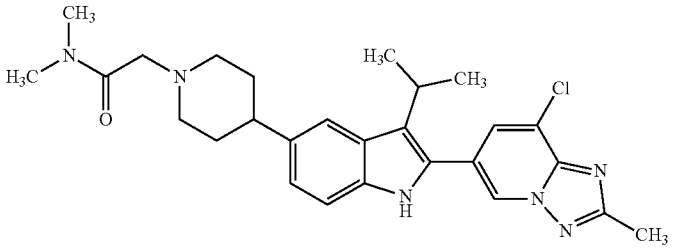
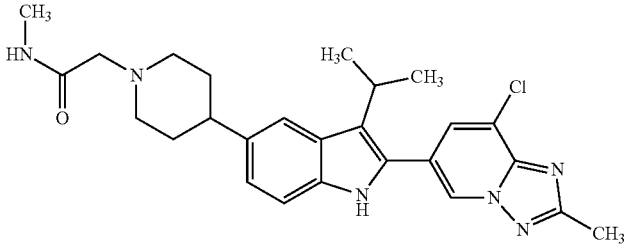
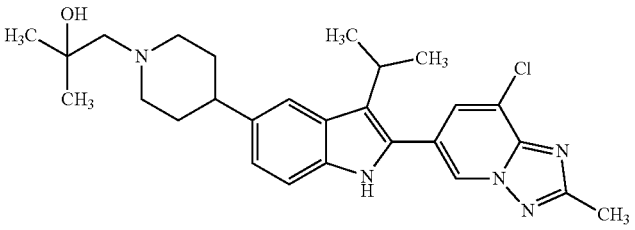
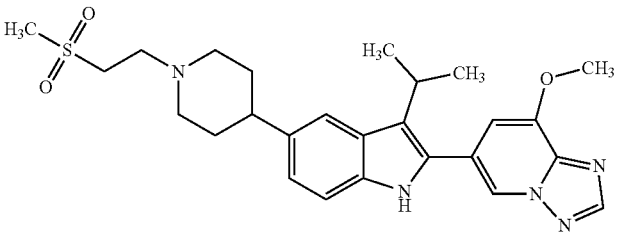
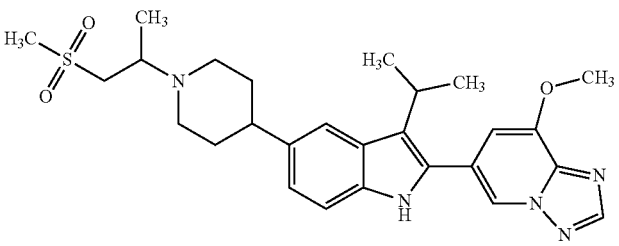
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
259	EX-153		527.3	1.91	E
260	EX-96		493	1.73	E
261	EX-96		479	1.94	E
262	EX-96		480.3	1.61	E
263	EX-5		496.2	1.81	E
264	EX-5		510.2	5.65	I

TABLE 12-continued

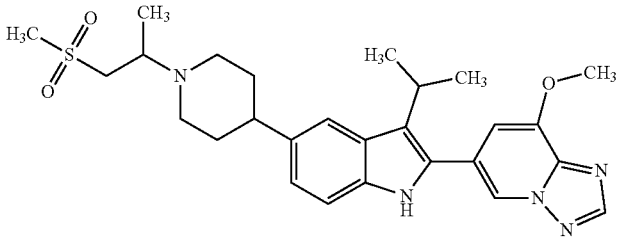
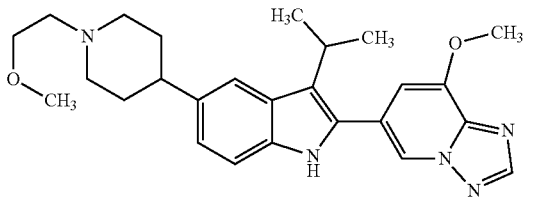
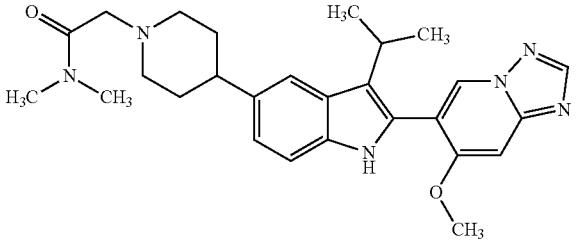
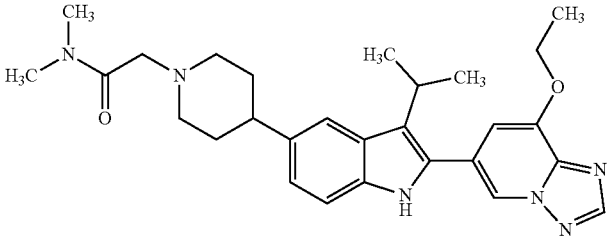
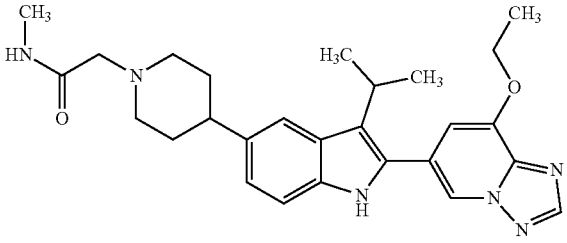
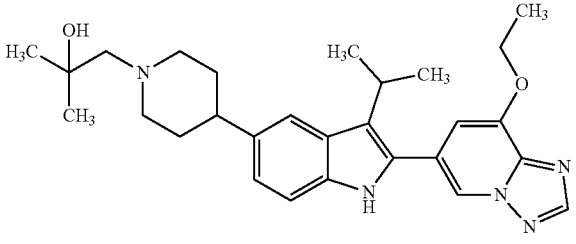
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
265	EX-5		510.1	5.63	I
266	EX-5		448.2	1.87	E
267	EX-131		475.3	1.58	E
268	EX-132		489	1.55	E
269	EX-132		475.3	1.95	E
270	EX-132		476.2	1.76	E

TABLE 12-continued

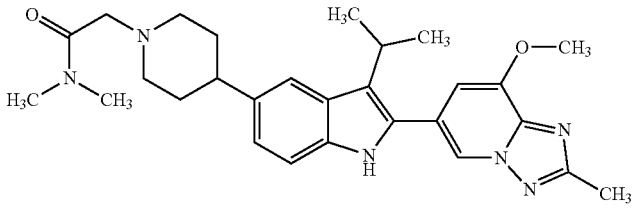
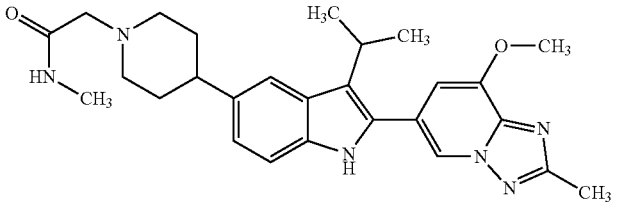
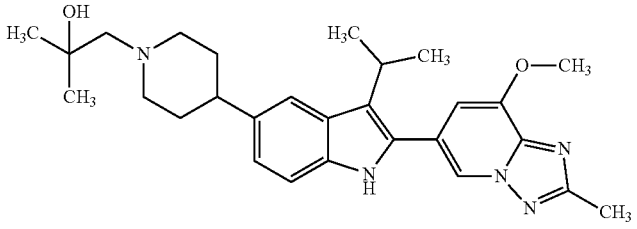
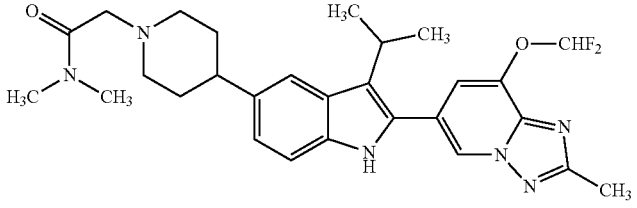
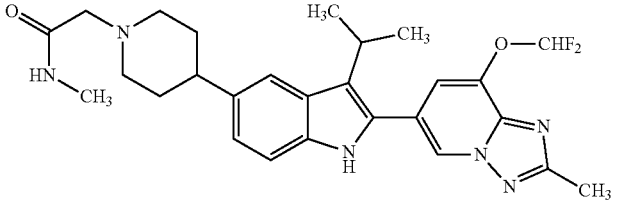
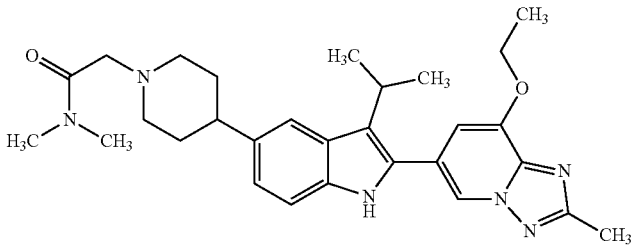
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
271	EX-133		489.3	1.71	E
272	EX-133		475.3	1.84	E
273	EX-133		476.3	1.7	E
274	EX-134		525.3	1.93	E
275	EX-134		511.3	1.98	E
276	EX-135		503.3	1.84	E

TABLE 12-continued

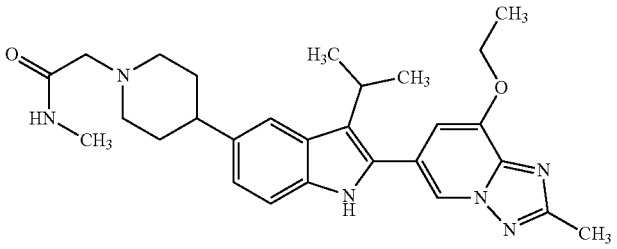
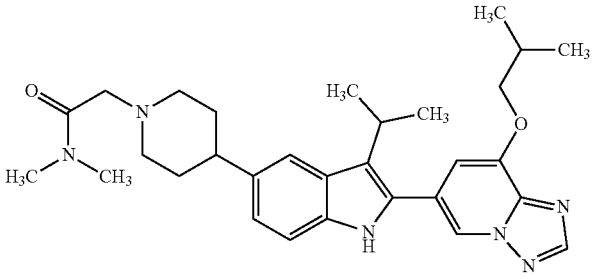
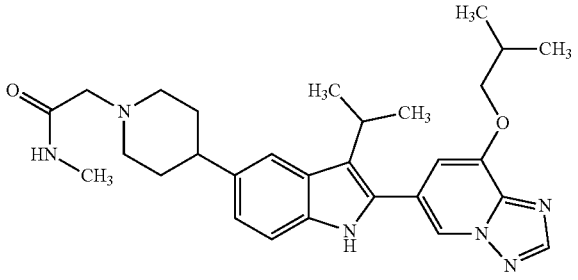
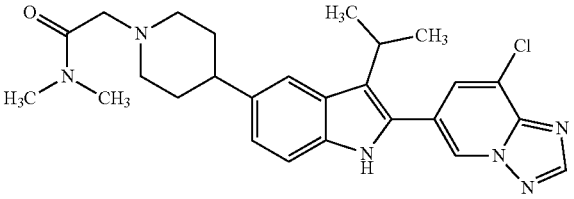
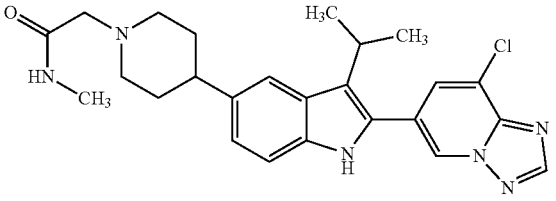
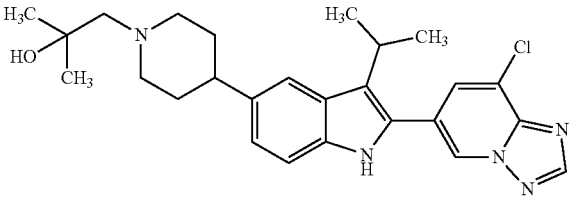
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
277	EX-135		489.3	2.09	E
278	EX-136		517.2	2.02	E
279	EX-136		503.4	1.93	E
280	EX-118		479	1.68	E
281	EX-118		465	1.85	E
282	EX-118		466	1.74	E

TABLE 12-continued

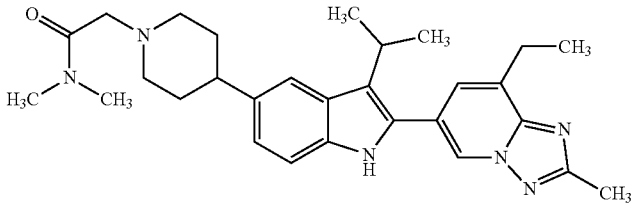
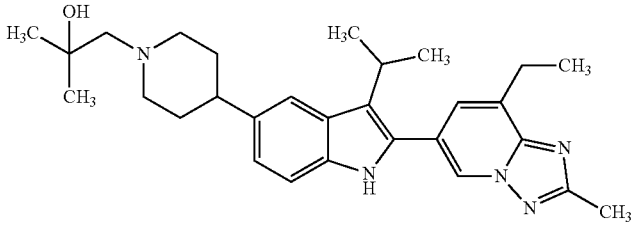
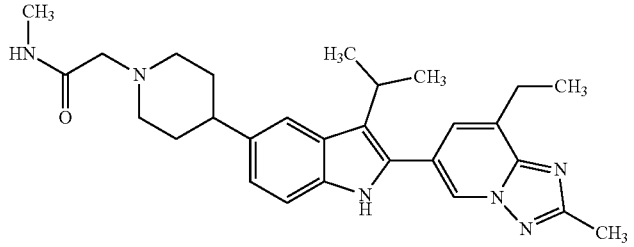
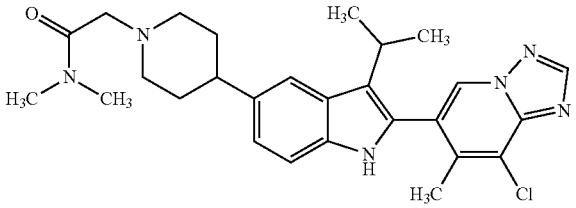
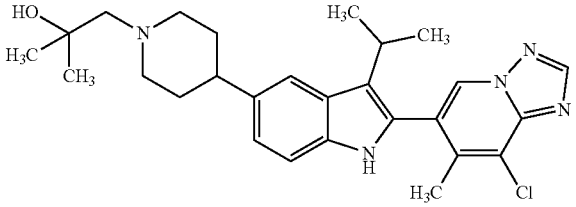
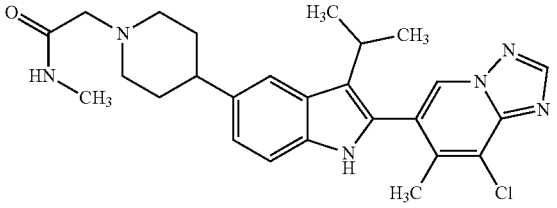
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
283	EX-137		487.2	1.81	E
284	EX-137		474.1	1.95	E
285	EX-137		473.2	1.98	E
286	EX-119		493.1	1.75	E
287	EX-119		480.1	1.47	E
288	EX-119		479.1	1.91	E

TABLE 12-continued

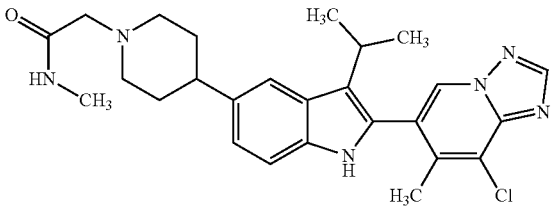
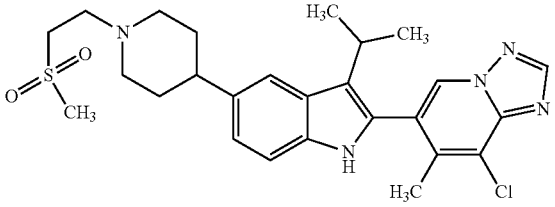
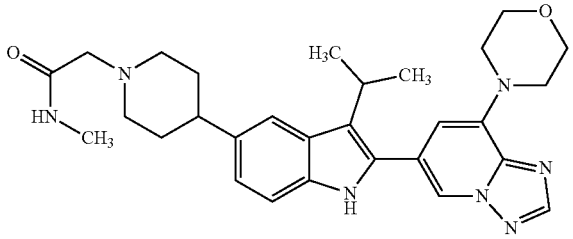
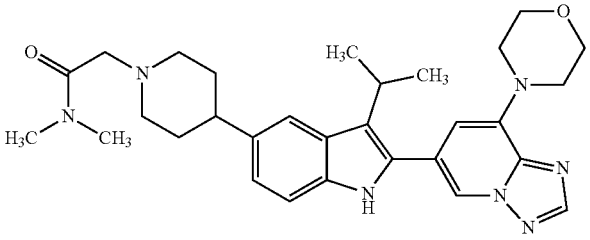
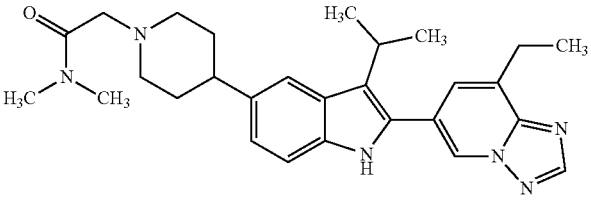
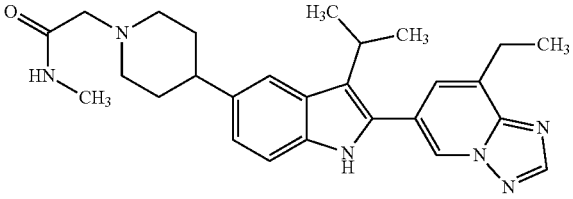
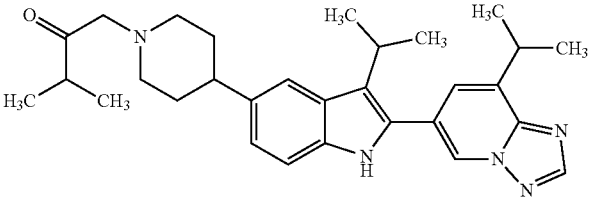
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
289	EX-119		479.2	1.91	E
290	EX-119		514.2	1.97	E
291	EX-143		516.3	1.88	E
292	EX-143		530.3	1.69	E
293	EX-94		473.3	1.75	E
294	EX-94		459.2	1.95	E
295	EX-95		487.3	1.91	E

TABLE 12-continued

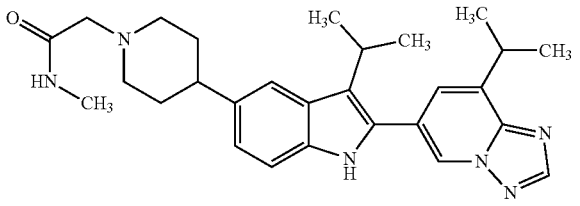
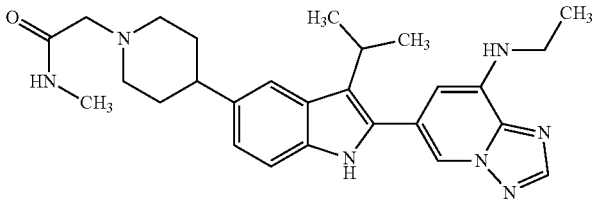
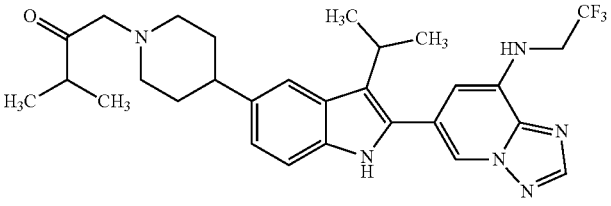
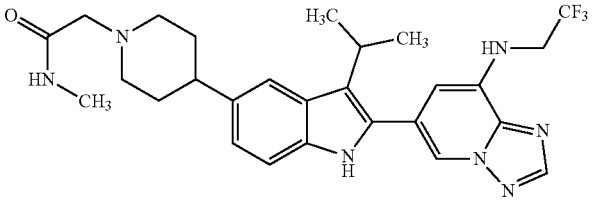
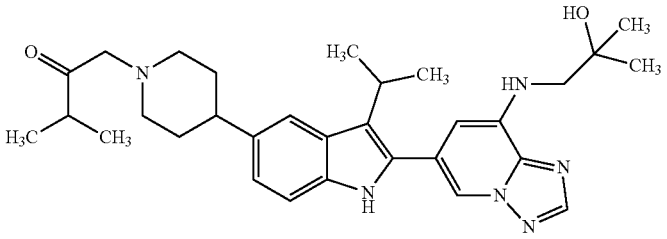
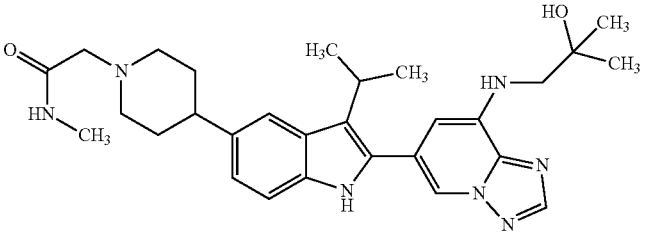
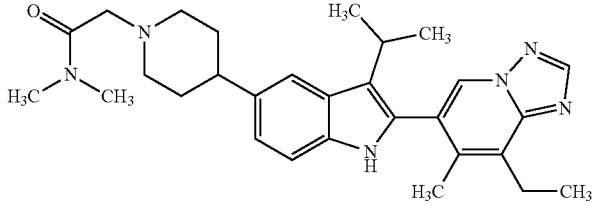
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
296	EX-95		473.3	2.1	E
297	EX-144		474.3	1.97	E
298	EX-145		542.3	1.83	E
299	EX-145		528.3	2.01	E
300	EX-146		532.3	1.62	E
301	EX-146		518.3	1.79	E
302	EX-98		487.3	1.76	E

TABLE 12-continued

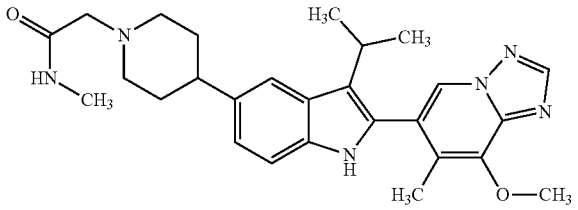
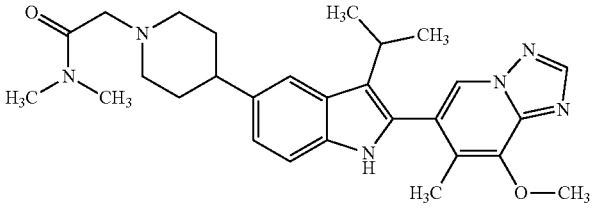
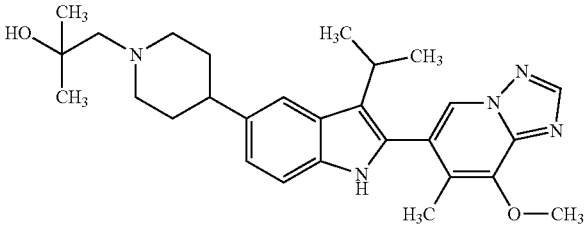
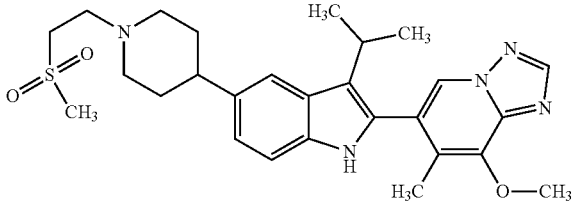
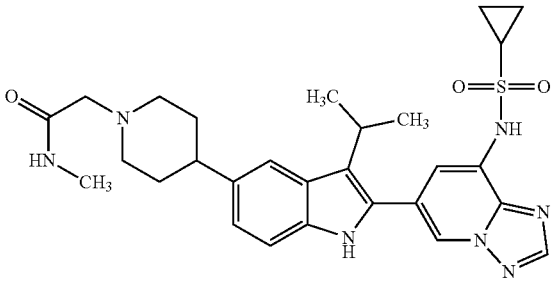
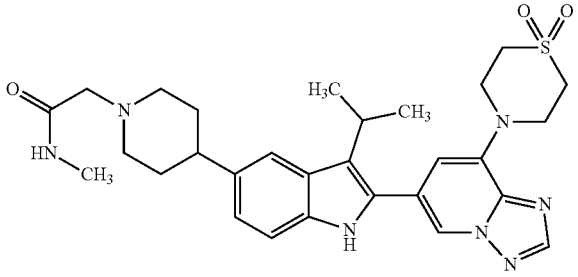
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
303	EX-140		475.3	1.9	E
304	EX-140		489.3	1.69	E
305	EX-140		476.3	1.72	E
306	EX-140		510.3	1.72	E
307	EX-147		550.3	1.32	F
308	EX-148		564.3	1.73	E

TABLE 12-continued

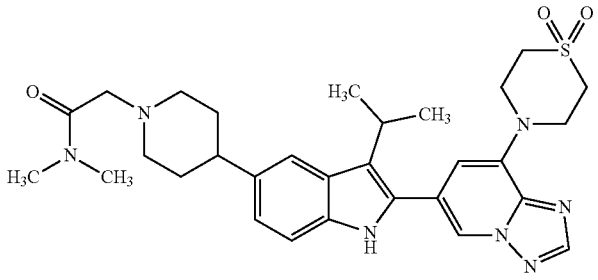
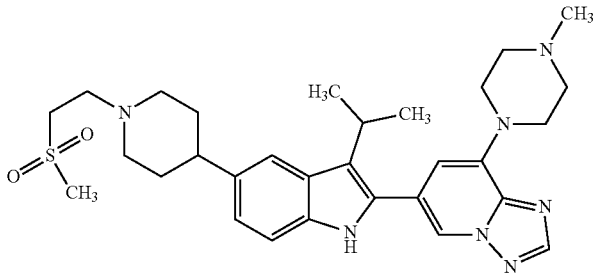
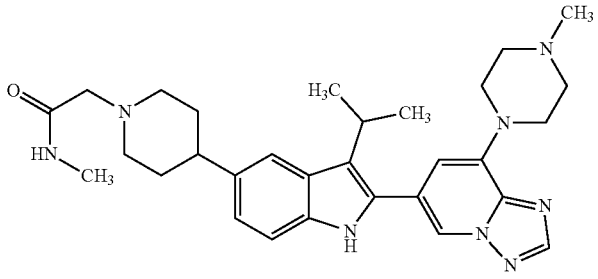
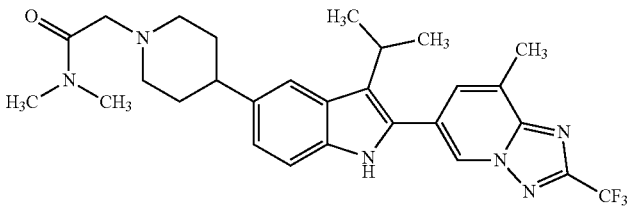
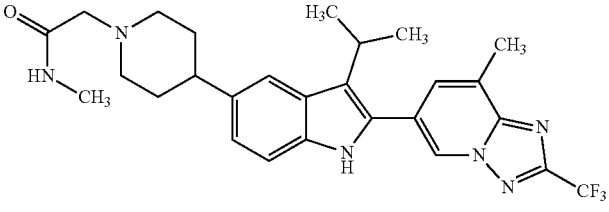
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
309	EX-148		578.3	1.56	E
310	EX-149		564.3	1.71	E
311	EX-149		529.3	1.64	E
312	EX-120		527.3	2.17	E
313	EX-120		513.2	2.38	E

TABLE 12-continued

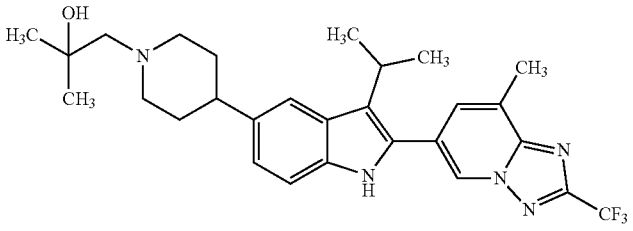
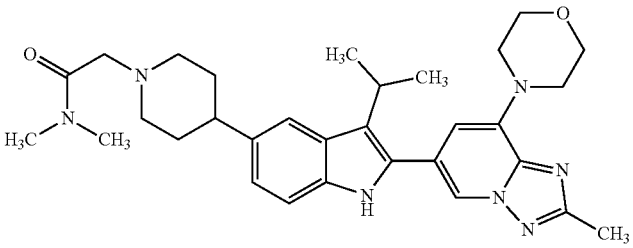
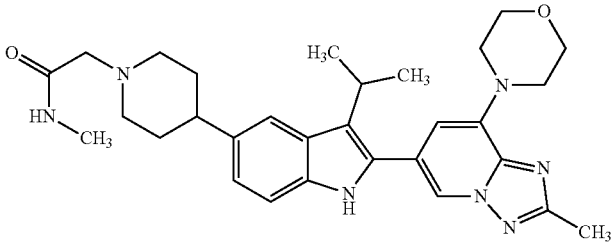
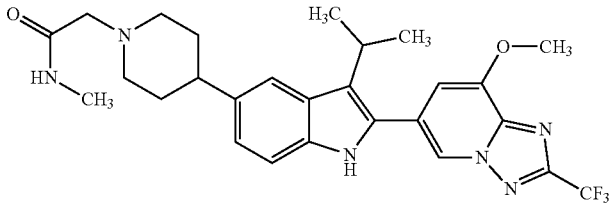
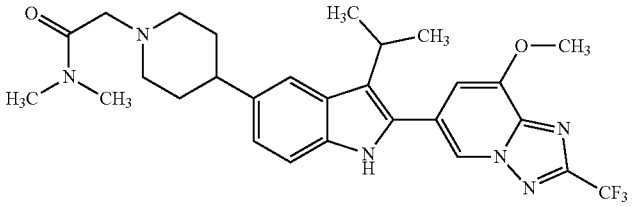
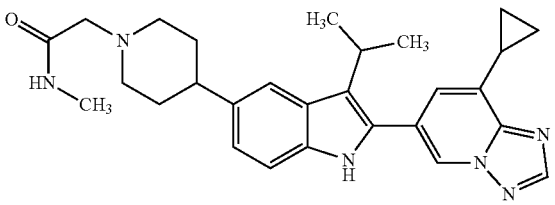
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
314	EX-120		514.2	2.26	E
315	EX-150		544.3	1.72	E
316	EX-150		530.3	1.91	E
317	EX-154		529.2	2.25	E
318	EX-154		543.2	2.08	E
319	EX-151		471.3	1.75	E

TABLE 12-continued

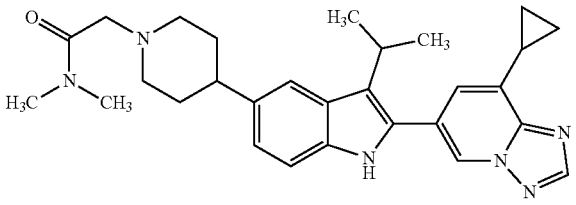
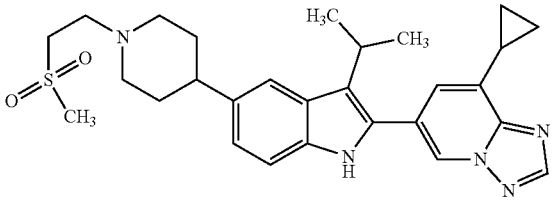
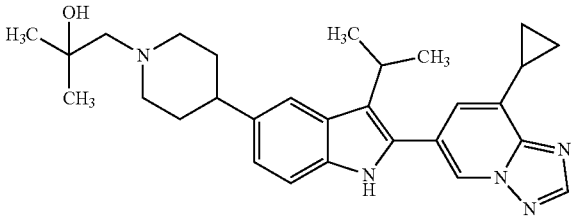
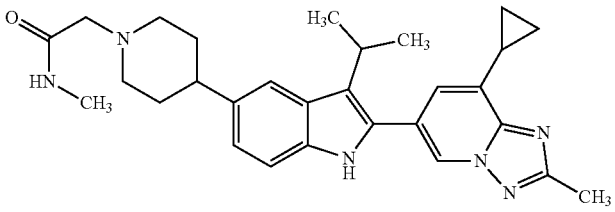
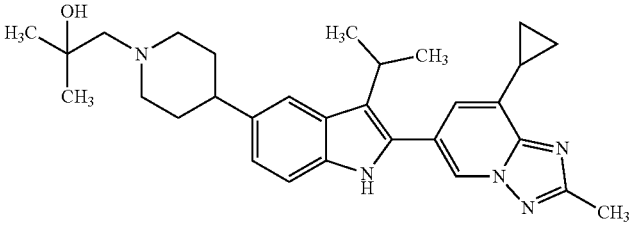
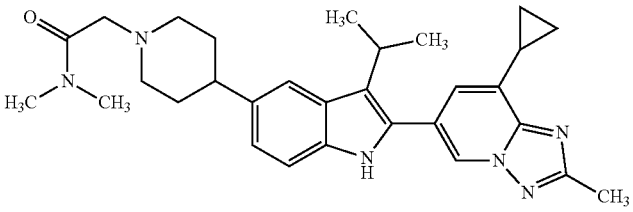
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
320	EX-151		485.3	1.27	F
321	EX-151		506.1	2.03	E
322	EX-151		472.2	1.86	E
323	EX-141		485.2	2.02	E
324	EX-141		486.2	1.89	E
325	EX-141		499.2	1.81	E

TABLE 12-continued

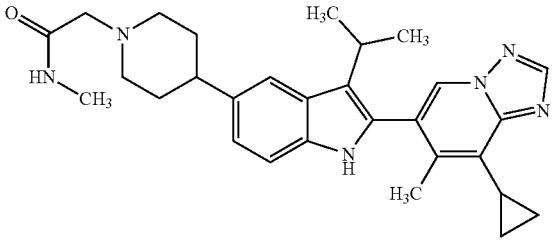
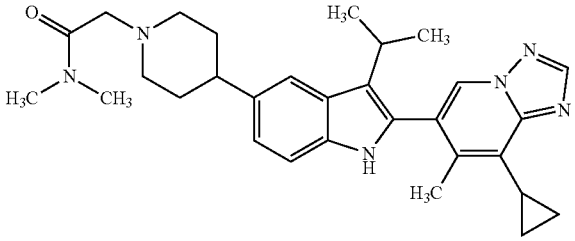
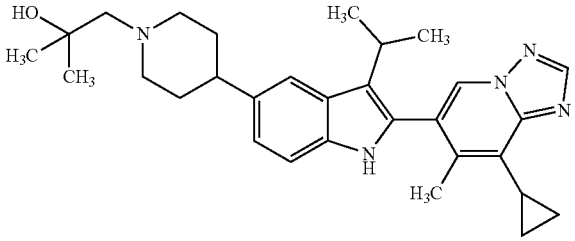
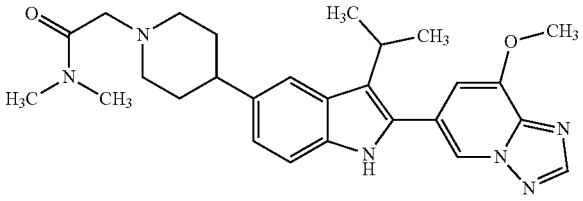
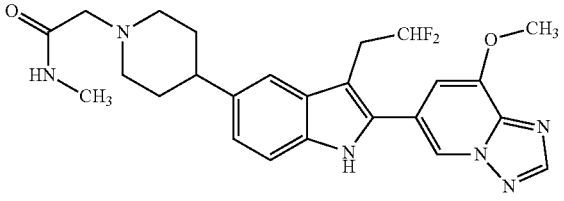
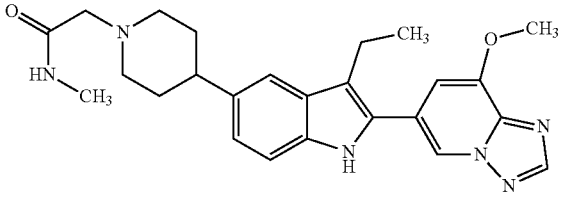
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
326	EX-152		485.1	2.05	E
327	EX-152		499.2	1.86	E
328	EX-152		486.2	1.92	E
329	EX-156		497.3	1.4	E
330	EX-156		483.2	1.55	E
331	EX-157		447.3	1.38	E

TABLE 12-continued

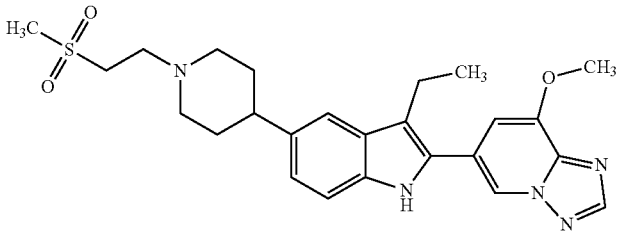
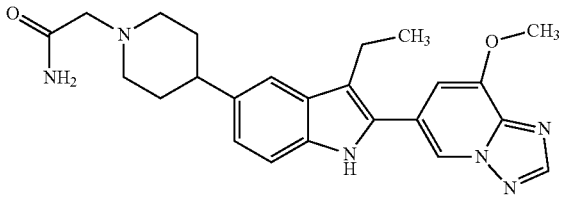
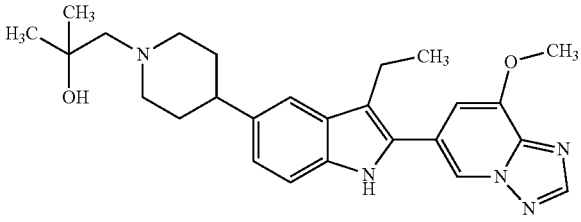
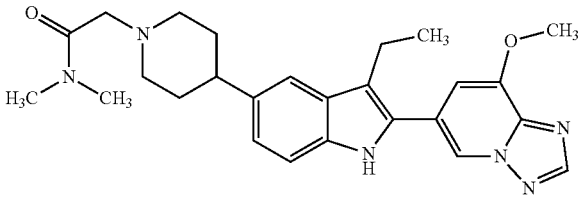
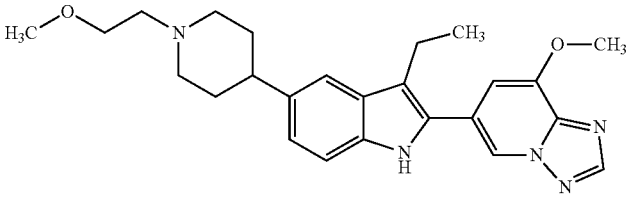
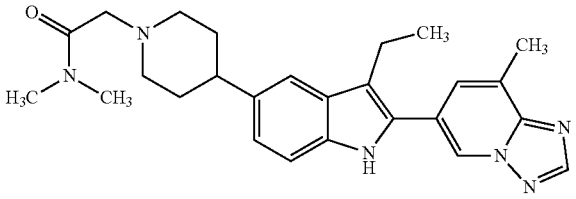
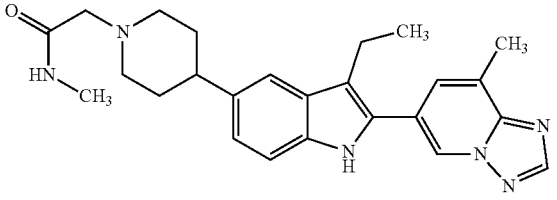
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
332	EX-157		482.3	1.44	E
333	EX-157		433.3	1.28	E
334	EX-157		448.3	1.26	E
335	EX-157		461.3	1.24	E
336	EX-157		434.3	1.22	E
337	EX-158		445.3	1.04	F
338	EX-158		431.3	1.44	E

TABLE 12-continued

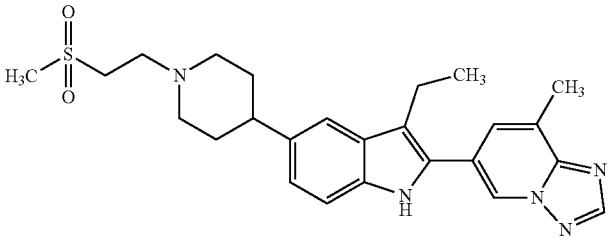
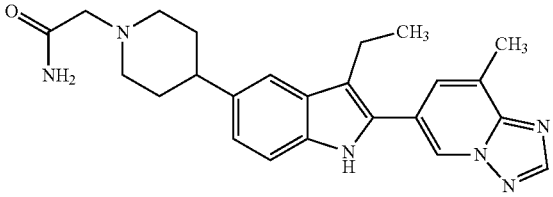
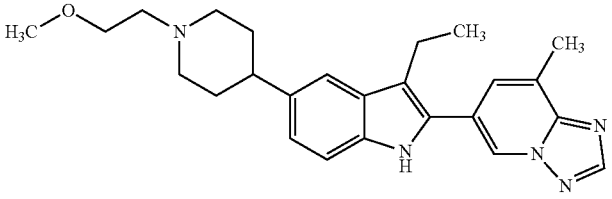
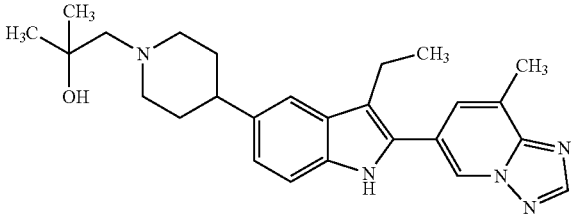
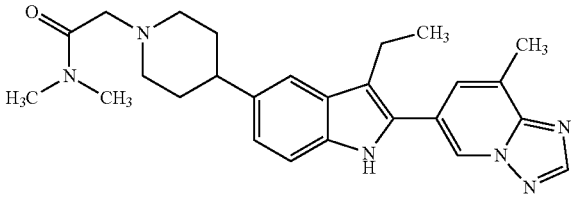
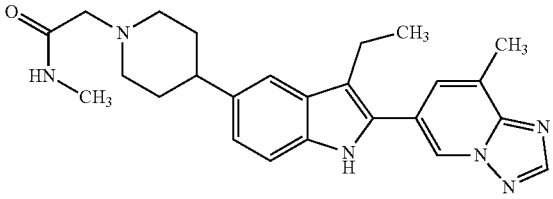
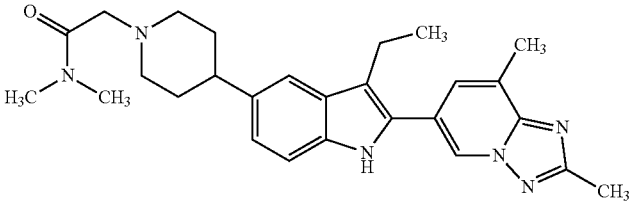
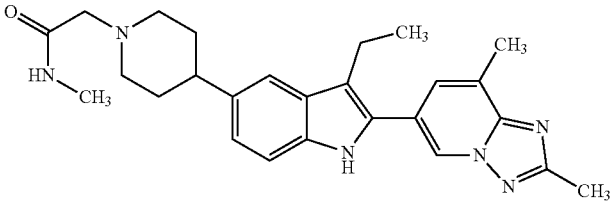
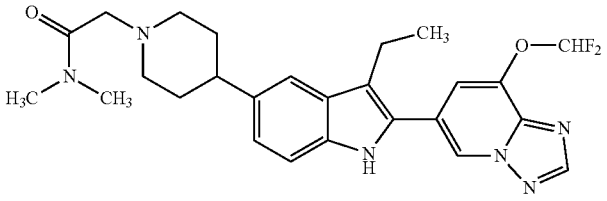
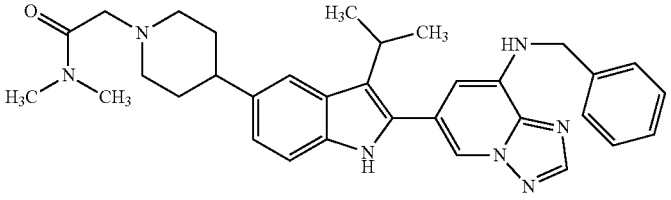
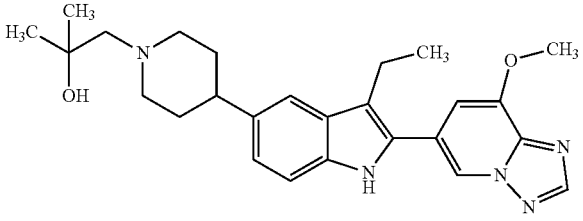
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
339	EX-158		455.3	1.5	E
340	EX-158		417.3	1.33	E
341	EX-158		418.3	1.26	E
342	EX-158		432.3	1.31	E
343	EX-161		481.3	1.45	E
344	EX-161		467.2	1.58	E
345	EX-162		495.2	1.53	E

TABLE 12-continued

Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
346	EX-162		481.2	1.68	E
347	EX-160		511.3	1.17	E
348	EX-159		550.3	1.97	E
349	EX-156		484.2	1.42	E

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The following examples were prepared according to the general procedure of Example 26.

TABLE 13

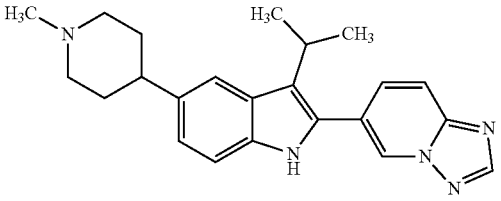
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
350	EX-1		374.0	1.05	QC-ACN-TFA-XB

TABLE 13-continued

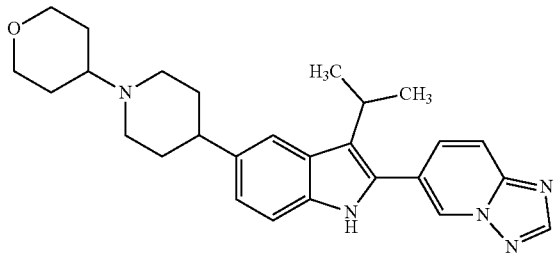
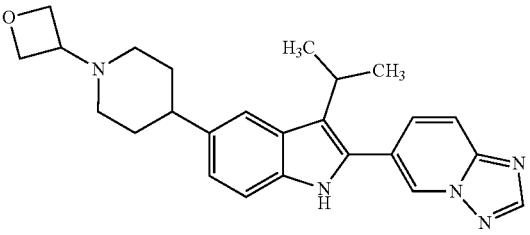
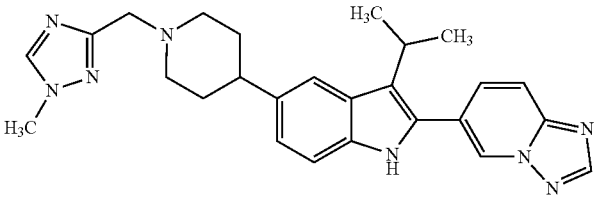
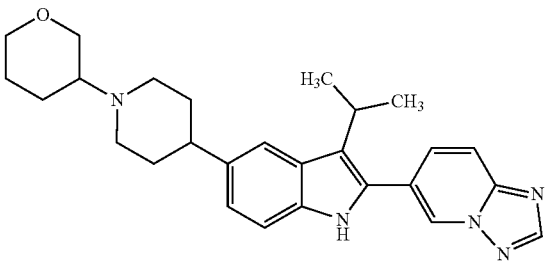
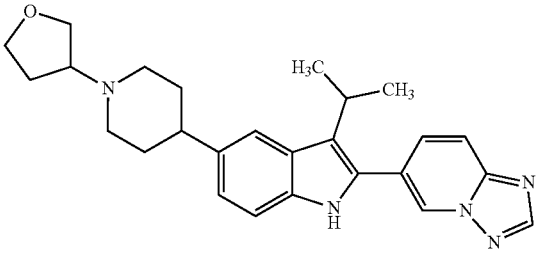
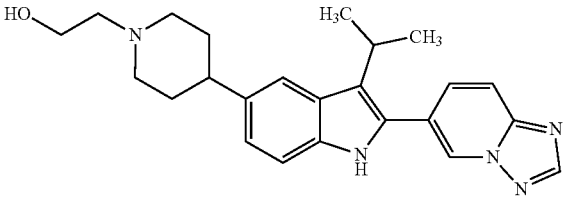
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
351	EX-1		444.4	1.53	QC-ACN-AA-XB
352	EX-1		416.4	1.02	QC-ACN-TFA-XB
353	EX-1		455.2	1.06	QC-ACN-TFA-XB
354	EX-1		444.4	1.17	QC-ACN-TFA-XB
355	EX-1		430.4	1.24	QC-ACN-AA-XB
356	EX-1		404.4	1.09	QC-ACN-AA-XB

TABLE 13-continued

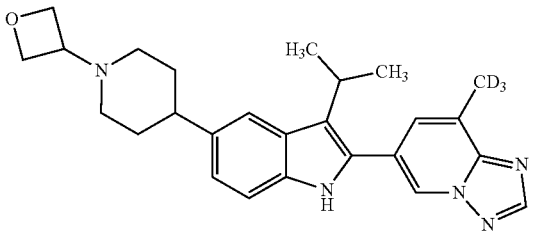
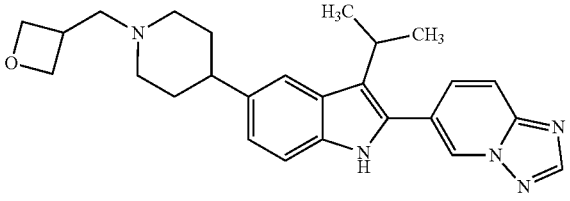
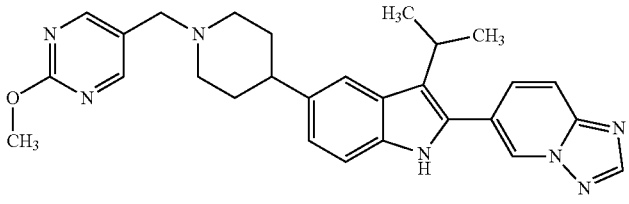
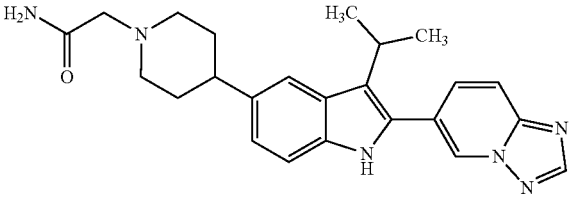
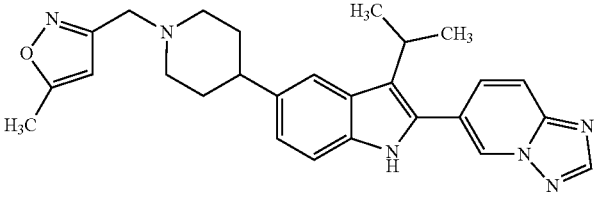
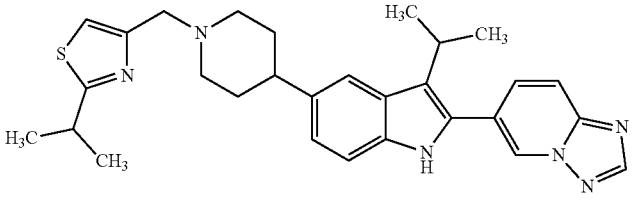
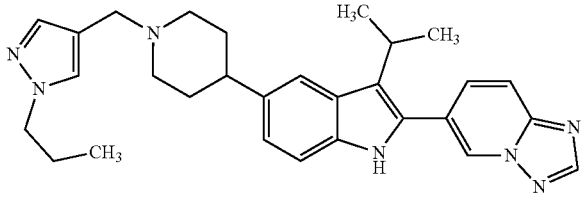
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
357	EX-117		433.2	0.66	TS1
358	EX-1		430.4	1.13	QC-ACN-TFA-XB
359	EX-1		481.9	1.79	QC-ACN-AA-XB
360	EX-1		417.04, 416.86	0.92	QC-ACN-TFA-XB
361	EX-1		455.2	1.89	QC-ACN-AA-XB
362	EX-1		499.2	1.96	QC-ACN-AA-XB
363	EX-1		482.4	1.44	QC-ACN-AA-XB

TABLE 13-continued

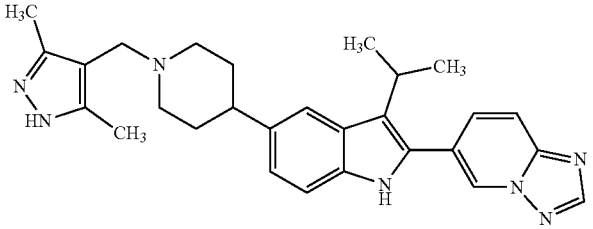
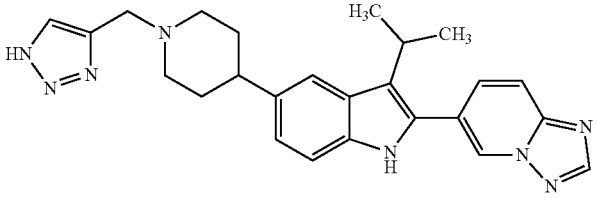
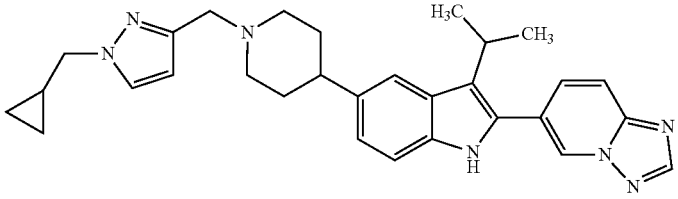
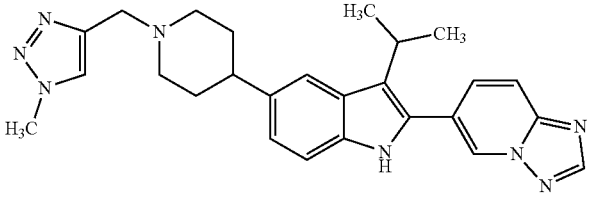
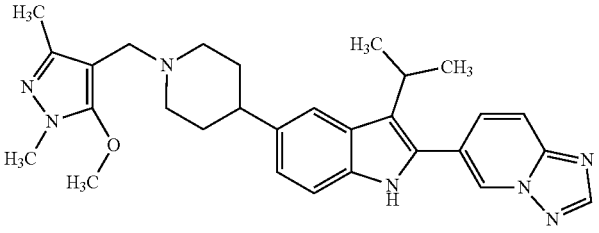
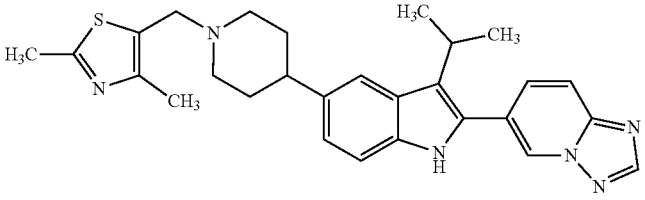
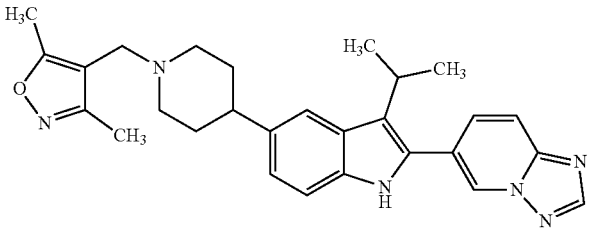
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
364	EX-1		468.4	1.15	QC-ACN-TFA-XB
365	EX-1		441.3	1.09	QC-ACN-TFA-XB
366	EX-1		494.2	1.45	QC-ACN-TFA-XB
367	EX-1		455.0	1.31	QC-ACN-AA-XB
368	EX-1		498.4	1.41	QC-ACN-AA-XB
369	EX-1		485.2	1.96	QC-ACN-AA-XB
370	EX-1		469.3	1.85	QC-ACN-AA-XB

TABLE 13-continued

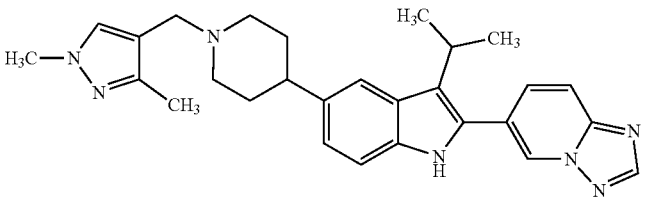
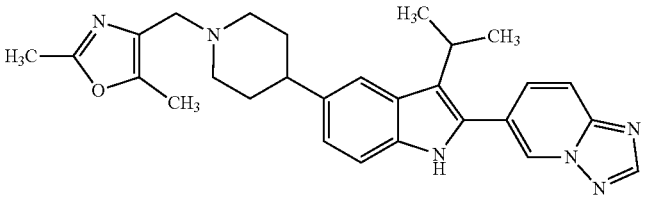
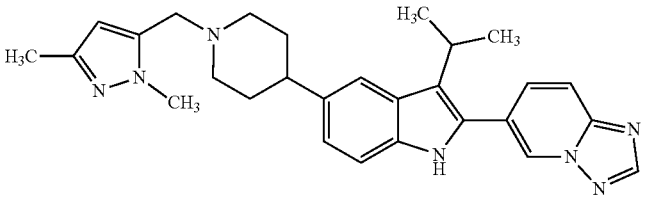
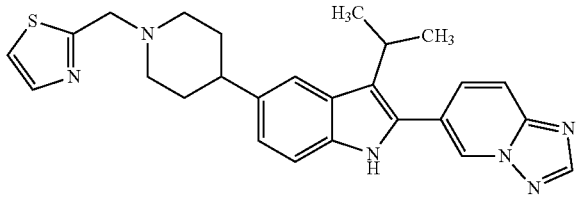
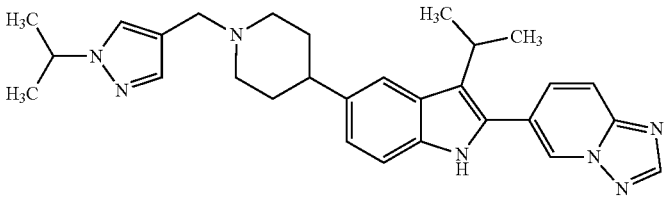
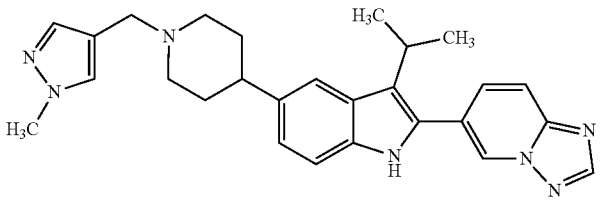
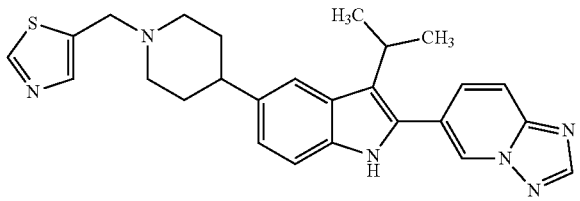
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
371	EX-1		468.4	1.21	QC-ACN-TFA-XB
372	EX-1		469.0	1.54	QC-ACN-AA-XB
373	EX-1		468.0	1.87	QC-ACN-AA-XB
374	EX-1		456.9	1.96	QC-ACN-AA-XB
375	EX-1		482.4	1.42	QC-ACN-AA-XB
376	EX-1		454.0	1.25	QC-ACN-AA-XB
377	EX-1		457.2	1.16	QC-ACN-TFA-XB

TABLE 13-continued

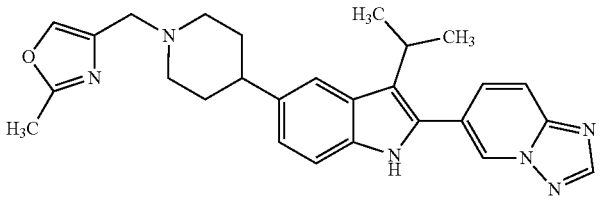
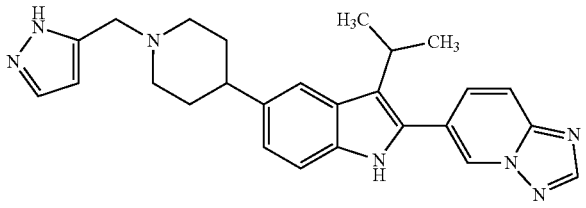
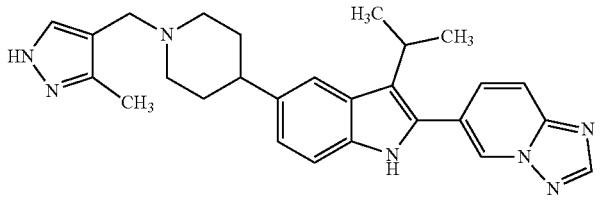
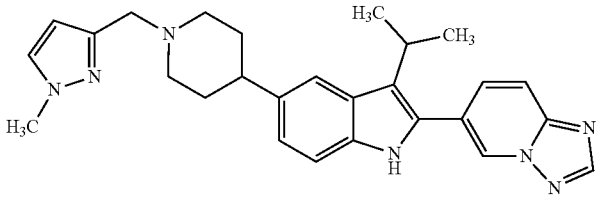
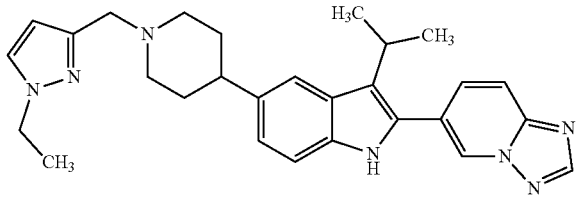
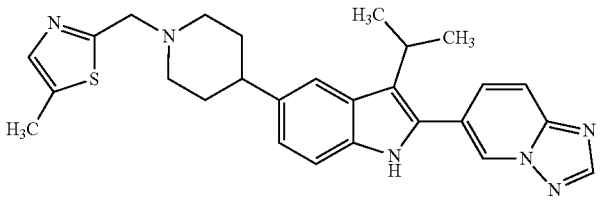
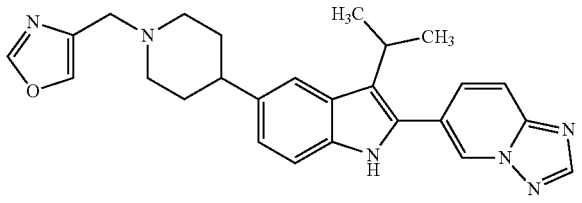
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
378	EX-1		455.4	1.25	QC-ACN-TFA-XB
379	EX-1		440.2	1.14	QC-ACN-TFA-XB
380	EX-1		454.3	1.19	QC-ACN-AA-XB
381	EX-1		454.4	1.32	QC-ACN-AA-XB
382	EX-1		468.4	1.33	QC-ACN-AA-XB
383	EX-1		471.3	2.04	QC-ACN-AA-XB
384	EX-1		221.2	1.45	QC-ACN-AA-XB

TABLE 13-continued

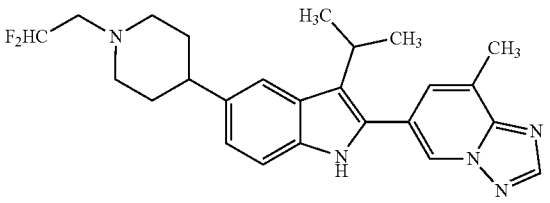
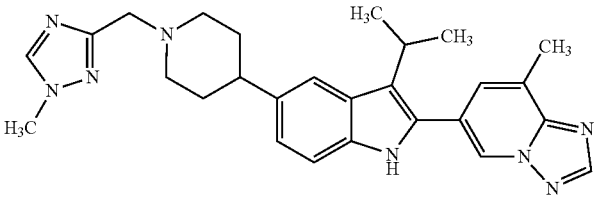
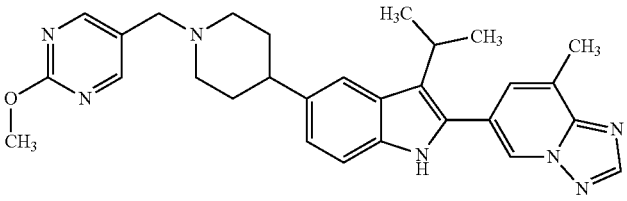
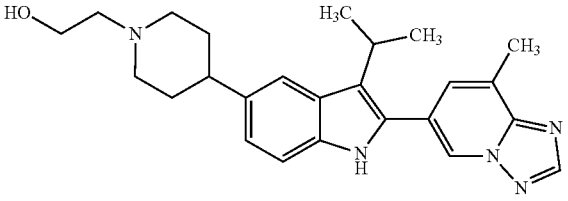
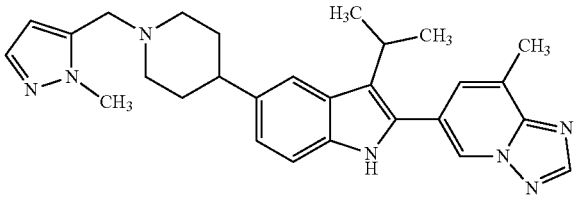
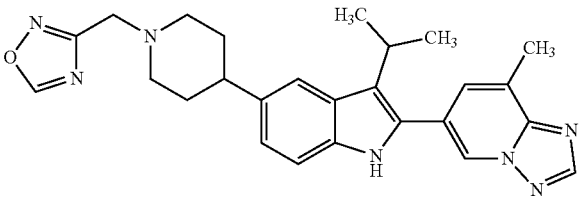
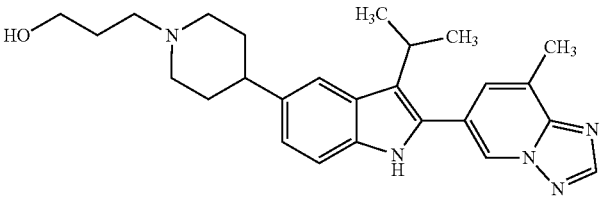
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
385	EX-2		438.2	1.21	QC-ACN-TFA-XB
386	EX-2		469.4	1.2	QC-ACN-TFA-XB
387	EX-2		496.1	1.79	QC-ACN-AA-XB
388	EX-2		418.0	1.16	QC-ACN-AA-XB
389	EX-2		468.2	1.9	QC-ACN-AA-XB
390	EX-2		456.4	1.86	QC-ACN-AA-XB
391	EX-2		432.4	1.19	QC-ACN-AA-XB

TABLE 13-continued

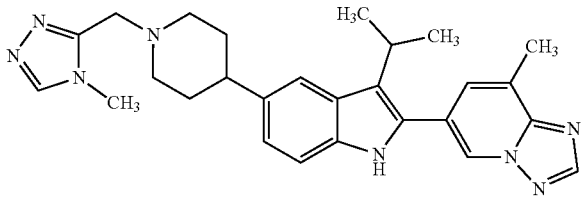
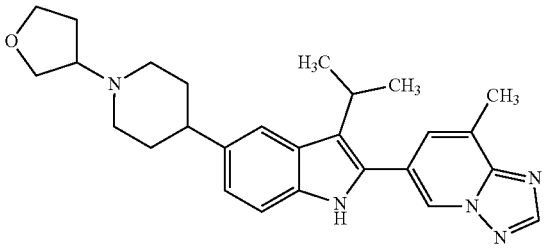
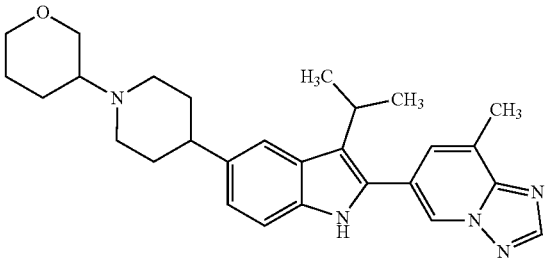
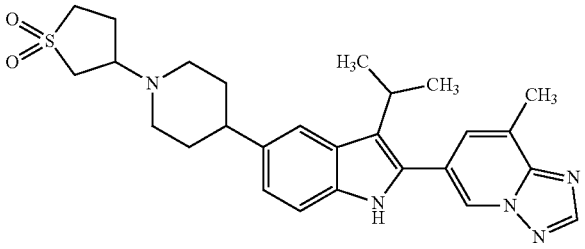
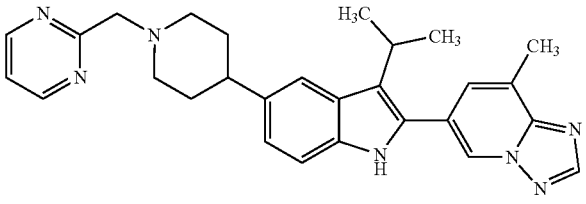
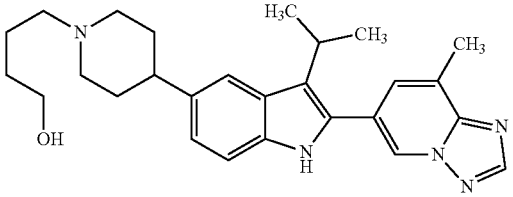
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
392	EX-2		469.2	1.52	QC-ACN-AA-XB
393	EX-2		444.0	1.58	QC-ACN-AA-XB
394	EX-2		458.0	1.58	QC-ACN-AA-XB
395	EX-2		492.1	1.63	QC-ACN-AA-XB
396	EX-2		466.0	1.5	QC-ACN-AA-XB
397	EX-2		446.0	1.1	QC-ACN-TFA-XB

TABLE 13-continued

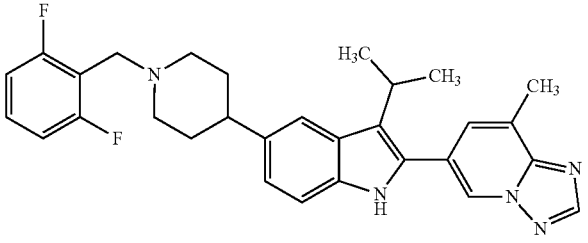
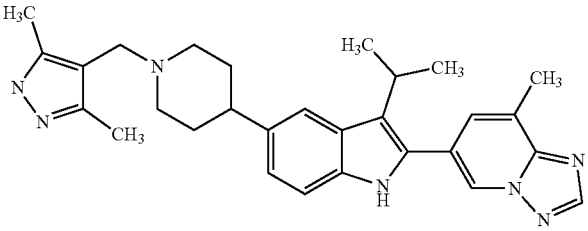
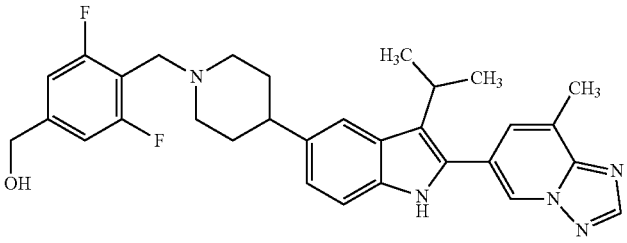
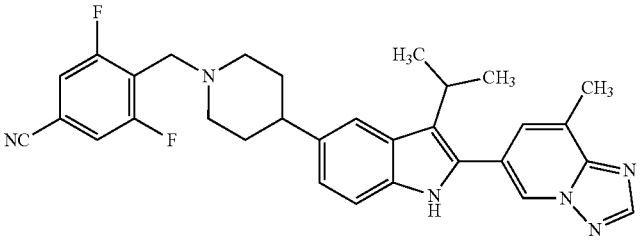
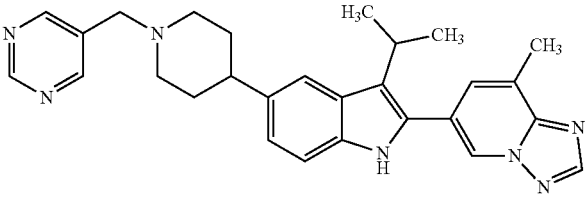
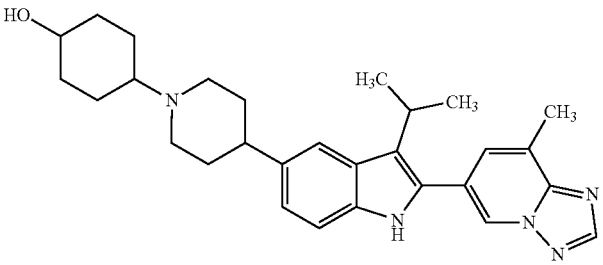
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
398	EX-2		500.0	2.37	QC-ACN-AA-XB
399	EX-2		482.0	1.31	QC-ACN-AA-XB
400	EX-2		530.0	1.92	QC-ACN-AA-XB
401	EX-2		525.1	2.35	QC-ACN-AA-XB
402	EX-2		455.4	1.72	QC-ACN-AA-XB
403	EX-2		472.4	1.24	QC-ACN-AA-XB

TABLE 13-continued

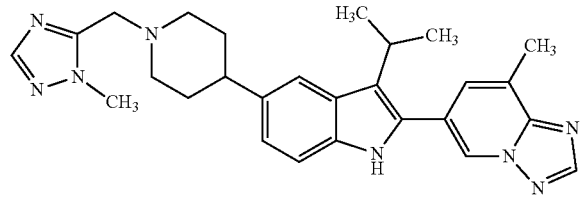
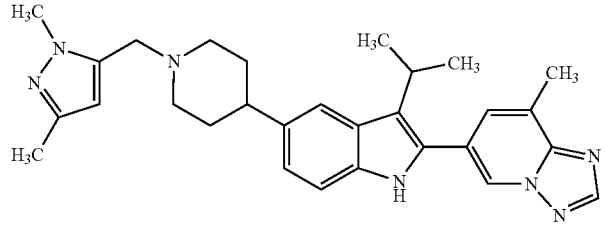
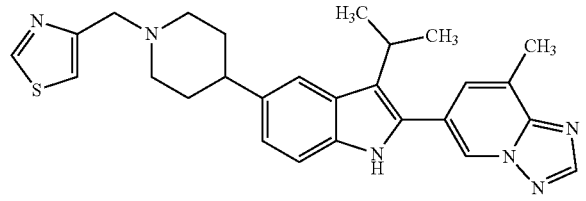
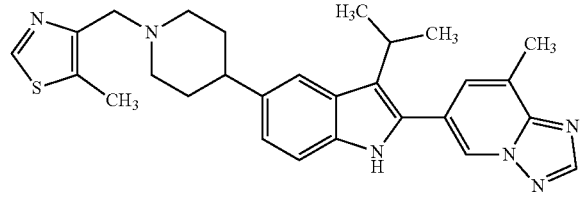
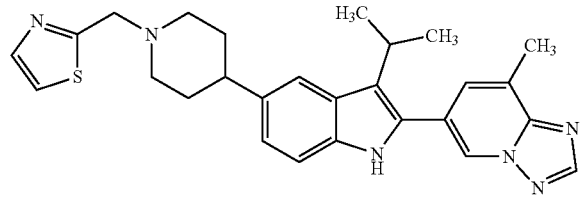
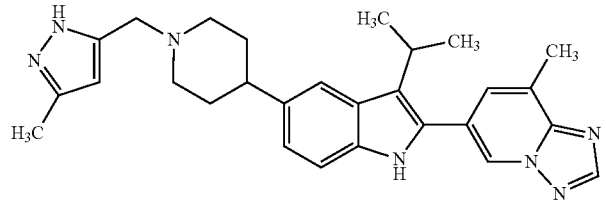
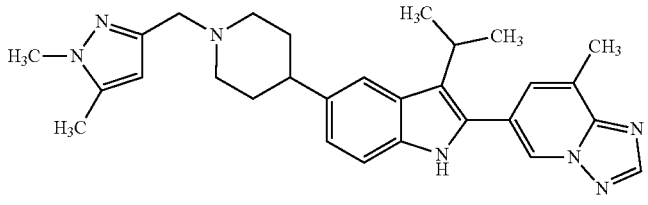
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
404	EX-2		469.0	1.77	QC-ACN-AA-XB
405	EX-2		482.0	1.96	QC-ACN-AA-XB
406	EX-2		471.0	1.6	QC-ACN-AA-XB
407	EX-2		485.3	1.99	QC-ACN-AA-XB
408	EX-2		471.0	2.18	QC-ACN-AA-XB
409	EX-2		468.0	1.4	QC-ACN-AA-XB
410	EX-2		482.2	1.52	QC-ACN-AA-XB

TABLE 13-continued

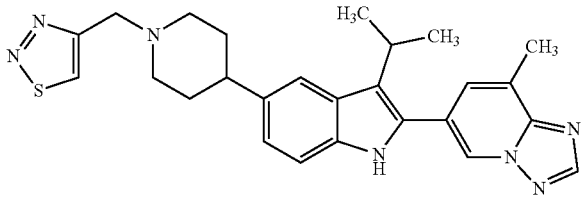
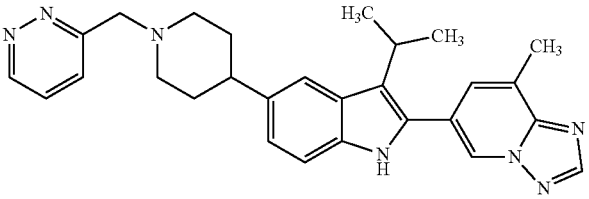
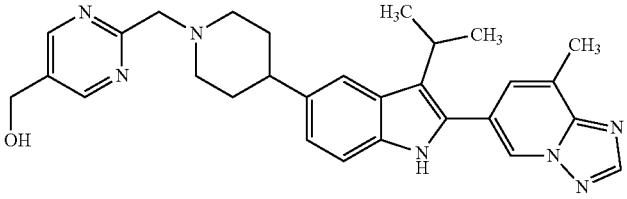
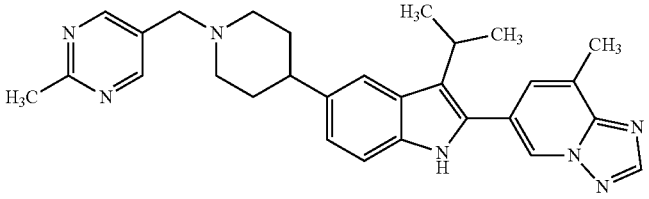
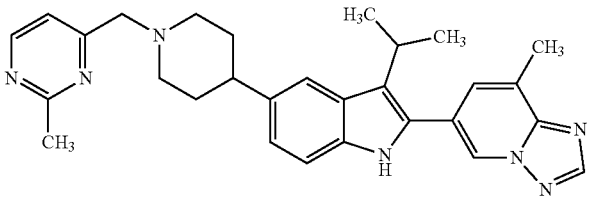
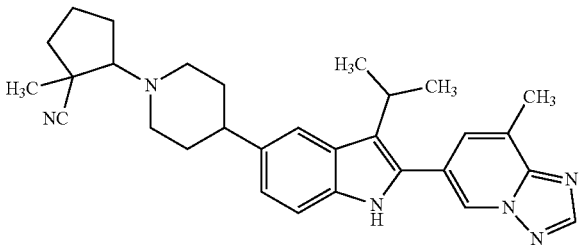
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
411	EX-2		472.1	1.36	QC-ACN-TFA-XB
412	EX-2		466.4	1.28	QC-ACN-TFA-XB
413	EX-2		496.4	1.38	QC-ACN-AA-XB
414	EX-2		480.0	1.76	QC-ACN-AA-XB
415	EX-2		480.2	1.77	QC-ACN-AA-XB
416	EX-2		481.0	1.32	QC-ACN-TFA-XB

TABLE 13-continued

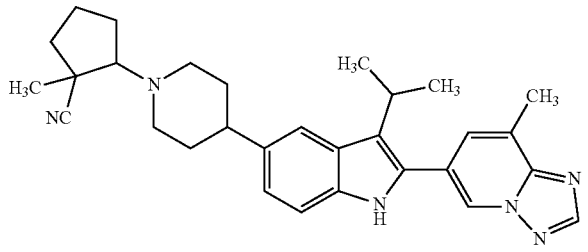
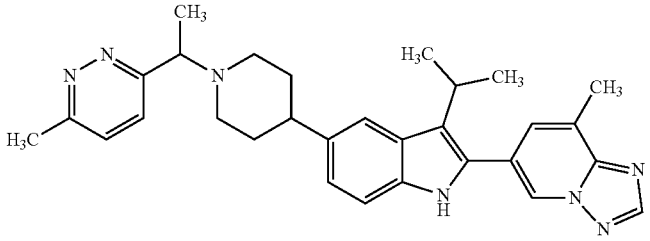
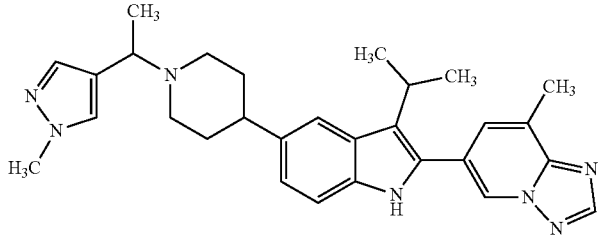
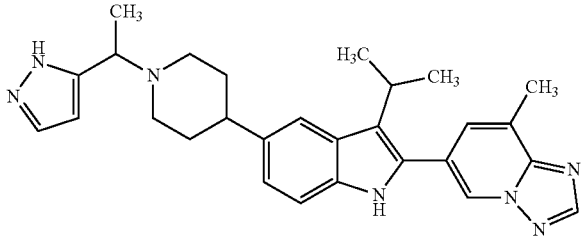
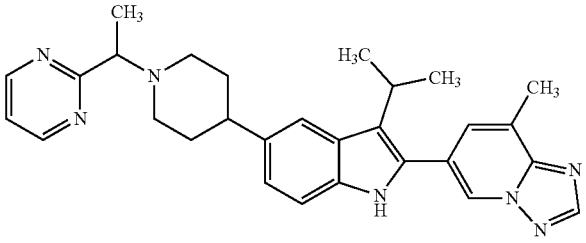
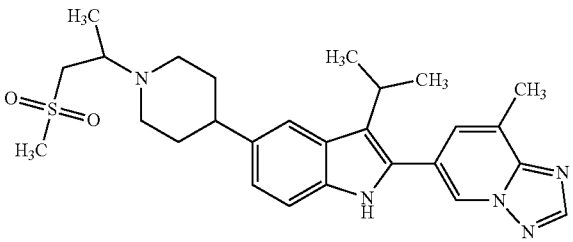
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
417	EX-2		481.0	1.32	QC-ACN-TFA-XB
418	EX-2		493.9	1.69	QC-ACN-AA-XB
419	EX-2		482.4	1.26	QC-ACN-AA-XB
420	EX-2		468.2	1.22	QC-ACN-TFA-XB
421	EX-2		480.5	1.47	QC-ACN-AA-XB
422	EX-2		494.1	1.87	QC-ACN-AA-XB

TABLE 13-continued

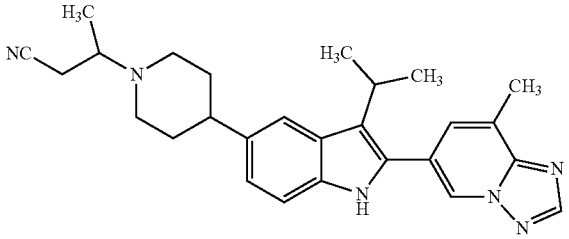
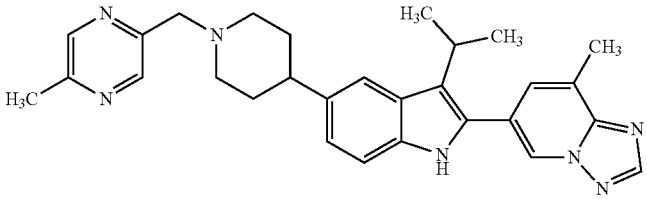
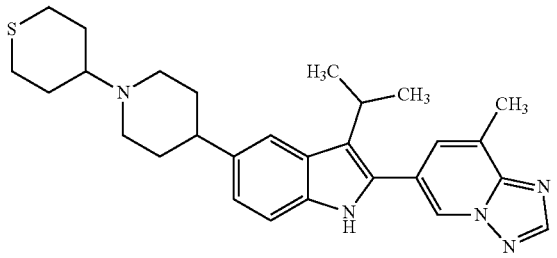
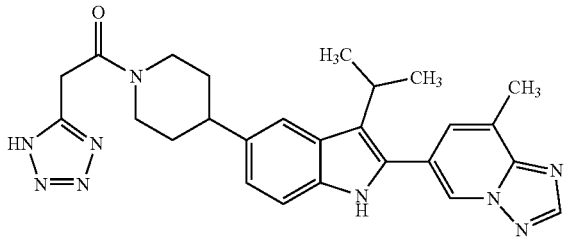
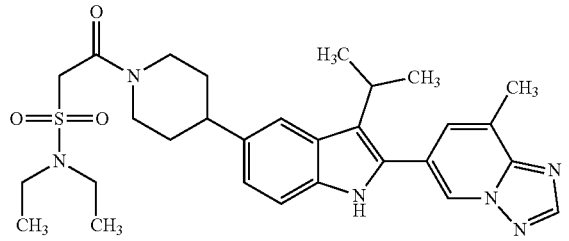
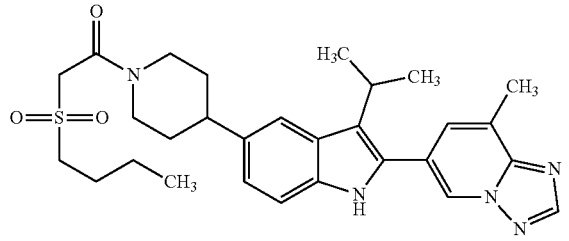
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
423	EX-2		441.0	1.36	QC-ACN-TFA-XB
424	EX-2		480.0	1.83	QC-ACN-AA-XB
425	EX-2		474.1	1.67	QC-ACN-AA-XB
426	EX-2		484.1	1.15	QC-ACN-AA-XB
427	EX-2		551.1	2.25	QC-ACN-AA-XB
428	EX-2		536.5	1.53	QC-ACN-TFA-XB

TABLE 13-continued

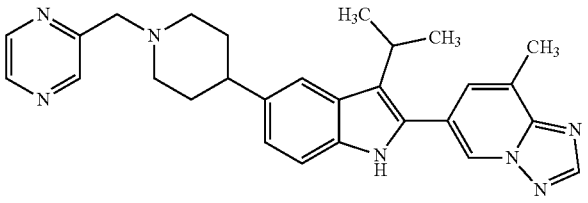
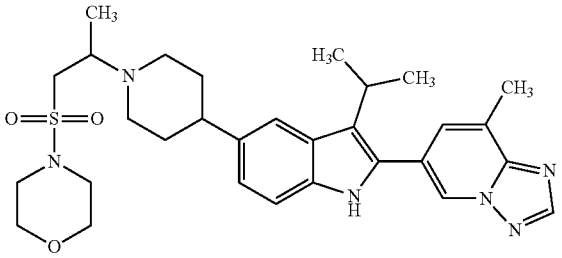
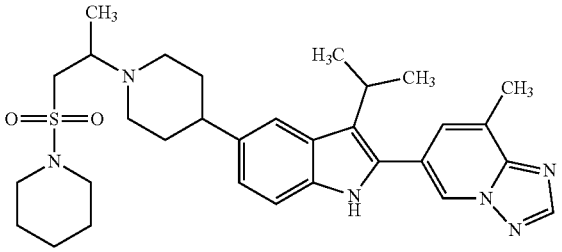
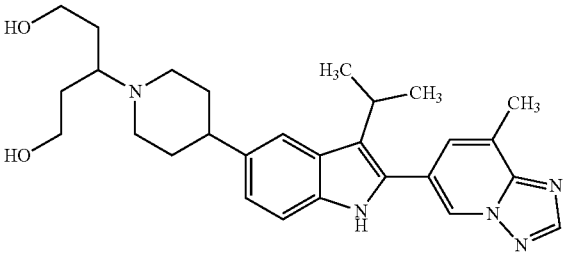
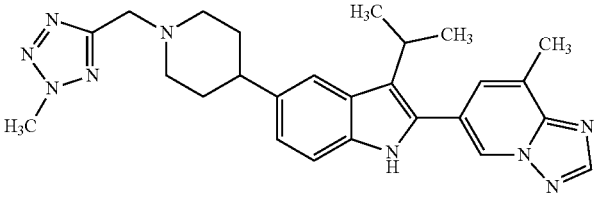
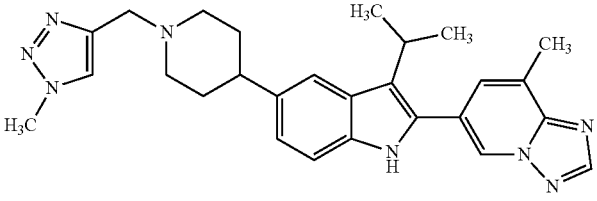
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
429	EX-2		466.3	1.25	QC-ACN-TFA-XB
430	EX-2		565.4	1.89	QC-ACN-AA-XB
431	EX-2		563.4	2.17	QC-ACN-AA-XB
432	EX-2		476.3	1.25	QC-ACN-AA-XB
433	EX-2		470.3	1.92	QC-ACN-AA-XB
434	EX-2		469.2	1.27	QC-ACN-TFA-XB

TABLE 13-continued

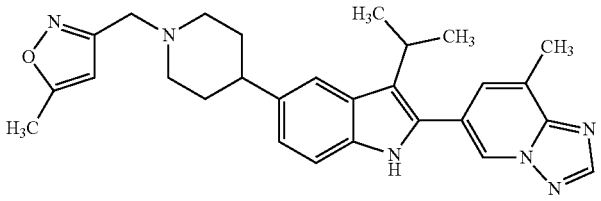
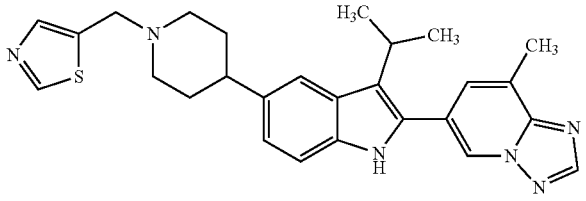
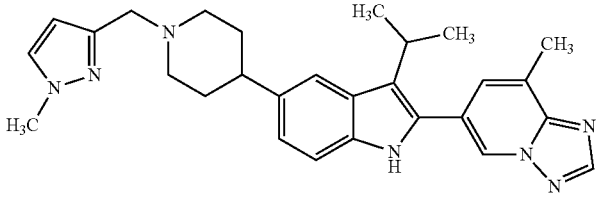
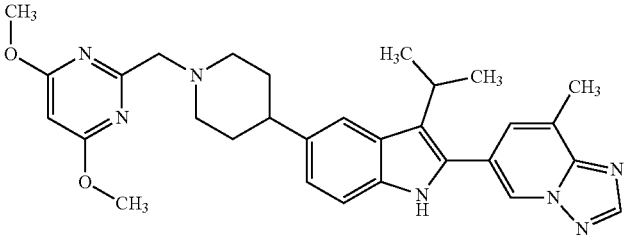
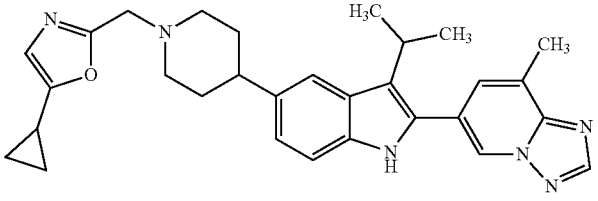
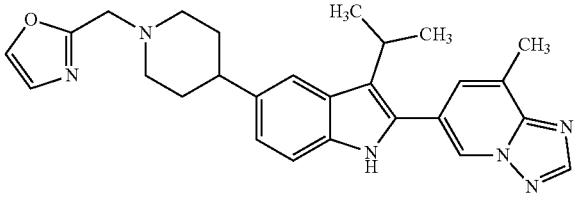
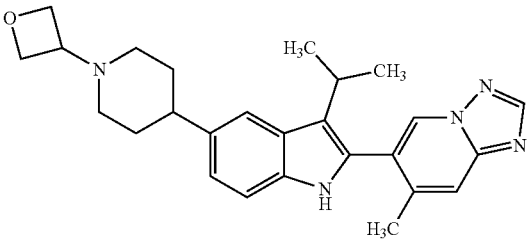
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
435	EX-2		469.2	1.9	QC-ACN-AA-XB
436	EX-2		471.1	1.93	QC-ACN-AA-XB
437	EX-2		468.2	1.49	QC-ACN-AA-XB
438	EX-2		526.2	1.54	QC-ACN-TFA-XB
439	EX-2		496.2	1.34	QC-ACN-TFA-XB
440	EX-2		455.2	1.28	QC-ACN-TFA-XB
441	EX-3		430.4	1.66	QC-ACN-AA-XB

TABLE 13-continued

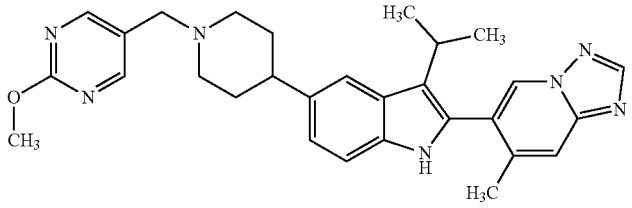
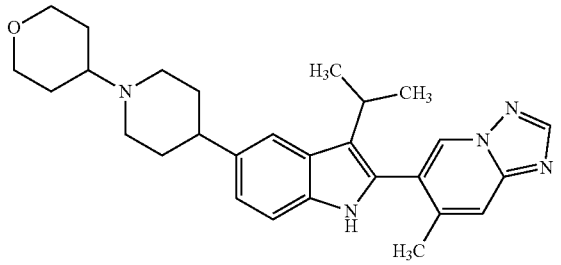
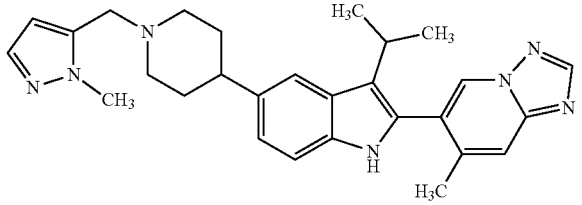
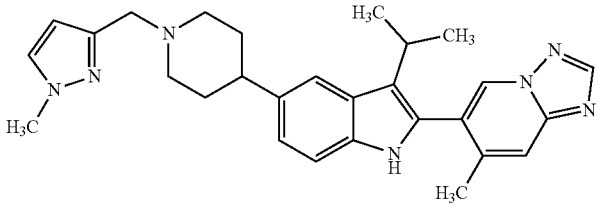
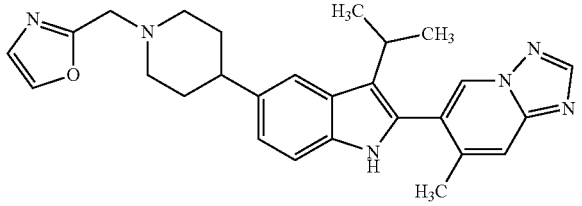
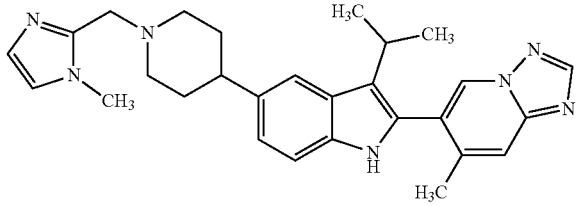
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
442	EX-3		496.2	1.08	QC-ACN-TFA-XB
443	EX-3		458.2	1.05	QC-ACN-TFA-XB
444	EX-3		468.4	1.81	QC-ACN-AA-XB
445	EX-3		468.3	1.1	QC-ACN-TFA-XB
446	EX-3		455.4	1.78	QC-ACN-AA-XB
447	EX-3		469.3	0.98	QC-ACN-TFA-XB

TABLE 13-continued

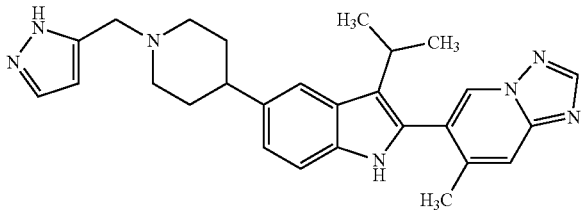
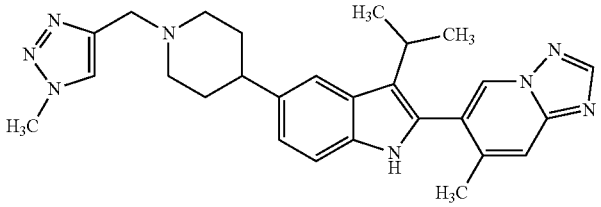
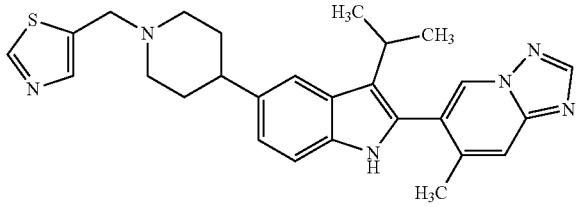
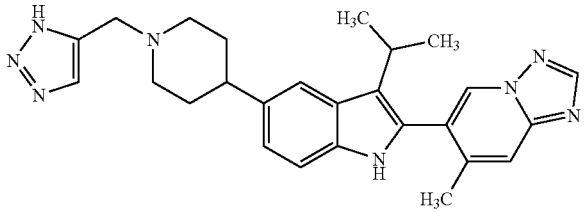
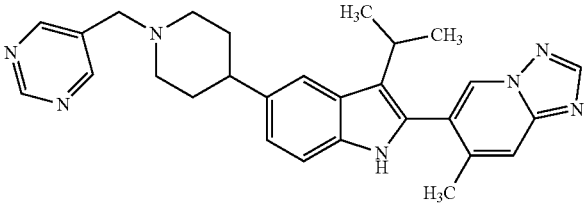
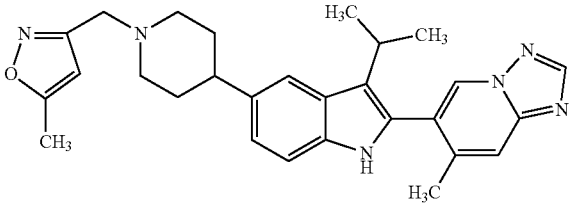
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
448	EX-3		454.0	1.3	QC-ACN-AA-XB
449	EX-3		469.4	1.33	QC-ACN-AA-XB
450	EX-3		471.0	1.79	QC-ACN-AA-XB
451	EX-3		455.0	1.5	QC-ACN-AA-XB
452	EX-3		465.9	1.69	QC-ACN-AA-XB
453	EX-3		469.0	1.95	QC-ACN-AA-XB

TABLE 13-continued

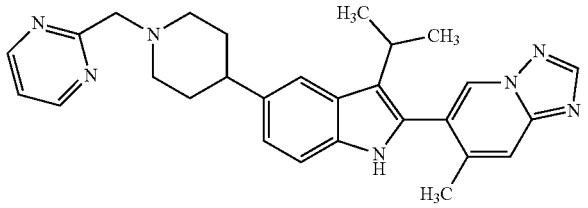
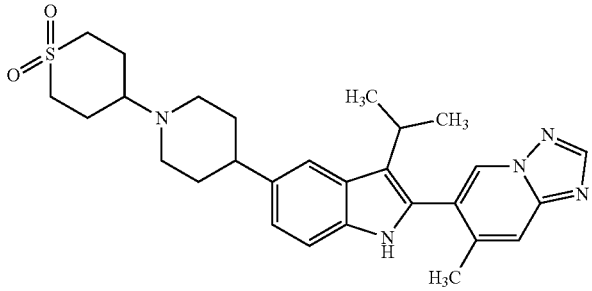
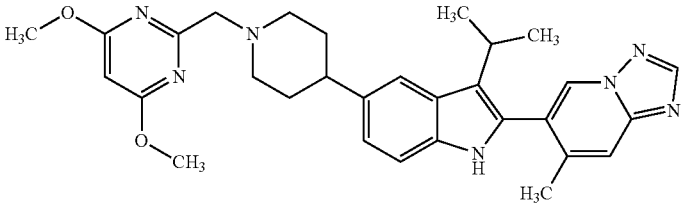
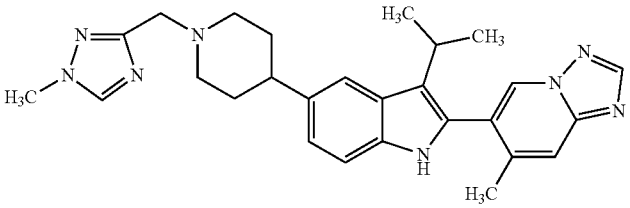
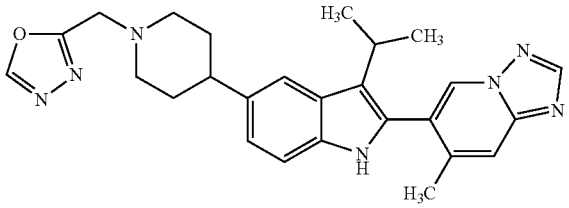
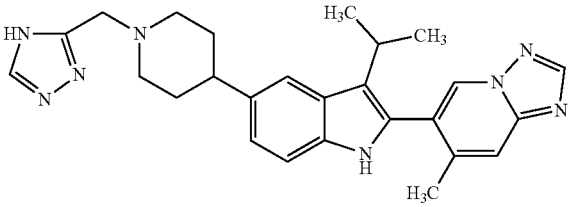
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
454	EX-3		466.2	1.46	QC-ACN-AA-XB
455	EX-3		506.0	1.69	QC-ACN-AA-XB
456	EX-3		526.0	2.05	QC-ACN-AA-XB
457	EX=3		469.1	1.42	QC-ACN-AA-XB
458	EX-3		456.2	1.77	QC-ACN-AA-XB
459	EX-3		455.4	1.05	QC-ACN-TFA-XB

TABLE 13-continued

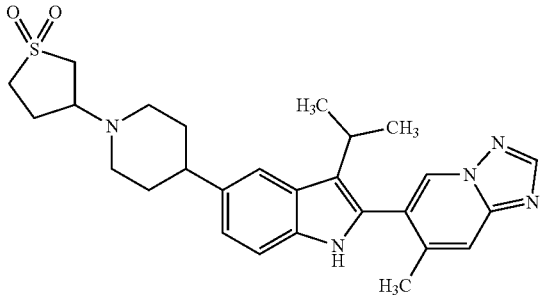
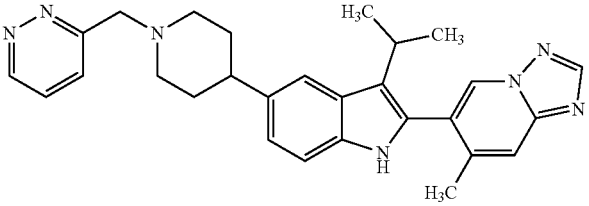
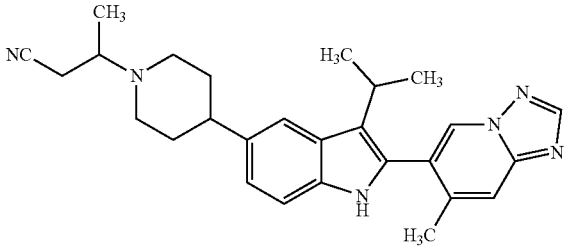
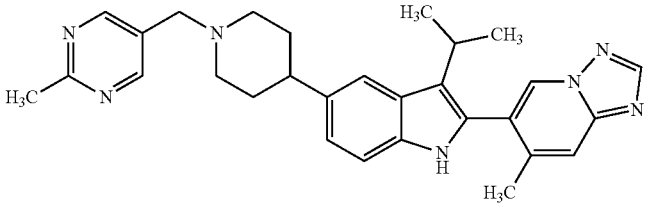
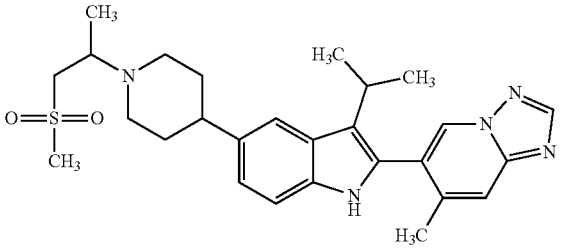
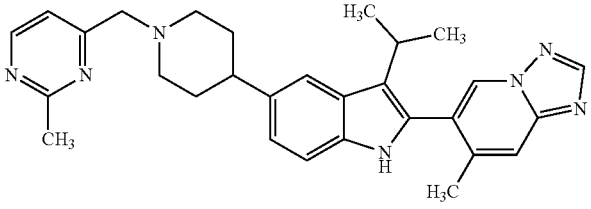
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
460	EX-3		492.4	1.21	QC-ACN-TFA-XB
461	EX-3		466.1	1	QC-ACN-TFA-XB
462	EX-3		441.0	1.84	QC-ACN-AA-XB
463	EX-3		480.1	1.05	QC-ACN-TFA-XB
464	EX-3		494.1	1.73	QC-ACN-AA-XB
465	EX-3		480.4	1.71	QC-ACN-AA-XB

TABLE 13-continued

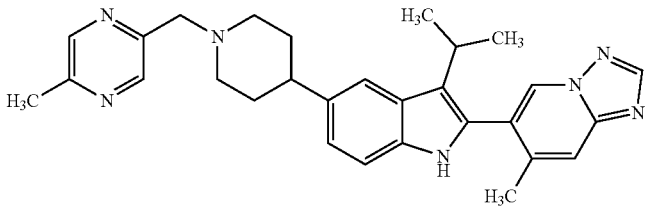
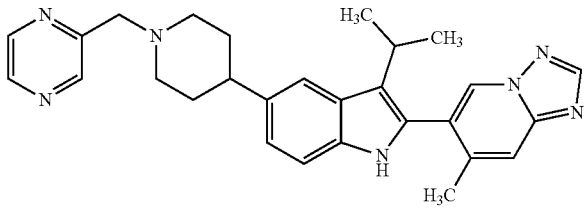
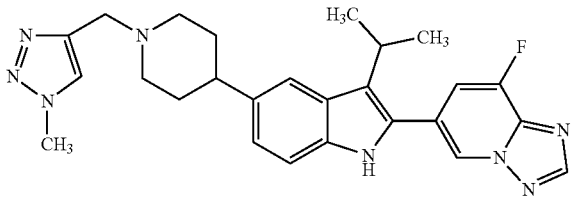
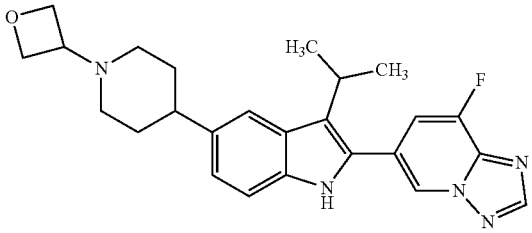
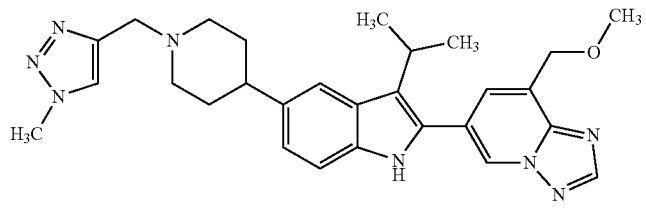
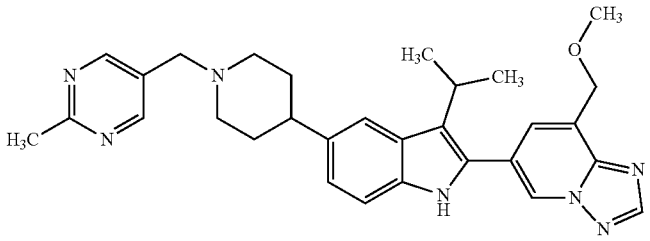
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
466	EX-3		480.0	1.33	QC-ACN-TFA-XB
467	EX-3		466.0	1.85	QC-ACN-AA-XB
468	EX-112		473.0	1.31	QC-ACN-TFA-XB
469	EX-112		434.1	1.18	QC-ACN-TFA-XB
470	EX-6		499.1	1.37	QC-ACN-AA-XB
471	EX-6		510.1	1.75	QC-ACN-AA-XB

TABLE 13-continued

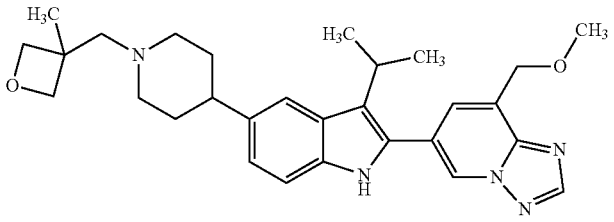
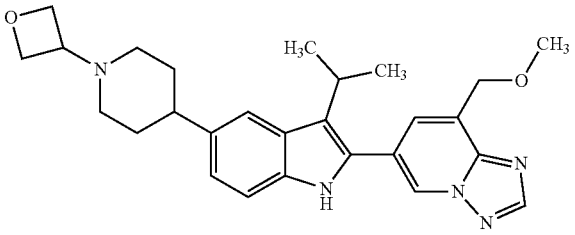
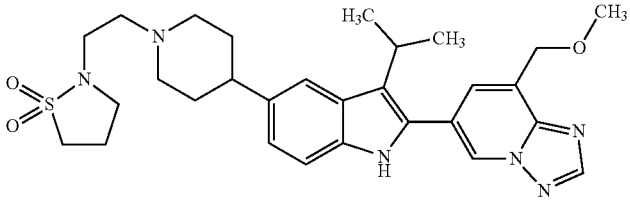
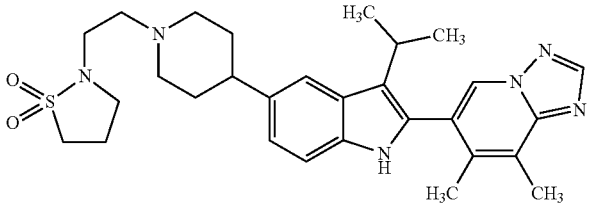
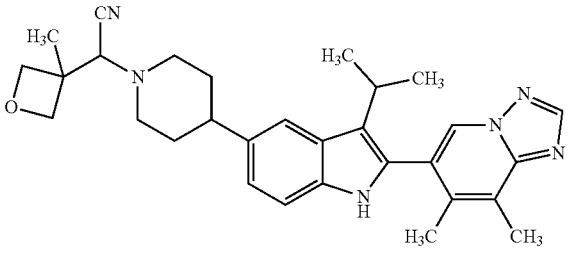
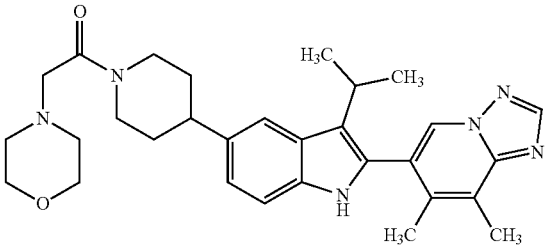
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
472	EX-6		488.1	1.74	QC-ACN-AA-XB
473	EX-6		460.1	1.65	QC-ACN-AA-XB
474	EX-6		551.0	1.69	QC-ACN-AA-XB
475	EX-4		535.4	1.43	QC-ACN-AA-XB
476	EX-4		497.4	1.94	QC-ACN-TFA-XB
477	EX-4		515.0	1.29	QC-ACN-TFA-XB

TABLE 13-continued

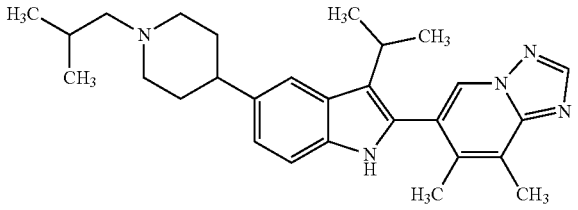
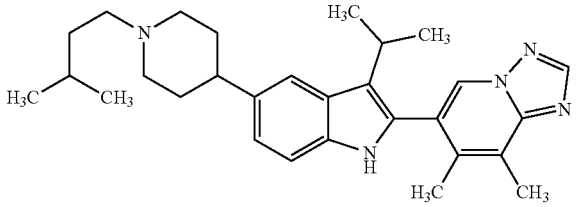
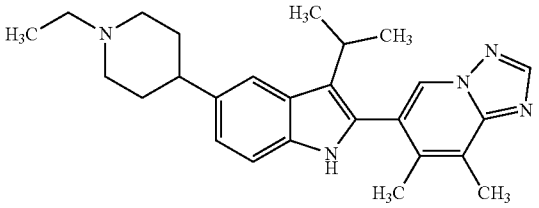
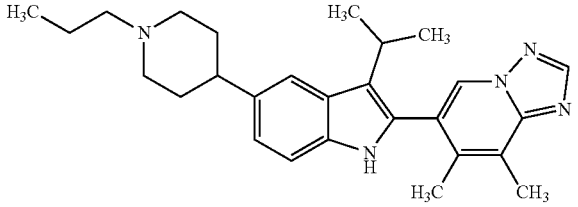
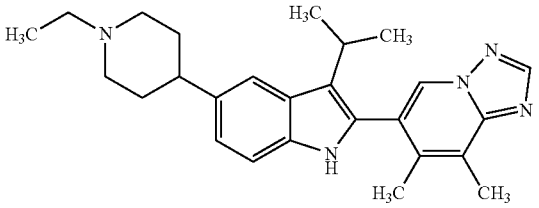
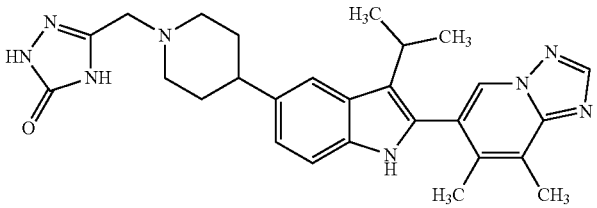
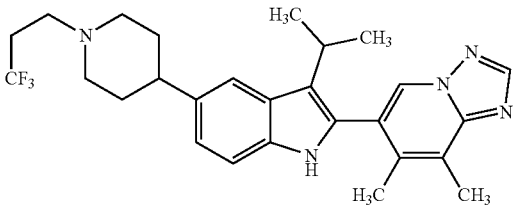
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
478	EX-4		444.1	1.74	QC-ACN-AA-XB
479	EX-4		458.4	1.58	QC-ACN-TFA-XB
480	EX-4		416.1	1.32	QC-ACN-AA-XB
481	EX-4		430.0	1.62	QC-ACN-AA-XB
482	EX-4		416.1	1.54	QC-ACN-TFA-XB
483	EX-4		485.2	1.44	QC-ACN-AA-XB
484	EX-4		484.3	2.29	QC-ACN-AA-XB

TABLE 13-continued

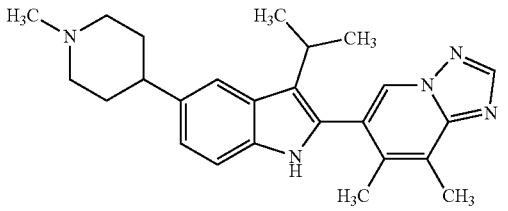
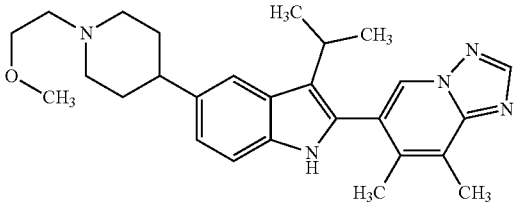
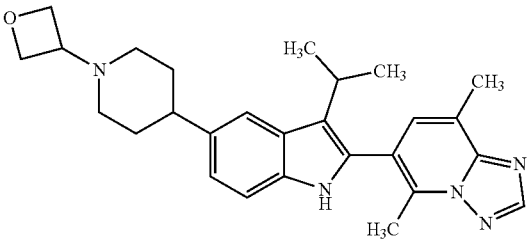
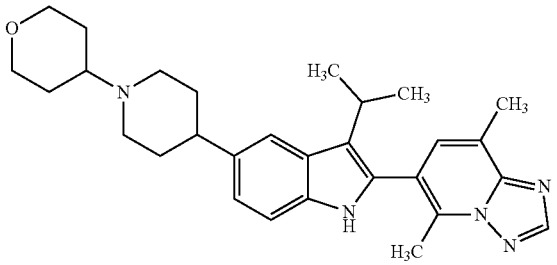
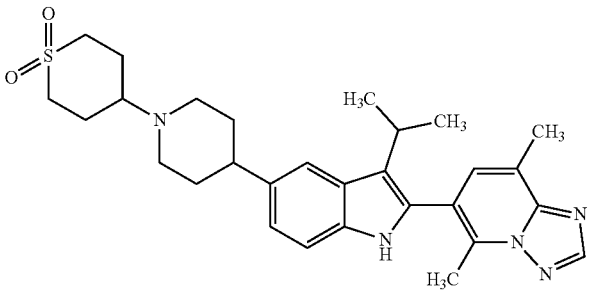
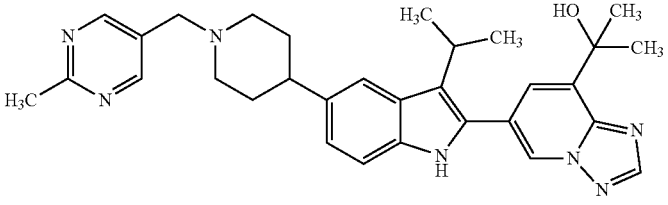
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
485	EX-4		402.2	1.29	QC-ACN-AA-XB
486	EX-4		446.2	1.38	QC-ACN-AA-XB
487	EX-110		444.3	1.77	QC-ACN-AA-XB
488	EX-110		471.9	1.28	QC-ACN-AA-XB
489	EX-110		520.4	1.23	QC-ACN-TFA-XB
490	EX-100		524.2	1.8	QC-ACN-AA-XB

TABLE 13-continued

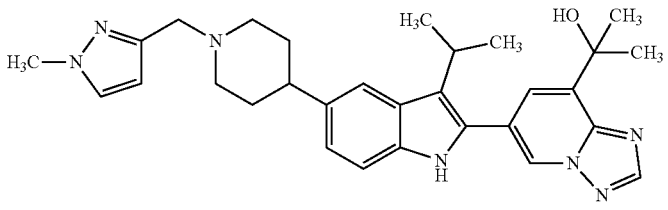
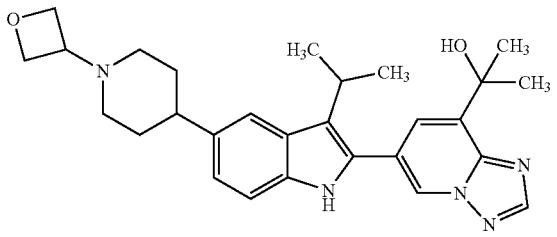
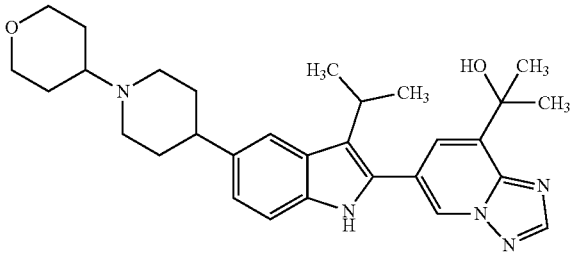
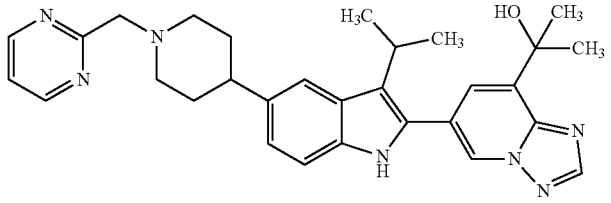
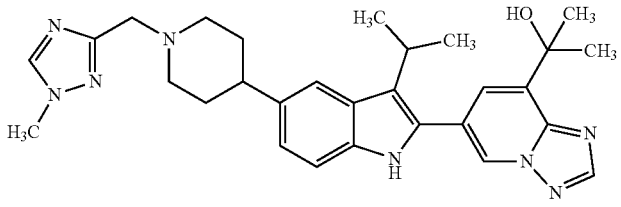
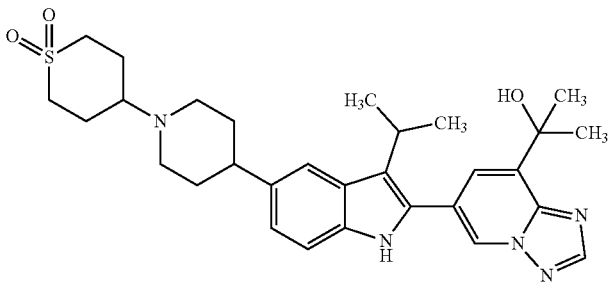
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
491	EX-100		512.2	1.53	QC-ACN-AA-XB
492	EX-100		474.4	1.15	QC-ACN-TFA-XB
493	EX-100		502.1	1.35	QC-ACN-AA-XB
494	EX-100		510.4	1.22	QC-ACN-TFA-XB
495	EX-100		513.4	1.15	QC-ACN-TFA-XB
496	EX-100		550.1	1.46	QC-ACN-AA-XB

TABLE 13-continued

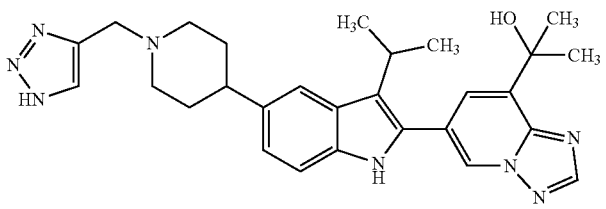
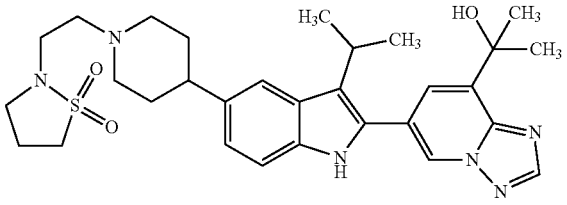
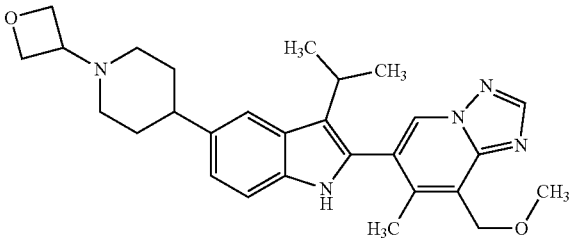
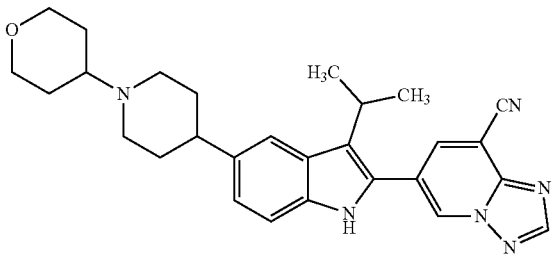
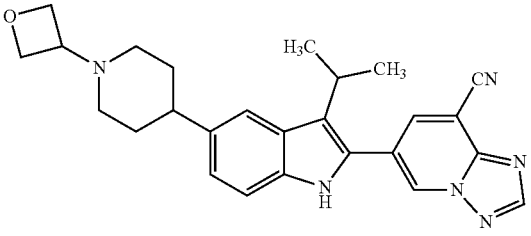
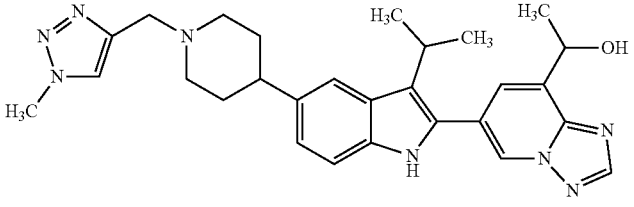
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
497	EX-100		499.1	1.38	QC-ACN-AA-XB
498	EX-100		565.3	1.38	QC-ACN-AA-XB
499	EX-101		474.1	1.09	QC-ACN-TFA-XB
500	EX-111		469.2	1.42	QC-ACN-AA-XB
501	EX-111		441.2	1.18	QC-ACN-AA-XB
502	EX-102		499.3	1.08	QC-ACN-TFA-XB

TABLE 13-continued

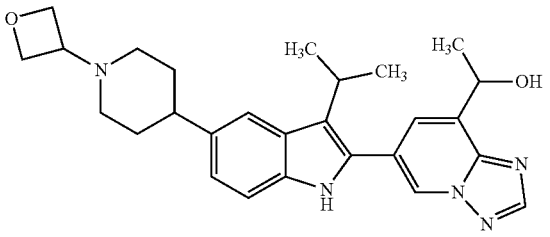
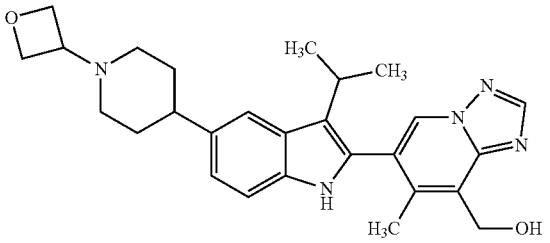
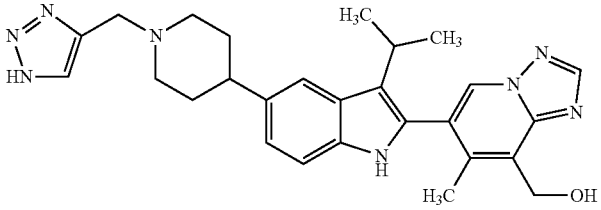
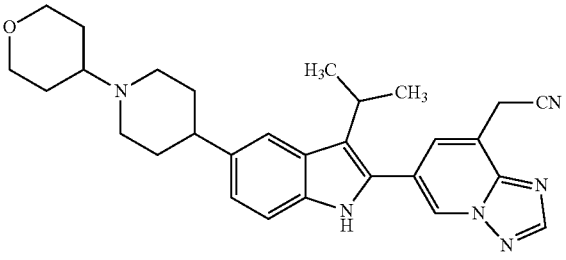
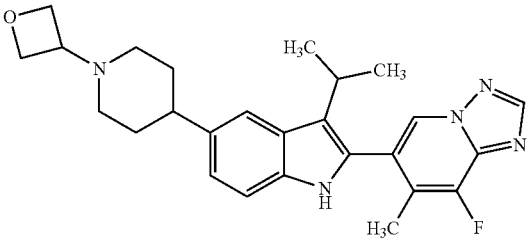
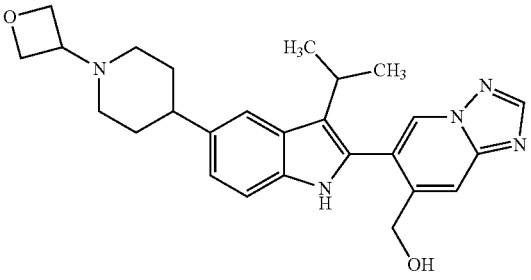
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
503	EX-102		460.3	1.06	QC-ACN-TFA-XB
504	EX-104		460.2	1.49	QC-ACN-AA-XB
505	EX-104		485.3	0.97	QC-ACN-TFA-XB
506	EX-105		483.2	1.26	QC-ACN-TFA-XB
507	EX-107		447.9	1.35	QC-ACN-AA-XB
508	EX-108		446.3	1.53	QC-ACN-AA-XB

TABLE 13-continued

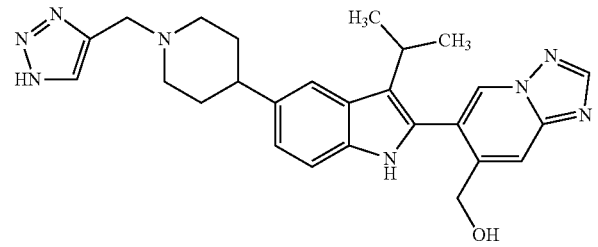
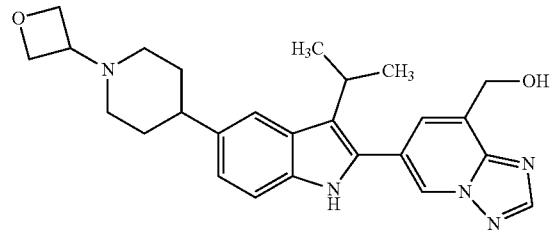
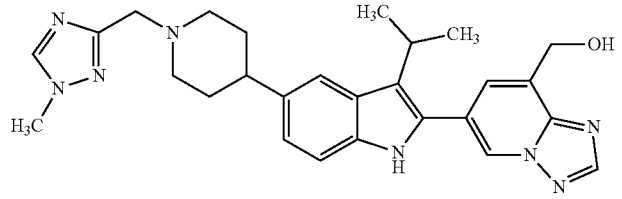
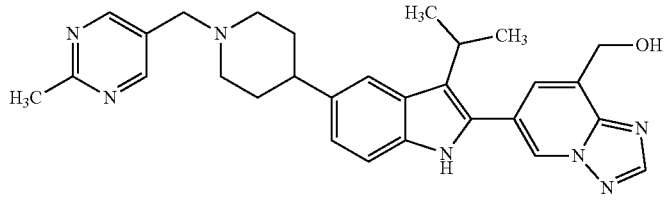
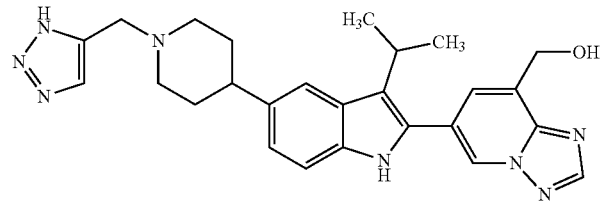
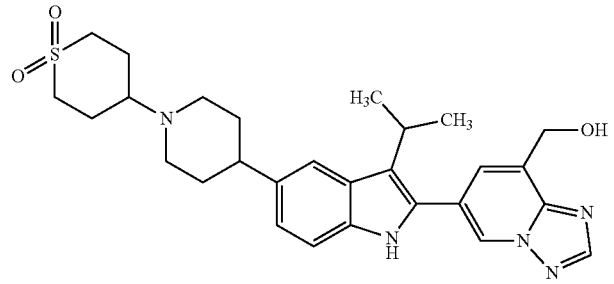
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
509	EX-108		485.1	0.92	QC-ACN-TFA-XB
510	EX-113		446.0	1.39	QC-ACN-AA-XB
511	EX-113		485.3	1.16	QC-ACN-AA-XB
512	EX-113		496.4	1.04	QC-ACN-TFA-XB
513	EX-113		471.1	1	QC-ACN-TFA-XB
514	EX-113		522.4	1.34	QC-ACN-AA-XB

TABLE 13-continued

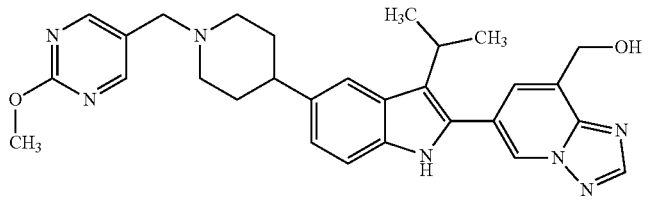
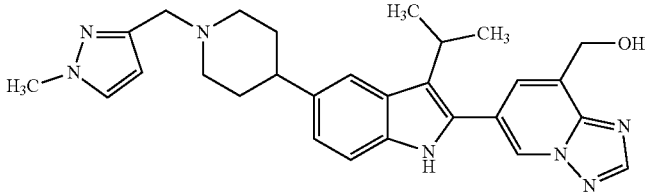
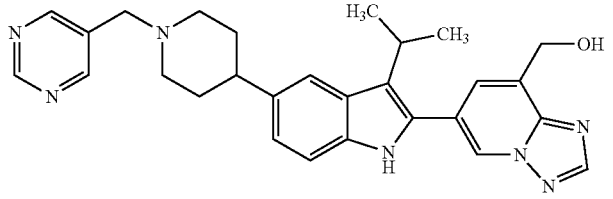
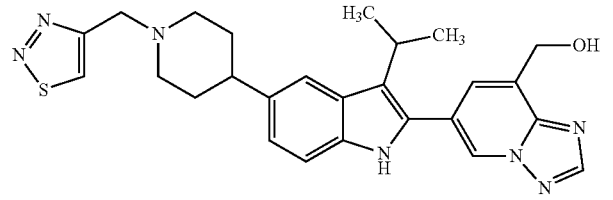
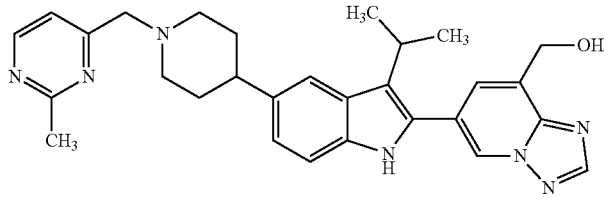
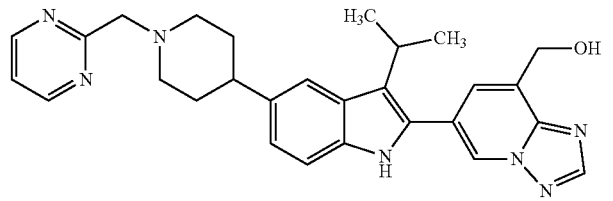
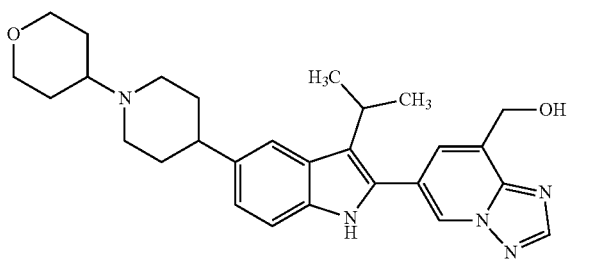
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
515	EX-113		512.4	1.56	QC-ACN-AA-XB
516	EX-113		484.1	1.27	QC-ACN-AA-XB
517	EX-113		482.1	1.45	QC-ACN-AA-XB
518	EX-113		488.0	1.26	QC-ACN-TFA-XB
519	EX-113		496.4	1.55	QC-ACN-AA-XB
520	EX-113		482.1	1.31	QC-ACN-AA-XB
521	EX-113		474.3	1.03	QC-ACN-TFA-XB

TABLE 13-continued

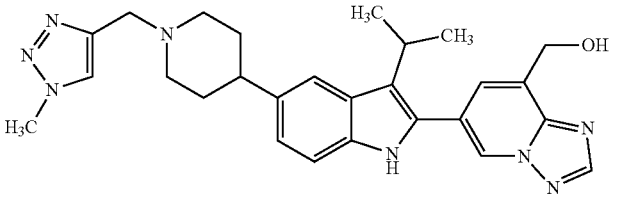
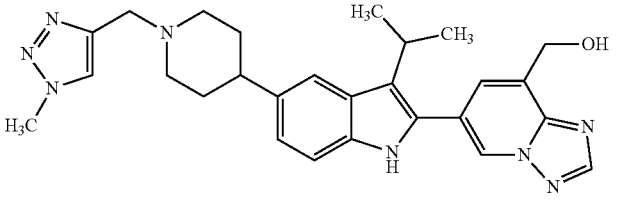
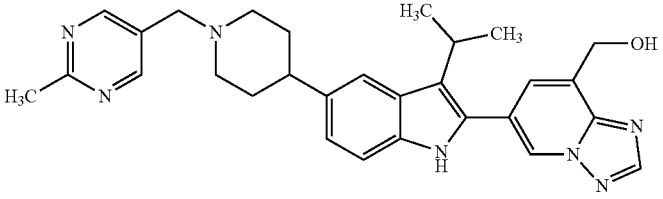
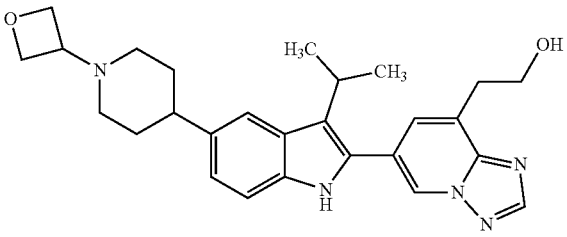
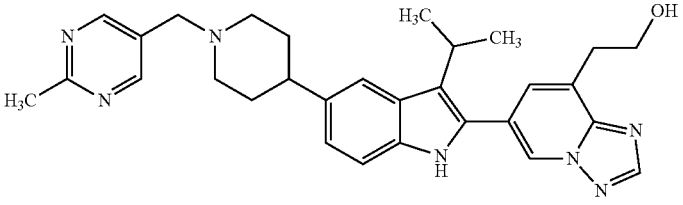
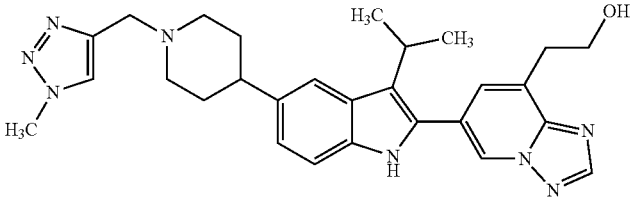
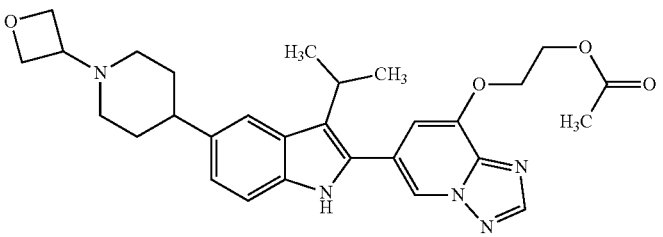
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
522	EX-113		486.1	1.46	QC-ACN-AA-XB
523	EX-113		485.2	1.01	QC-ACN-TFA-XB
524	EX-113		496.0	1.39	QC-ACN-AA-XB
525	EX-114		460.3	1.44	QC-ACN-AA-XB
526	EX-114		510.0	1.48	QC-ACN-AA-XB
527	EX-114		499.3	1.02	QC-ACN-TFA-XB
528	EX-116		518.0	1.71	QC-ACN-AA-XB

TABLE 13-continued

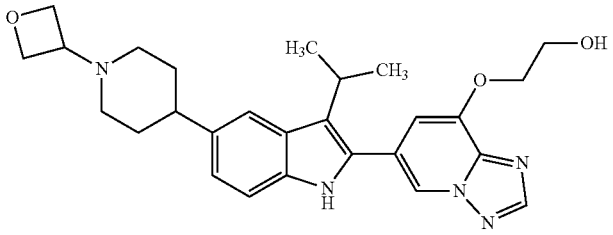
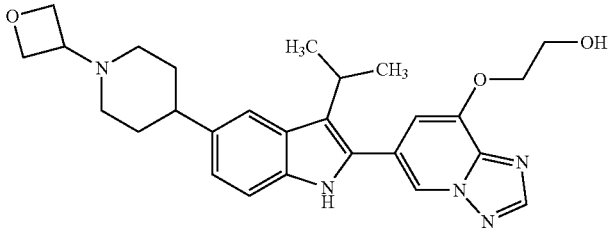
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
529	EX-116		475.9	1.11	QC-ACN-TFA-XB
530	EX-116		476.0	1.3	QC-ACN-AA-XB

TABLE 14

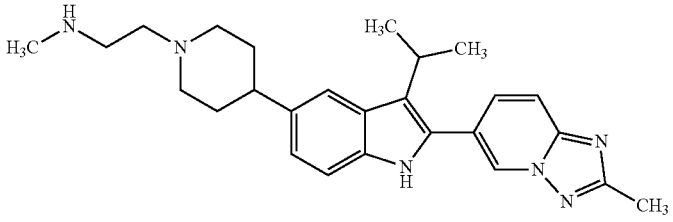
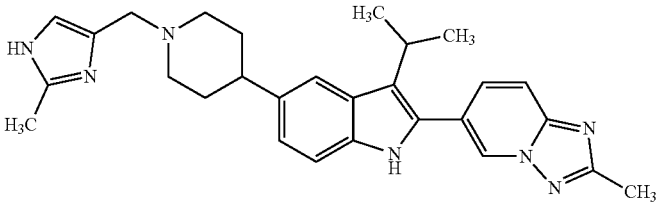
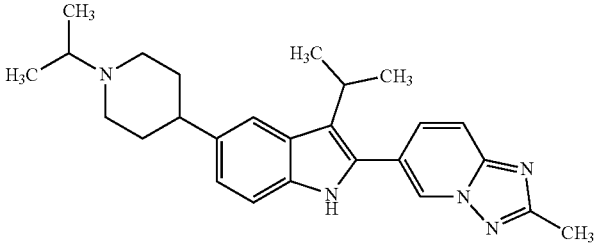
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
531	EX-122		431.3	0.93	E
532	EX-122		467.3	1.56	E
533	EX-122		416.3	1.48	E

TABLE 14-continued

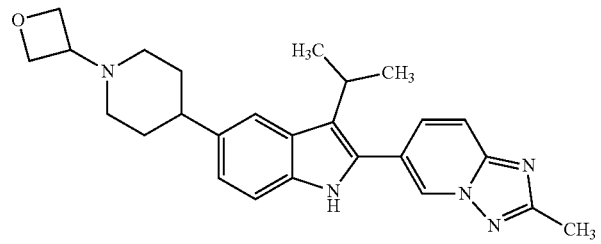
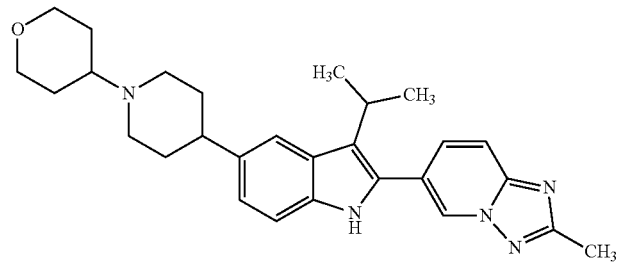
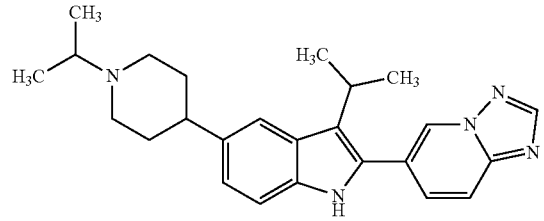
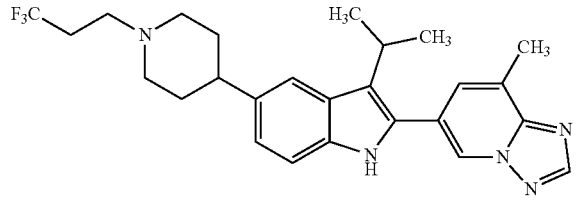
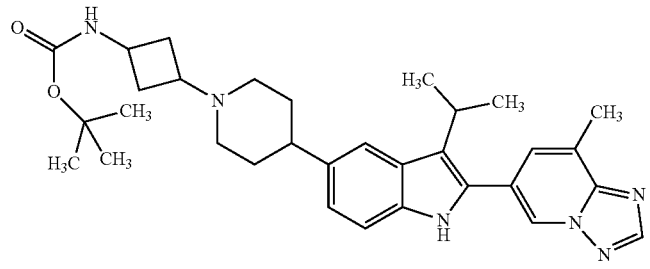
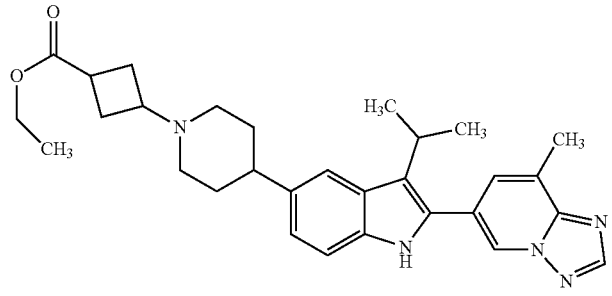
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
534	EX-122		430.3	1.8	E
535	EX-122		458.3	1.45	E
536	EX-1		402.3	1.47	E
537	EX-2		470.2	2.5	E
538	EX-2		543	2.12	E
539	EX-2		500	2.11	E

TABLE 14-continued

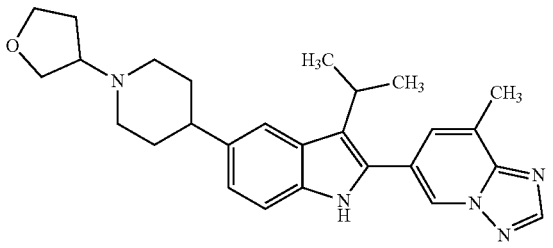
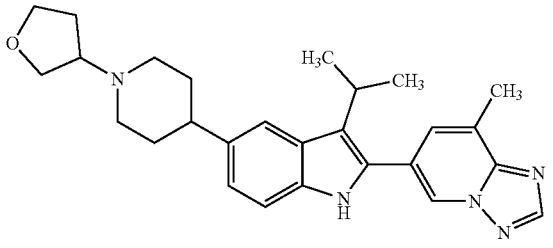
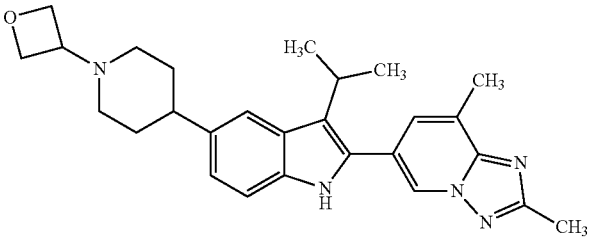
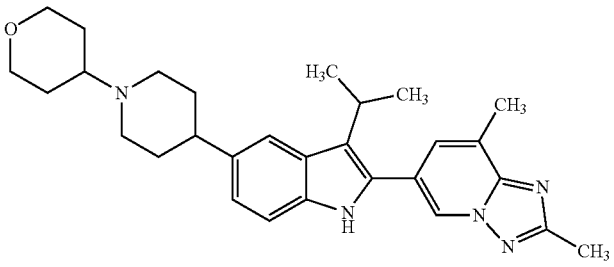
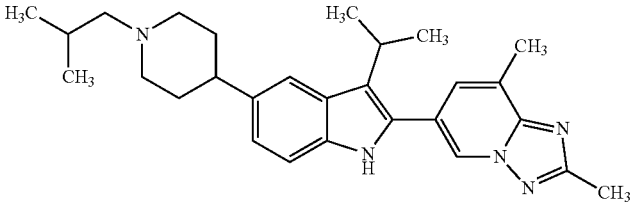
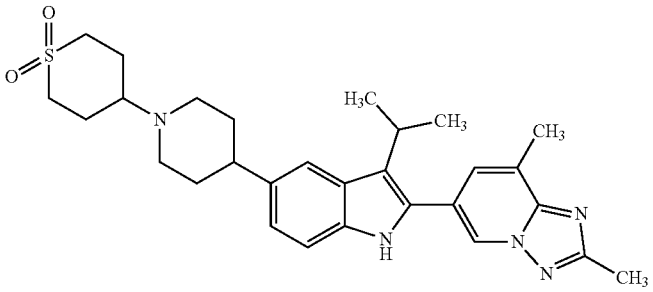
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
540	EX-2		444.2	1.71	E
541	EX-2		444.2	1.72	E
542	EX-124		444.3	1.74	E
543	EX-124		473.3	1.71	E
544	EX-124		444	1.82	E
545	EX-124		520.3	1.93	E

TABLE 14-continued

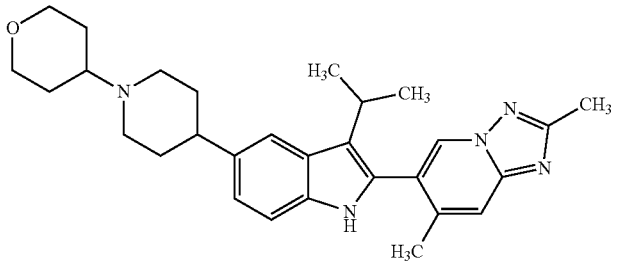
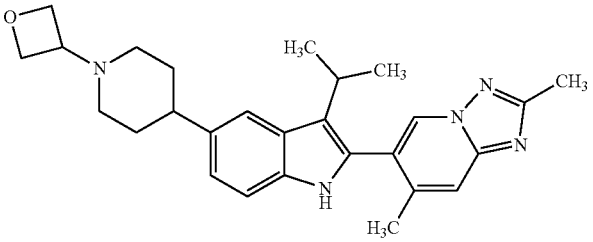
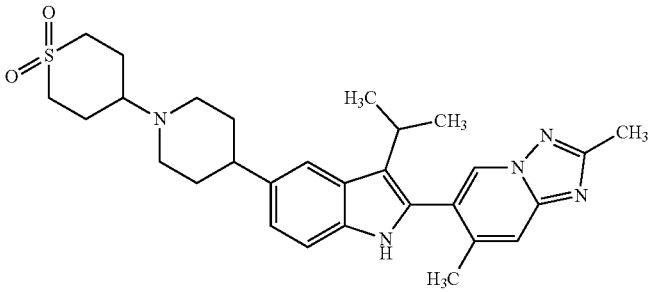
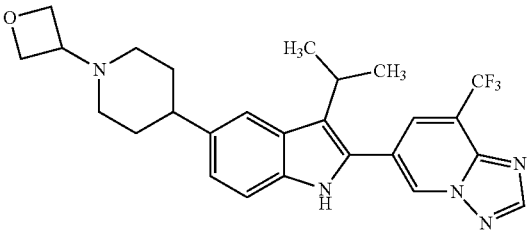
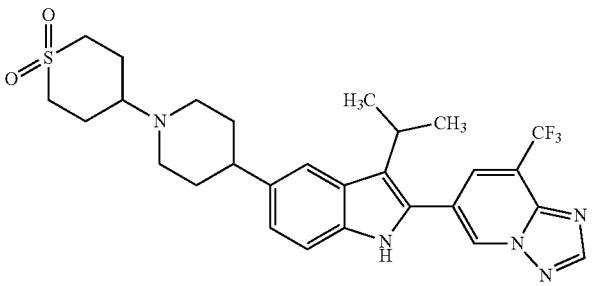
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
546	EX-125		472.3	1.56	E
547	EX-125		444.4	1.69	E
548	EX-125		520	1.58	E
549	EX-128		484	2.03	E
550	EX-128		560	1.88	E

TABLE 14-continued

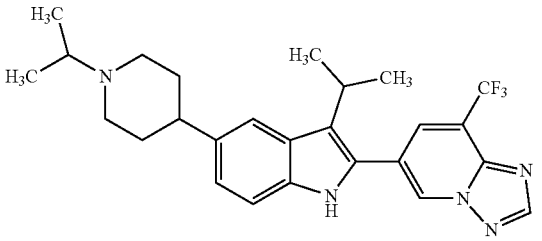
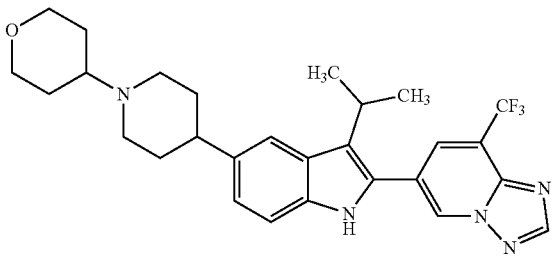
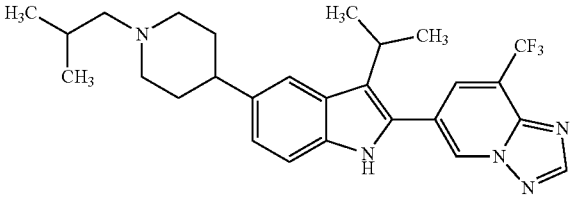
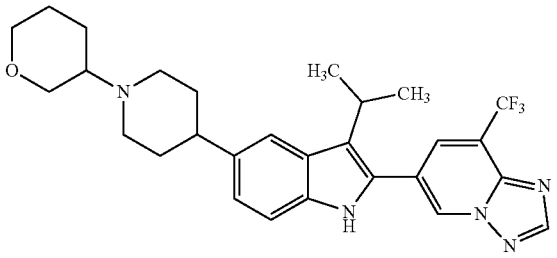
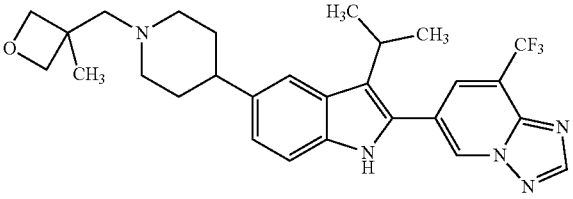
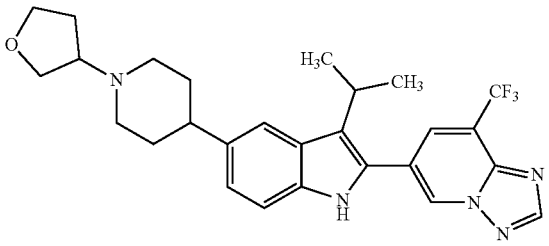
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
551	EX-128		470	1.56	E
552	EX-128		512	2.5	D
553	EX-128		484.2	2.24	E
554	EX-128		512.1	2.13	E
555	EX-128		512.3	2.15	E
556	EX-128		498.2	1.51	F

TABLE 14-continued

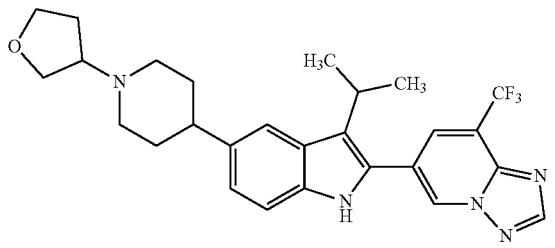
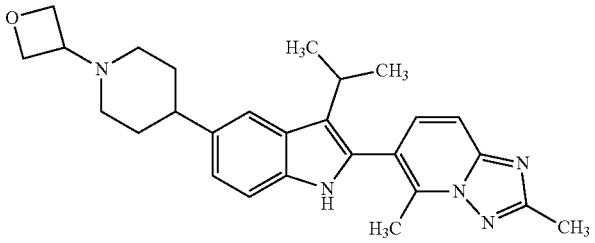
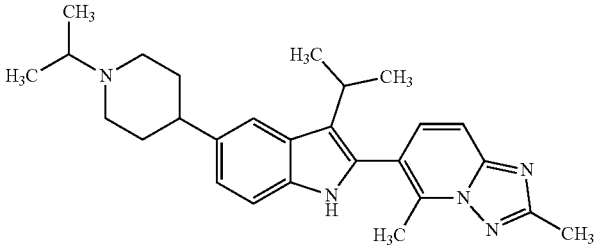
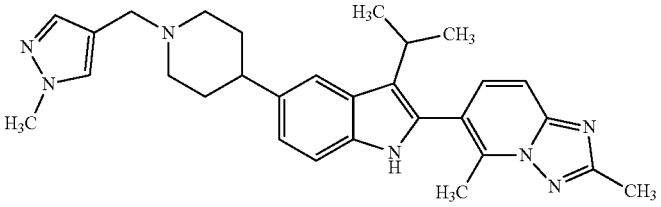
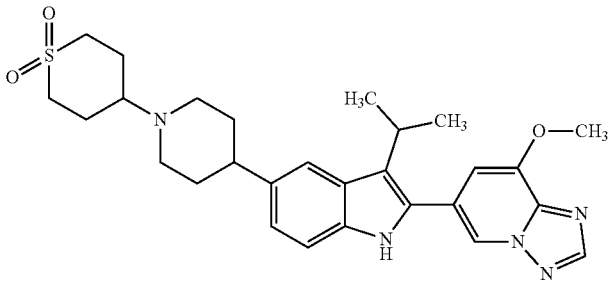
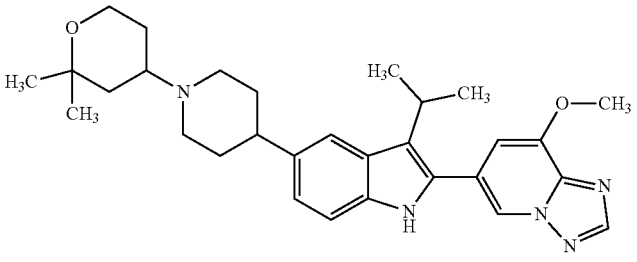
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
557	EX-128		498.2	2.03	E
558	EX-155		444.3	1.65	E
559	EX-155		430.3	1.53	E
560	EX-155		482.3	1.5	E
561	EX-5		522.4	1.51	E
562	EX-5		502.3	1.71	E

TABLE 14-continued

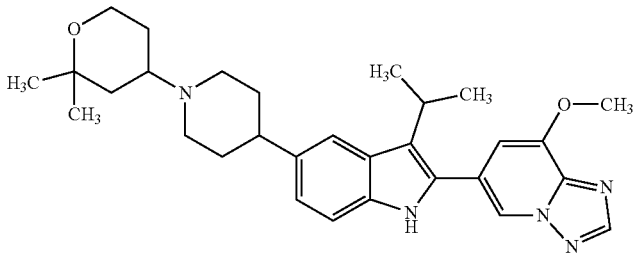
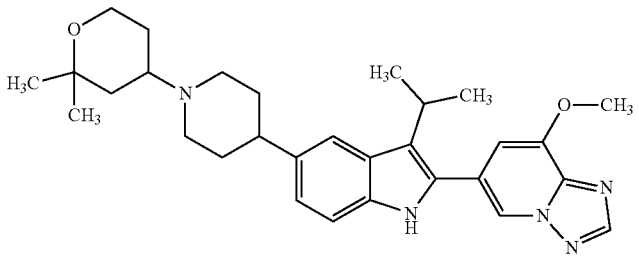
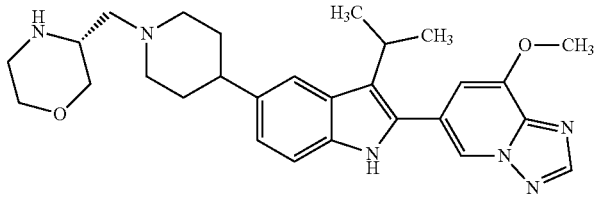
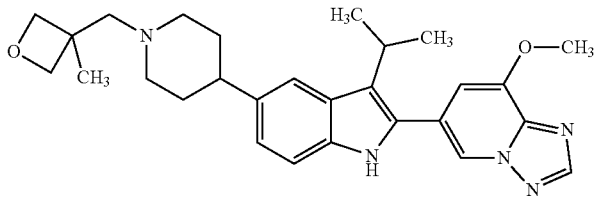
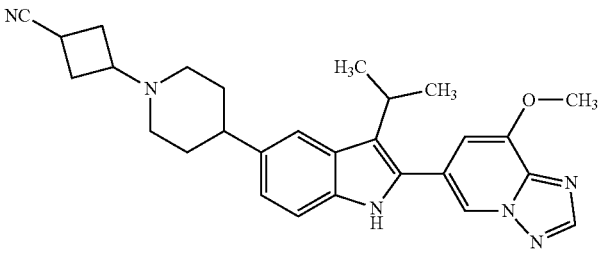
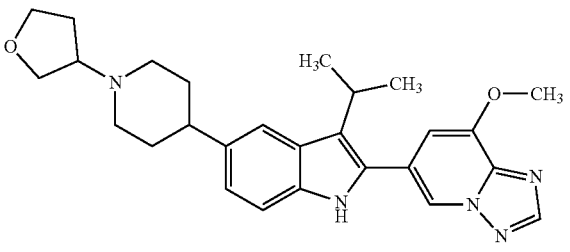
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
563	EX-5		502.2	6.03	I
564	EX-5		502.4	6.06	I
565	EX-5		489.3	1.55	E
566	EX-5		474.3	1.86	E
567	EX-5		469.2	1.89	E
568	EX-5		460.2	1.87	D

TABLE 14-continued

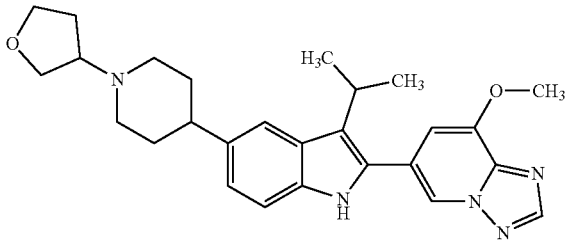
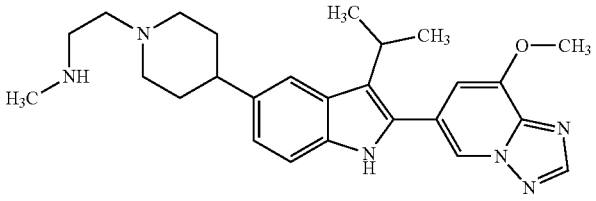
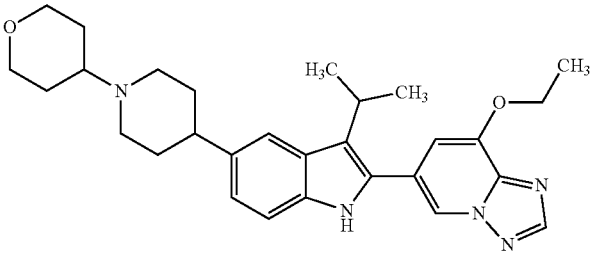
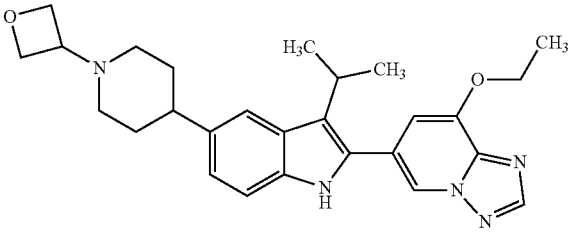
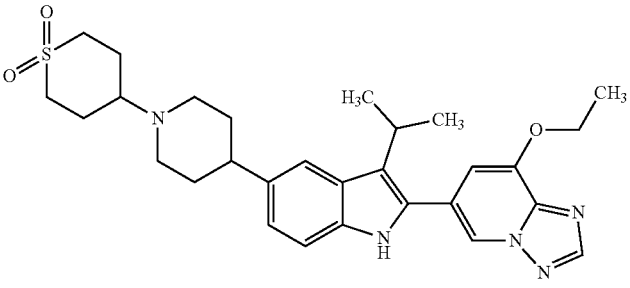
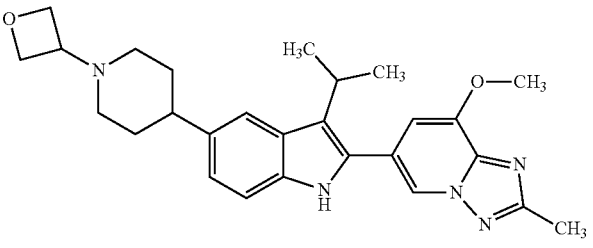
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
569	EX-5		460.1	1.73	E
570	EX-5		447.1	1.44	E
571	EX-132		488	1.66	E
572	EX-132		460.1	1.34	F
573	EX-132		536	1.9	E
574	EX-133		460.2	1.94	E

TABLE 14-continued

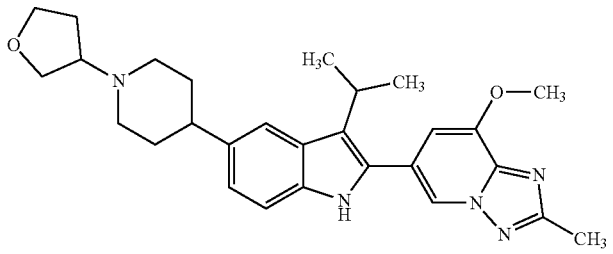
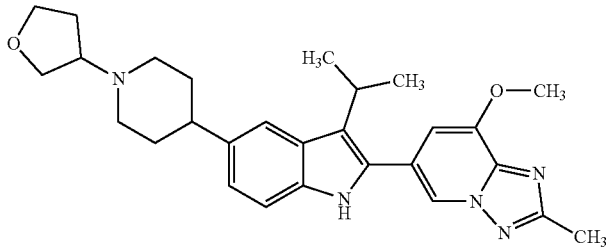
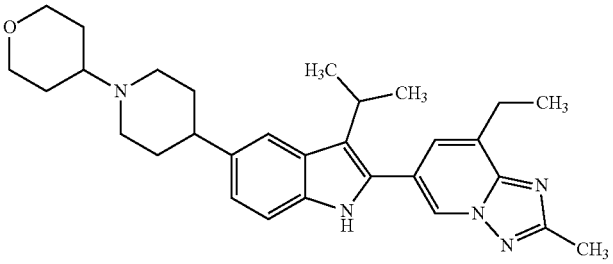
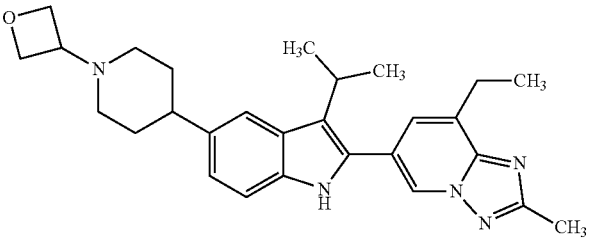
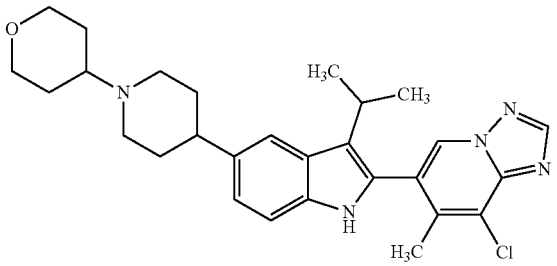
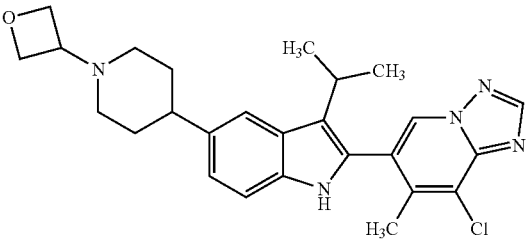
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
575	EX-133		474.2	1.92	D
576	EX-133		474.2	1.94	D
577	EX-137		486.2	1.8	E
578	EX-137		458.3	1.96	E
579	EX-119		492.2	1.7	E
580	EX-119		464.2	2.1	E

TABLE 14-continued

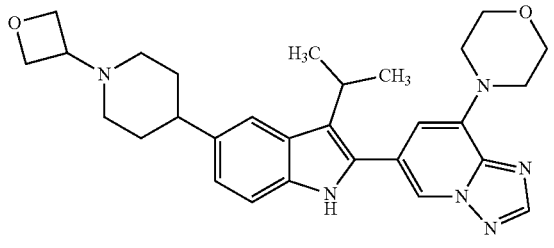
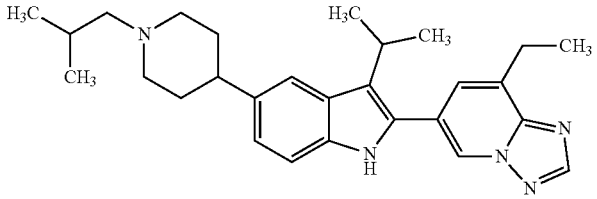
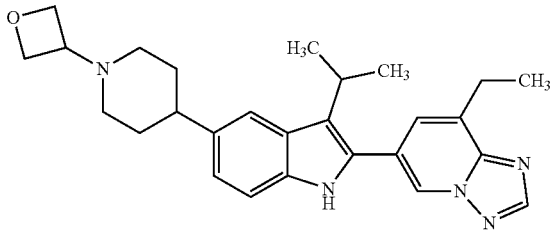
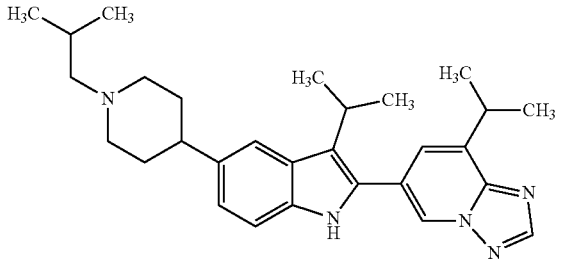
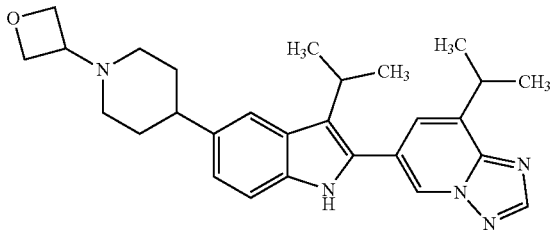
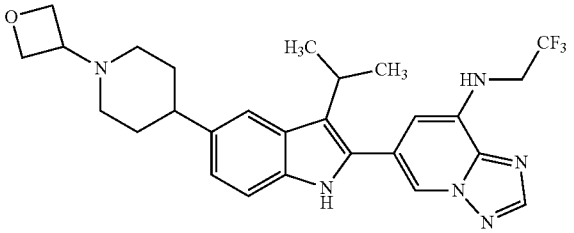
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
581	EX-143		501.3	2.01	E
582	EX-94		444.3	2.07	E
583	EX-94		444.3	2.08	E
584	EX-95		458.3	2.25	E
585	EX-95		458.2	2.24	E
586	EX-145		513.2	2.15	E

TABLE 14-continued

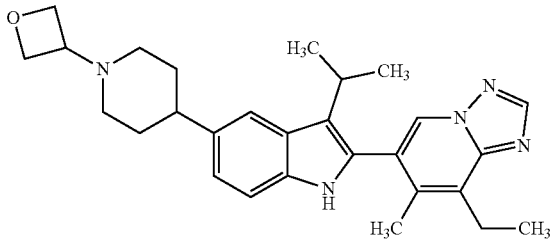
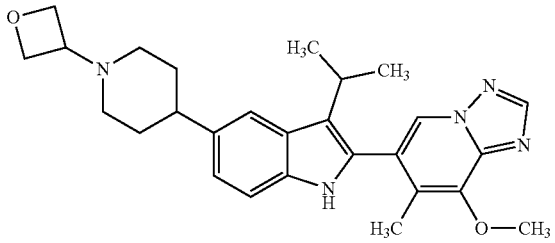
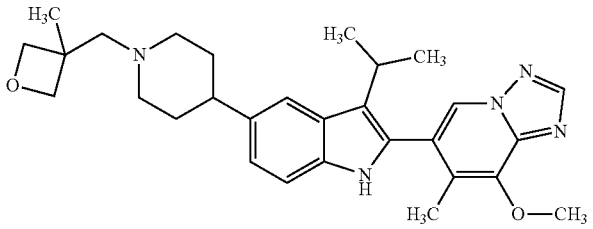
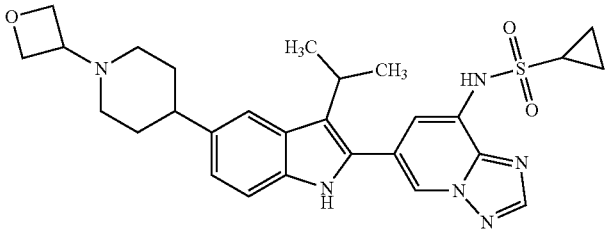
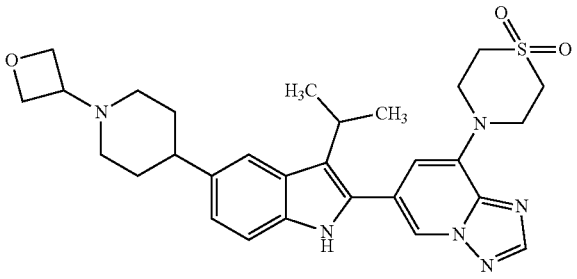
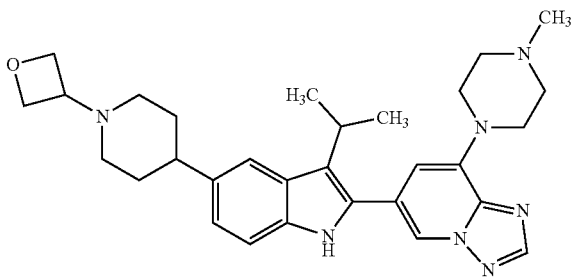
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
587	EX-98		458.3	2.11	E
588	EX-140		460.2	2.04	E
589	EX-140		488.3	2.05	E
590	EX-147		535.2	1.32	F
591	EX-148		549.2	1.87	E
592	EX-149		514.3	1.76	E

TABLE 14-continued

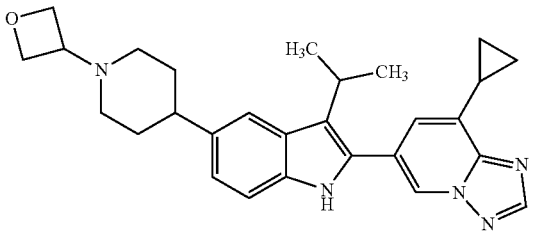
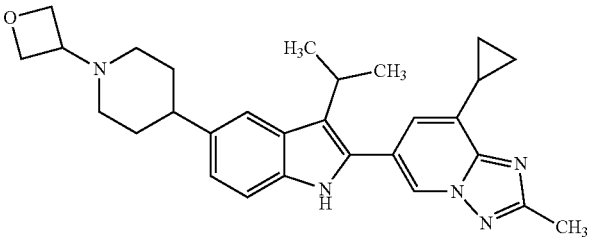
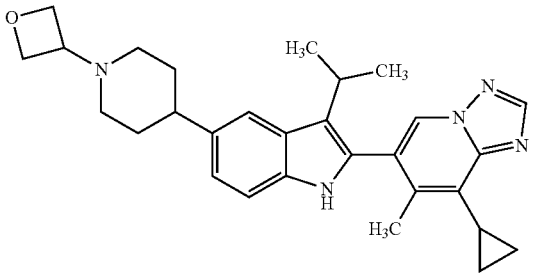
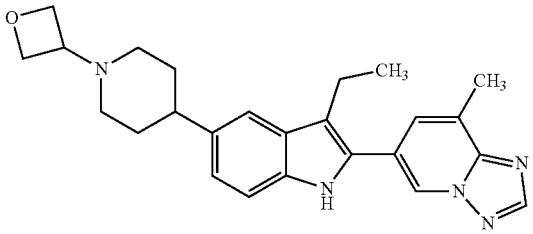
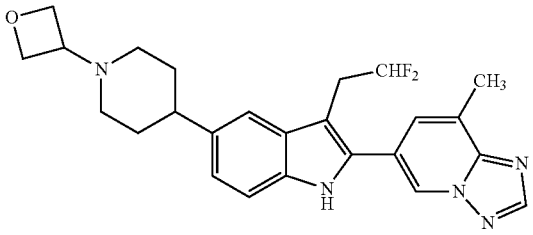
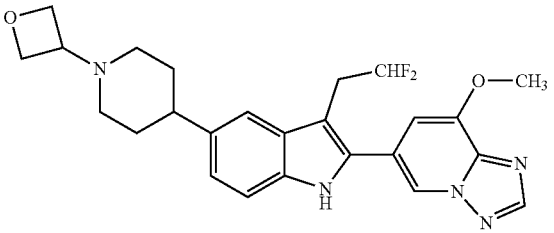
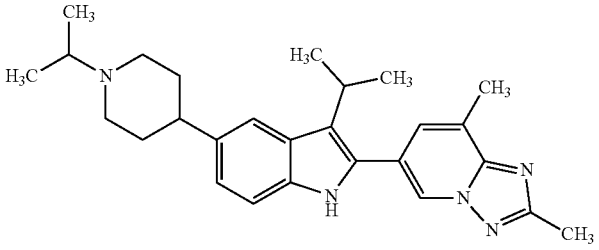
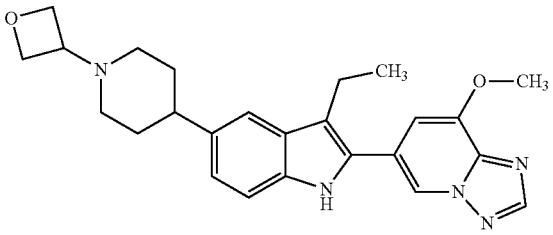
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
593	EX-151		456.3	1.88	E
594	EX-141		470.3	1.92	E
595	EX-152		470.1	2.21	E
596	EX-158		416.3	1.54	E
597	EX-161		452.2	1.67	E
598	EX-156		468.2	1.67	E

TABLE 14-continued

Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
599	EX-124		430.3	1.49	E
600	EX-157		432.3	1.49	E

The following examples were prepared according to the general methods disclosed in Examples 46 and 47.

TABLE 15

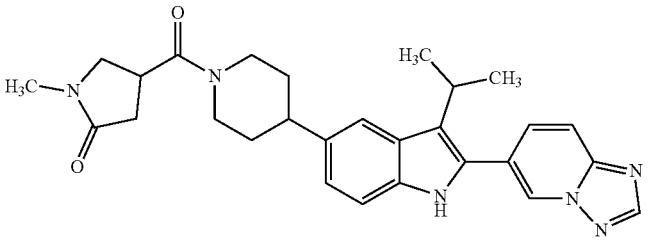
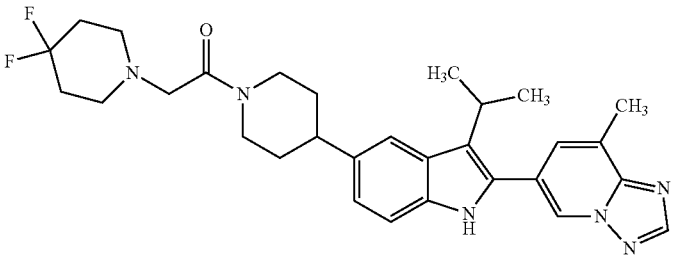
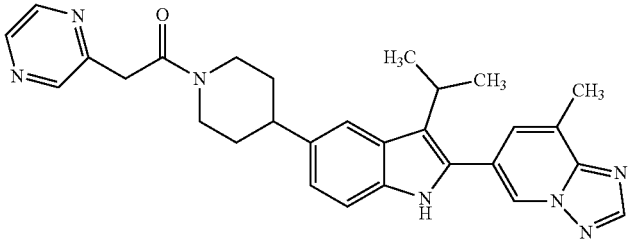
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
601	EX-1		484.9	1.43	QC-ACN-AA-XB
602	EX-2		535.2	1.95	QC-ACN-AA-XB
603	EX-2		494.2	1.65	QC-ACN-AA-XB

TABLE 15-continued

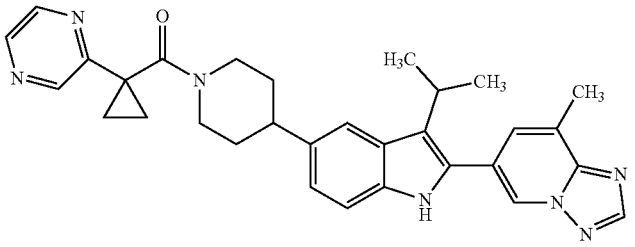
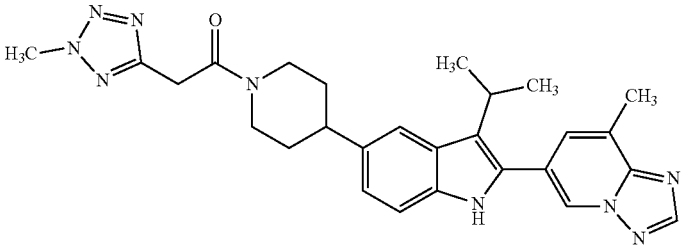
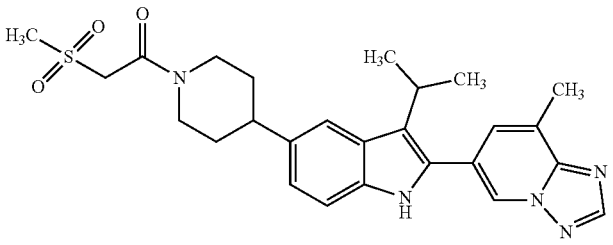
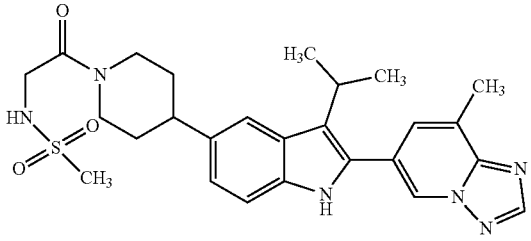
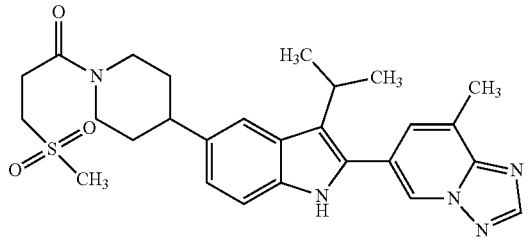
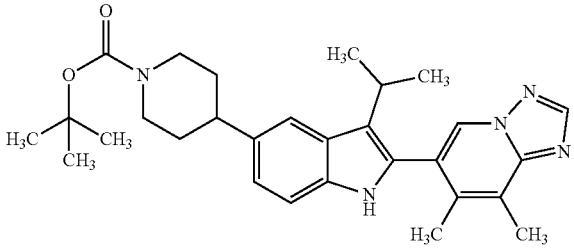
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
604	EX-2		520.3	1.78	QC-ACN-TFA-XB
605	EX-2		498.0	1.63	QC-ACN-TFA-XB
606	EX-2		494.2	1.68	QC-ACN-AA-XB
607	EX-2		509.4	1.66	QC-ACN-AA-XB
608	EX-2		508.2	1.64	QC-ACN-AA-XB
609	EX-4		488.0	2.39	QC-ACN-AA-XB

TABLE 15-continued

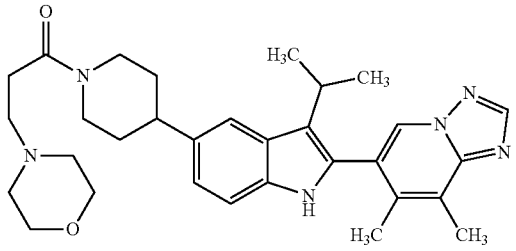
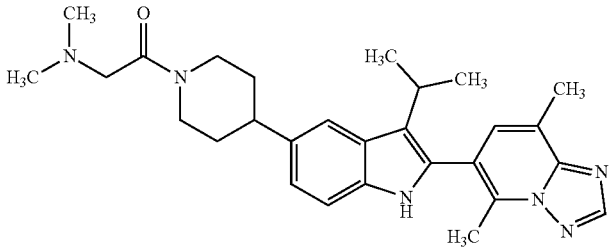
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
610	EX-4		529.4	1.63	QC-ACN-AA-XB
611	EX-110		473.4	1.37	QC-ACN-AA-XB

TABLE 16

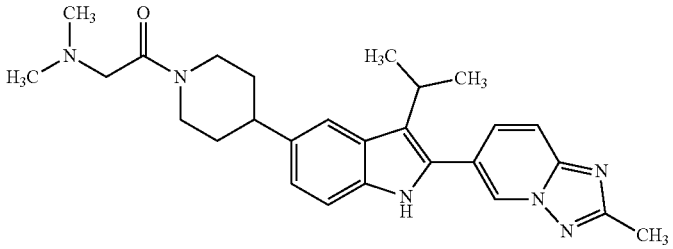
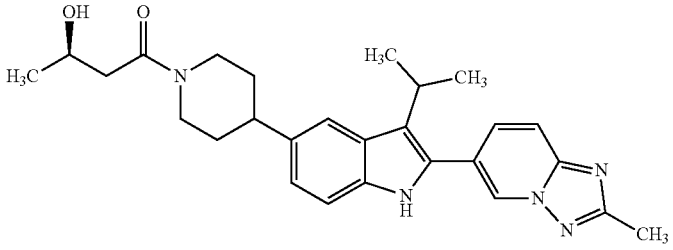
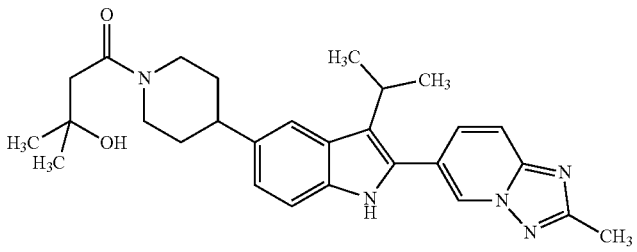
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
612	EX-122		459.3	2.76	D
613	EX-122		460.3	1.64	E
614	EX-122		474.3	1.83	E

TABLE 16-continued

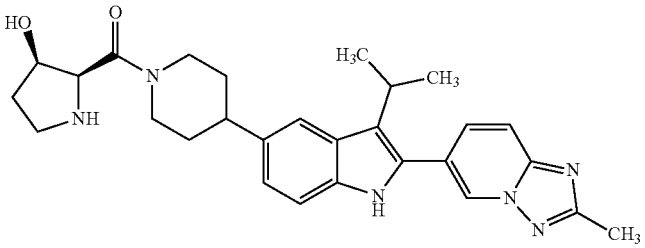
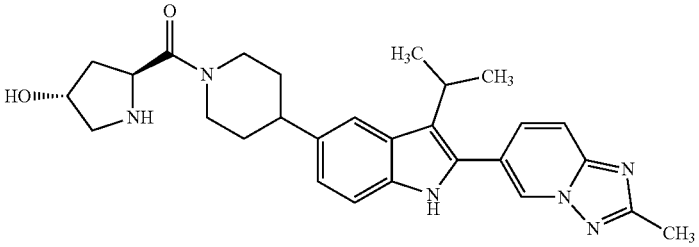
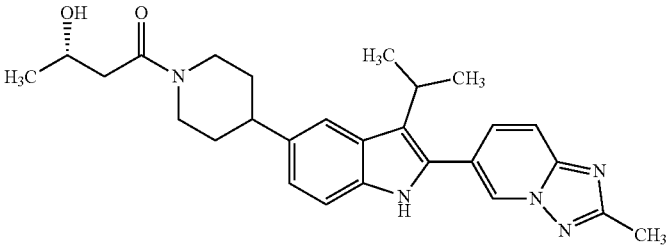
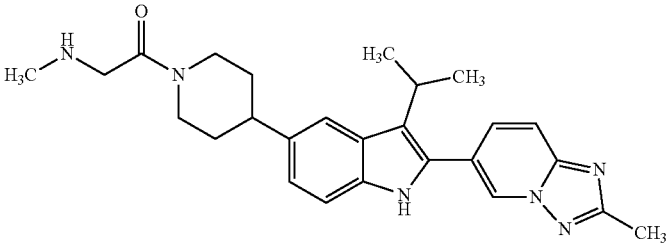
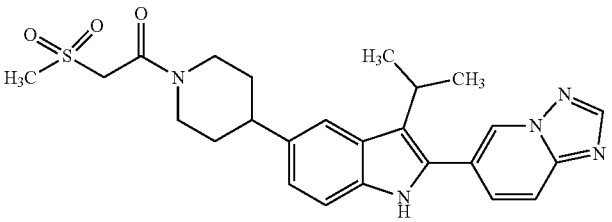
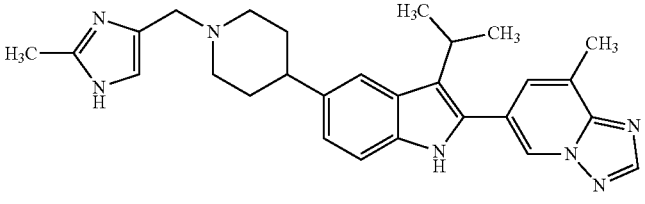
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
615	EX-122		487.3	1.36	E
616	EX-122		487.3	1.3	E
617	EX-122		460.3	1.67	E
618	EX-122		445.2	1.38	E
619	EX-1		480.2	1.67	E
620	EX-2		468.3	1.23	F

TABLE 16-continued

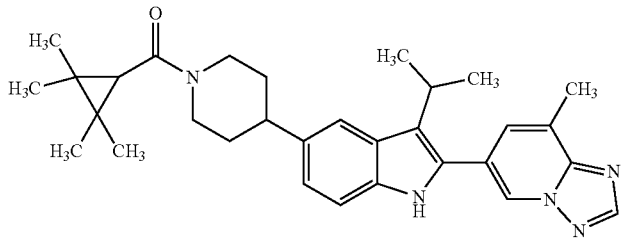
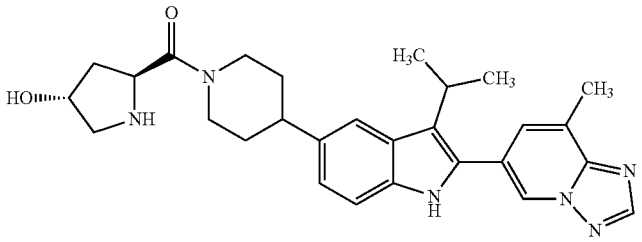
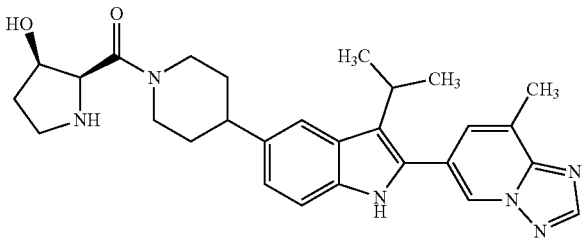
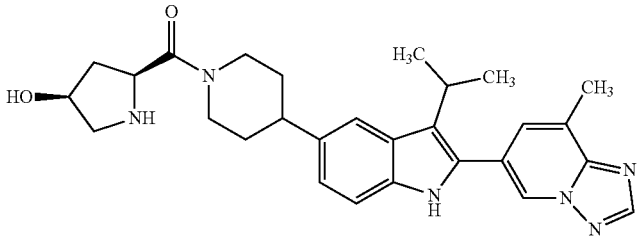
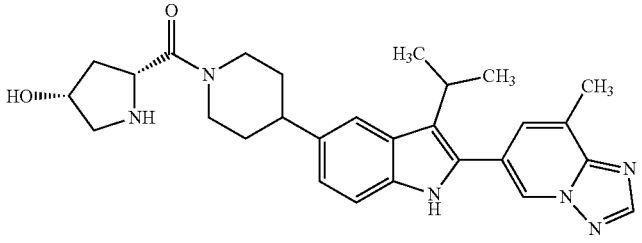
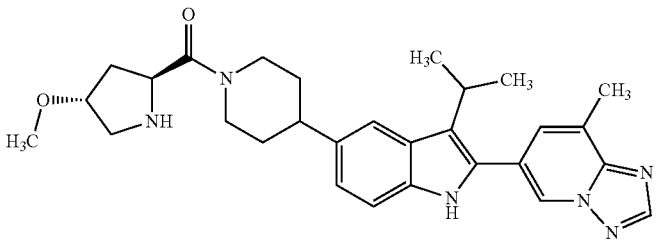
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
621	EX-2		498.5	2.29	E
622	EX-2		487.3	1.42	F
623	EX-2		487.3	1.4	E
624	EX-2		487.3	1.3	F
625	EX-2		487	1.4	E
626	EX-2		501.2	1.46	F

TABLE 16-continued

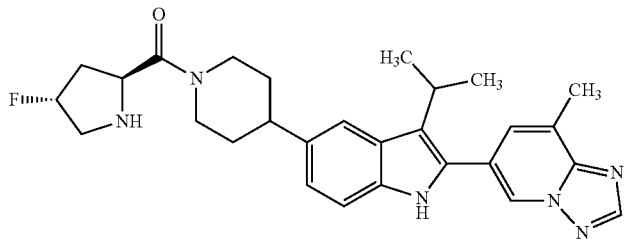
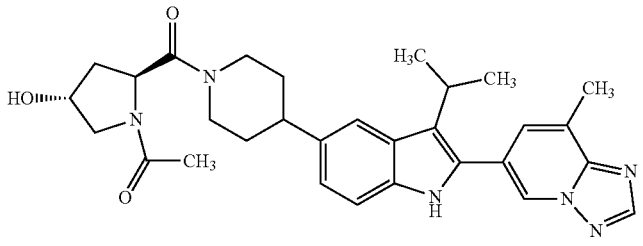
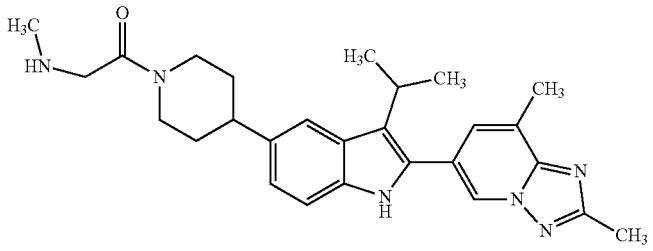
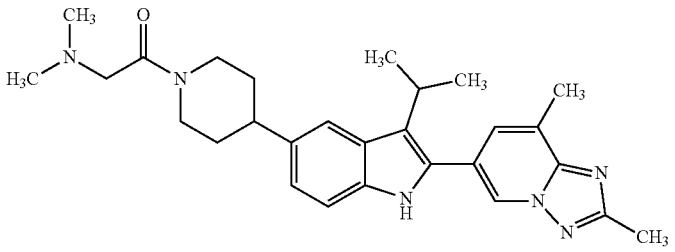
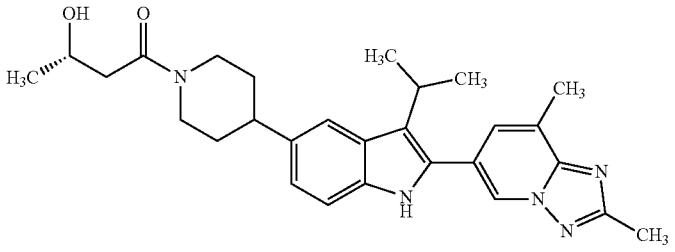
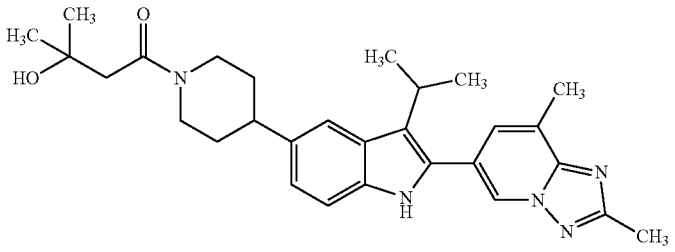
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
627	EX-2		489.1	1.74	E
628	EX-2		529.3	1.5	E
629	EX-124		459.3	1.95	D
630	EX-124		473.3	2.35	D
631	EX-124		474.3	1.85	E
632	EX-124		488.3	1.96	E

TABLE 16-continued

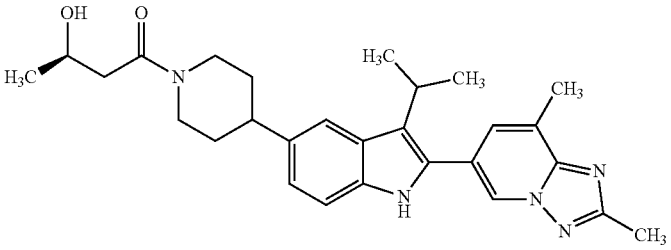
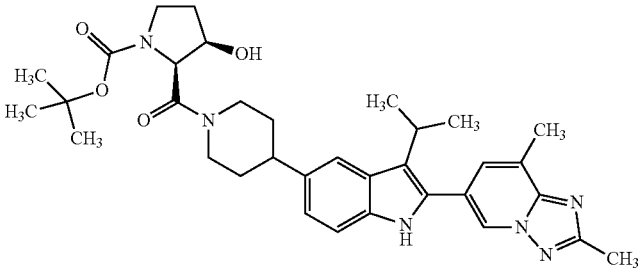
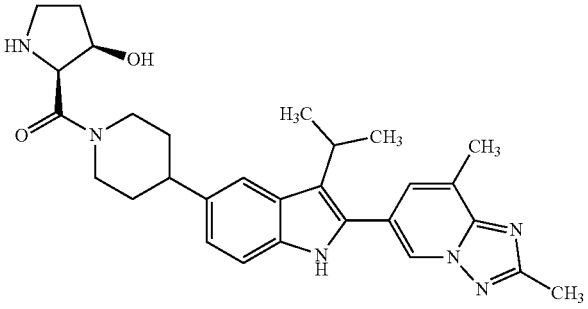
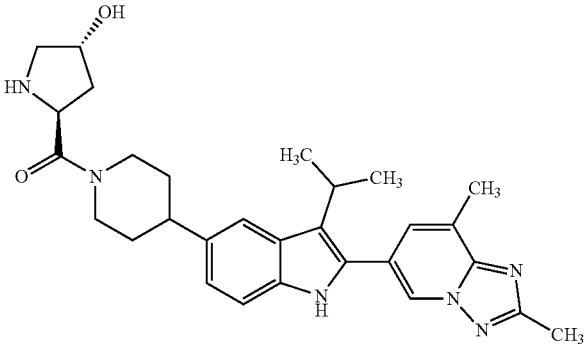
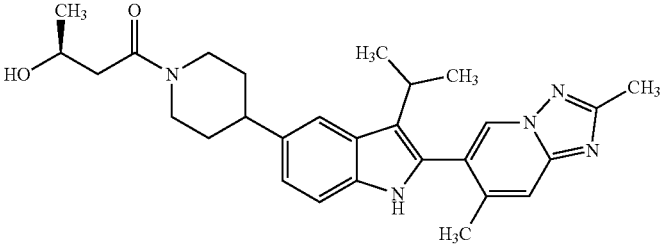
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
633	EX-124		474.3	1.82	E
634	EX-124		601	1.92	E
635	EX-124		501.3	1.36	E
636	EX-124		501.3	1.88	D
637	EX-125		474.3	1.71	E

TABLE 16-continued

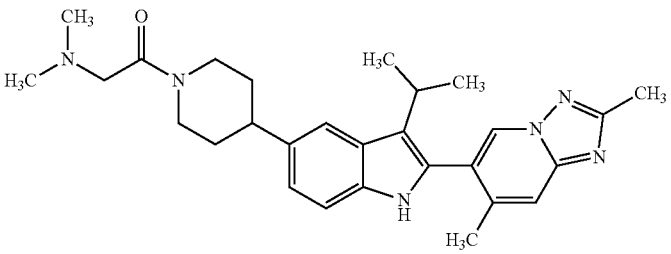
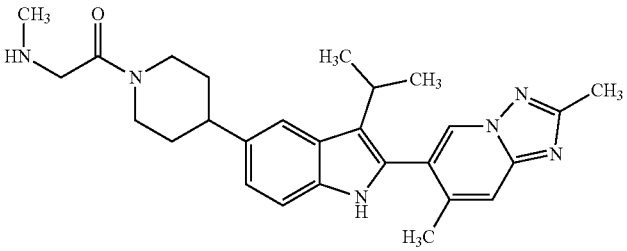
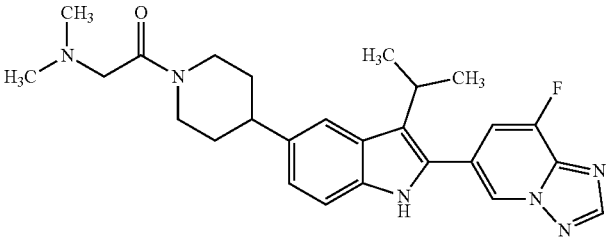
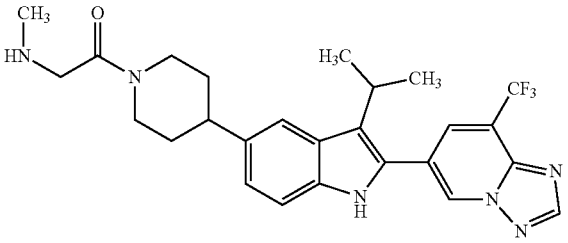
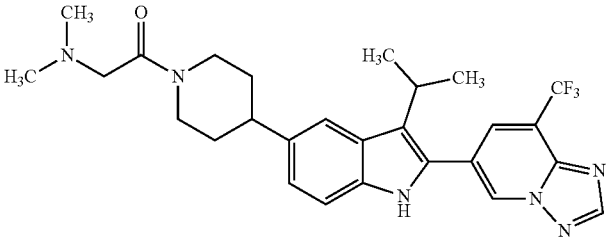
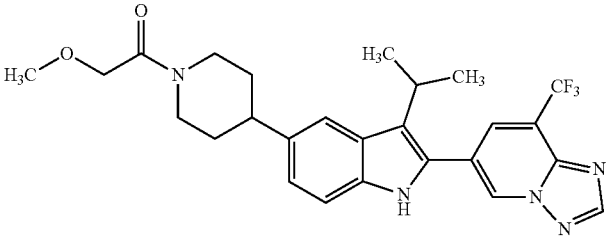
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
638	EX-125		473	1.54	E
639	EX-125		459	1.21	E
640	EX-112		463.4	1.06	F
641	EX-128		499.3	1.59	E
642	EX-128		513.3	1.75	E
643	EX-128		500.3	1.83	E

TABLE 16-continued

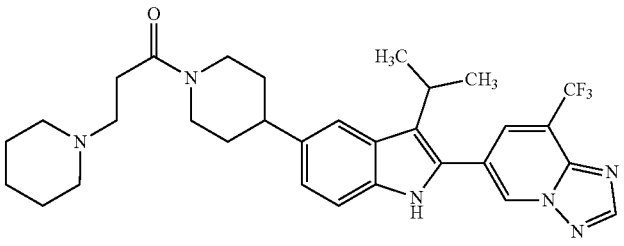
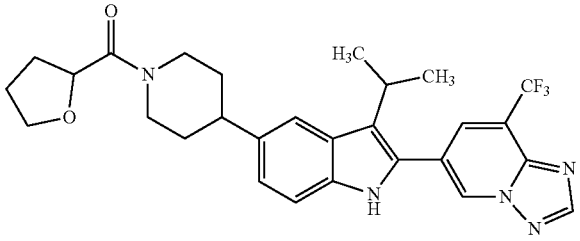
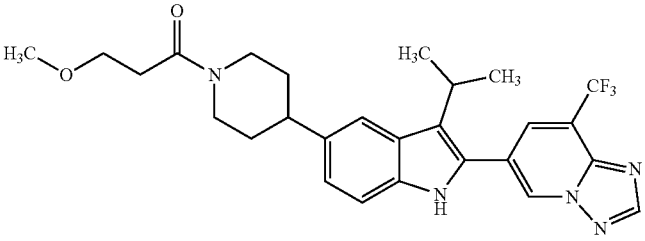
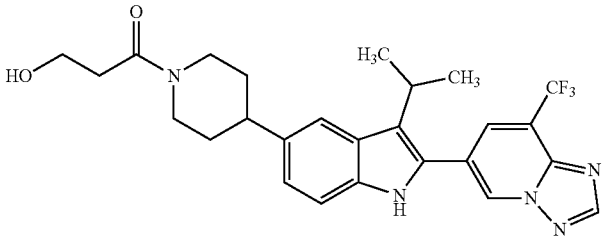
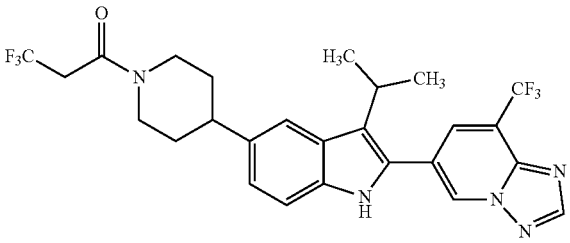
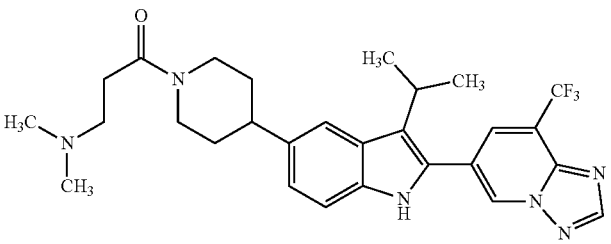
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
644	EX-128		567.4	1.7	E
645	EX-128		526.4	1.9	E
646	EX-128		514.4	1.88	E
647	EX-128		500.3	1.64	E
648	EX-128		538.3	2.07	E
649	EX-128		527.4	1.48	E

TABLE 16-continued

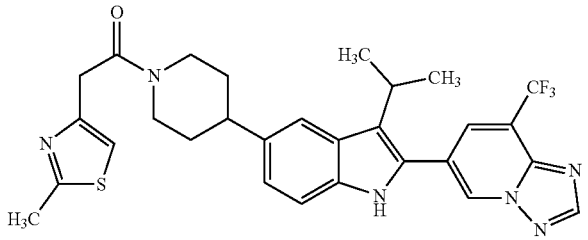
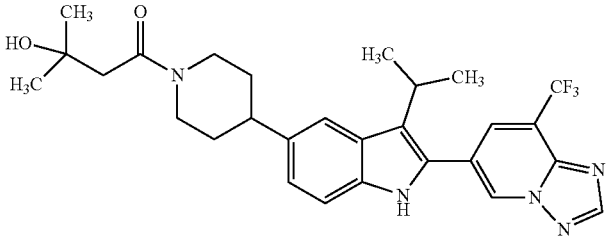
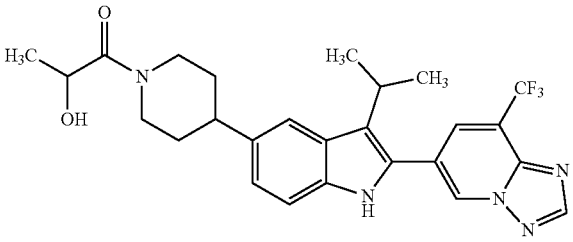
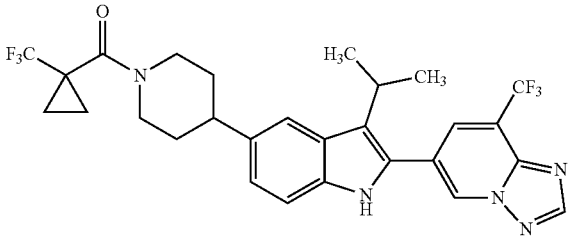
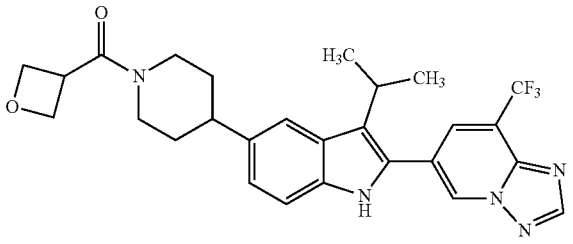
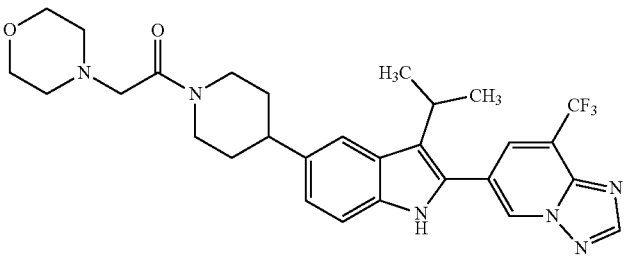
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
650	EX-128		567.3	1.95	E
651	EX-128		528.2	1.92	E
652	EX-128		500.2	1.77	E
653	EX-128		564.3	2.22	E
654	EX-128		512.3	1.68	E
655	EX-128		555.4	1.82	E

TABLE 16-continued

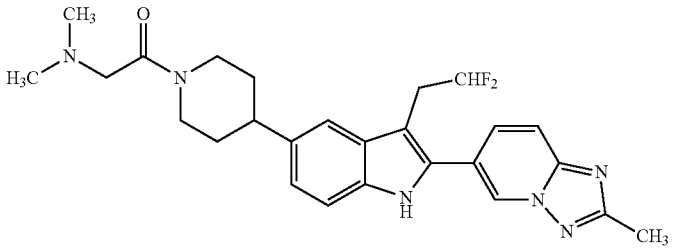
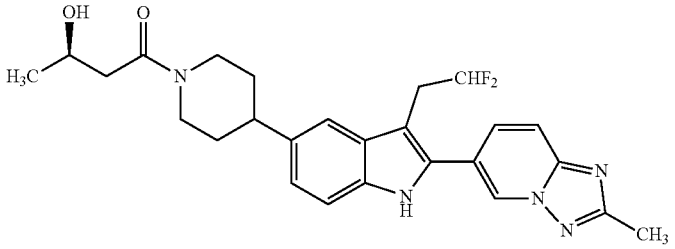
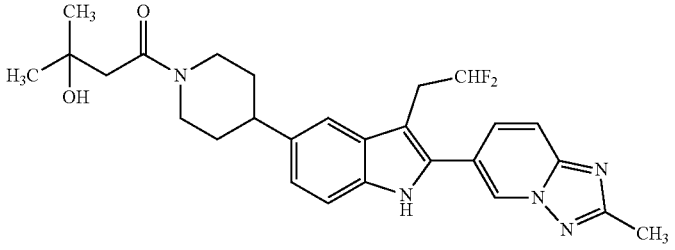
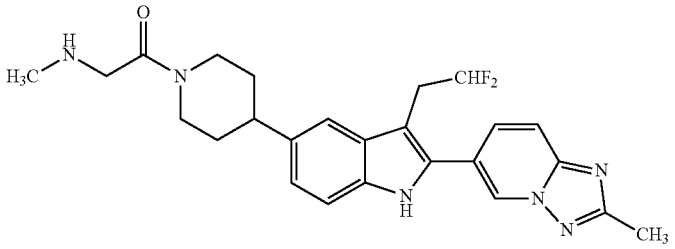
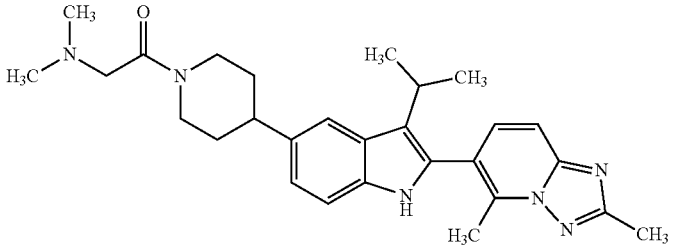
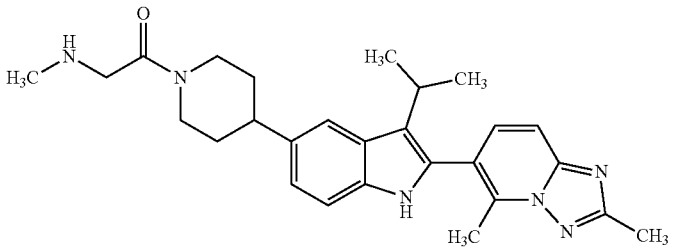
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
656	EX-142		481.3	1.49	E
657	EX-142		482.2	1.7	E
658	EX-142		496.2	1.72	E
659	EX-142		467.3	1.4	E
660	EX-155		473	1.6	E
661	EX-155		459	1.49	E

TABLE 16-continued

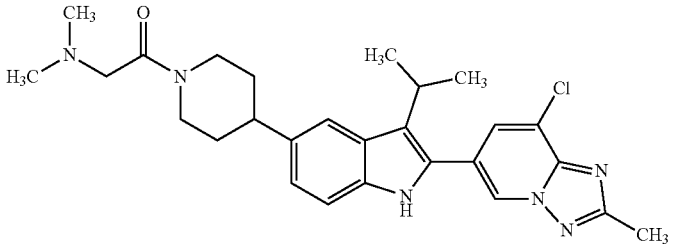
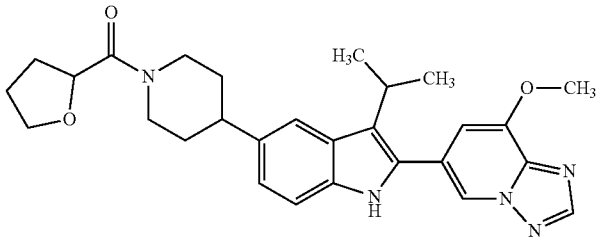
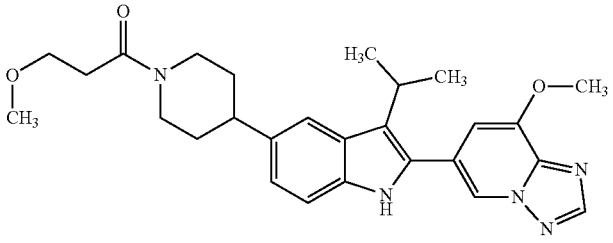
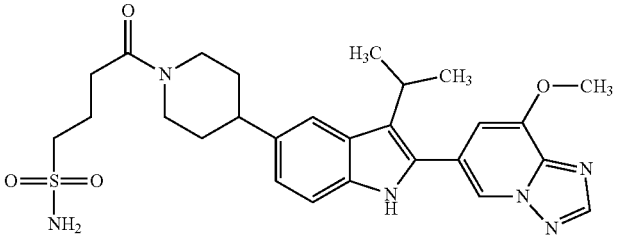
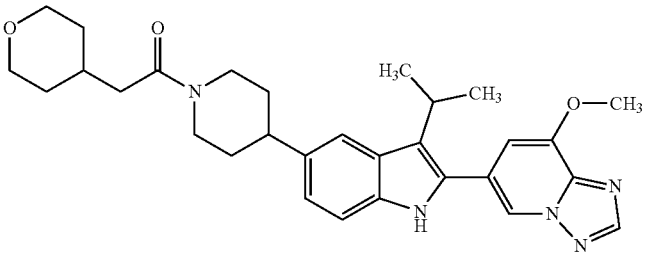
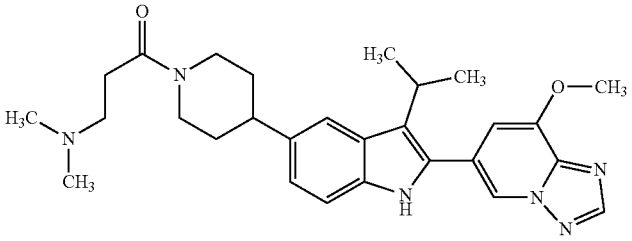
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
662	EX-96		493.3	1.46	E
663	EX-5		488.4	1.62	E
664	EX-5		476.4	1.59	E
665	EX-5		539.4	1.38	E
666	EX-5		516.4	1.69	E
667	EX-5		489.4	1.32	E

TABLE 16-continued

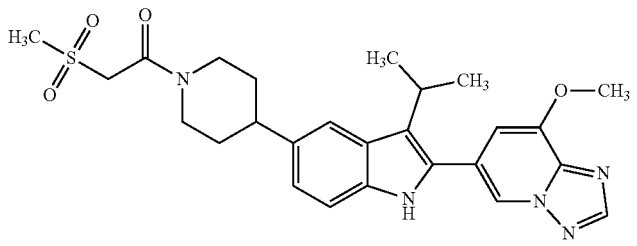
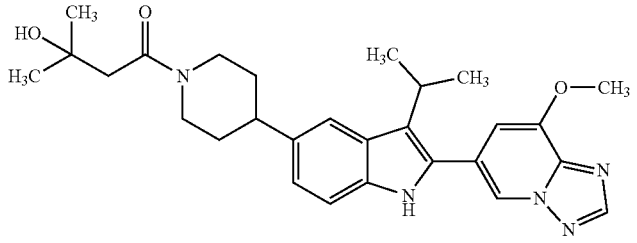
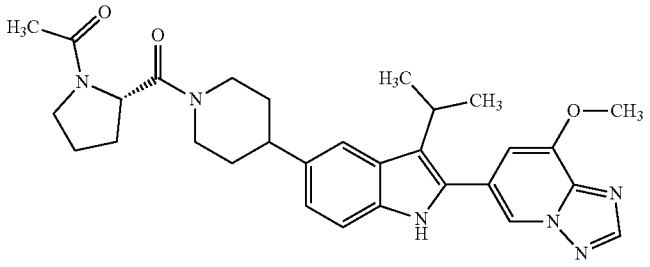
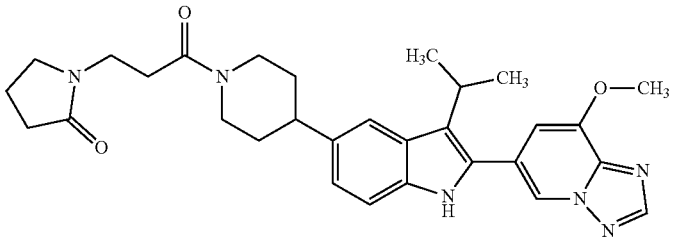
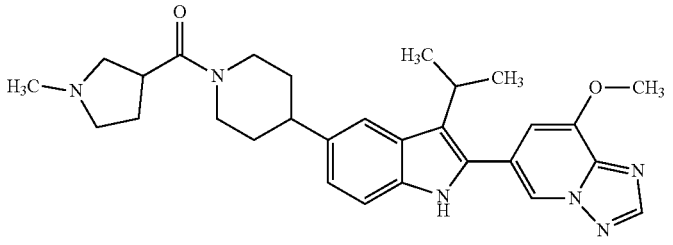
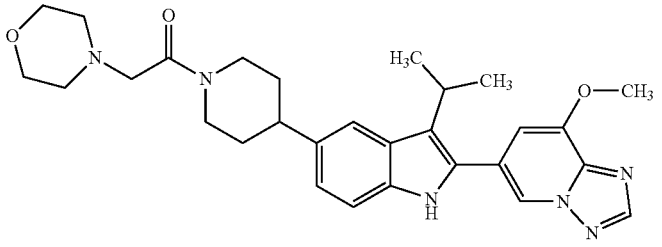
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
668	EX-5		510.3	1.43	E
669	EX-5		490.4	1.64	E
670	EX-5		529.4	1.46	E
671	EX-5		529.3	1.46	E
672	EX-5		501.1	1.16	E
673	EX-5		517.4	1.55	E

TABLE 16-continued

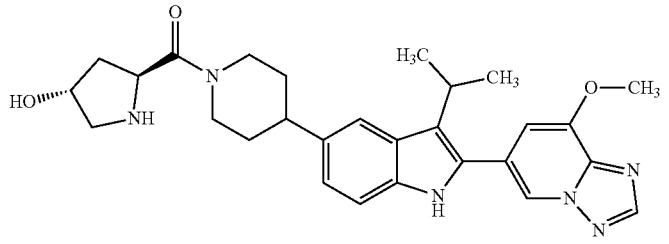
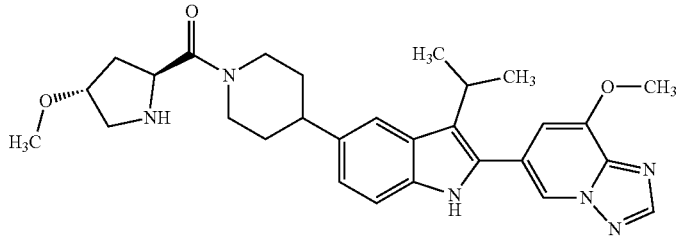
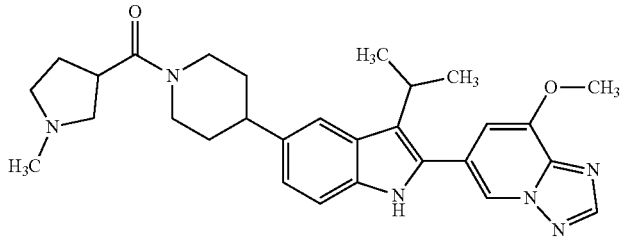
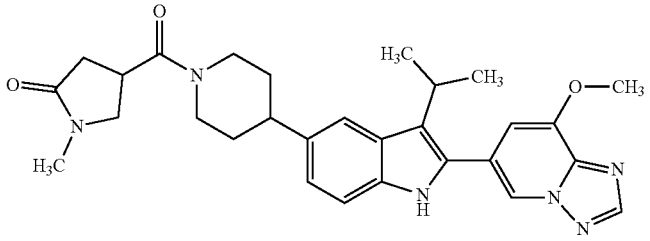
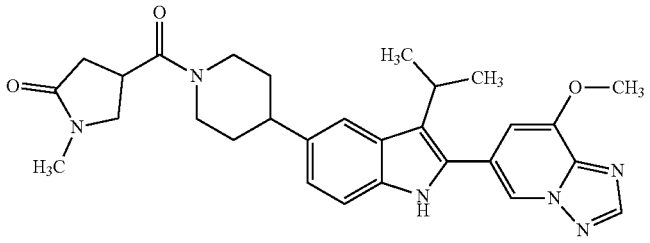
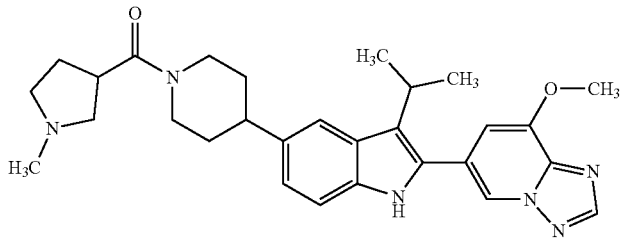
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
674	EX-5		503.1	1.37	E
675	EX-5		517.3	1.56	E
676	EX-5		501.3	1.43	E
677	EX-5		515.2	7.94	I
678	EX-5		515.2	7.95	I
679	EX-5		501.3	1.43	E

TABLE 16-continued

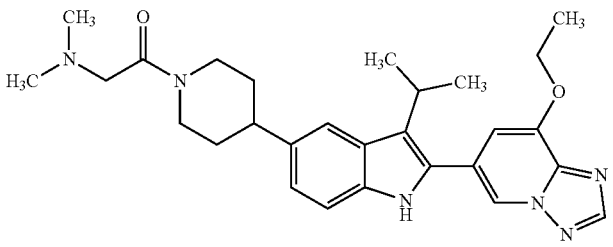
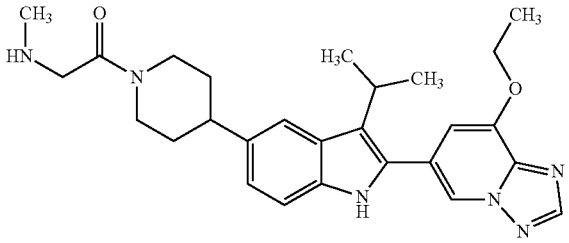
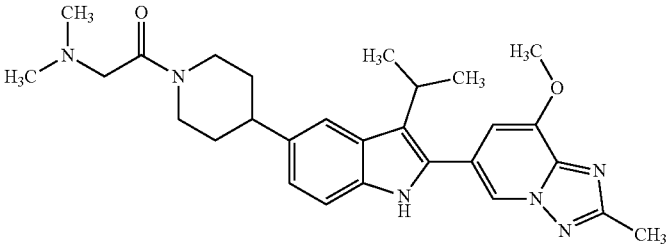
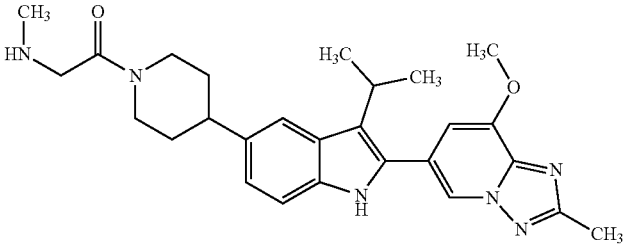
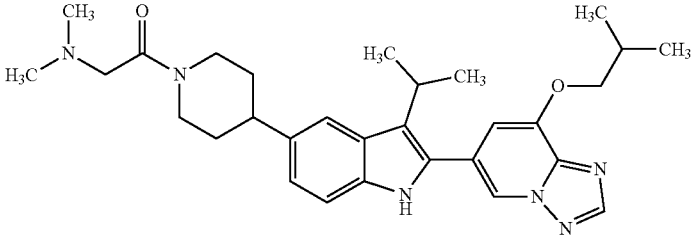
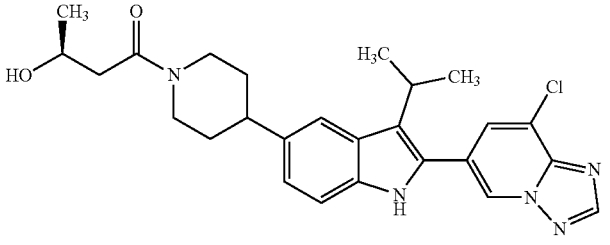
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
680	EX-132		489.1	1.62	E
681	EX-132		475.1	1.48	E
682	EX-133		489.3	1.6	E
683	EX-133		475.3	1.42	E
684	EX-136		517.4	1.65	E
685	EX-118		480.2	1.02	E

TABLE 16-continued

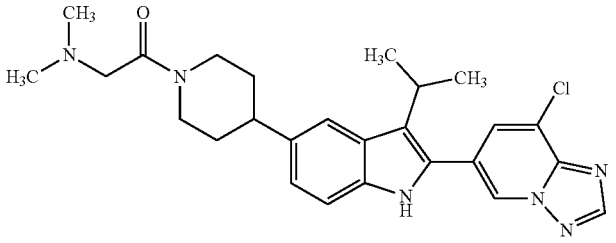
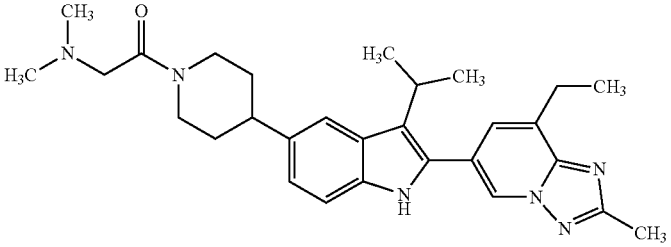
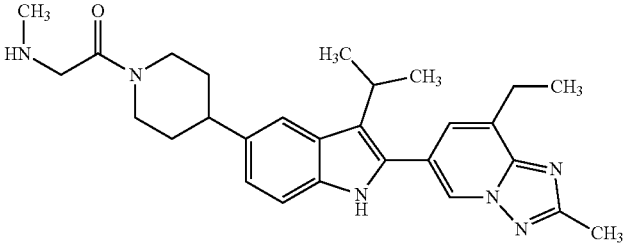
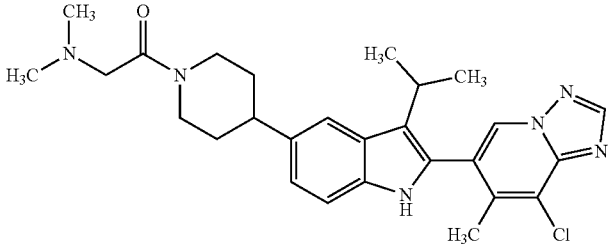
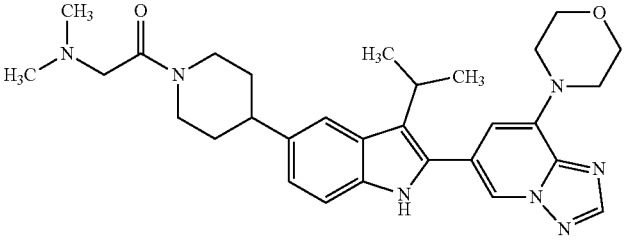
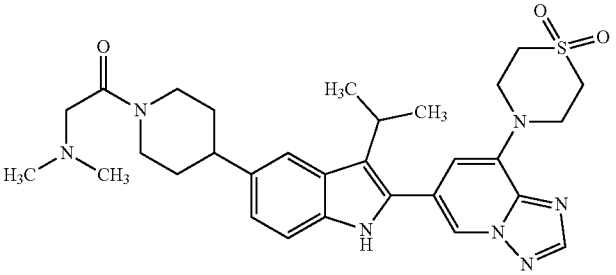
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
686	EX-118		479.2	1.6	E
687	EX-137		487.4	1.64	E
688	EX-137		473.3	1.59	E
689	EX-119		493.1	1.68	E
690	EX-143		530.4	1.4	E
691	EX-148		578.3	1.52	E

TABLE 16-continued

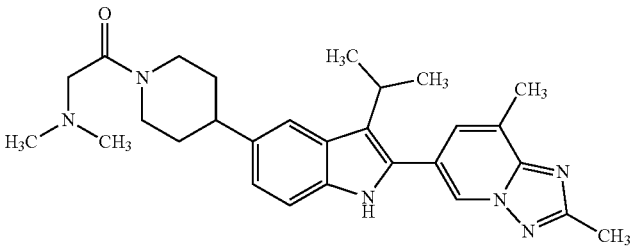
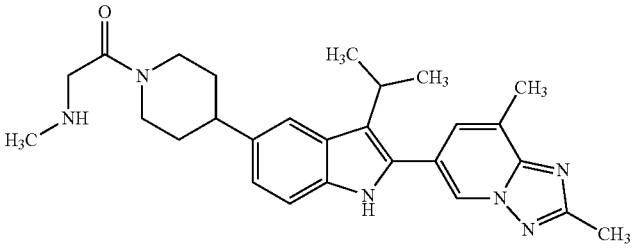
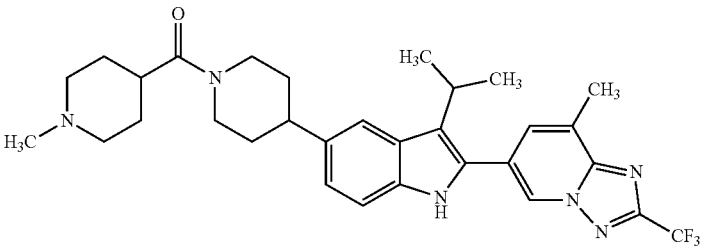
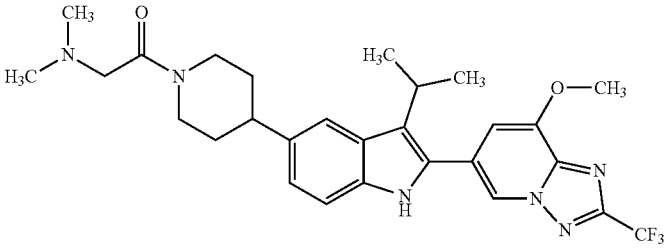
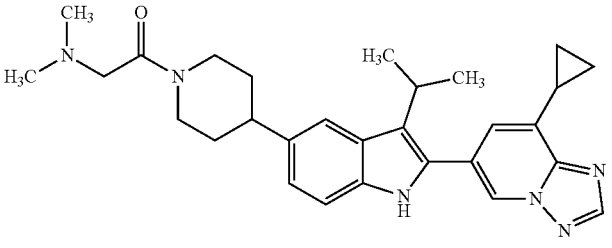
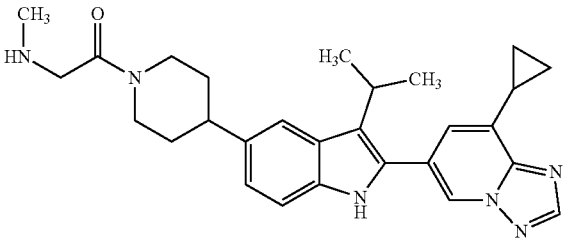
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
692	EX-120		527.3	2.08	E
693	EX-120		513.3	1.93	E
694	EX-120		567.3	1.97	E
695	EX-154		543.2	1.98	E
696	EX-151		485.3	1.5	E
697	EX-151		471.2	1.56	E

TABLE 16-continued

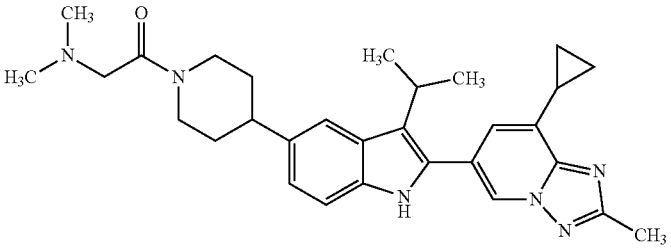
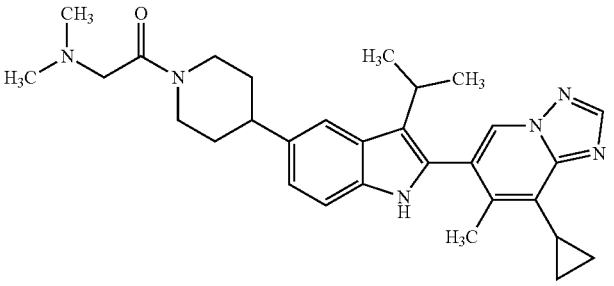
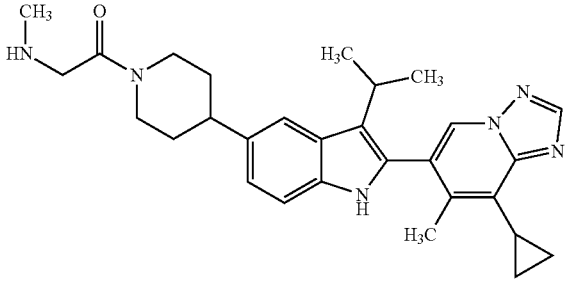
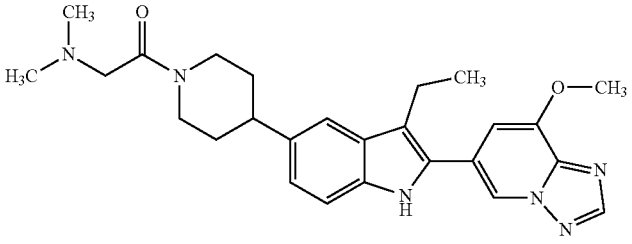
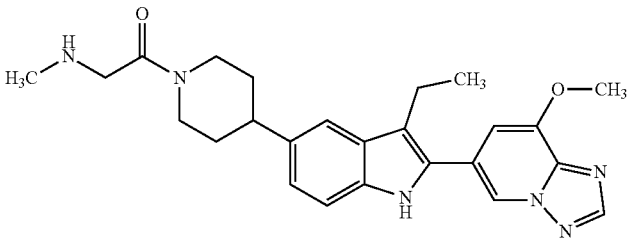
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
698	EX-141		499.2	1.75	E
699	EX-152		499.2	1.77	E
700	EX-152		485.2	1.62	E
701	EX-157		461.3	1.19	E
702	EX-157		447.3	1.08	E

TABLE 16-continued

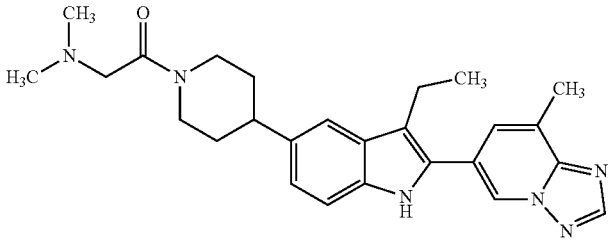
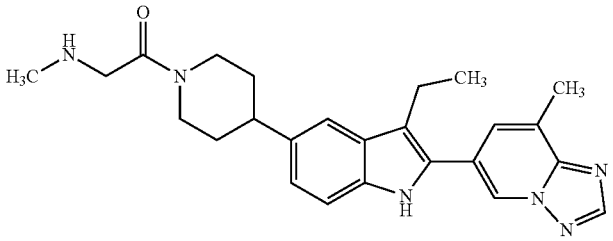
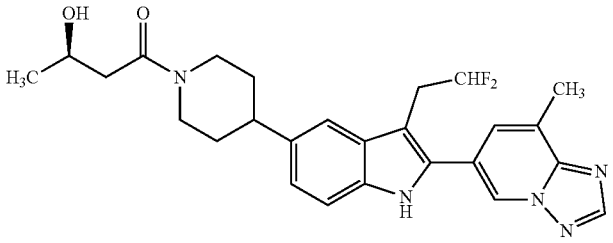
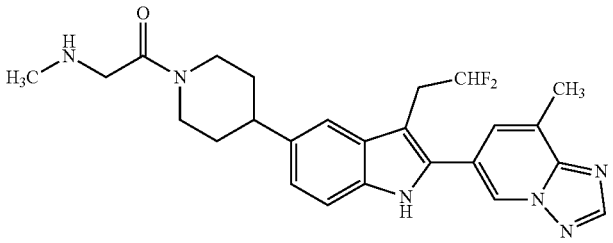
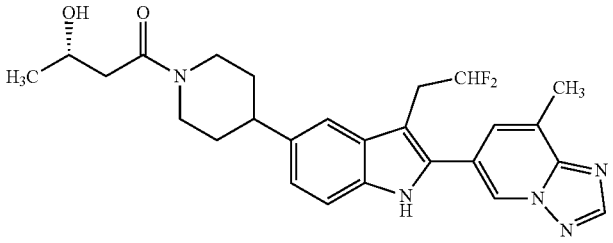
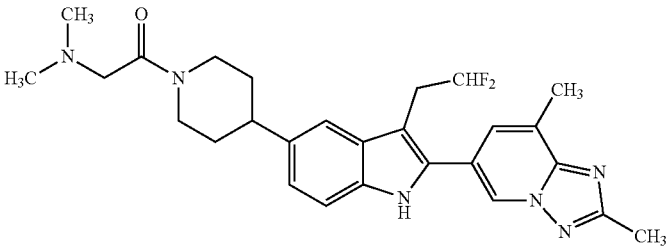
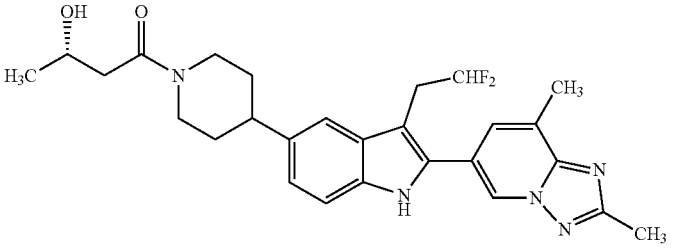
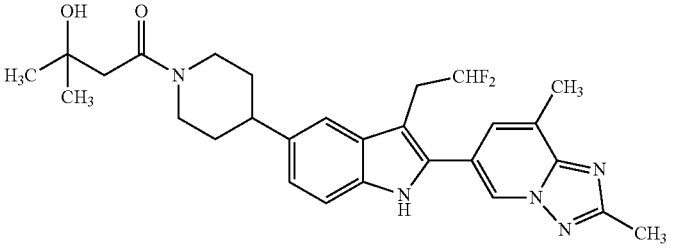
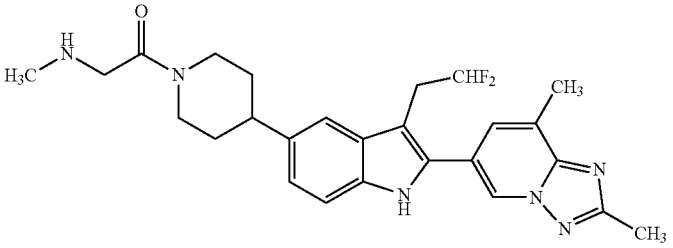
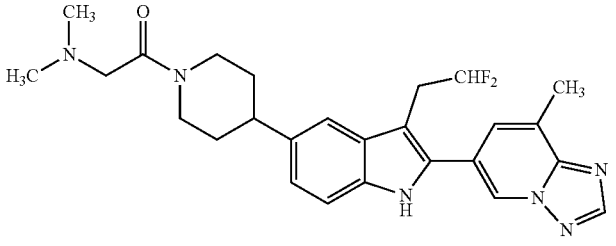
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
703	EX-158		445.3	1.24	E
704	EX-158		431.3	1.12	E
705	EX-161		482.2	1.57	E
706	EX-161		467.2	1.27	E
707	EX-161		482.2	1.58	E
708	EX-161		495.2	1.48	E

TABLE 16-continued

Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
709	EX-161		496.2	1.68	E
710	EX-161		510.3	1.82	E
711	EX-161		481.3	1.37	E
712	EX-161		481.2	1.41	E

The following examples were prepared according to the general process disclosed in Example 68.

TABLE 17

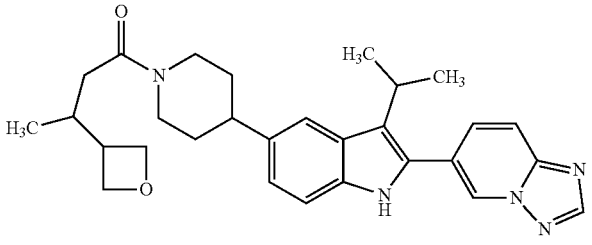
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
713	EX-1		487.2	1.17	QC-ACN-TFA-XB

TABLE 17-continued

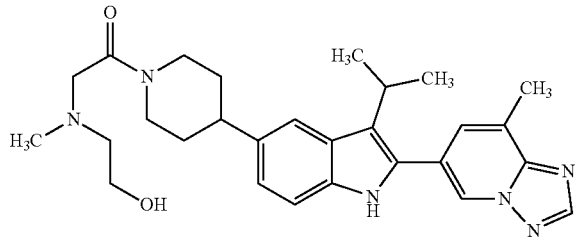
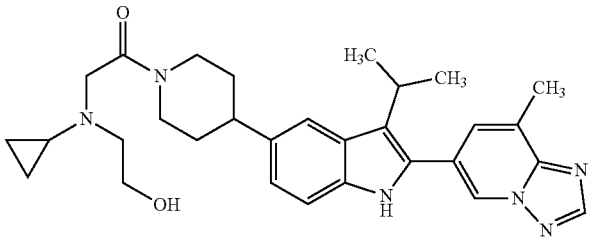
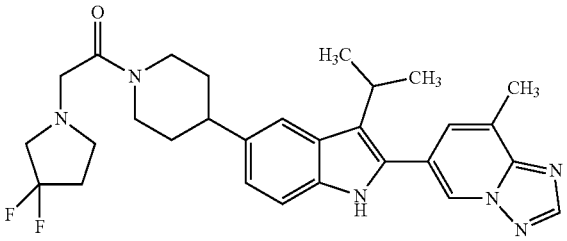
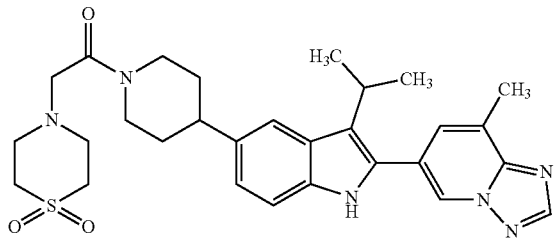
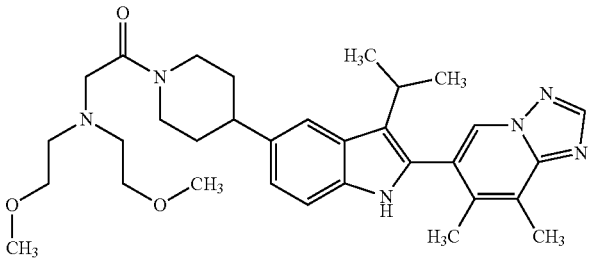
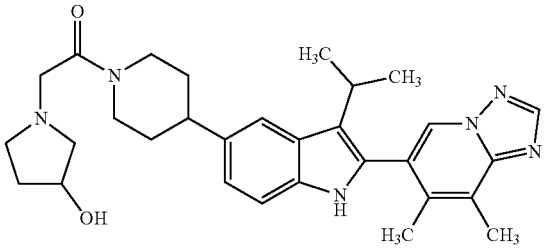
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
714	EX-2		489.1	1.26	QC-ACN-TFA-XB
715	EX-2		515.2	2.36	QC-ACN-AA-XB
716	EX-2		520.9	2.55	QC-ACN-AA-XB
717	EX-2		549.1	2.08	QC-ACN-AA-XB
718	EX-4		561.4	1.46	QC-ACN-TFA-XB
719	EX-4		258.1	1.22	QC-ACN-TFA-XB

TABLE 17-continued

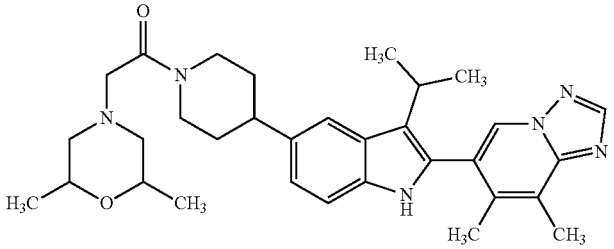
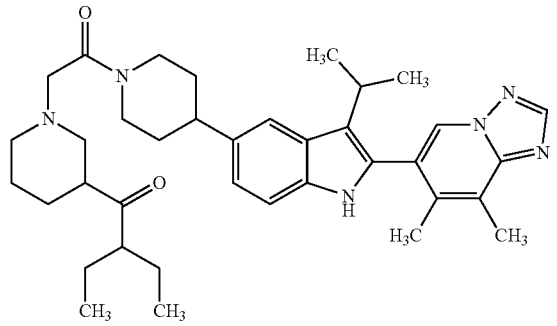
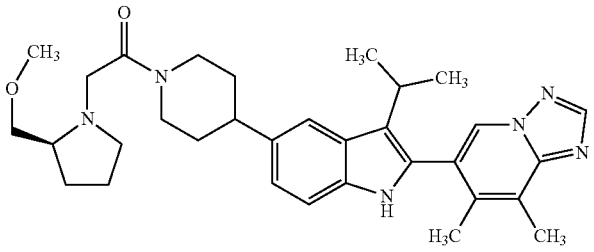
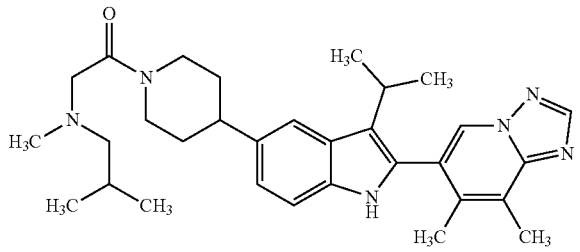
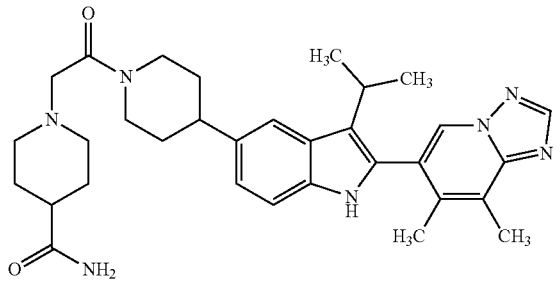
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
720	EX-4		543.1	1.97	QC-ACN-AA-XB
721	EX-4		612.2	1.83	QC-ACN-AA-XB
722	EX-4		543.3	1.78	QC-ACN-AA-XB
723	EX-4		258.4	1.44	QC-ACN-TFA-XB
724	EX-4		556.3	1.2	QC-ACN-TFA-XB

TABLE 17-continued

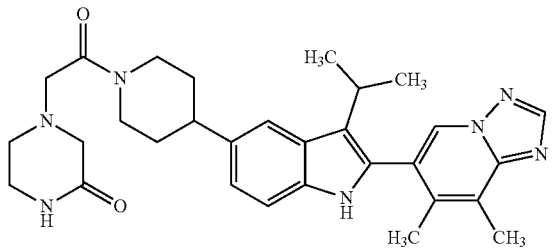
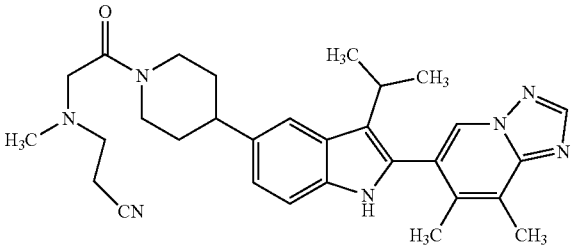
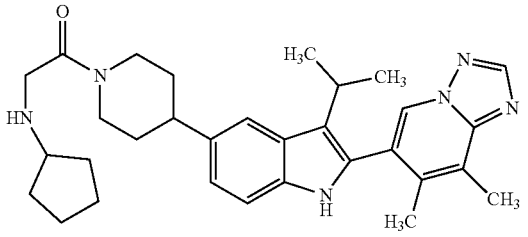
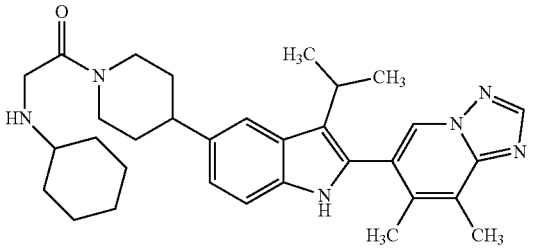
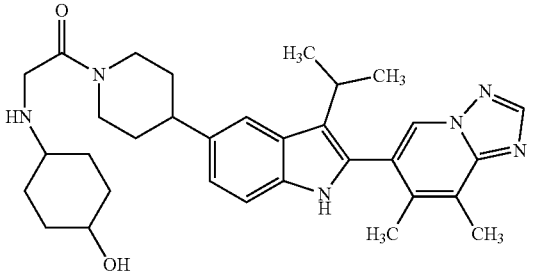
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
725	EX-4		528.2	1.68	QC-ACN-AA-XB
726	EX-4		512.1	1.87	QC-ACN-AA-XB
727	EX-4		513.2	1.53	QC-ACN-TFA-XB
728	EX-4		527.2	1.77	QC-ACN-AA-XB
729	EX-4		543.3	1.39	QC-ACN-AA-XB

TABLE 17-continued

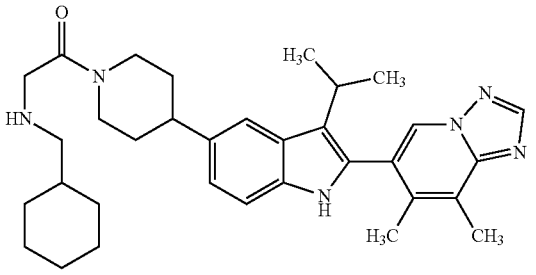
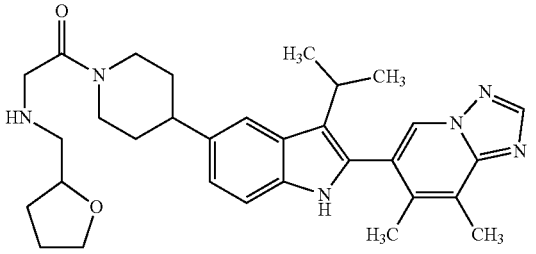
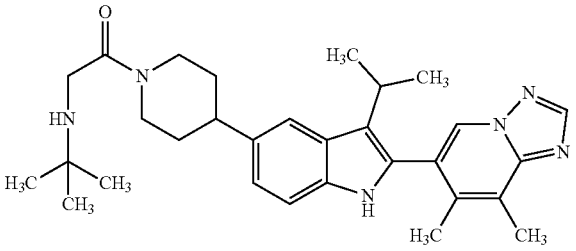
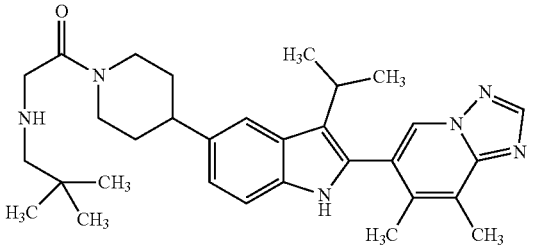
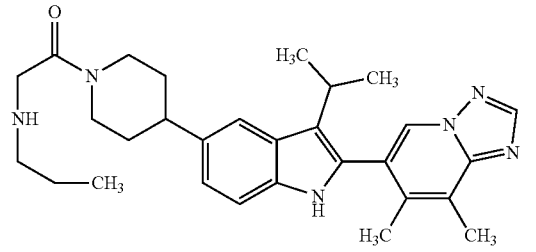
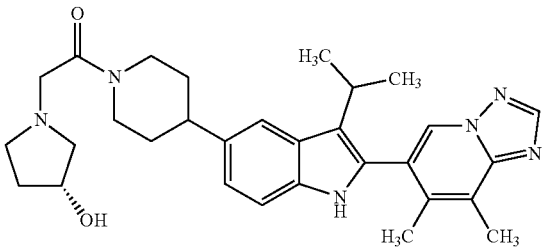
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
730	EX-4		271.4	1.59	QC-ACN-TFA-XB
731	EX-4		529.3	1.6	QC-ACN-AA-XB
732	EX-4		501.2	1.49	QC-ACN-AA-XB
733	EX-4		515.3	1.84	QC-ACN-AA-XB
734	EX-4		244.2	1.33	QC-ACN-TFA-XB
735	EX-4		515.1	1.41	QC-ACN-TFA-XB

TABLE 17-continued

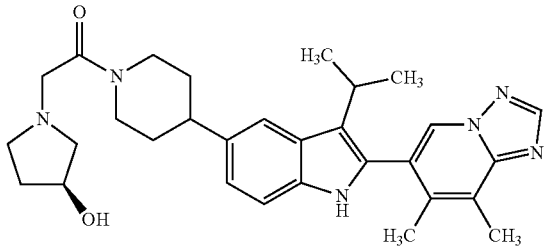
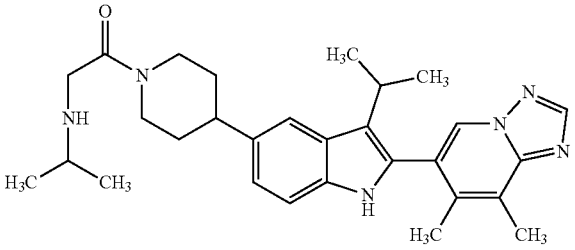
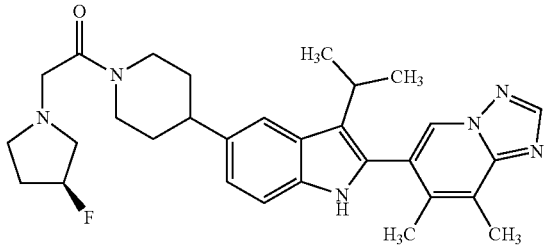
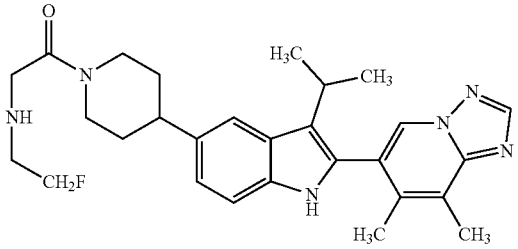
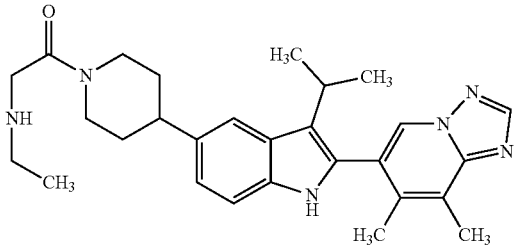
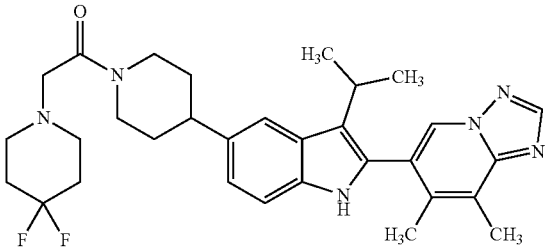
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
736	EX-4		515.1	1.54	QC-ACN-AA-XB
737	EX-4		487.1	1.54	QC-ACN-AA-XB
738	EX-4		259.4	1.29	QC-ACN-TFA-XB
739	EX-4		246.4	1.24	QC-ACN-TFA-XB
740	EX-4		473.2	1.37	QC-ACN-AA-XB
741	EX-4		549.0	2.01	QC-ACN-AA-XB

TABLE 17-continued

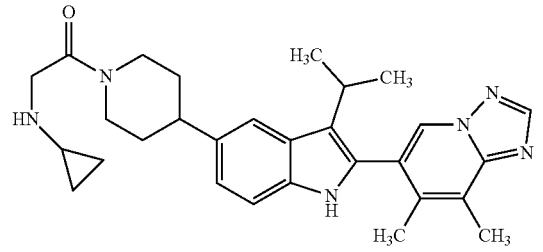
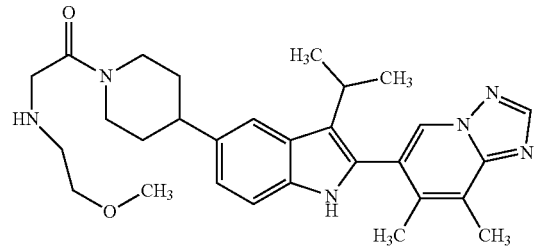
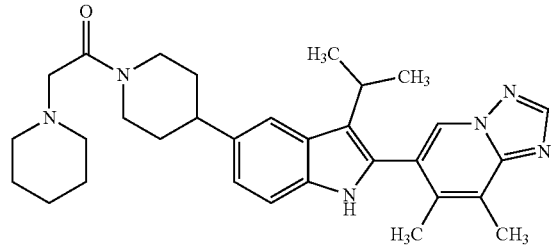
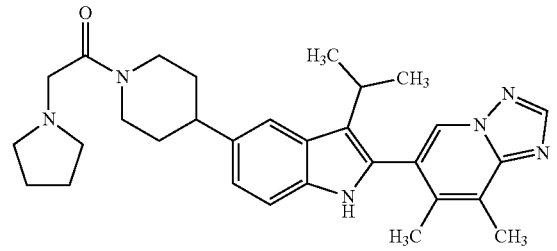
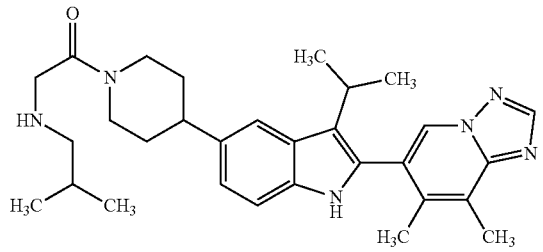
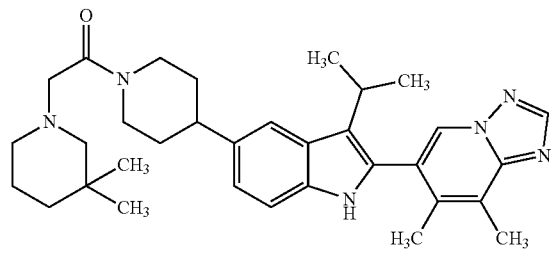
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
742	EX-4		485.1	1.76	QC-ACN-AA-XB
743	EX-4		503.0	1.57	QC-ACN-AA-XB
744	EX-4		513.4	1.73	QC-ACN-AA-XB
745	EX-4		250.3	1.3	QC-ACN-TFA-XB
746	EX-4		501.4	1.41	QC-ACN-TFA-XB
747	EX-4		541.1	2.28	QC-ACN-AA-XB

TABLE 17-continued

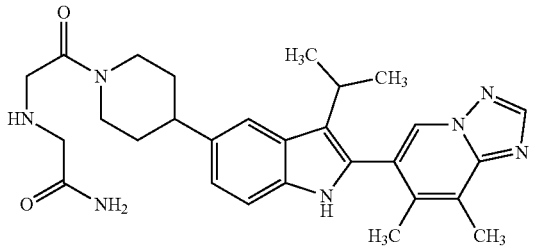
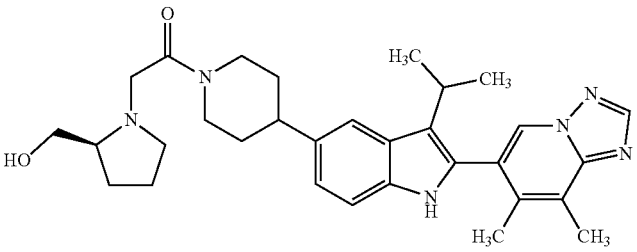
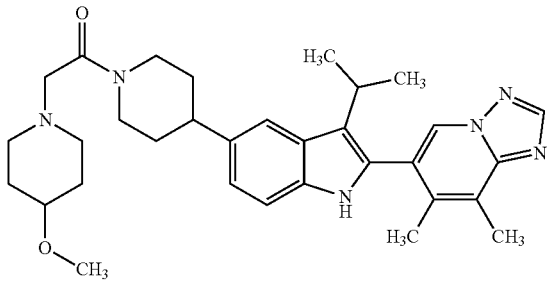
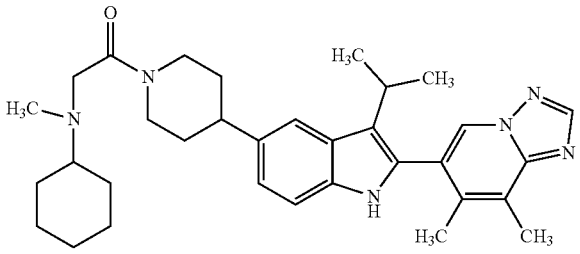
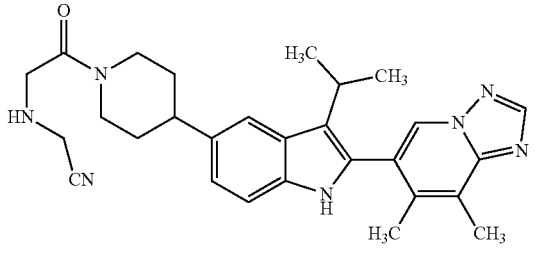
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
748	EX-4		502.4	1.37	QC-ACN-TFA-XB
749	EX-4		529.0	1.34	QC-ACN-TFA-XB
750	EX-4		543.1	1.76	QC-ACN-AA-XB
751	EX-4		541.14 541.14		QC-ACN-TFA-XB
752	EX-4		484.4	1.47	QC-ACN-TFA-XB

TABLE 17-continued

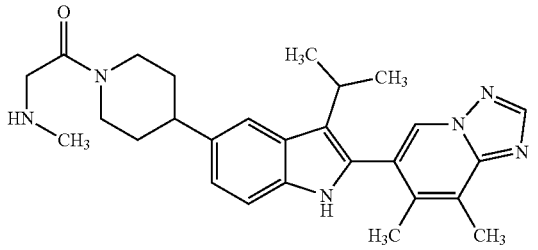
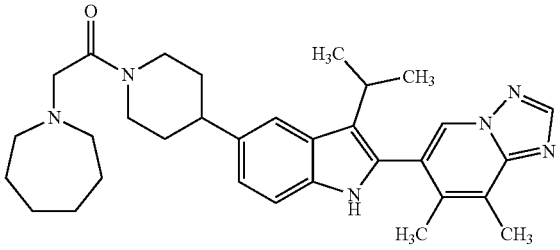
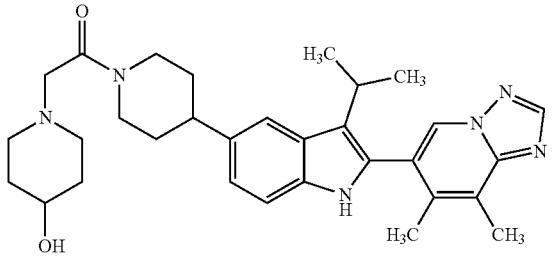
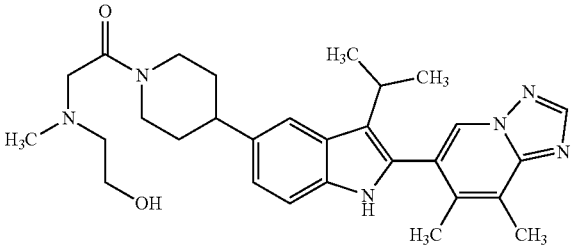
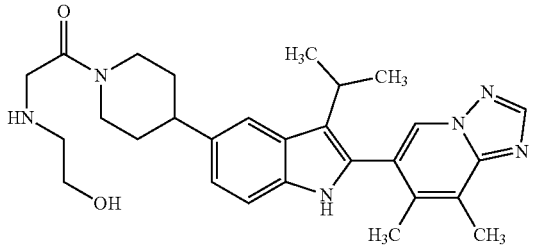
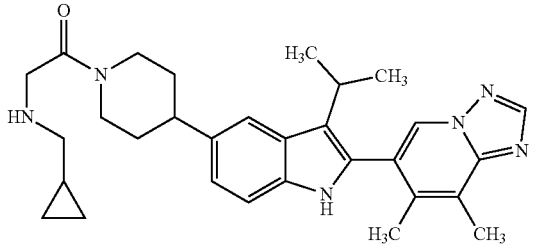
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
753	EX-4		459.0	1.4	QC-ACN-AA-XB
754	EX-4		264.4	1.41	QC-ACN-TFA-XB
755	EX-4		529.3	1.46	QC-ACN-AA-XB
756	EX-4		252.3	1.22	QC-ACN-TFA-XB
757	EX-4		489.2	1.28	QC-ACN-AA-XB
758	EX-4		250.3	1.35	QC-ACN-TFA-XB

TABLE 17-continued

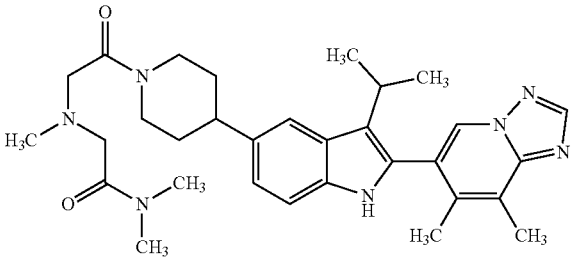
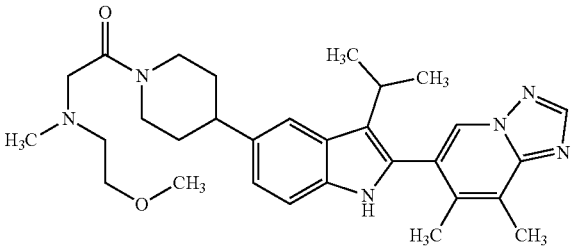
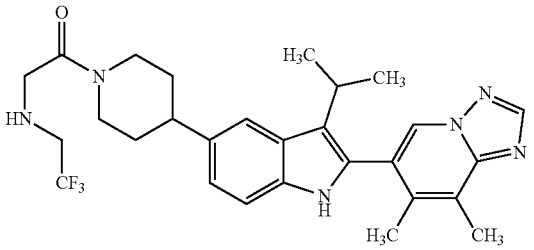
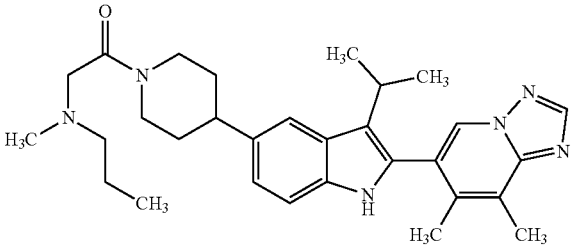
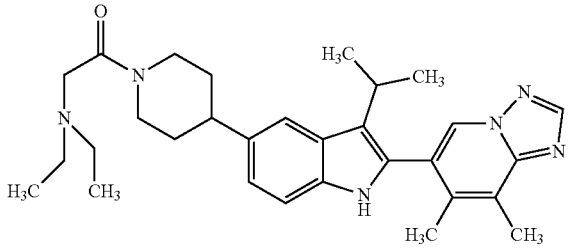
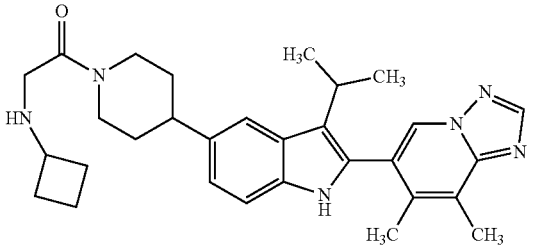
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
759	EX-4		544.1	1.64	QC-ACN-AA-XB
760	EX-4		517.5	1.32	QC-ACN-TFA-XB
761	EX-4		527.2	1.86	QC-ACN-AA-XB
762	EX-4		501.1	1.74	QC-ACN-AA-XB
763	EX-4		501.2	1.58	QC-ACN-AA-XB
764	EX-4		499.5	1.37	QC-ACN-TFA-XB

TABLE 17-continued

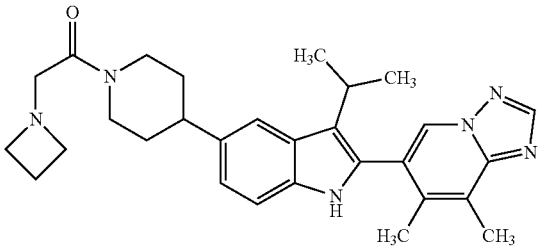
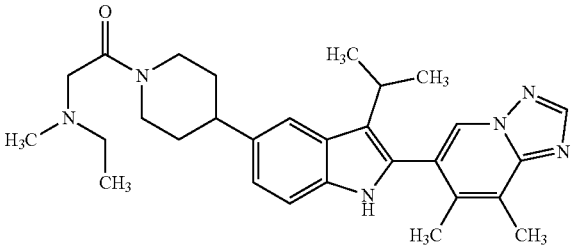
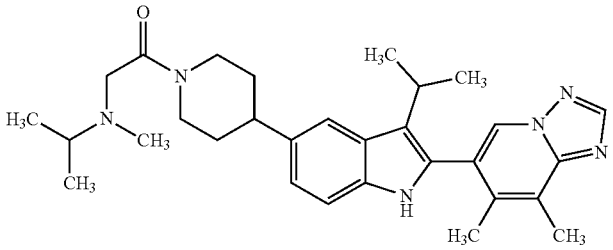
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
765	EX-4		485.4	1.35	QC-ACN-AA-XB
766	EX-4		487.5	1.32	QC-ACN-TFA-XB
767	EX-4		501.4	1.37	QC-ACN-TFA-XB

TABLE 18

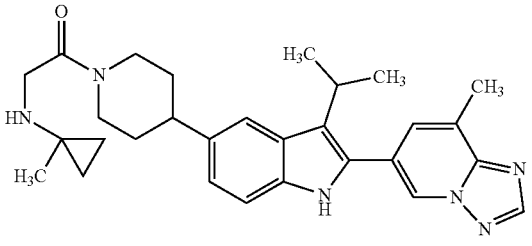
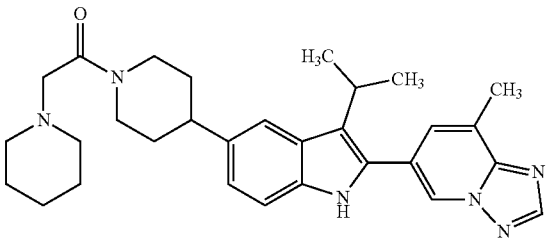
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
768	EX-2		485.4	1.72	E
769	EX-2		499.4	1.62	E

TABLE 18-continued

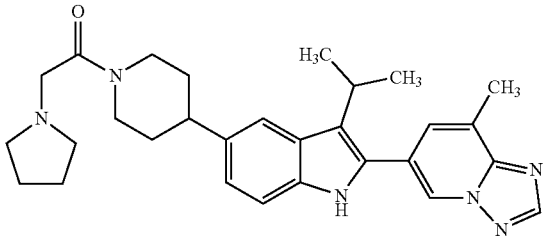
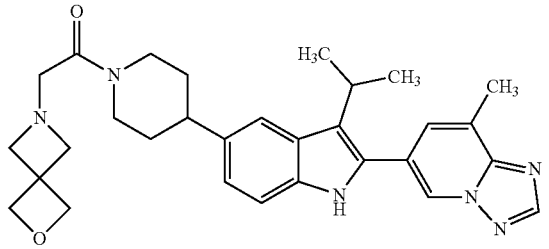
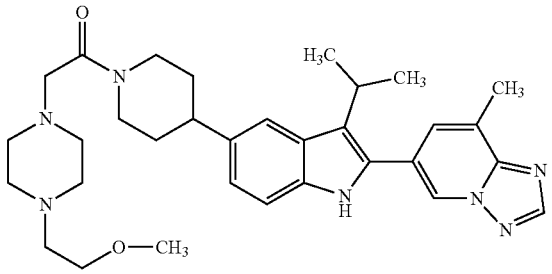
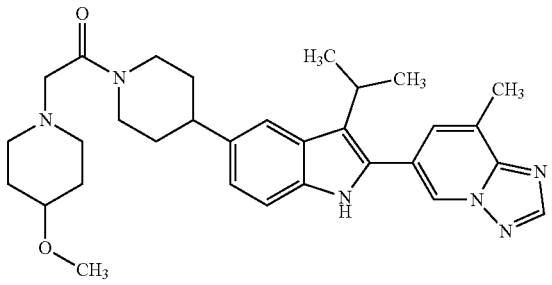
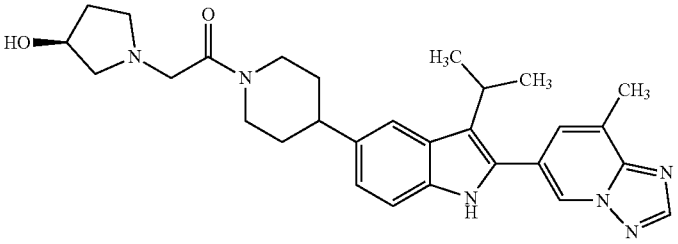
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
770	EX-2		485.4	1.35	E
771	EX-2		513.4	1.37	E
772	EX-2		558.5	1.53	E
773	EX-2		529.4	1.65	E
774	EX-2		501.4	1.29	E

TABLE 18-continued

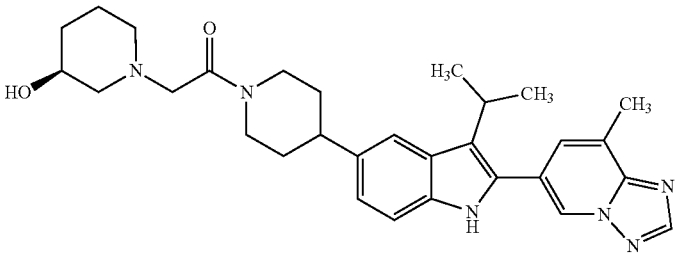
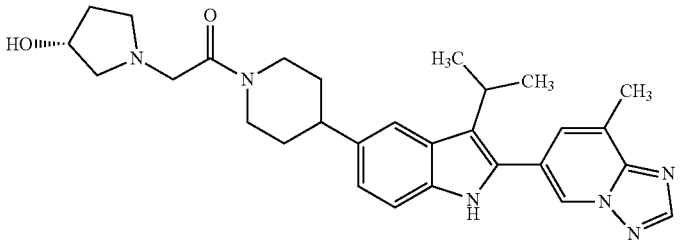
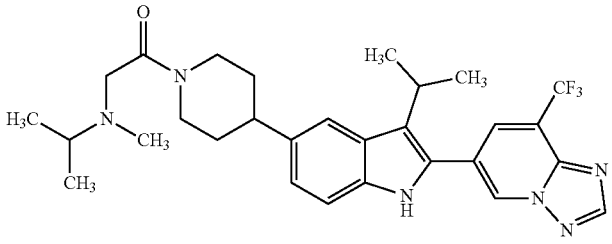
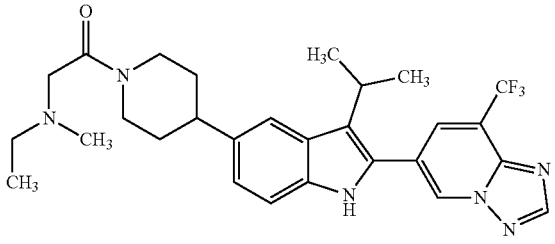
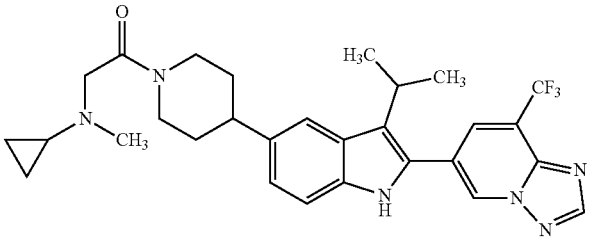
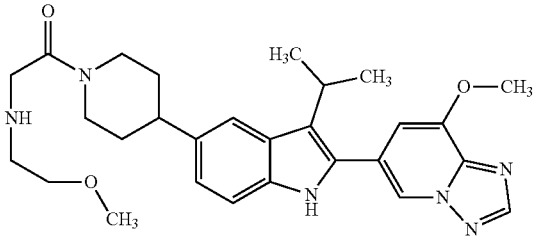
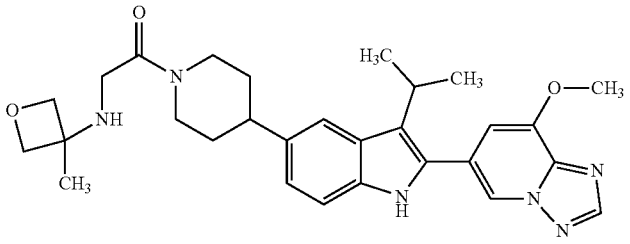
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
775	EX-2		515.4	1.47	E
776	EX-2		501.4	1.29	E
777	EX-128		541.4	1.51	F
778	EX-128		527.4	1.44	F
779	EX-128		539.4	2.14	E
780	EX-5		505.3	1.55	E

TABLE 18-continued

Ex. No.	Template Starting Material	Structure	LCMS MH+	Rt (min)	HPLC Method
781	EX-5		517.3	1.69	E

The following examples were prepared according to the general process described in Example 74.

TABLE 19

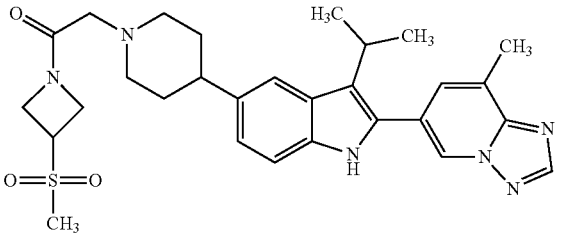
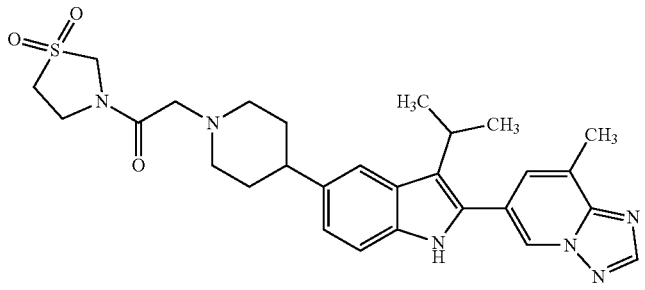
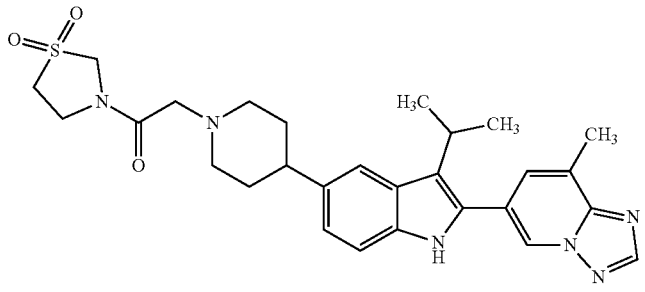
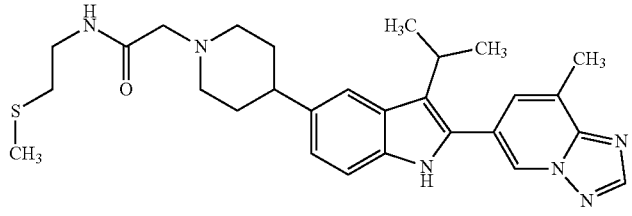
Ex. No.	Template Starting Material	Structure	LCMS MH+	Rt (min)	HPLC Method
782	EX-2		549.2	1.29	QC-ACN-TFA-XB
783	EX-2		535.4	1.31	QC-ACN-TFA-XB
784	EX-2		535.32	1.64	QC-ACN-AA-XB
785	EX-2		505.1	1.77	QC-ACN-AA-XB

TABLE 19-continued

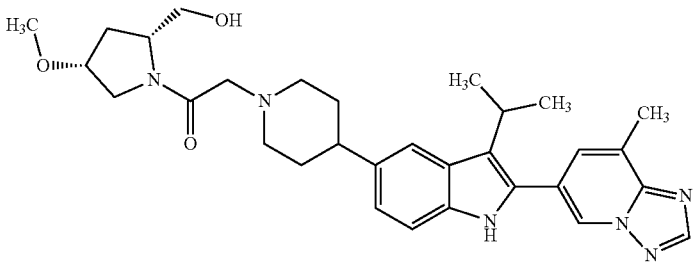
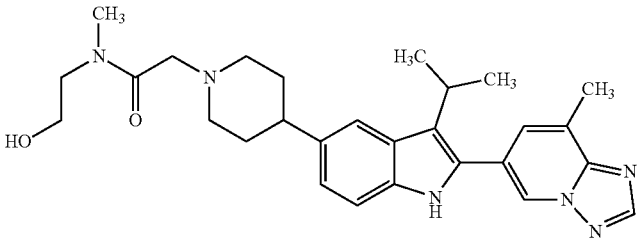
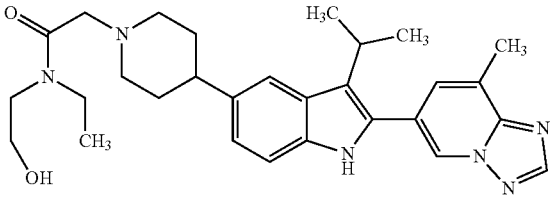
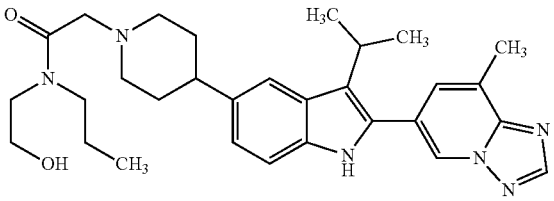
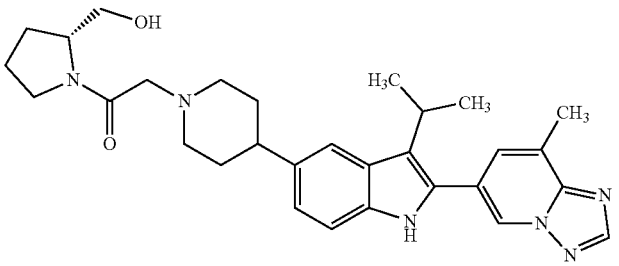
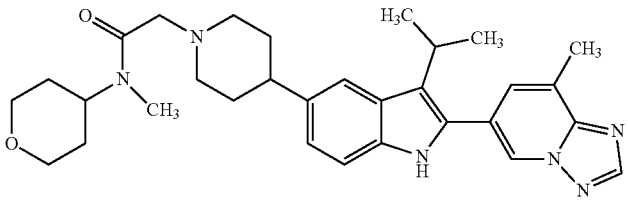
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
786	EX-2		545.2	1.55	QC-ACN-AA-XB
787	EX-2		511.1	1.21	QC-ACN-TFA-XB
788	EX-2		503.2	1.26	QC-ACN-TFA-XB
789	EX-2		517.4	1.35	QC-ACN-TFA-XB
790	EX-2		515.2	1.54	QC-ACN-AA-XB
791	EX-2		529.4	1.58	QC-ACN-AA-XB

TABLE 19-continued

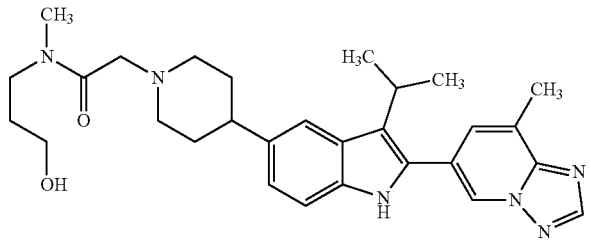
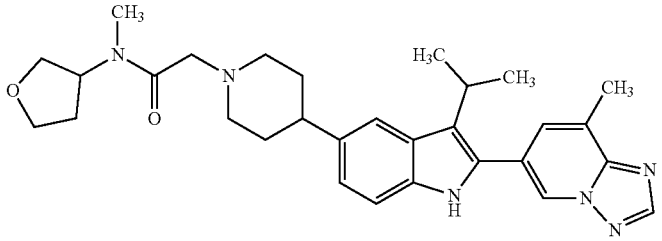
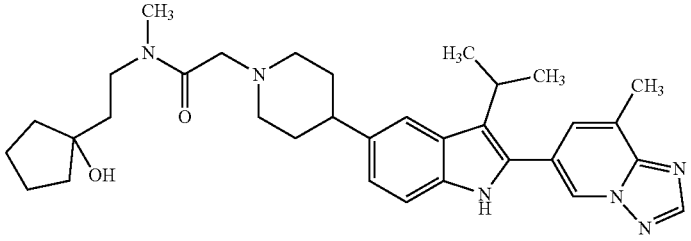
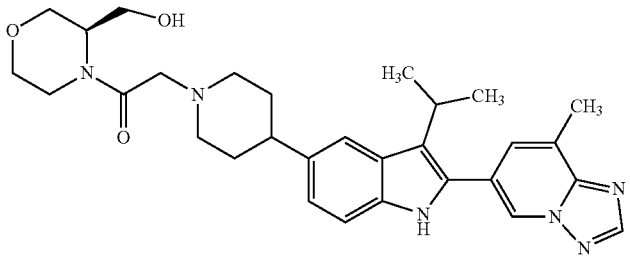
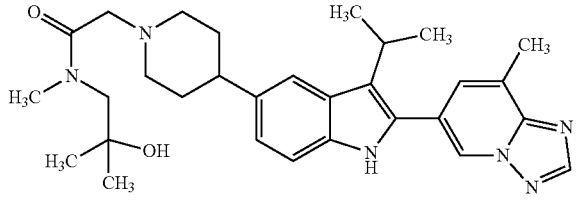
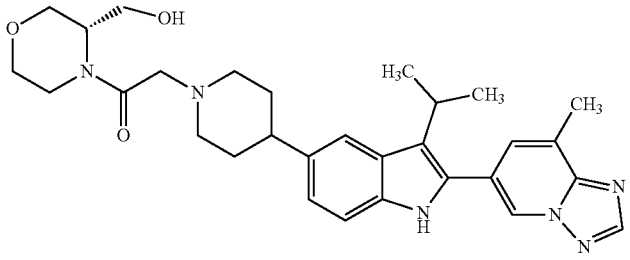
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
792	EX-2		503.2	1.49	QC-ACN-AA-XB
793	EX-2		515.2	1.33	QC-ACN-TFA-XB
794	EX-2		579.2	1.44	QC-ACN-TFA-XB
795	EX-2		531.2	1.22	QC-ACN-TFA-XB
796	EX-2		517.2	1.6	QC-ACN-AA-XB
797	EX-2		531.2	1.25	QC-ACN-TFA-XB

TABLE 19-continued

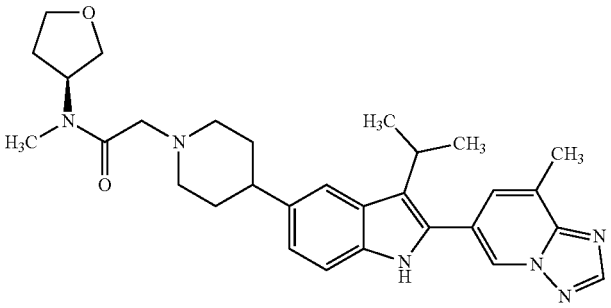
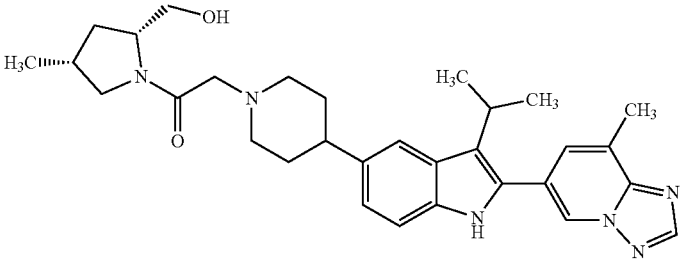
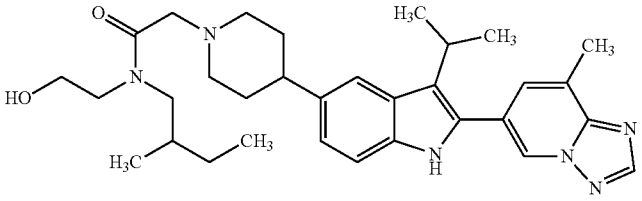
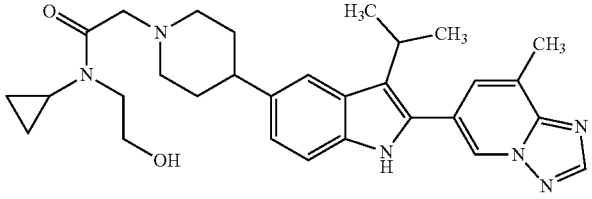
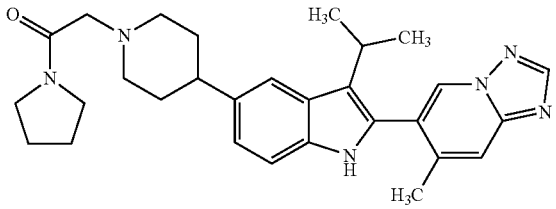
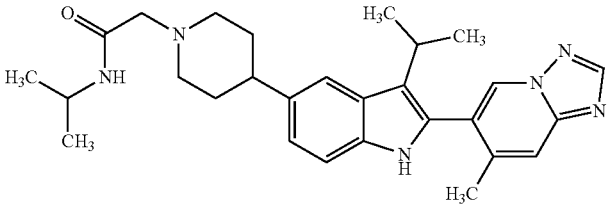
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
798	EX-2		515.2	1.63	QC-ACN-AA-XB
799	EX-2		529.3	1.7	QC-ACN-AA-XB
800	EX-2		545.2	1.56	QC-ACN-TFA-XB
801	EX-2		515.4	1.24	QC-ACN-TFA-XB
802	EX-3		485.0	1.33	QC-ACN-TFA-XB
803	EX-3		473.1	1.76	QC-ACN-AA-XB

TABLE 19-continued

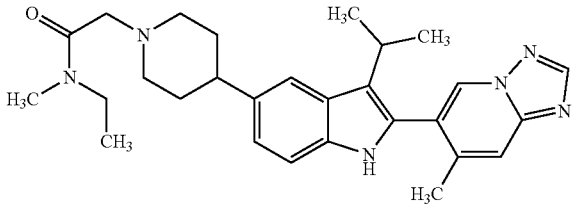
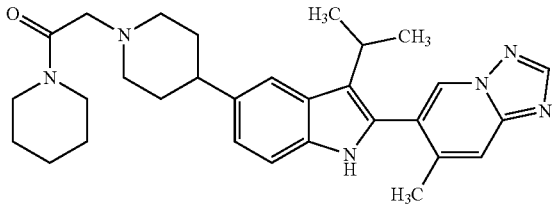
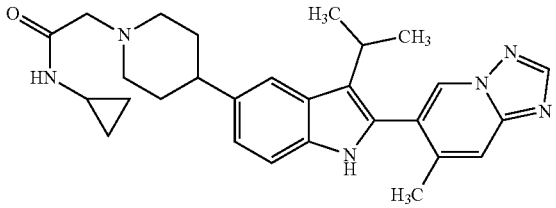
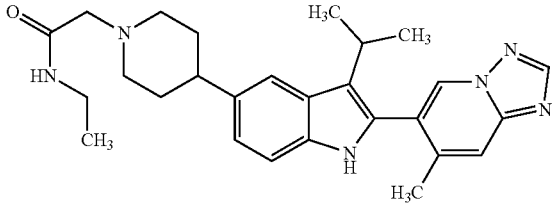
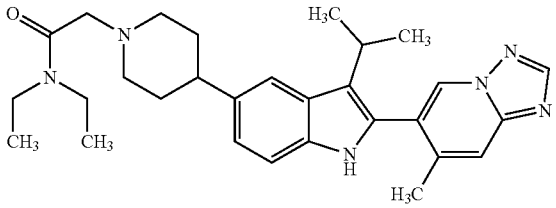
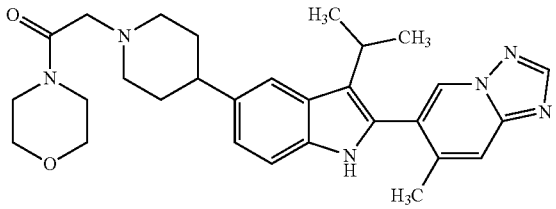
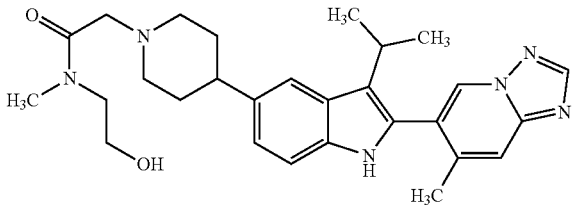
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
804	EX-3		473.0	1.63	QC-ACN-AA-XB
805	EX-3		499.2	1.42	QC-ACN-TFA-XB
806	EX-3		471.4	1.59	QC-ACN-AA-XB
807	EX-3		459.1	1.25	QC-ACN-TFA-XB
808	EX-3		487.4	1.35	QC-ACN-TFA-XB
809	EX-3		501.3	1.5	QC-ACN-AA-XB
810	EX-3		489.3	1.23	QC-ACN-TFA-XB

TABLE 19-continued

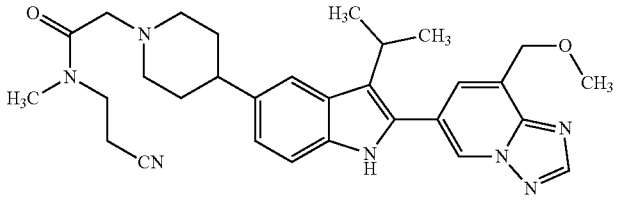
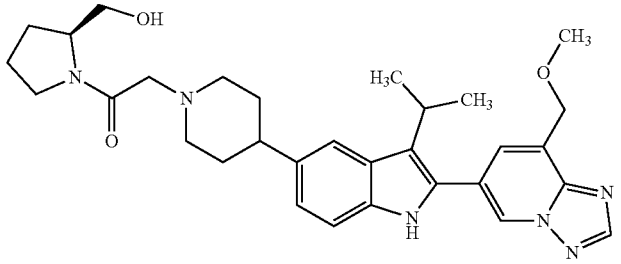
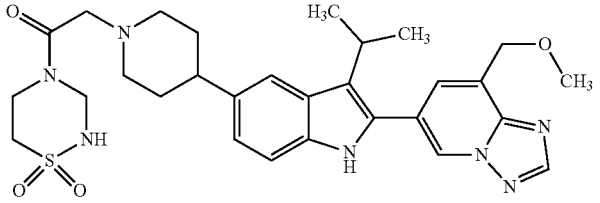
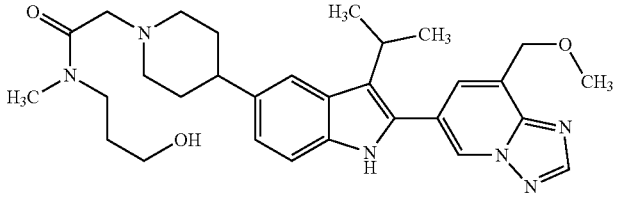
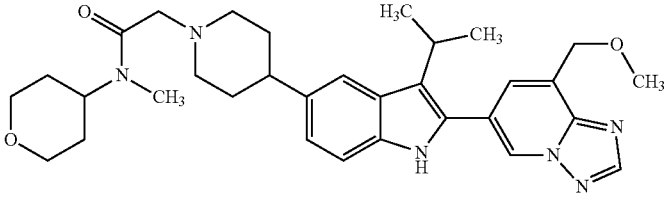
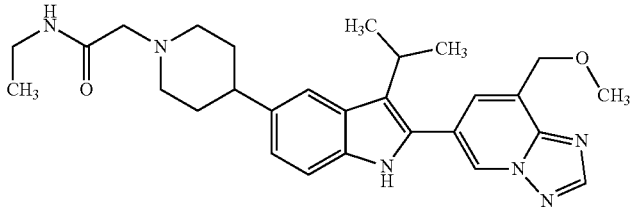
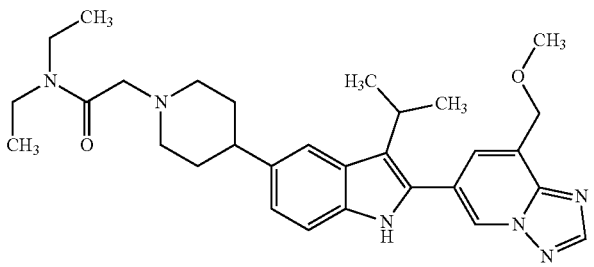
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
811	EX-6		528.0	1.46	QC-ACN-AA-XB
812	EX-6		545.0	1.31	QC-ACN-TFA-XB
813	EX-6		580.1	1.58	QC-ACN-AA-XB
814	EX-6		533.2	1.48	QC-ACN-AA-XB
815	EX-6		558.9	1.53	QC-ACN-AA-XB
816	EX-6		489.0	1.63	QC-ACN-AA-XB
817	EX-6		517.0	1.58	QC-ACN-AA-XB

TABLE 19-continued

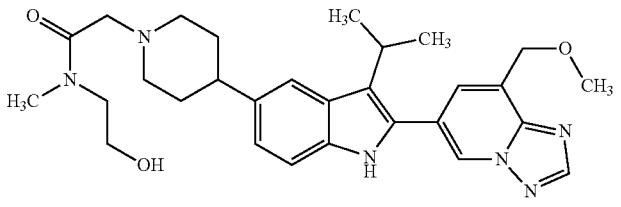
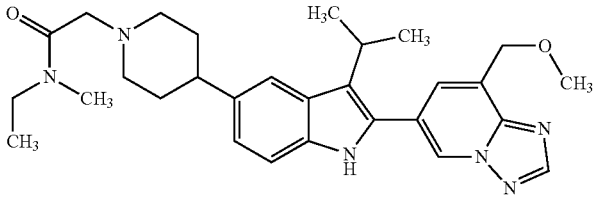
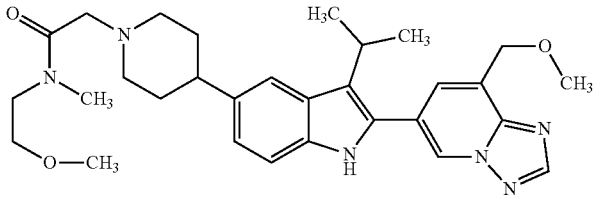
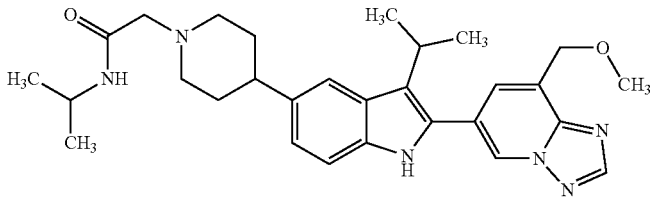
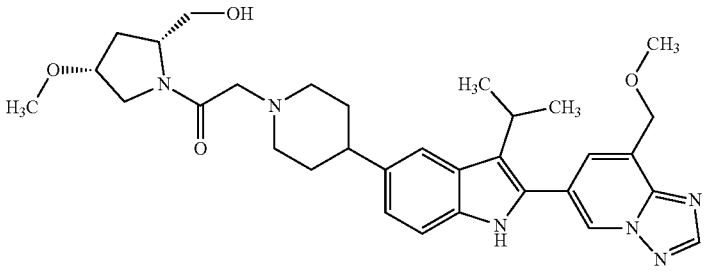
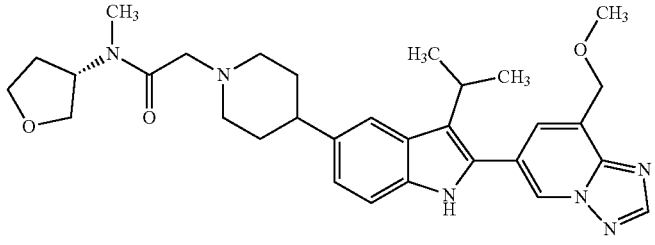
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
818	EX-6		519.0	1.28	QC-ACN-AA-XB
819	EX-6		503.0	1.44	QC-ACN-TFA-XB
820	EX-6		532.9	1.37	QC-ACN-TFA-XB
821	EX-6		503.0	1.3	QC-ACN-TFA-XB
822	EX-6		575.0	1.39	QC-ACN-AA-XB
823	EX-6		545.0	1.43	QC-ACN-AA-XB

TABLE 19-continued

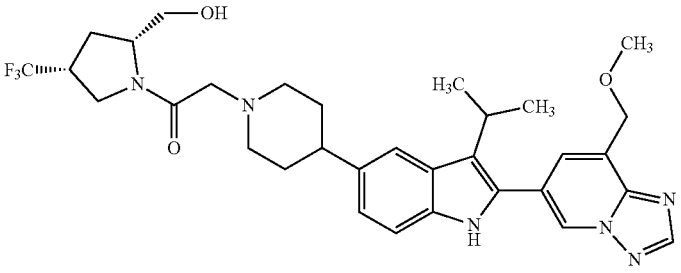
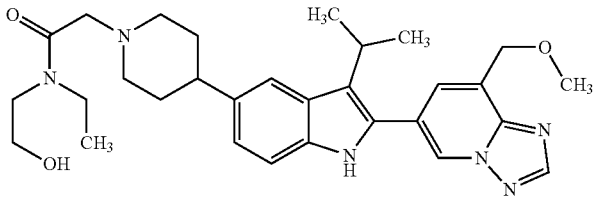
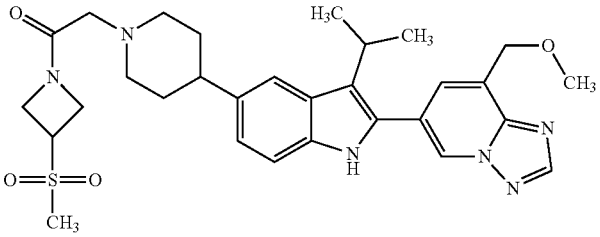
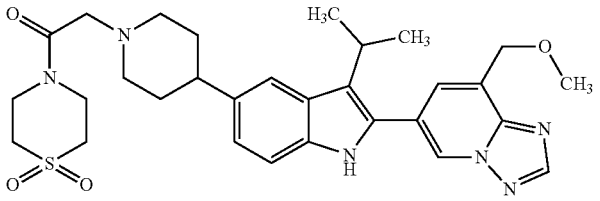
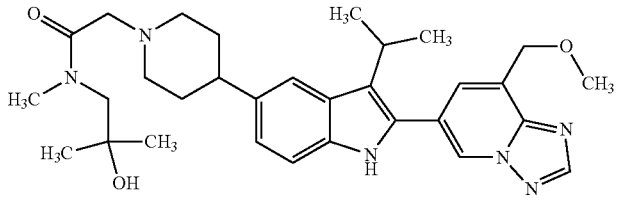
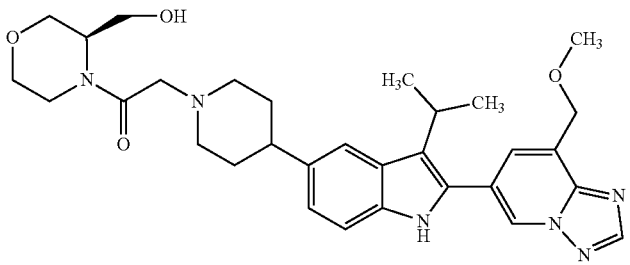
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
824	EX-6		613.3	1.62	QC-ACN-AA-XB
825	EX-6		533.0	1.4	QC-ACN-AA-XB
826	EX-6		578.9	1.46	QC-ACN-AA-XB
827	EX-6		579.0	1.45	QC-ACN-AA-XB
828	EX-6		547.0	1.34	QC-ACN-TFA-XB
829	EX-6		561.0	1.27	QC-ACN-TFA-XB

TABLE 19-continued

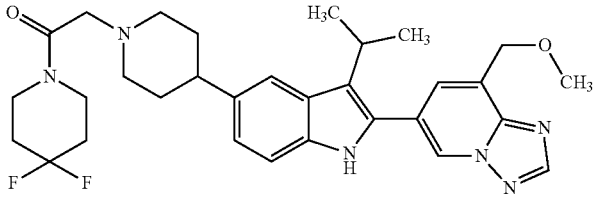
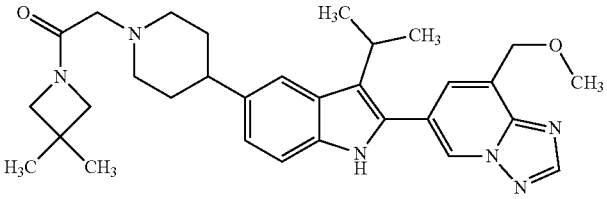
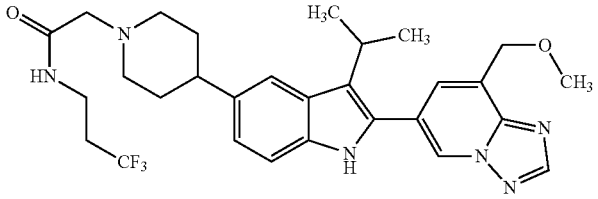
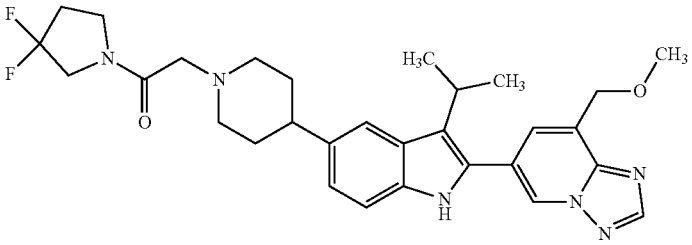
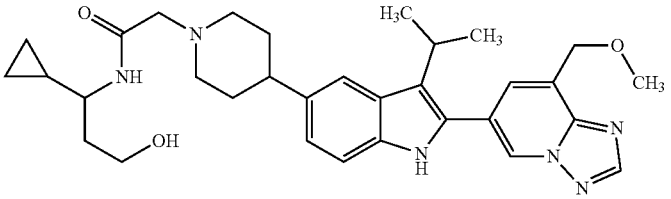
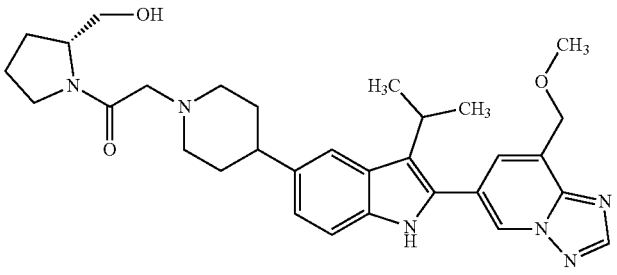
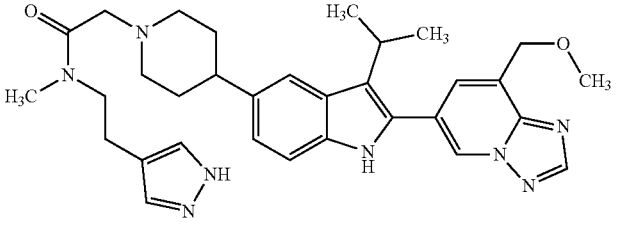
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
830	EX-6		565.1	1.66	QC-ACN-AA-XB
831	EX-6		529.3	1.69	QC-ACN-AA-XB
832	EX-6		557.0	1.85	QC-ACN-AA-XB
833	EX-6		551.0	1.63	QC-ACN-AA-XB
834	EX-6		559.1	1.63	QC-ACN-AA-XB
835	EX-6		545.0	1.31	QC-ACN-TFA-XB
836	EX-6		569.1	1.3	QC-ACN-AA-XB

TABLE 19-continued

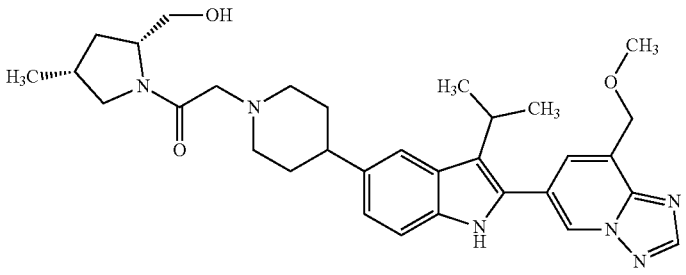
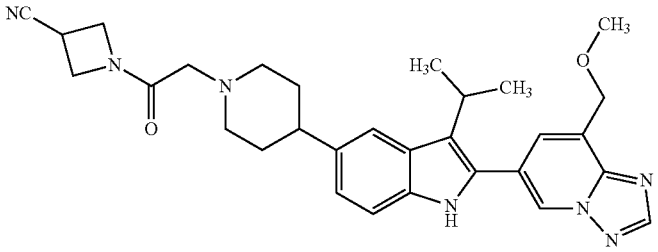
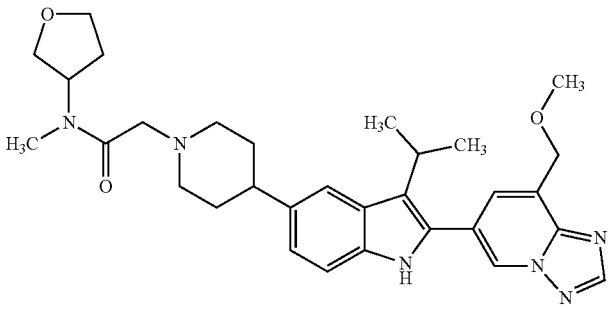
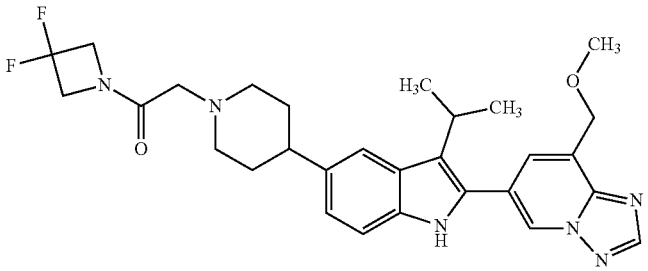
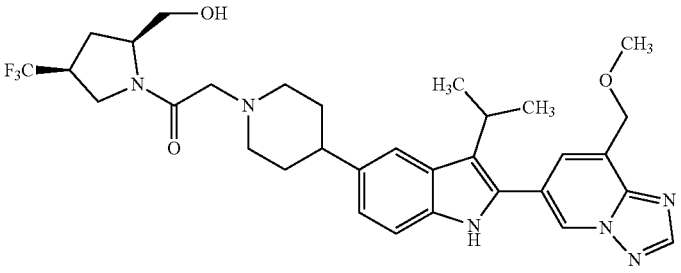
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
837	EX-6		559.1	1.31	QC-ACN-TFA-XB
838	EX-6		526.0	1.8	QC-ACN-AA-XB
839	EX-6		545.0	1.59	QC-ACN-AA-XB
840	EX-6		537.1	1.74	QC-ACN-AA-XB
841	EX-6		613.0	1.79	QC-ACN-AA-XB

TABLE 19-continued

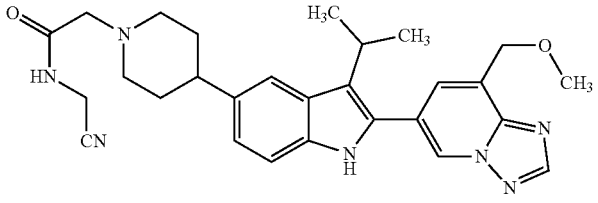
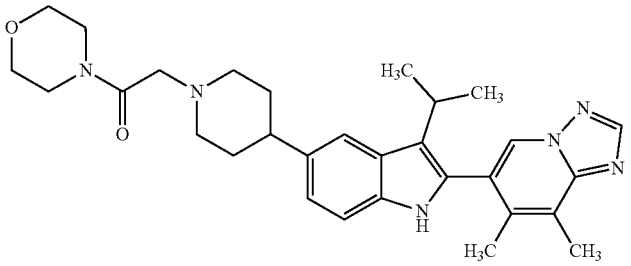
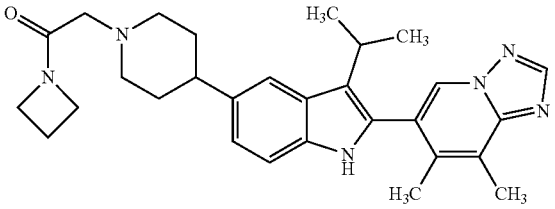
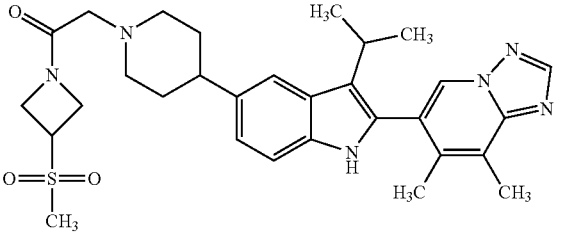
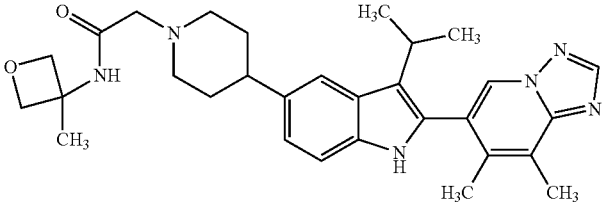
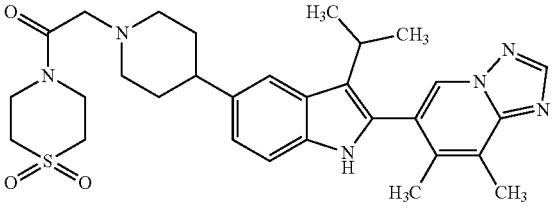
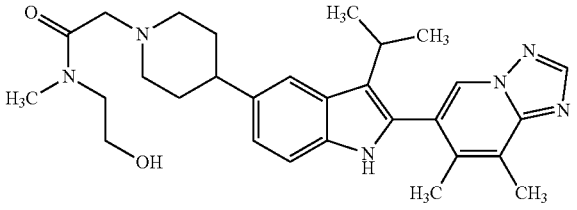
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
842	EX-6		514.2	1.57	QC-ACN-AA-XB
843	EX-4		515.2	1.32	QC-ACN-TFA-XB
844	EX-4		485.4	1.74	QC-ACN-AA-XB
845	EX-4		563.3	1.56	QC-ACN-AA-XB
846	EX-4		515.1	1.32	QC-ACN-TFA-XB
847	EX-4		563.1	1.45	QC-ACN-AA-XB
848	EX-4		503.2	1.29	QC-ACN-TFA-XB

TABLE 19-continued

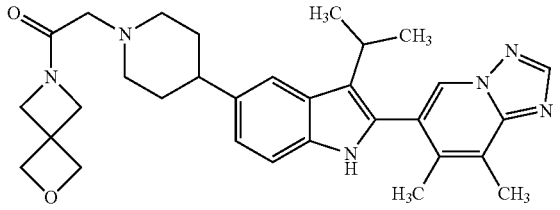
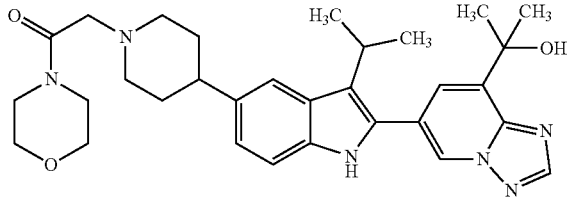
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
849	EX-4		527.2	1.67	QC-ACN-AA-XB
850	EX-100		545.0	1.3	QC-ACN-TFA-XB

TABLE 20

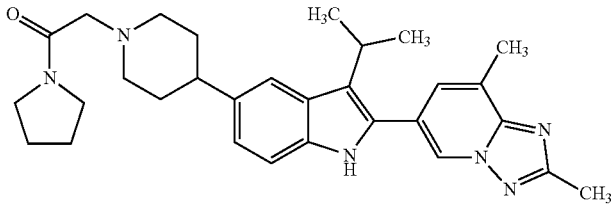
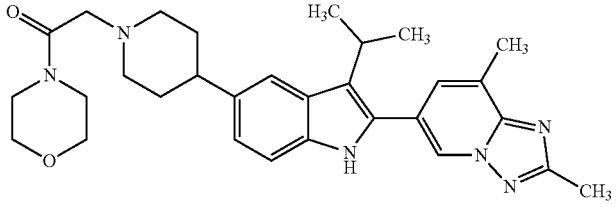
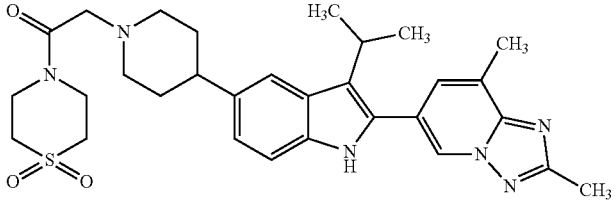
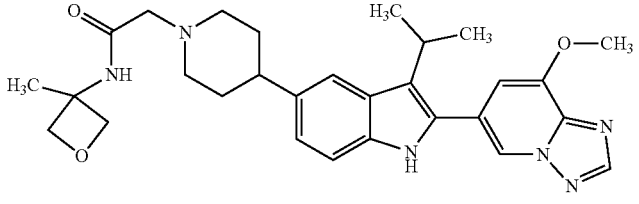
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
851	EX-124		499	1.83	E
852	EX-124		515	1.75	E
853	EX-124		563.3	1.76	E
854	Ex-5		517.2	1.86	E

TABLE 20-continued

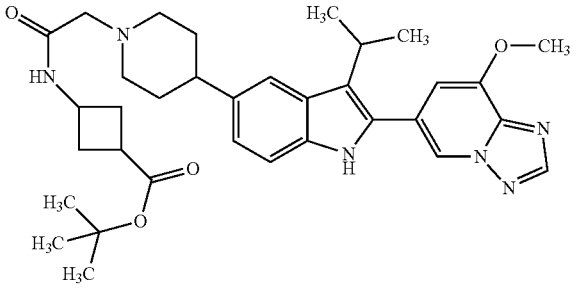
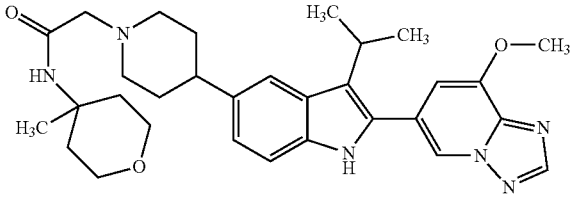
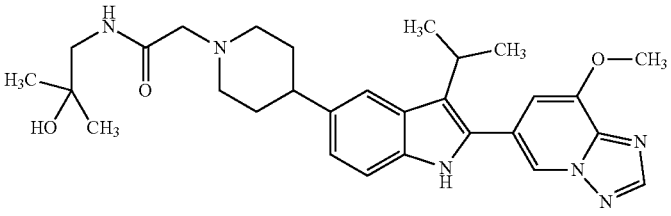
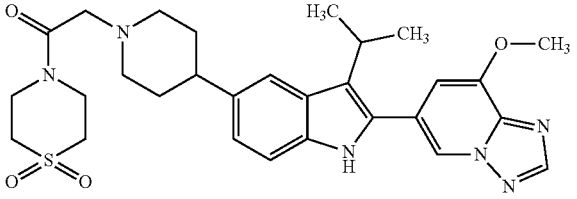
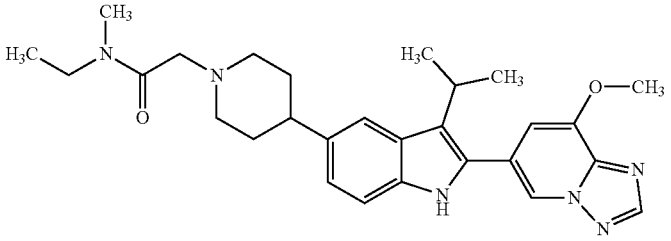
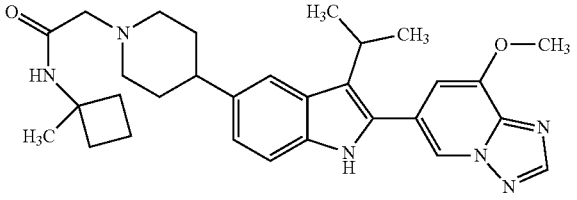
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
855	EX-5		602.4	1.89	E
856	EX-5		545.4	1.72	E
857	EX-5		519.3	1.49	E
858	EX-5		565.3	1.44	E
859	EX-5		489.3	1.46	E
860	EX-5		515.3	1.92	E

TABLE 20-continued

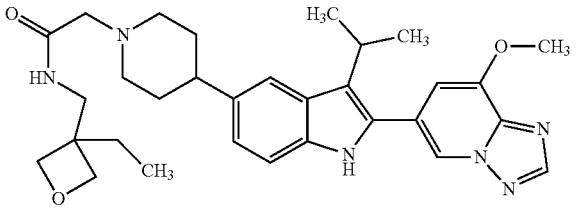
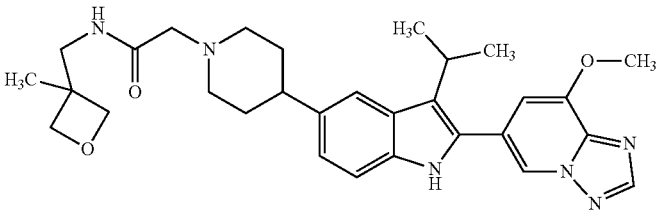
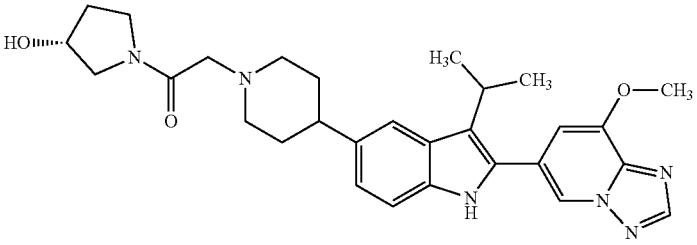
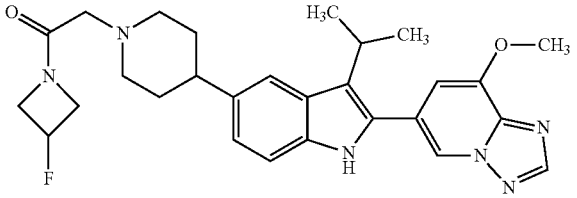
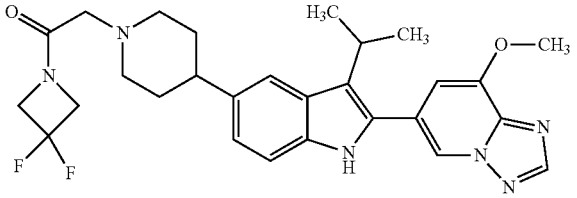
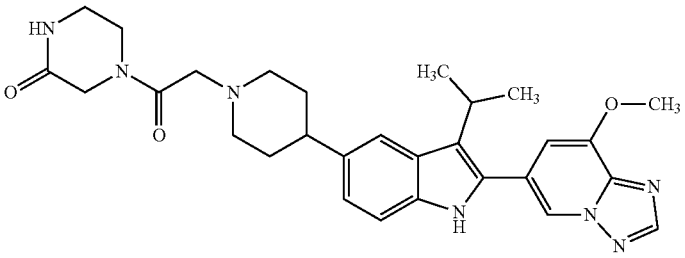
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
861	EX-5		545.3	1.9	E
862	EX-5		531.3	1.79	E
863	EX-5		517.3	1.21	E
864	EX-5		505.3	1.56	E
865	EX-5		523.3	1.18	F
866	EX-5		530.3	1.23	E

TABLE 20-continued

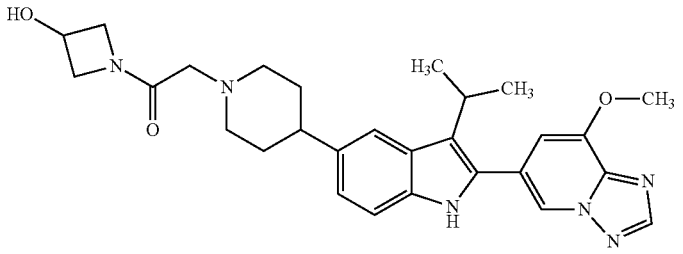
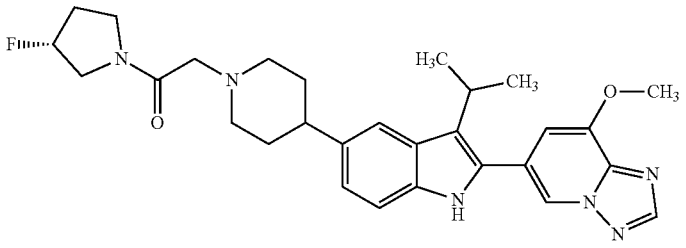
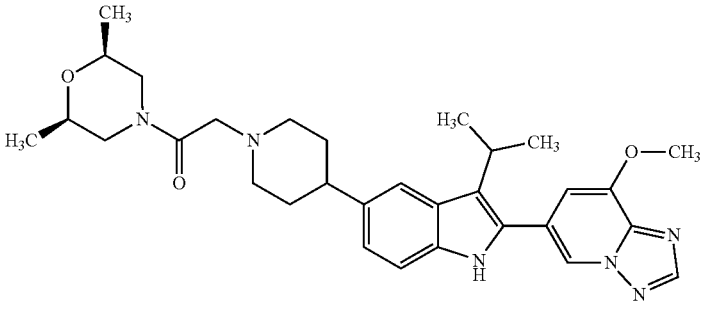
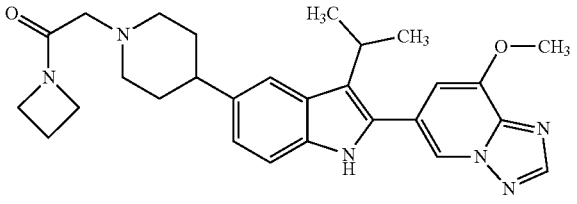
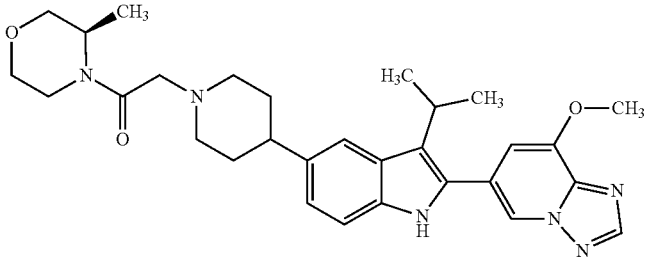
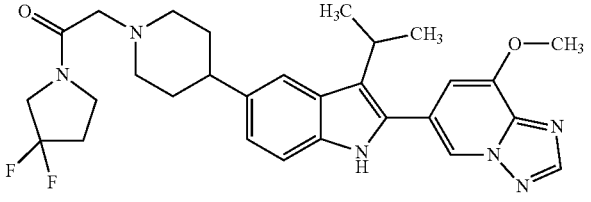
Ex. No.	Fragment Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
867	EX-5		503.3	1.26	E
868	EX-5		519.3	1.15	F
869	EX-5		545.4	1.69	E
870	EX-5		487.3	1.5	E
871	EX-5		531.3	1.16	F
872	EX-5		537.3	1.71	E

TABLE 20-continued

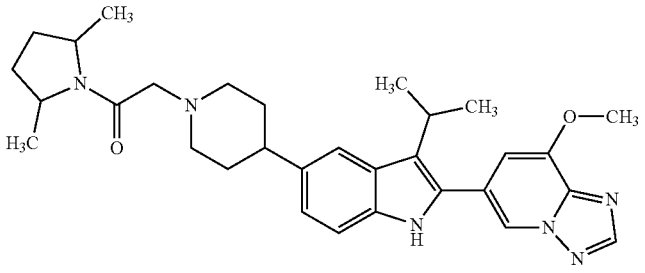
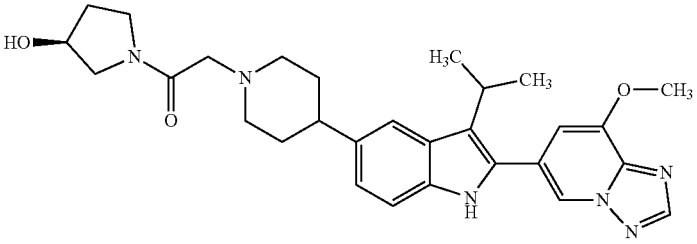
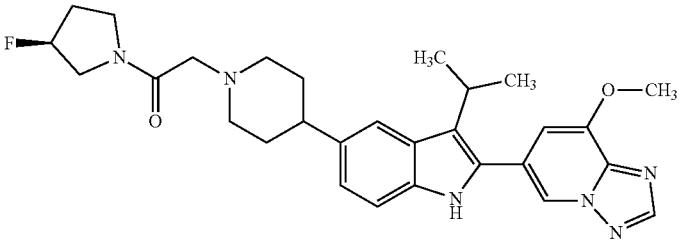
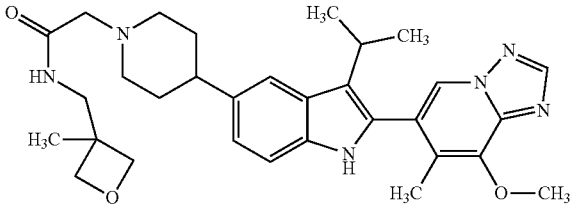
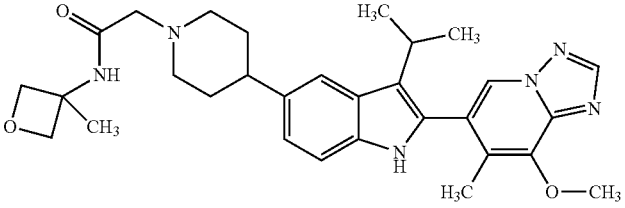
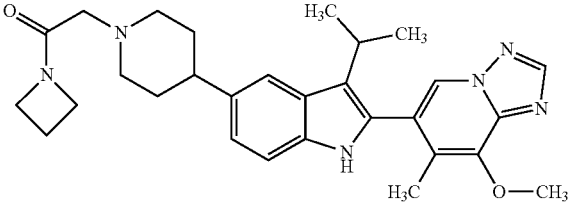
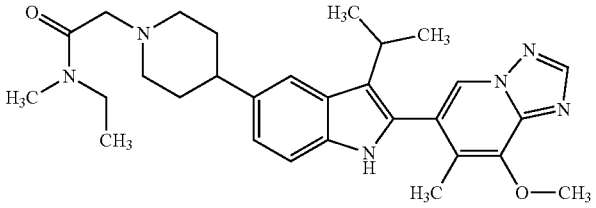
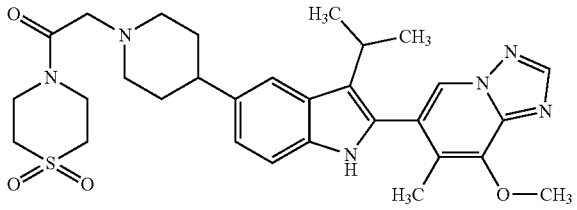
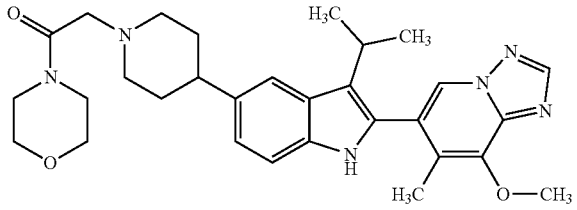
Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
873	EX-5		529.4	1.77	E
874	EX-5		517.3	1.02	F
875	EX-5		519.3	1.51	E
876	EX-140		545.3	1.73	E
877	EX-140		531.3	1.73	E
878	EX-140		501.4	1.21	F

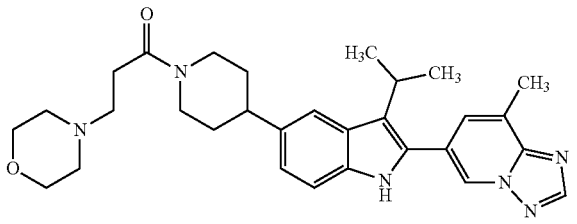
TABLE 20-continued

Ex. No.	Fragment Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
879	EX-140		503.4	1.29	F
880	EX-140		579.3	1.6	E
881	EX-140		531.3	1.56	E

Example 882

1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidi n-1-yl)-3-morpholinopropan-1-one

(882)



To a two dram vial were added the TFA salt of 6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (0.025 g, 0.053 mmol), CH_3CN, HATU (1.0 equiv.), TEA (3.0 equiv.), and 3-morpholinopropanoic acid (0.250 g, 1.570 mmol). The reaction vial was capped and stirred overnight at room temperature. The mixture was diluted with solvent (90:10:0.1 CH_3CN: Water: TFA) and filtered. The crude material was purified via preparative LC/MS with the following conditions: Column:) (Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 10-70% B over 19 minutes, then a 3-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 1-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl) piperidi n-1-yl)-3-morpholinopropan-1-one (21.2 mg, 0.041 mmol, 78% yield). LCMS MH+: 515.2 HPLC Ret. Time 1.52 min. Method QC-ACN-AA-XB. ^1H NMR (500 MHz, DMSO-d_6) δ 8.85-8.72 (m, 1H), 8.55-8.48 (m, 1H), 7.63-7.50 (m, 2H), 7.36-7.22 (m, 1H), 7.06-6.94 (m, 1H), 4.63-4.51 (m, 1H), 4.06-3.98 (m, 1H), 3.63-3.56 (m, 5H), 3.30-3.20 (m, 1H), 2.70-2.53 (m, 11H), 2.46-2.39 (m, 3H), 1.89-1.79 (m, 2H), 1.70-1.59 (m, 1H), 1.53-1.46 (m, 1H), 1.45-1.39 (m, 6H).

The following examples were prepared according to the general process described in Example 882.

TABLE 21

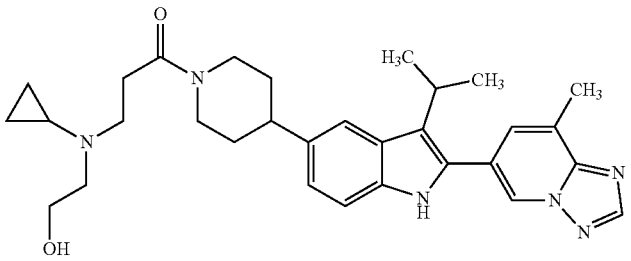
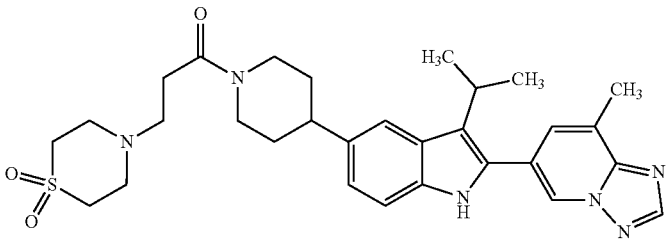
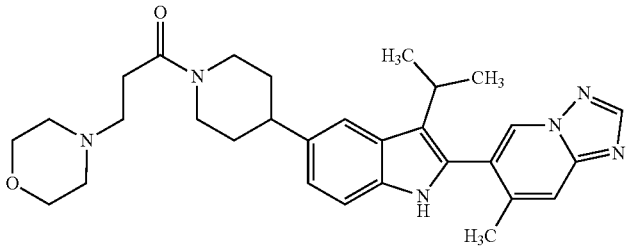
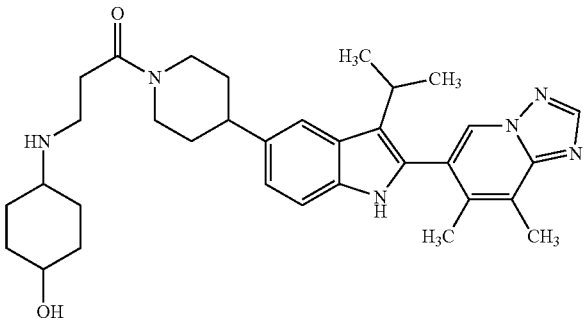
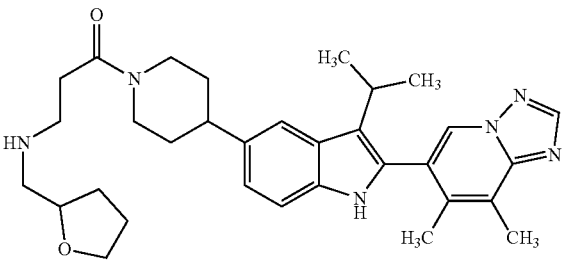
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
883	EX-2		529.0	1.63	QC-ACN-AA-XB
884	EX-2		563.2	1.29	QC-ACN-TFA-XB
885	EX-3		515.5	1.56	QC-ACN-AA-XB
886	EX-4		557.2	1.28	QC-ACN-TFA-XB
887	EX-4		543.2	1.44	QC-ACN-AA-XB

TABLE 21-continued

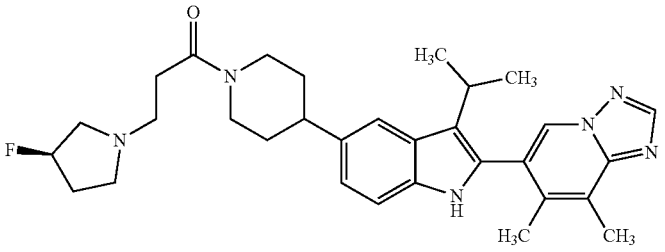
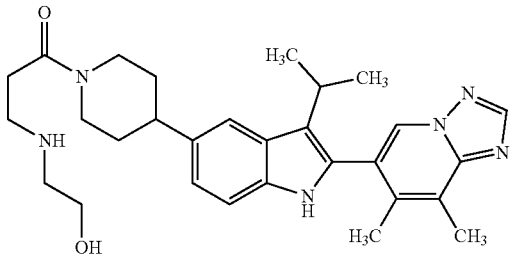
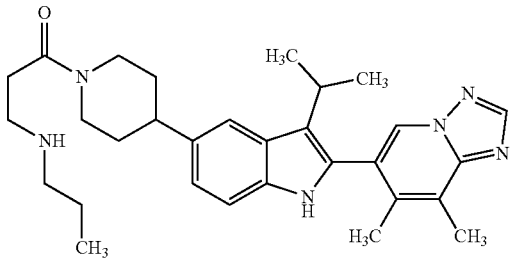
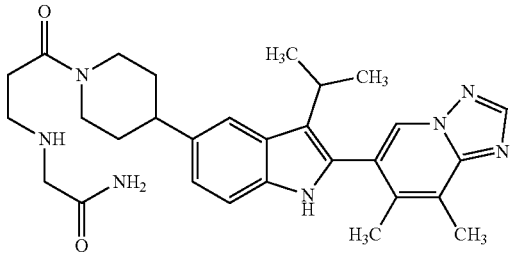
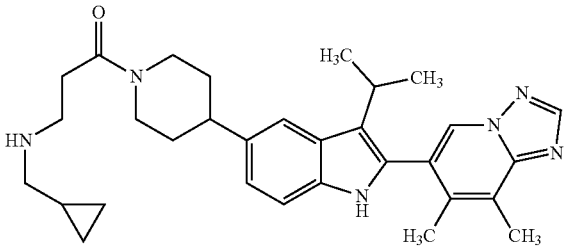
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
888	EX-4		531.2	1.32	QC-ACN-TFA-XB
889	EX-4		503.1	1.3	QC-ACN-AA-XB
890	EX-4		501.2	1.42	QC-ACN-AA-XB
891	EX-4		516.1	1.33	QC-ACN-AA-XB
892	EX-4		513.1	1.44	QC-ACN-AA-XB

TABLE 21-continued

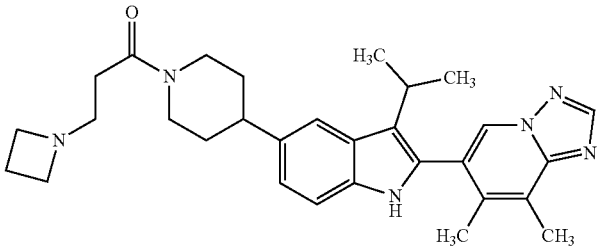
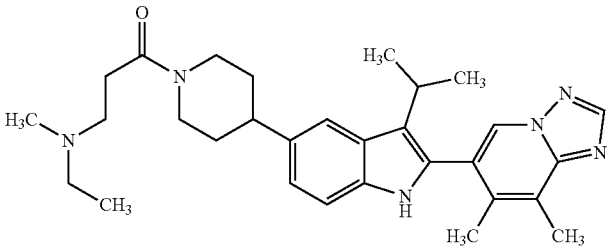
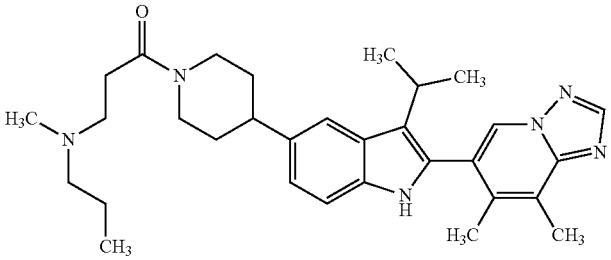
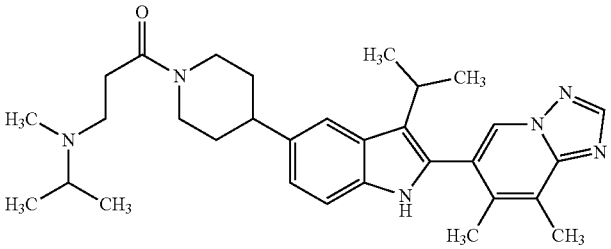
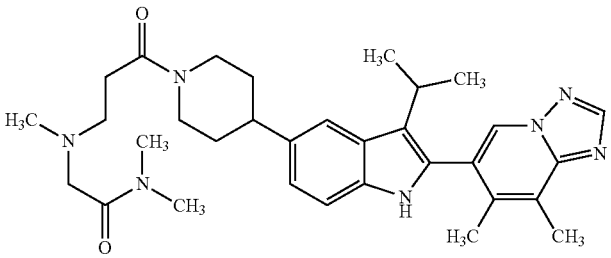
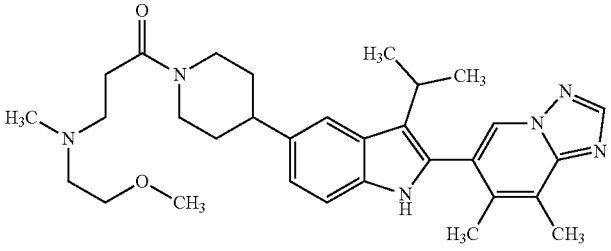
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
893	EX-4		499.2	1.28	QC-ACN-TFA-XB
894	EX-4		501.2	1.31	QC-ACN-TFA-XB
895	EX-4		515.2	1.45	QC-ACN-AA-XB
896	EX-4		515.2	1.35	QC-ACN-TFA-XB
897	EX-4		558.2	1.42	QC-ACN-AA-XB
898	EX-4		531.2	1.35	QC-ACN-TFA-XB

TABLE 21-continued

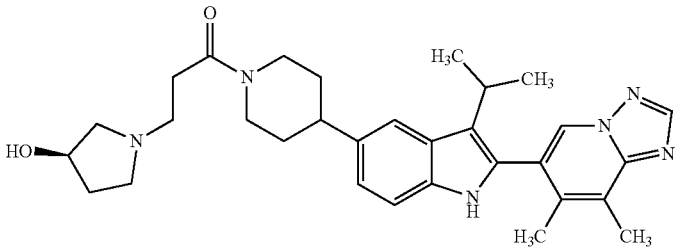
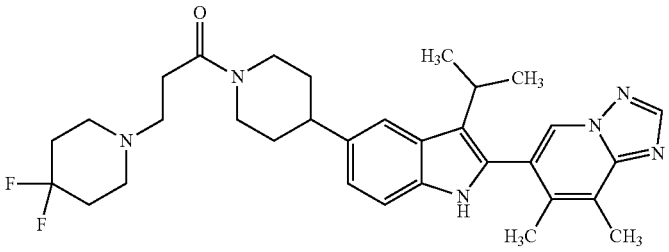
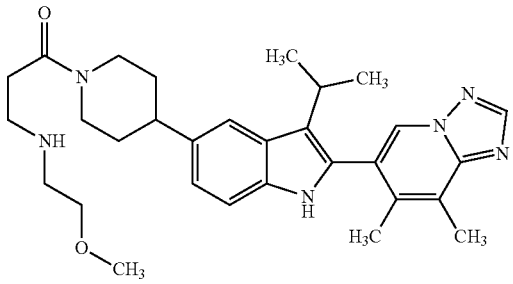
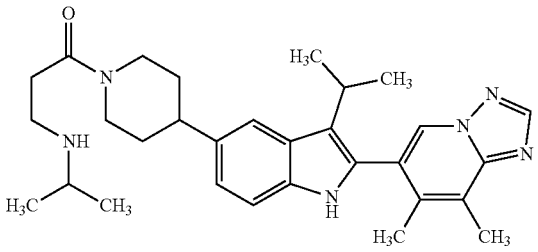
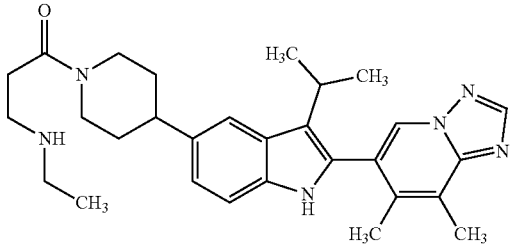
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
899	EX-4		529.2	1.32	QC-ACN-AA-XB
900	EX-4		563.2	1.37	QC-ACN-TFA-XB
901	EX-4		517.2	1.32	QC-ACN-TFA-XB
902	EX-4		501.2	1.33	QC-ACN-TFA-XB
903	EX-4		487.1	1.29	QC-ACN-TFA-XB

TABLE 21-continued

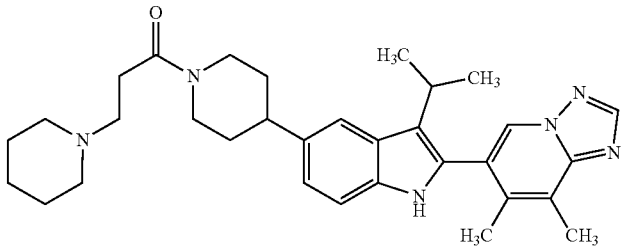
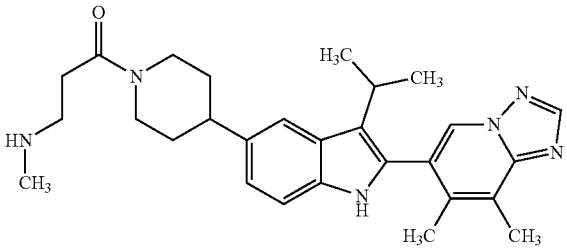
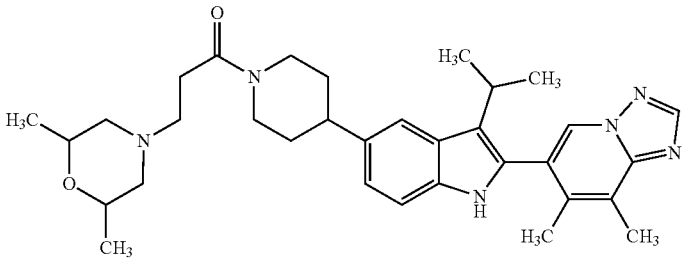
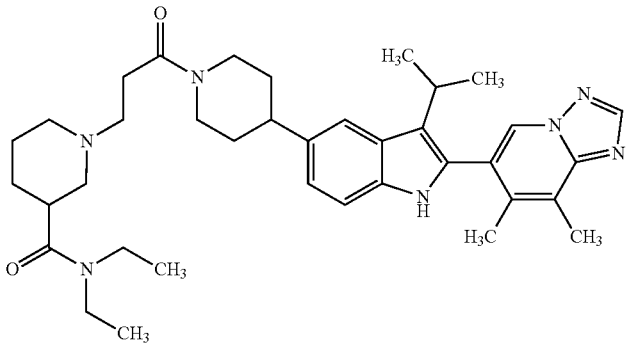
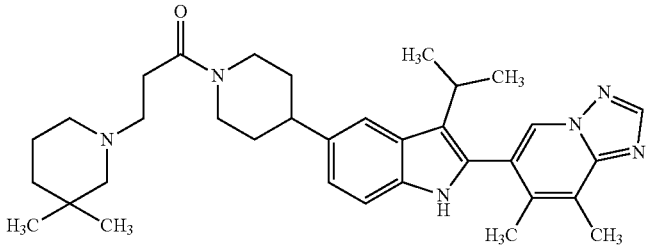
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
904	EX-4		527.0	1.35	QC-ACN-TFA-XB
905	EX-4		473.1	1.31	QC-ACN-AA-XB
906	EX-4		557.2	1.65	QC-ACN-AA-XB
907	EX-4		626.2	1.56	QC-ACN-AA-XB
908	EX-4		555.2	1.62	QC-ACN-AA-XB

TABLE 21-continued

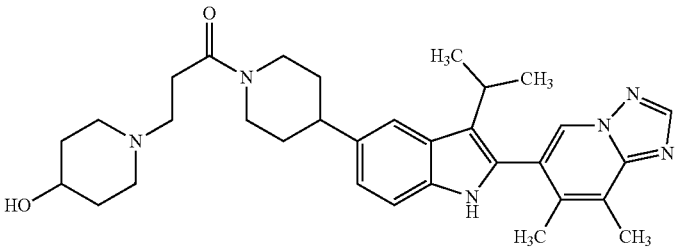
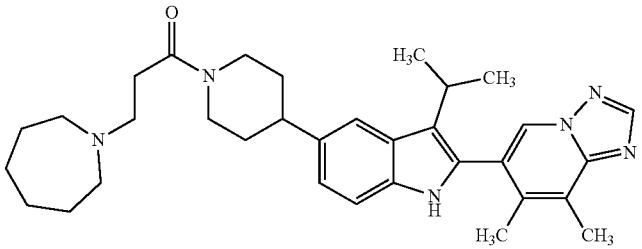
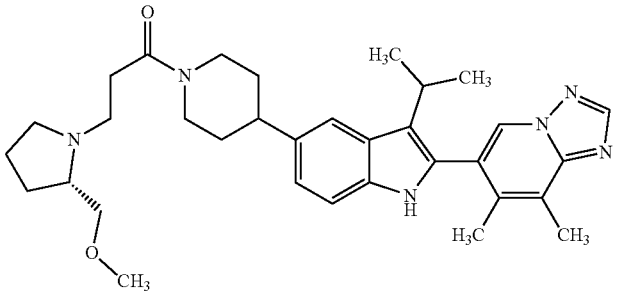
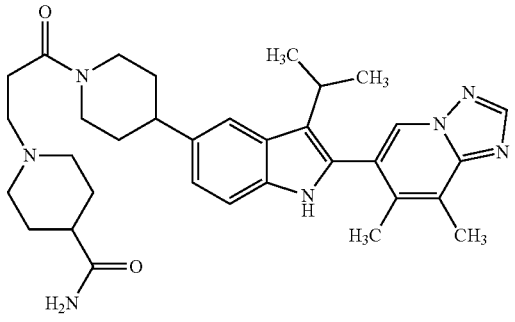
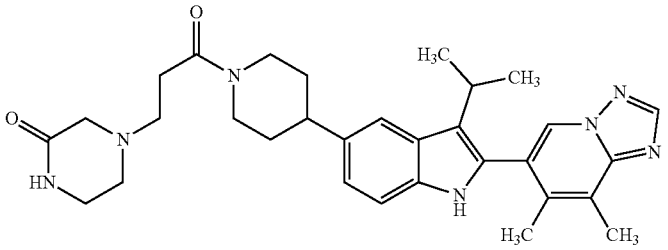
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
909	EX-4		543.2	1.32	QC-ACN-AA-XB
910	EX-4		541.2	1.5	QC-ACN-AA-XB
911	EX-4		557.2	1.48	QC-ACN-AA-XB
912	EX-4		570.2	1.31	QC-ACN-AA-XB
913	EX-4		542.2	1.44	QC-ACN-AA-XB

TABLE 21-continued

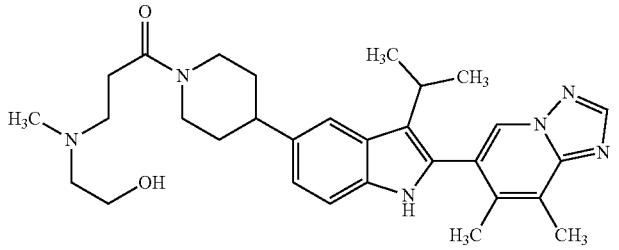
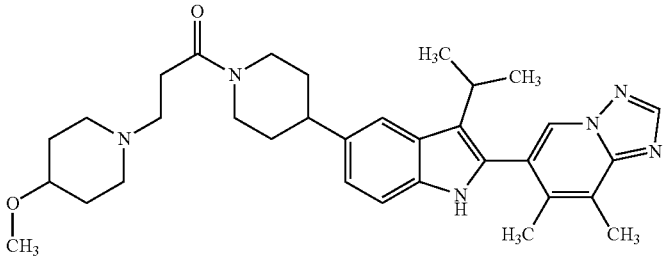
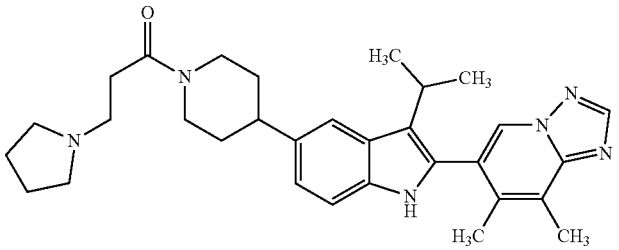
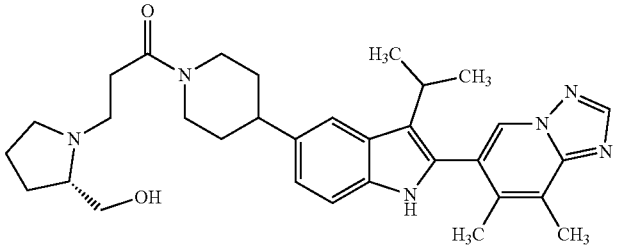
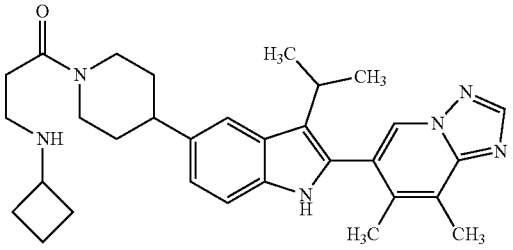
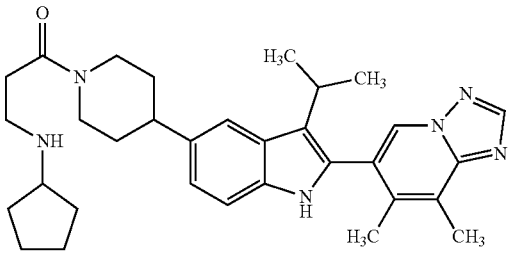
Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
914	EX-4		517.2	1.32	QC-ACN-AA-XB
915	EX-4		557.2	1.43	QC-ACN-AA-XB
916	EX-4		513.1	1.38	QC-ACN-AA-XB
917	EX-4		543.2	1.35	QC-ACN-AA-XB
918	EX-4		513.2	1.39	QC-ACN-TFA-XB
919	EX-4		527.2	1.42	QC-ACN-TFA-XB

TABLE 21-continued

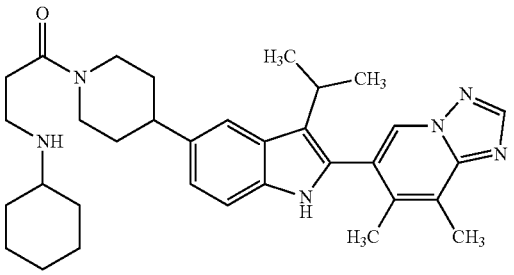
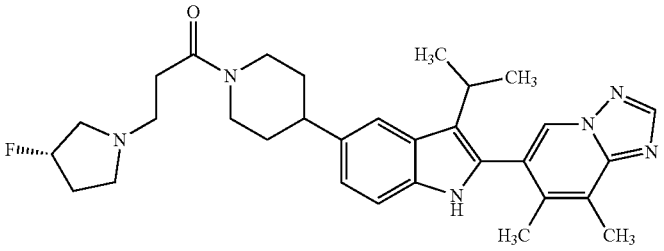
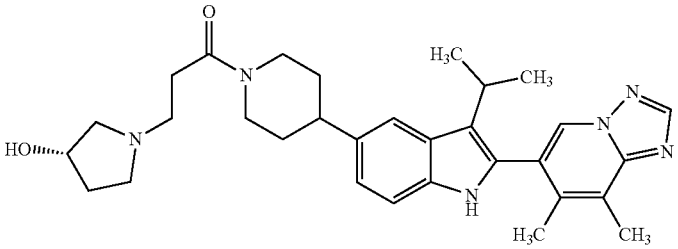
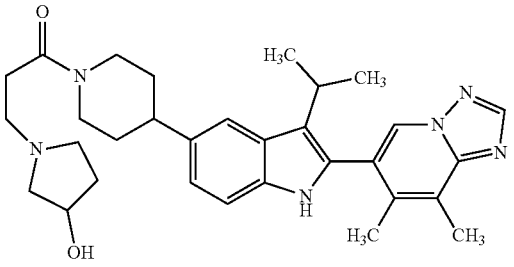
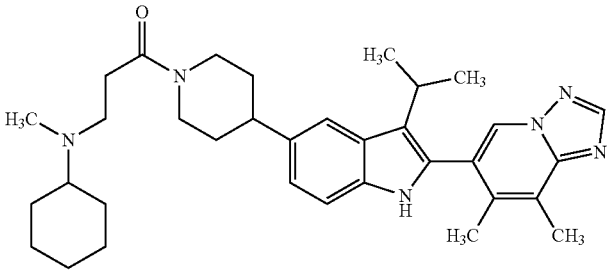
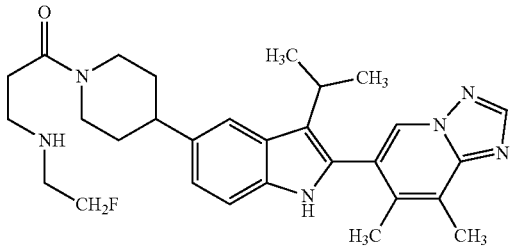
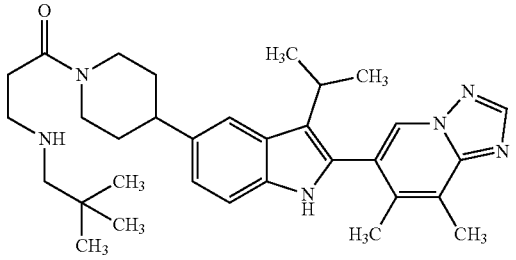
Ex. No.	Template Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
920	EX-4		541.2	1.49	QC-ACN-TFA-XB
921	EX-4		531.2	1.49	QC-ACN-AA-XB
922	EX-4		529.2	1.32	QC-ACN-AA-XB
923	EX-4		529.2	1.32	QC-ACN-AA-XB
924	EX-4		555.2	1.52	QC-ACN-TFA-XB

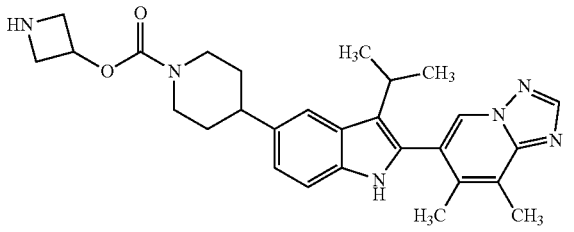
TABLE 21-continued

Ex. No.	Template Starting Material	Structure	LCMS MH+	R_t (min)	HPLC Method
925	EX-4		505.2	1.31	QC-ACN-TFA-XB
926	EX-4		529.3	1.54	QC-ACN-TFA-XB

Example 927

Azetidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate

(927)



1-(tert-butoxycarbonyl)azetidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (15 mg, 0.026 mmol) and 2:1 trifluoroacetic acid:dichloromethane (1.2 mL, 0.026 mmol) were combined in a 1-dram vial containing a stir bar. The resulting clear, yellow solution was stirred at room temperature for 30 min. After completion of the reaction, toluene (150 μL) was added to the reaction mixture. The reaction mixture was stirred briefly and excess solvent was evaporated. The residue was taken up in DMF (1.5 mL) and purified by semi-preparative HPLC on a C-18 column on the Shimadzu instrument, eluting with water/acetonitrile/TFA. Excess solvent was evaporated from product-containing fractions to afford azetidin-3-yl 4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate, TFA (14.9 mg, 0.025 mmol, 96% yield) as a white solid. LCMS MH+: 487.3. HPLC Ret. Time 1.40 min. Method QC-ACN-TFA-XB. ^{1}H NMR (400 MHz, METHANOL-d_4) δ 8.68 (s, 1H), 8.58 (s, 1H), 7.60 (s, 1H), 7.33 (d, J=8.3 Hz, 1H), 7.08 (dd, J=8.4, 1.5 Hz, 1H), 5.33-5.24 (m, 1H), 4.45 (dd, J=12.7, 7.0 Hz, 2H), 4.38-4.25 (m, 2H), 4.21 (br. s., 2H), 3.17-3.06 (m, 1H), 2.98 (dq, J=13.6, 6.8 Hz, 4H), 2.88 (tt, J=12.0, 3.3 Hz, 1H), 2.67 (s, 3H), 2.30 (s, 3H), 1.96 (d, J=12.0 Hz, 2H), 1.75 (br. s., 2H), 1.40 (d, J=7.1 Hz, 6H).

The following examples were prepared according to the general process described in Example 929.

TABLE 22

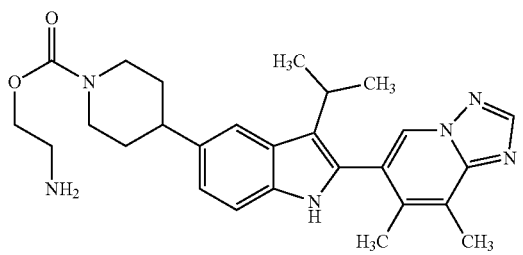
Ex. No.	Structure	LCMS MH+	R_t (min)	HPLC Method
928		475.1	1.45	QC-ACN-TFA-XB

TABLE 22-continued

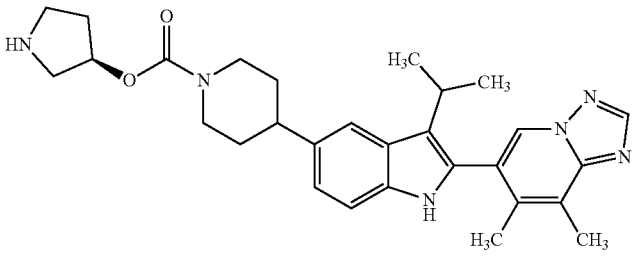
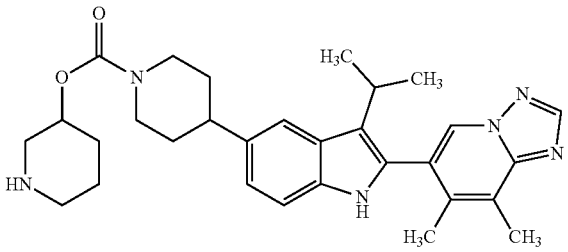
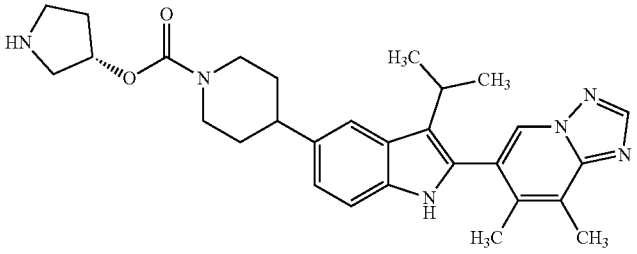
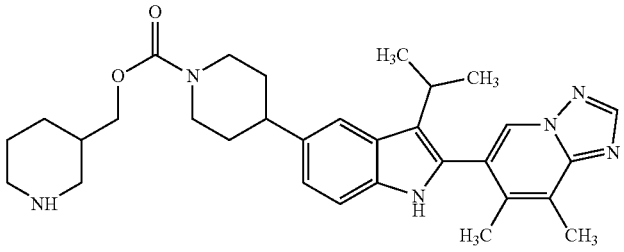
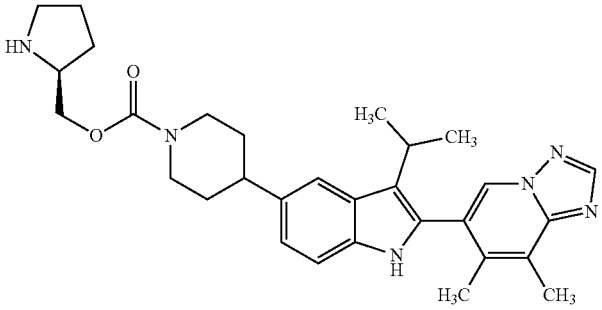
Ex. No.	Structure	LCMS MH^+	R_t (min)	HPLC Method
929		501.4	1.48	QC-ACN-TFA-XB
930		515.4	1.42	QC-ACN-TFA-XB
931		501.4	1.37	QC-ACN-TFA-XB
932		529.3	1.54	QC-ACN-AA-XB
933		515.4	1.4	QC-ACN-TFA-XB

TABLE 22-continued

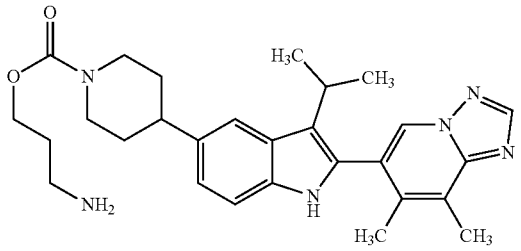
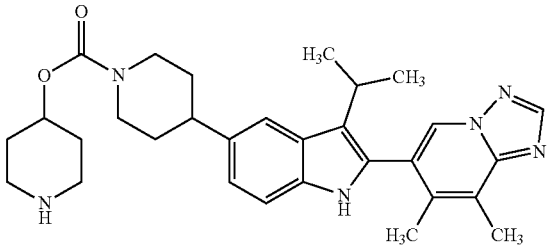
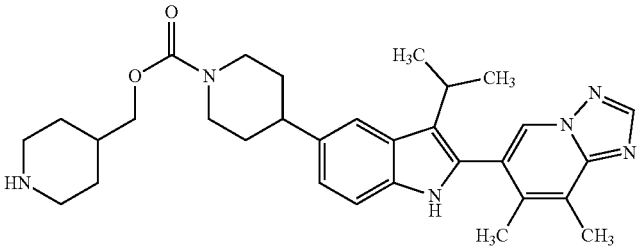
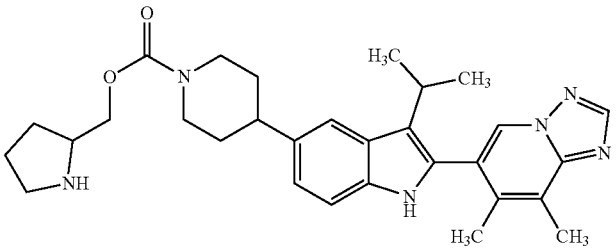
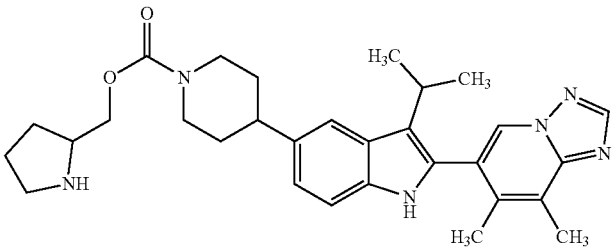
Ex. No.	Structure	LCMS MH^+	R_t (min)	HPLC Method
934		489.4	1.36	QC-ACN-TFA-XB
935		515.4	1.4	QC-ACN-TFA-XB
936		529.4	1.52	QC-ACN-AA-XB
937		515.0	1.52	QC-ACN-TFA-XB
938		515.0	1.58	QC-ACN-AA-XB

TABLE 22-continued

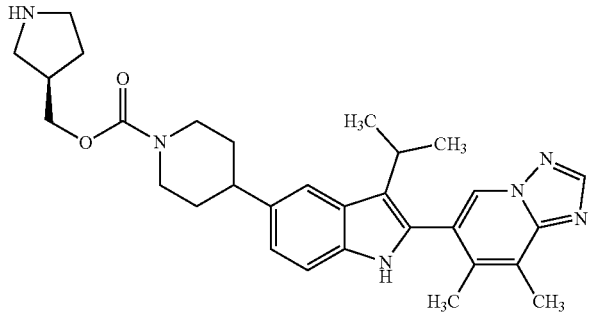
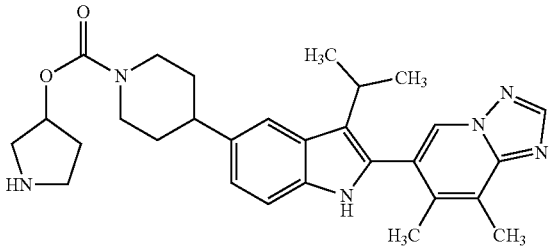
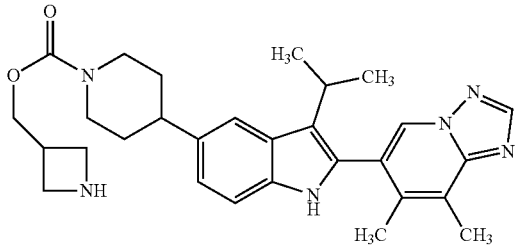
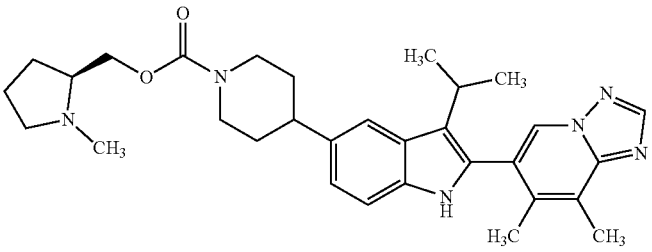
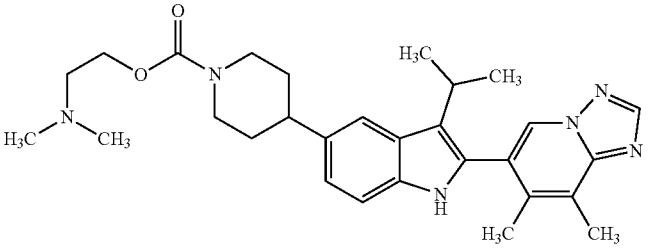
Ex. No.	Structure	LCMS MH^+	R_t (min)	HPLC Method
939		515.1	1.52	QC-ACN-TFA-XB
940		501.1	1.55	QC-ACN-AA-XB
941		501.4	1.37	QC-ACN-TFA-XB
942		528.9	1.64	QC-ACN-AA-XB
943		503.4	1.35	QC-ACN-TFA-XB

TABLE 22-continued

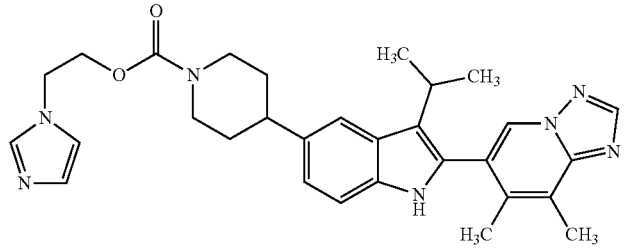
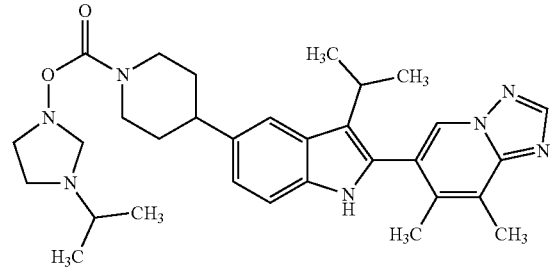
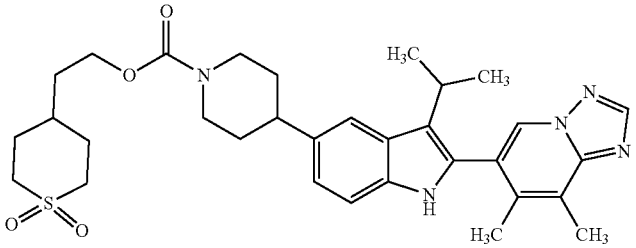
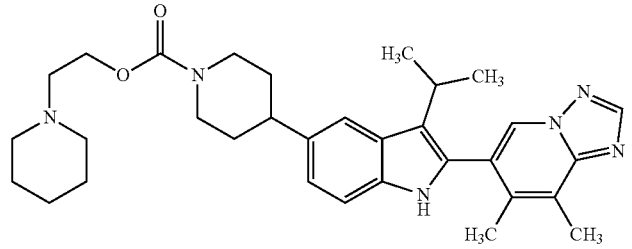
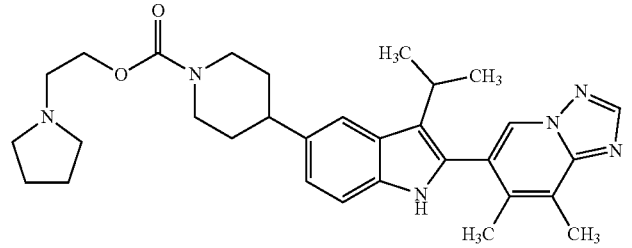
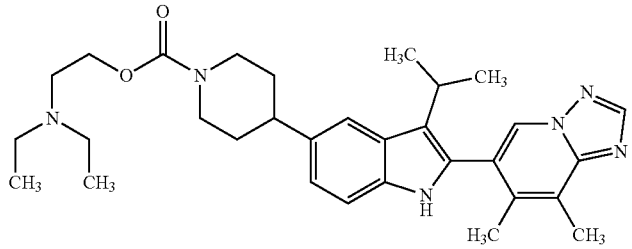
Ex. No.	Structure	LCMS MH+	R_t (min)	HPLC Method
944		526.3	1.37	QC-ACN-TFA-XB
945		543.5	1.45	QC-ACN-TFA-XB
946		593.4	1.45	QC-ACN-TFA-XB
947		543.5	1.45	QC-ACN-TFA-XB
948		529.5	1.41	QC-ACN-TFA-XB
949		531.3	1.47	QC-ACN-TFA-XB

TABLE 22-continued

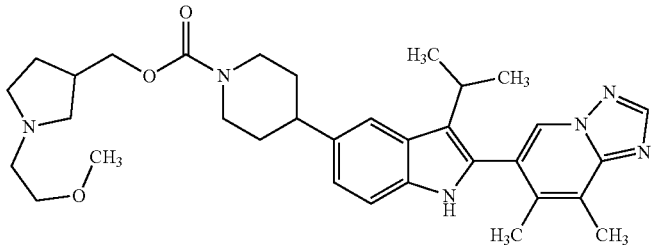
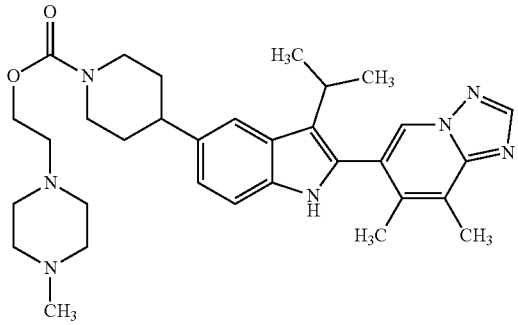
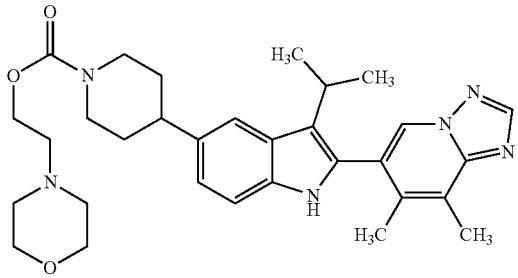
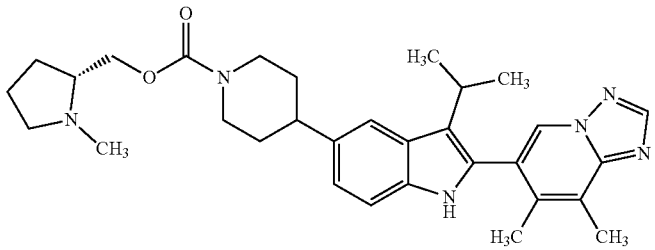
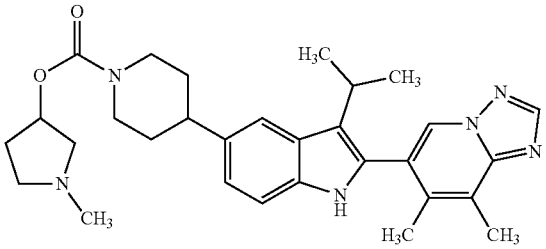
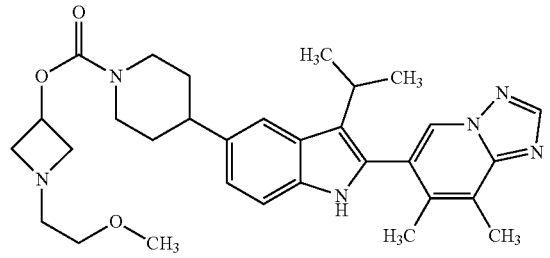
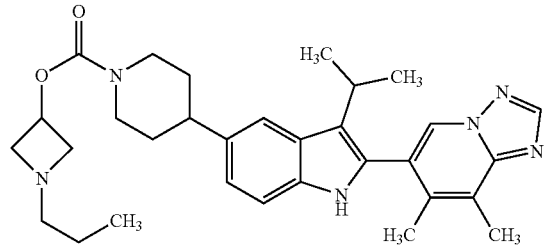
Ex. No.	Structure	LCMS MH^+	R_t (min)	HPLC Method
950		573.1	1.55	QC-ACN-AA-XB
951		558.1	1.48	QC-ACN-AA-XB
952		545.0	1.8	QC-ACN-AA-XB
953		265.2	1.52	QC-ACN-TFA-XB
954		515.1	1.67	QC-ACN-AA-XB

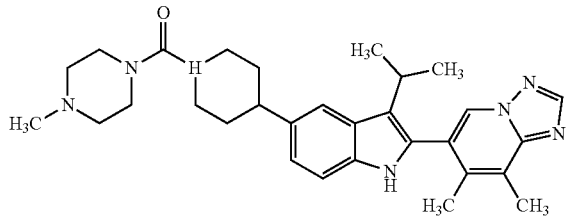
TABLE 22-continued

Ex. No.	Structure	LCMS MH^+	R_t (min)	HPLC Method
955		545.1	1.76	QC-ACN-AA-XB
956		529.1	1.59	QC-ACN-TFA-XB

Example 957

(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(4-methylpiperazin-1-yl)methanone

(957)



6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (10 mg, 0.026 mmol) was dissolved in THF (0.25 mL). Phenyl carbonochloridate (6.06 mg, 0.039 mmol) was added to the solution. The reaction mixture was stirred overnight at room temperature. The reaction mixture was blown down on a ZYmark Turbovap at 45° C. for 1 h. The residue was dissolved in NMP (0.25 mL). Next, 1-methylpiperazine (7.75 mg, 0.077 mmol) and DIPEA (6.76 μl, 0.039 mmol) were added to the NMP solution of the intermediate. The reaction mixture was stirred at 100° C. overnight. Crude samples with final volume of 1.8 mL in DMF/NMP in a stubby tube were purified via preparative LC/MS with the following conditions: Column:)(Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 20-60% B over 20 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford (4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)(4-methylpiperazin-1-yl) methanone (4 mg, 7.63 μmol, 29.6% yield). LCMS MH^+: 514.4. HPLC Ret. Time 1.29 min. Method QC-ACN-TFA-XB.

The following examples were prepared according to the general process described in Example 957.

TABLE 23

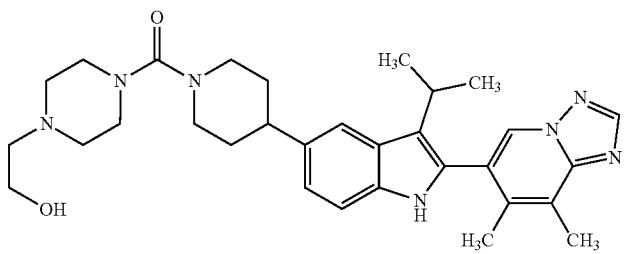
Ex. No.	Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
958	EX-4		565.9	1.57	QC-ACN-AA-XB

TABLE 23-continued

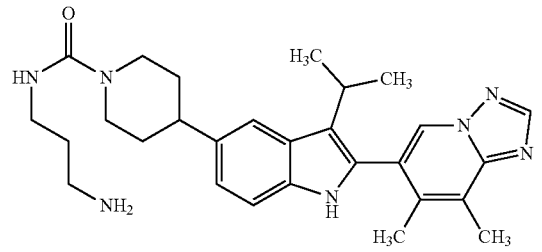
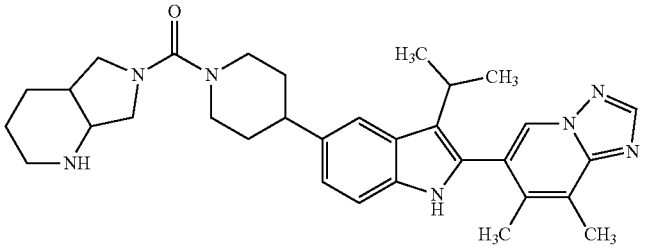
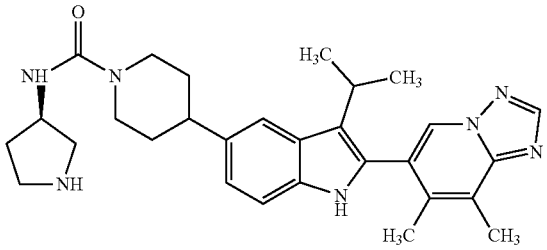
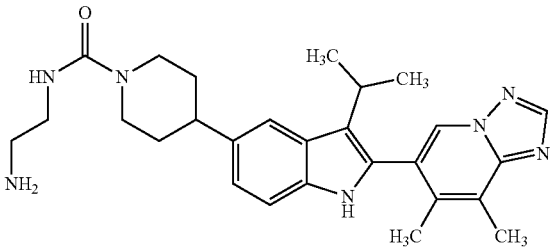
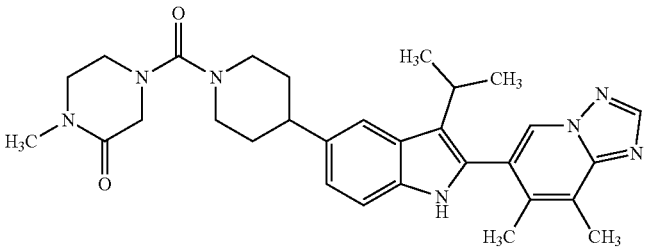
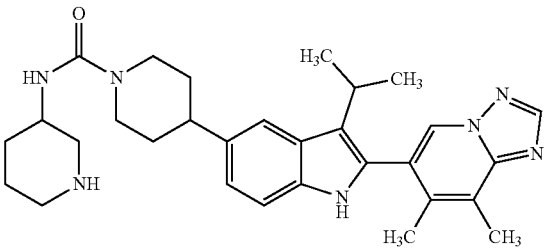
Ex. No.	Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
959	EX-4		488.3	1.27	QC-ACN-TFA-XB
960	EX-4		540.5	1.46	QC-ACN-TFA-XB
961	EX-4		500.0	1.31	QC-ACN-AA-XB
962	EX-4		474.4	1.27	QC-ACN-AA-XB
963	EX-4		528.5	1.56	QC-ACN-AA-XB
964	EX-4		514.2	1.36	QC-ACN-AA-XB

TABLE 23-continued

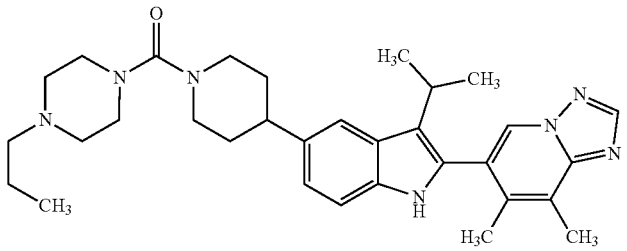
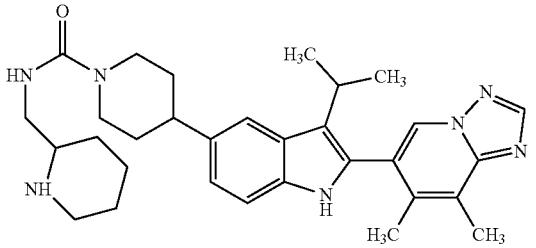
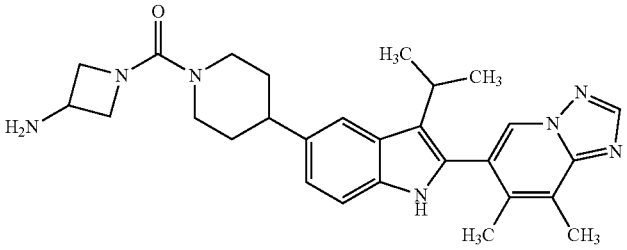
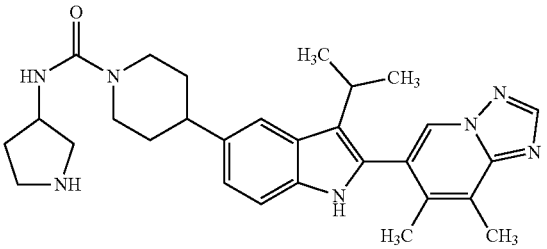
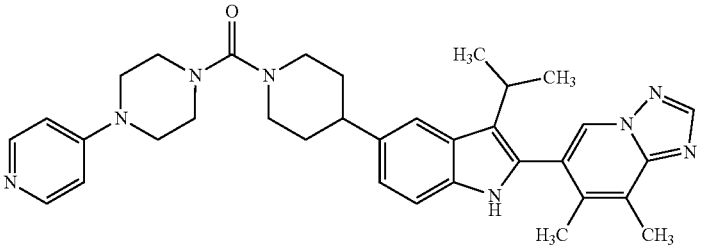
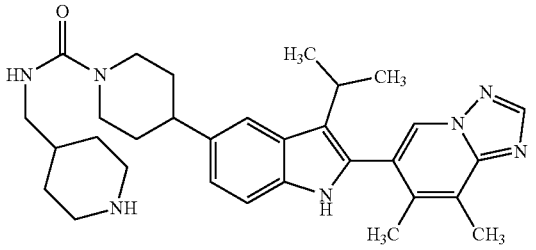
Ex. No.	Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
965	EX-4		542.6	1.83	QC-ACN-AA-XB
966	EX-4		528.5	1.39	QC-ACN-TFA-XB
967	EX-4		486.0	1.55	QC-ACN-AA-XB
968	EX-4		500.5	1.31	QC-ACN-AA-XB
969	EX-4		577.6	1.45	QC-ACN-TFA-XB
970	EX-4		528.5	1.33	QC-ACN-TFA-XB

TABLE 23-continued

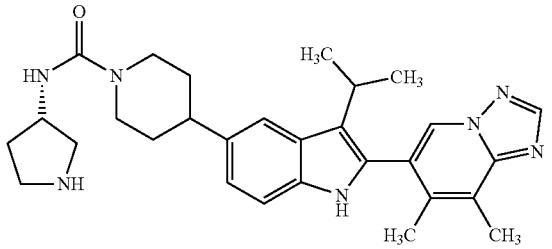
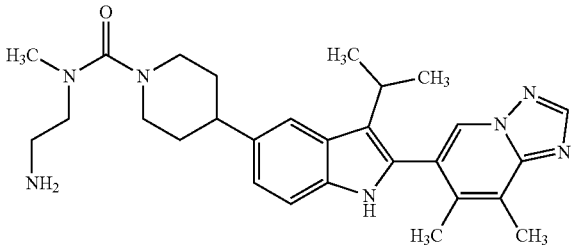
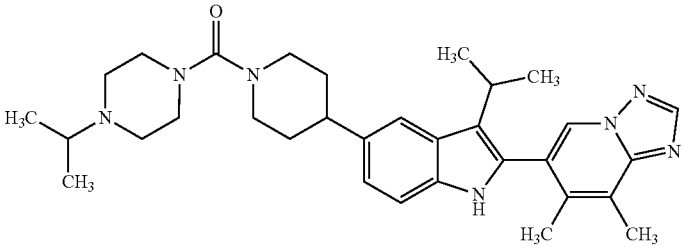
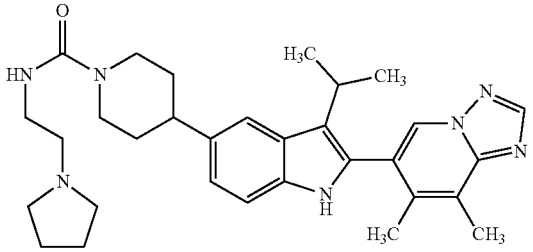
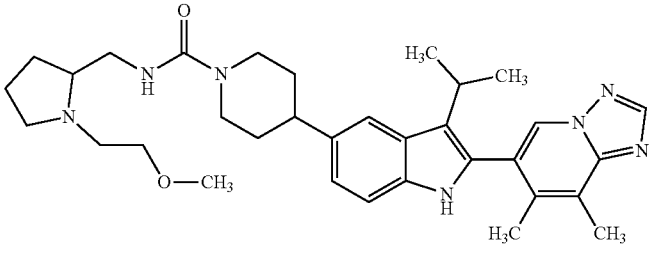
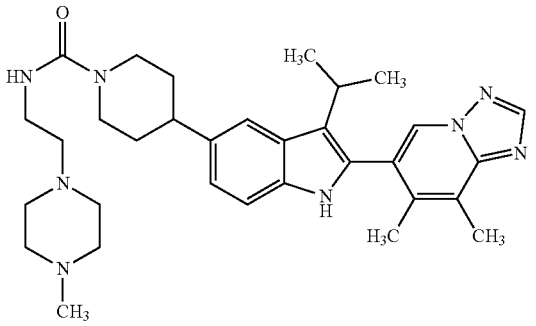
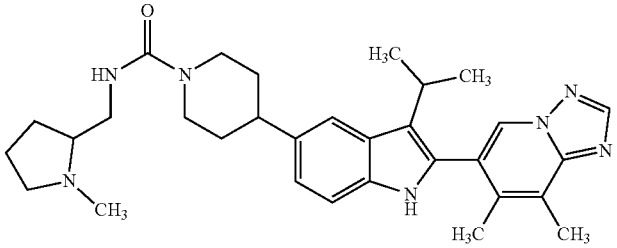
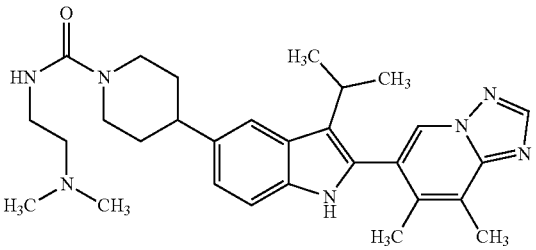
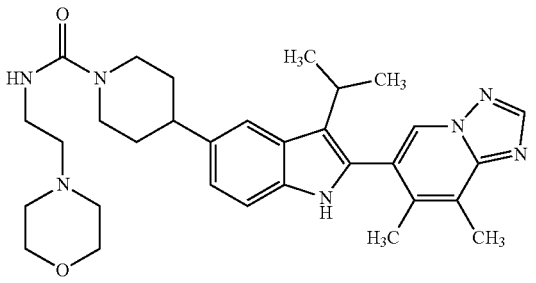
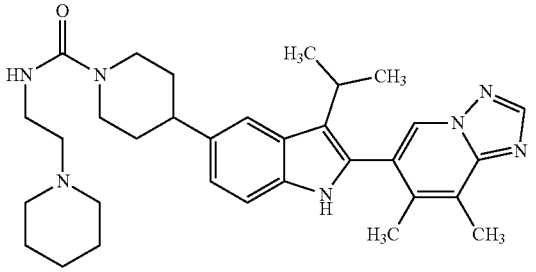
Ex. No.	Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
971	EX-4		500.3	1.3	QC-ACN-TFA-XB
972	EX-4		488.0	1.43	QC-ACN-TFA-XB
973	EX-4		542.0	1.68	QC-ACN-AA-XB
974	EX-4		528.4	1.32	QC-ACN-TFA-XB
975	EX-4		572.5	1.45	QC-ACN-TFA-XB

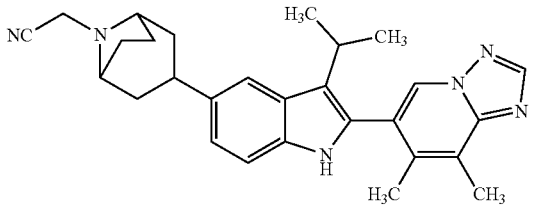
TABLE 23-continued

Ex. No.	Starting Material	Structure	LCMS MH^+	R_t (min)	HPLC Method
976	EX-4		557.3	1.3	QC-ACN-AA-XB
977	EX-4		528.4	1.36	QC-ACN-TFA-XB
978	EX-4		502.4	1.33	QC-ACN-AA-XB
979	EX-4		544.5	1.3	QC-ACN-TFA-XB
980	EX-4		542.6	1.41	QC-ACN-TFA-XB

Example 981

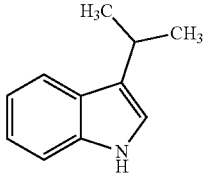
2-(3-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-8-a zabicyclo [3.2.1]octan-8-yl)acetonitrile

(981)



Intermediate 981A: 3-isopropyl-1H-indole

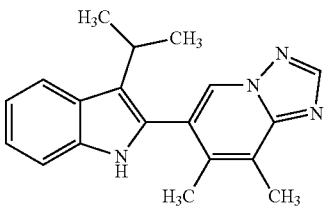
(981A)



To a 500 mL round bottom flask were added 2,2,2-trichloroacetic acid (23.60 g, 144 mmol), toluene (150 mL), and triethylsilane (46.1 mL, 289 mmol). With stirring, the solution was heated to 70° C. and a solution of 1H-indole (11.28 g, 96 mmol) and acetone (8.48 mL, 116 mmol) in 75 mL of toluene was added drop-wise via an addition funnel. The reaction mixture was heated to 90° C. for 2.5 hours. The reaction mixture was cooled to room temperature, then to 5° C. To this were added 1.5 M dibasic potassium phosphate solution and diethyl ether. The layers were separated and the organic layer was washed with brine, dried over Na_2SO_4, filtered and concentrated. The residue was purified on silica gel using ethyl acetate/hexane as the eluent to afford 3-isopropyl-1H-indole (12 g, 78%) as a white solid. LC retention time=1.04 min [A1]. MS (E^+) m/z: 160.2 (M+H). ^1H NMR (400 MHz, CHLOROFORM-d) δ 7.72-7.65 (m, 1H), 7.41-7.36 (m, 1H), 7.21 (d, J=0.9 Hz, 1H), 7.14 (s, 1H), 6.99 (dd, J=2.2, 0.7 Hz, 1H), 3.31-3.17 (m, 1H), 1.40 (d, J=6.8 Hz, 6H).

Intermediate 981B: 6-(3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine

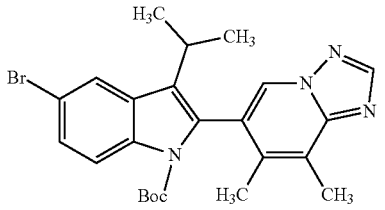
(981B)



To a 100 mL round bottom flask were added 3-isopropyl-1H-indole (1.000 g, 6.28 mmol) and DCE (10 mL). NBS (1.062 g, 5.97 mmol) was dissolved in 10 mL of DCE and added to the reaction mixture drop-wise via an addition funnel over 15 minutes. The reaction was quenched with 5 mL of a 10% sodium sulfite solution. The volatiles were removed. Next, THF (10 mL), 7,8-dimethyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,2,4]triazolo[1,5-a] pyridine (1.54 g, 5.56 mmol), $PdCl_2(dppf)$-CH_2Cl_2 adduct (0.25 g, 0.314 μmol), and 3 M tribasic potassium phosphate solution (6.3 mL, 18.8 mmol) were added. The reaction vessel was capped and pump/purged with nitrogen gas three times. The reaction mixture was set to heat at 70° C. for 1 hour. The mixture was cooled to room temperature and concentrated. The crude residue was taken up in DCM (3 mL), filtered and purified on silica gel using ethyl acetate/hexane to afford 6-(3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (0.8 g, 41.8%) as a white foam. LC retention time=2.04 min [D1]. MS (E^+) m/z: 305.0 (M+H). ^1H NMR (400 MHz, METHANOL-d_4) δ 8.54-8.44 (m, 1H), 8.38-8.28 (m, 1H), 7.56 (d, J=1.1 Hz, 1H), 7.45 (d, J=8.4 Hz, 1H), 7.13-7.01 (m, 2H), 3.28-3.16 (m, 1H), 2.66 (s, 3H), 2.32 (s, 3H), 1.38 (d, J=6.8 Hz, 6H).

Intermediate 981C: tert-butyl 5-bromo-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole-1-carboxylate

(981C)



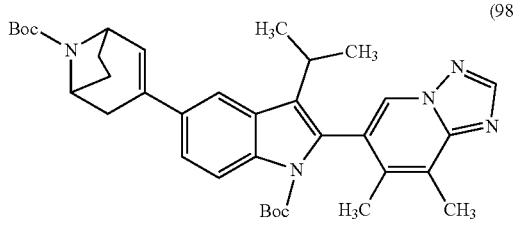
To a 40 mL reaction vial were added 6-(3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (0.450 g, 1.478 mmol), AcOH (4 mL), water (0.5 mL), and NBS (0.263 g, 1.478 mmol). The vial was sealed and stirred at 80° C. for 30 minutes. The reaction mixture was cooled to room temperature and 1 mL of a 10% sodium sulfite was added. This mixture was concentrated, dissolved in DCM/MeOH, filtered, and purified on silica gel using ethyl acetate/hexane to afford 5-bromo-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole as a tan solid. LC retention time=1.01 min [A1]. MS (E^+) m/z: 83/385 (M+H). ^1H NMR (400 MHz, DMSO-d_6) δ 11.26 (s, 1H), 8.82 (s, 1H), 8.48 (s, 1H), 7.70 (d, J=8.4 Hz, 1H), 7.52 (d, J=1.5 Hz, 1H), 7.16 (dd, J=8.6, 1.8 Hz, 1H), 2.88 (br d, J=14.1 Hz, 1H), 2.60 (s, 3H), 2.15 (s, 3H), 1.43-1.15 (m, 5H), 1.18-1.09 (m, 1H).

To this material were added DMAP (0.010 g, 0.0148 mmol), THF (10 mL), and BOC-anhydride (0.59 g, 2.95 mmol). The reaction mixture was stirred for 2 hours at room temperature, concentrated to a viscous oil, diluted with DCM, and washed with dilute 1N HCl. The organic was washed with water and then brine. The solution was dried over Na_2SO_4, filtered, and concentrated. The residue was purified on silica gel using ethyl acetate/hexane to afford tert-butyl 5-bromo-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-3-isopropyl-1H-indole-1-car boxylate (0.45 g,

63%) as a yellowish solid. LC retention time=1.15 min [A1]. MS (E^+) m/z: 483/485 (M+H).

Intermediate 981D: tert-butyl 5-(8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]oct-2-en-3-yl)-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole-1-carboxylate

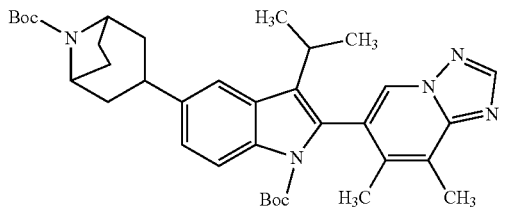
(981D)



To a mixture of tert-butyl 5-bromo-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole-1-carboxylate (0.130 g, 0.269 mmol), $PdCl_2(dppf)$-CH_2Cl_2 adduct (10.98 mg, 0.013 mmol), and (8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]oct-3-en-3-yl) boronic acid (0.071 g, 0.282 mmol) in a screw cap vial was added THF (2 mL) followed by 3 M aqueous solution of tripotassium phosphate (0.269 mL, 0.807 mmol). The vial was fitted with a Teflon lined septum cap. The system was evacuated under vacuum and backfilled with nitrogen gas. The procedure was repeated three times. The vial was sealed and heated at 75° C. for 18 hours. The reaction mixture was diluted with EtOAc (100 mL) and poured into a separatory funnel. The organic layer was washed with water (2×50 mL), saturated aqueous NaCl solution (50 mL), dried (Na_2SO_4), filtered and concentrated in vacuo to afford crude product. The crude product was purified on silica gel using 0-100% ethyl acetate/hexane. Following concentration of the fractions, the product was collected as a tan oil (0.11 g, 65%). LC retention time=1.19 min [A1]. MS (E^+) m/z: 612.2 (M+H).

Intermediate 981E: tert-butyl 5-(8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]octan-3-yl)-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole-1-carboxylate

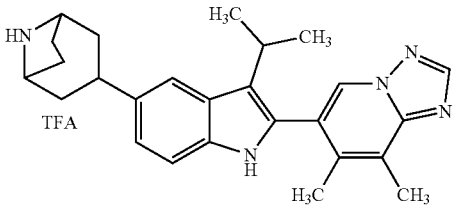
(981E)



In a Parr bottle, tert-butyl 5-(8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]oct-2-en-3-yl)-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole-1-carboxylate (0.11 g, 0.18 mmol) was suspended in ethyl acetate (3 mL) and treated with 10 mol % of 5% Pd/C (0.057 g, 0.027 mmol). Following degassing, the reaction mixture was placed under a hydrogen gas atmosphere (50 psi) and shaken for 16 hours at room temperature. Following the removal of the hydrogen atmosphere and back-filling with nitrogen gas, the reaction mixture was diluted with MeOH, filtered through celite, and concentrated to afford tert-butyl 5-(8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]octan-3-yl)-2-(7,8-dimethyl-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole-1-carboxylate (0.11 g, 100%) as a mixture of isomers. LC retention time=1.20 min [A1]. MS (E^+) m/z: 614.4 (M+H).

Intermediate 981F: 6-(5-(8-azabicyclo[3.2.1]octan-3-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine TFA salt

(981F)



To a solution of tert-butyl 5-(8-(tert-butoxycarbonyl)-8-azabicyclo[3.2.1]octan-3-yl)-2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indole-1-carboxylate (0.025 g, 0.041 mmol) was added DCM (0.5 mL) in a 2 dram reaction vial. To this was added TFA (1 mL) and the reaction vial was capped. The reaction mixture was stirred for 2 hours at room temperature. The volatiles were removed under a stream of nitrogen gas. The yield was considered quantitative. This material was used as is for final derivatization to prepare the compounds shown in Table 24. One example is described below for Example 981.

Example 981

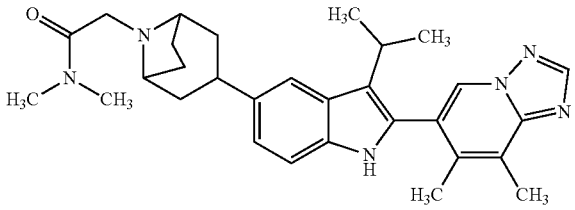
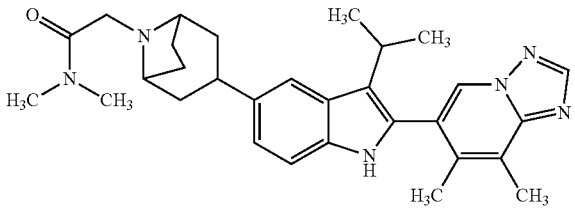
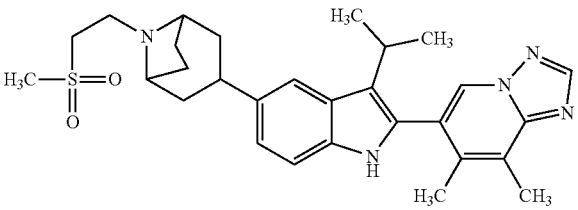
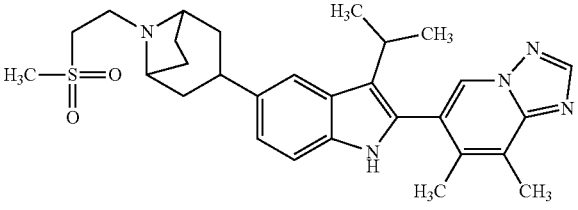
In a 2 dram reaction vial were added 6-(5-(8-azabicyclo[3.2.1]octan-3-yl)-3-isopropyl-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine, TFA salt (0.021 g, 0.041 mmol), NMP, DBU (0.025 mL, 0.164 mmol), and drop-wise, bromoacetonitrile (0.017 g, 0.15 mmol). The reaction mixture was stirred for 1 hour at room temperature, then diluted with water, and filtered through a 0.45 micron syringe filter. The crude material was purified via preparative LC/MS with the following conditions: Column:)(Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 40-80% B over 25 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation. The material was further purified via preparative LC/MS with the following conditions: Column:)(Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 35-75% B over 20 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation.

2-(3-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)-8-azabicyclo[3.2.1]octan-8-yl) acetonitrile (0.0021 g, 6.4% yield) was collected as a mix-

ture of isomers. Two analytical LC/MS injections were used to determine the final purity. LC retention time 2.18 min [C1]. MS (E^+) m/z: 453.0 (M+H). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.95 (br d, J=18.2 Hz, 1H), 8.73-8.64 (m, 1H), 8.69 (br s, 1H), 8.52-8.39 (m, 1H), 8.46 (s, 1H), 7.62 (s, 1H), 7.62 (br d, J=18.2 Hz, 1H), 7.19 (s, 1H), 7.23 (br s, 1H), 7.01-6.88 (m, 1H), 7.05-6.84 (m, 1H), 3.34 (br s, 1H), 3.17 (s, 1H), 3.13-3.01 (m, 1H), 2.99-2.93 (m, 1H), 2.88-2.76 (m, 1H), 2.57 (s, 2H), 2.15 (s, 2H), 2.02-1.94 (m, 1H), 1.90 (br d, J=8.2 Hz, 1H), 1.75 (br s, 4H), 1.68-1.57 (m, 1H), 1.29 (br s, 5H).

The following examples were prepared according to the general procedures disclosed in Example 981.

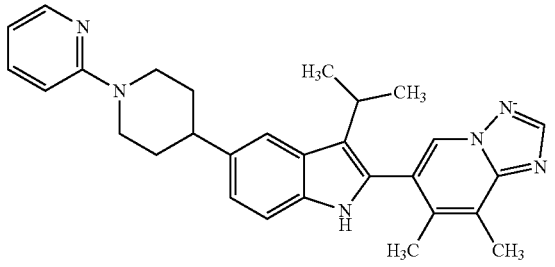
TABLE 24

Ex. No.	Structure	LCMS MH^+	R_t (min)	HPLC Method
982		499.1	1.57	C1
983		499.1	1.50	C1
984		520.0	1.58	C1
985		520.1	1.53	C1

Example 986

6-(3-isopropyl-5-(1-(pyridin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine

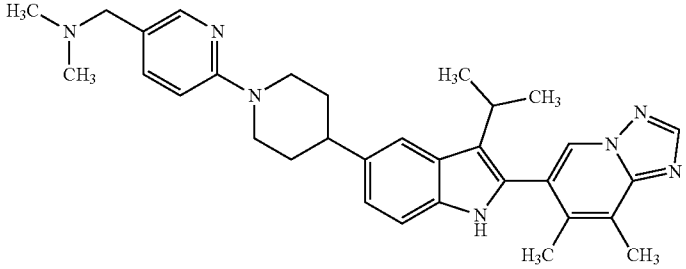
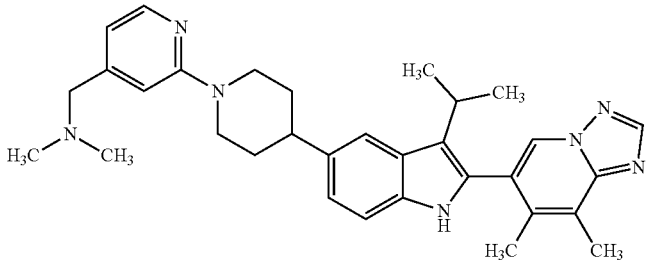
(986)



6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (19.4 mg, 0.050 mmol), 2-chloropyridine (6.2 mg, 0.055 mmol), 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene (5.8 mg, 10.00 μmol), $Pd_2(dba)_3$ (4.6 mg, 5.00 μmol) and Cs_2CO_3 (48.9 mg, 0.150 mmol) were suspended in dioxane (0.5 mL). The mixture was degassed with nitrogen gas for 5 minutes. The reaction vessel was sealed and heated to 90° C. for 2 hours. Upon completion, the reaction mixture was filtered, concentrated, dissolved in DMF, and purified via preparative LCMS using the following conditions: Column:)(Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 0.1% trifluoroacetic acid; Mobile Phase B: 95:5 acetonitrile: water with 0.1% trifluoroacetic acid; Gradient: 10-50% B over 19 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 6-(3-isopropyl-5-(1-(pyridin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine, TFA (10.1 mg, 0.017 mmol, 35% yield). LCMS retention time 1.25 [QC-ACN-TFA-XB]. MS (ES^+) m/z: 465.4 (M+H). ^1H NMR (500 MHz, DMSO-d_6) δ 8.81 (s, 1H), 8.63 (br d, J=7.9 Hz, 1H), 8.44-8.38 (m, 2H), 8.36 (br d, J=9.5 Hz, 1H), 7.82-7.73 (m, 1H), 7.67 (s, 1H), 7.48 (d, J=8.5 Hz, 1H), 7.28-7.24 (m, 1H), 7.22 (d, J=7.9 Hz, 1H), 7.12 (br d, J=8.5 Hz, 1H), 3.41 (br d, J=11.3 Hz, 2H), 3.11-2.93 (m, 3H), 2.85 (dt, J=14.0, 7.0 Hz, 1H), 2.42 (s, 3H), 2.06-1.96 (m, 2H), 1.96-1.82 (m, 5H), 1.35 (dd, J=16.5, 7.0 Hz, 6H).

The following examples were prepared in a manner similar to Example 986.

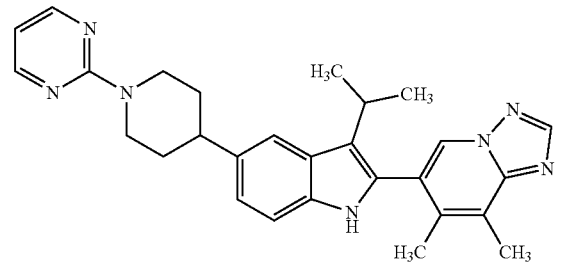
TABLE 25

Ex. No.	Structure	LCMS MH^+	R_t (min)	HPLC Method
987		522.5	0.96	QC-ACN-TFA-XB
988		522.5	0.95	QC-ACN-TFA-XB

Example 989

6-(3-isopropyl-5-(1-(pyrimidin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine

(989)

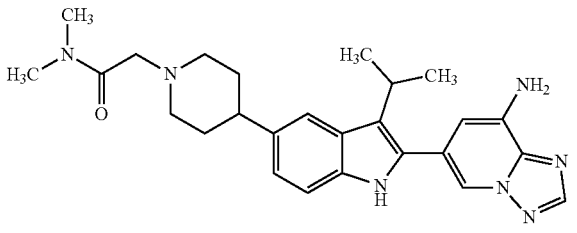


6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (19.4 mg, 0.050 mmol) and Et_3N-(0.021 mL, 0.150 mmol) were mixed in DMSO (1 mL). Next, 2-chloropyrimidine (6.9 mg, 0.060 mmol) was added. The reaction vial was sealed and heated to 90° C. for 2 hours. Upon completion, the reaction mixture was cooled to room temperature, diluted with water (0.05 mL) and 1 mL of DMSO, and purified on preparative LCMS via the following conditions: Column:) (Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 45-100% B over 20 minutes, then a 10-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to provide 6-(3-isopropyl-5-(1-(pyrimidin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (5.0 mg, 10.2 μmol, 20.4% yield). LCMS retention time 1.71 [QC-ACN-TFA-XB]. MS (ES^+) m/z: 466.3 (M+H).

Example 990

2-(4-(2-(8-amino-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide

(990)

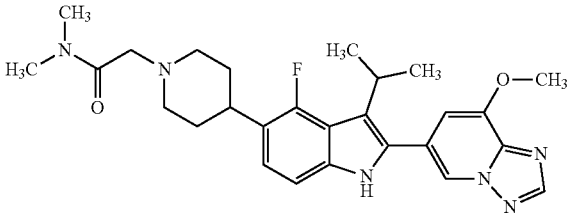


To a solution of 2-(4-(2-(8-(benzylamino)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl -1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (0.040 g, 0.073 mmol) in methanol (10.0 mL) was added Pd/C (0.023 g, 0.218 mmol). The reaction mixture was stirred at room temperature for 6 h under hydrogen. The reaction mixture was diluted with ethyl acetate:methanol (1:1) filtered and washed with excess ethyl acetate. The combined organic layers were evaporated to afford crude compound. The crude material was purified via preparative LC/MS with the following conditions: Column: Water XBridge C18, 19×150 mm, 5-μm particles; Mobile Phase A: 0.05% TFA; Mobile Phase B: acetonitrile; Gradient: 15-50% B over 20 minutes, then a 5-minute hold at 100% B; Flow: 15 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 2-(4-(2-(8-amino-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl) piperidin-1-yl)-N,N-dimethylacetamide (7.3 mg). LCMS retention time 1.44 min [E]. MS (E−) m/z: 460.3 (M−H). ^1H NMR (400 MHz, METHANOL-d_4) δ ppm 8.31-8.39 (m, 1H) 8.16 (d, J=1.47 Hz, 1H) 7.66 (s, 1H) 7.36 (d, J=8.31 Hz, 1H) 7.08 (d, J=8.80 Hz, 1H) 6.84-6.97 (m, 1H) 4.26 (s, 2H) 3.76 (d, J=13.21 Hz, 2H) 3.33-3.43 (m, 2H) 3.25 (br. s., 2H) 2.94-3.12 (m, 8H) 2.19 (br. s., 4H) 1.50 (d, J=7.09 Hz, 7H) 1.28 (br. s., 1H).

Example 991

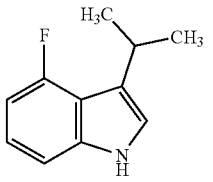
2-(4-(4-fluoro-3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide

(991)



Intermediate 991A: 4-fluoro-3-isopropyl-1H-indole

(991A)

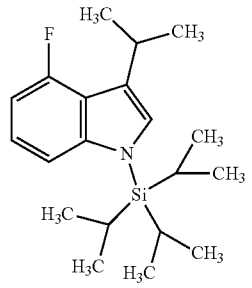


To a 40 mL vial with a red pressure-release cap were added 2,2,2-trichloroacetic acid (0.907 g, 5.55 mmol), toluene (7.40 mL) and triethylsilane (1.773 mL, 11.10 mmol). With stirring, the solution was heated to 70° C. and a solution of 4-fluoro-1H-indole (0.500 g, 3.70 mmol) and acetone (0.326 mL, 4.44 mmol) in 1 mL of toluene was added drop-wise via a syringe. The reaction mixture was stirred and heated to 90° C. for 3h, venting with a nitrogen line. The reaction mixture was allowed to cool to 5° C., and to the reaction mixture were added 1 M aqueous K_3PO_4 solution (~4 mL) and ethyl acetate (4 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2×5 mL). The combined organic extracts were dried over sodium sulfate and filtered, and excess solvent was evaporated off. The resulting red oil was taken up in DCM (~2 mL) and purified by flash chromatography to afford 4-fluoro-3-isopropyl-1H-indole as a yellow liquid (483.2 mg, 2.67 mmol, 72.2% yield). ^1H NMR (400 MHz, CHLOROFORM-

d) δ 7.97 (br s, 1H), 7.16-7.07 (m, 2H), 6.95 (d, J=2.2 Hz, 1H), 6.77 (ddd, J=11.3, 7.4, 1.1 Hz, 1H), 3.38 (dt, J=13.7, 6.8 Hz, 1H), 1.38 (dd, J=6.8, 0.6 Hz, 6H). HPLC Ret. Time 0.99 min. Method G.

Intermediate 991B: 4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indole

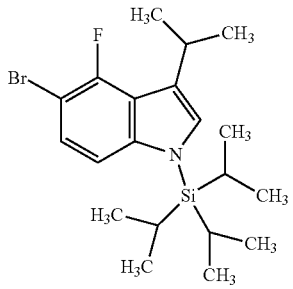
(991B)



4-fluoro-3-isopropyl-1H-indole (0.475 g, 2.68 mmol) was dissolved in THF (10.72 mL) in a 40 mL vial. The solution was cooled to 0° C. under a nitrogen atmosphere with an ice bath, and sodium hydride (0.214 g, 5.36 mmol) was added to the reaction mixture. The reaction mixture was allowed to warm to room temperature, then triisopropylsilyl chloride (0.860 mL, 4.02 mmol) was added dropwise via syringe. The reaction mixture was then stirred at 50° C. for 1 h. The reaction completed. The reaction mixture was cooled to 0° C. and quenched by addition of 1 M $KHSO_4$ (~4 mL) and water (4 mL). Ethyl acetate (4 mL) was added, and the phases were separated. The aqueous phase was extracted with ethyl acetate (2×3 mL). The combined organic phases were extracted with brine (1×4 mL), and excess solvent was evaporated off. The resulting yellow oil was taken up in DCM (~3.5 mL total volume) and purified by flash chromatography on a 24 g silica column, eluting with ethyl acetate and hexanes. The product 4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indole was obtained as a clear, colorless liquid (0.92 g, 2.48 mmol, 92% yield). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.24 (d, J=8.3 Hz, 1H), 7.03 (td, J=8.1, 5.4 Hz, 1H), 6.94 (s, 1H), 6.76 (dd, J=11.0, 7.8 Hz, 1H), 3.36 (spt, J=6.8 Hz, 1H), 1.36 (d, J=6.8 Hz, 6H), 1.16 (d, J=7.6 Hz, 18H). LCMS MH^-: 334.3. HPLC Ret. Time 1.43 min. Method G.

Intermediate 991C: 5-bromo-4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indole

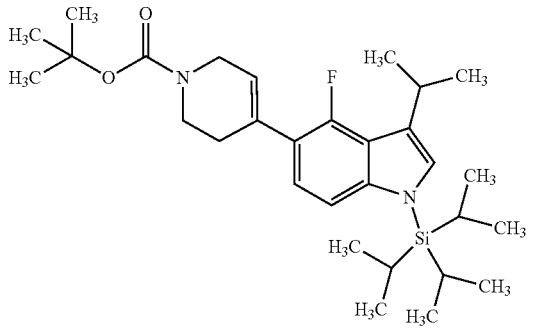
(991C)



Sec-butyllithium (2.144 mL, 3.00 mmol, 90% purity) was added to a −75° C. (dry ice/methanol bath) solution of 4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indole (0.910 g, 2.73 mmol) and 1,1,4,7,7-pentamethyldiethylenetriamine (0.572 mL, 2.73 mmol) in THF (13.64 mL) in an oven-dried 50 mL recovery flask under a nitrogen atmosphere. The solution was stirred for 6.5 h at −75° C. for 6 h. Next, 1,2-dibromotetrafluoroethane (0.325 mL, 2.73 mmol) was added to the reaction mixture. The solution was stirred for 10 min at −75° C., then allowed to warm to room temperature. The reaction progressed 50%. Excess solvent was evaporated from the reaction mixture. The resulting orange oil was taken up in DCM (total volume ~4 mL) and purified by flash chromatography on a 24 g silica column, eluting with hexanes. The product and remaining starting indole co-eluted. Fractions were pooled and excess solvent was evaporated off to yield 5-bromo-4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indole (1.07 g, 1.68 mmol, 65% yield) and 4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indole as a mixture in a clear, colorless liquid. The mixed products were taken forward directly. LCMS MH^-: 412.08. HPLC Ret. Time 1.50 min. Method G.

Intermediate 991D: tert-butyl 4-(4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indol-5-yl)-3,6-dihydropyridine-1(2H)-carboxylate

(991D)

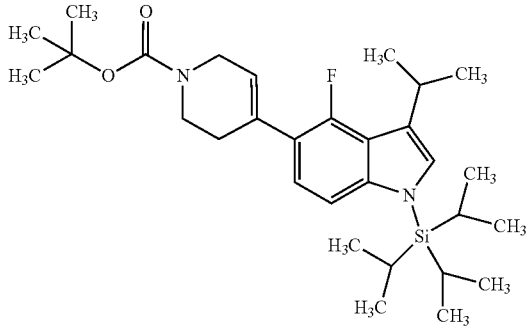


5-bromo-4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indole (650 mg, 1.576 mmol) was dissolved in THF (7880 μl) in a 40 mL scintillation vial with a red pressure-release cap and containing a Teflon-covered stir bar. Tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5,6-dihydropyridine-1(2H)-carboxylate (585 mg, 1.891 mmol) was added to the vial, followed by tripotassium phosphate (2364 μl, 4.73 mmol). The reaction mixture was degassed by bubbling nitrogen through the solution for 5 min, then 2nd generation XPhos precatalyst (31.0 mg, 0.039 mmol) was added to the reaction mixture. The clear, yellow reaction mixture was placed under a nitrogen atmosphere and heated to 60° C. with stirring for 6 h. The reaction mixture was allowed to cool to room temperature. The aqueous phase was removed, and excess THF was evaporated from the reaction. The resulting oil residue was taken up in DCM (~4 mL total volume) and purified by flash chromatography eluting with ethyl acetate and hexanes. The product fractions was concentrated and vacuumed to afford tert-butyl 4-(4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate as a pale yellow sticky solid (0.65 g, 1.14 mmol, 72.6% yield). ^{1}H NMR (400 MHz,

CHLOROFORM-d) δ 7.18 (d, J=8.6 Hz, 1H), 6.99-6.94 (m, 1H), 6.92 (s, 1H), 5.90 (br s, 1H), 4.10 (br s, 2H), 3.66 (br t, J=5.2 Hz, 2H), 3.36 (spt, J=6.8 Hz, 1H), 2.61 (br s, 2H), 1.53 (s, 9H), 1.35 (d, J=6.7 Hz, 6H), 1.16 (d, J=7.6 Hz, 18H). LCMS MH^+: 515.5. HPLC Ret. Time 1.53 min. Method G.

Intermediate 991E: tert-butyl 4-(4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indol-5-yl) piperidine-1-carboxylate

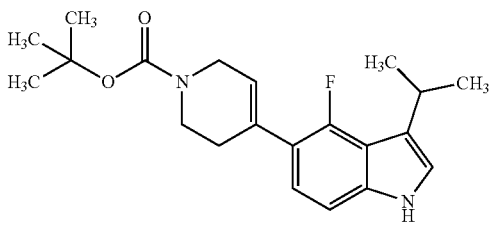
(991E)



5% Pd on Carbon (100 mg, 1.271 mmol) was weighed into a 20 mL scintillation vial containing a Teflon-coated stir bar with a red pressure-release cap. Tert-butyl 4-(4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (654.4 mg, 1.271 mmol) was dissolved in MeOH (12.71 mL) and transferred into the vial containing the Pd on C while under a nitrogen atmosphere. Ammonium formate (401 mg, 6.36 mmol) was added to the reaction mixture, and the vial was capped. The reaction mixture was stirred at 50° C. for 4 h. Additional ammonium formate (401 mg, 6.36 mmol) was added to the reaction mixture, and the reaction mixture was stirred at 60° C. for 3 h but did not reach completion. The reaction mixture was stirred at 50° C. overnight. The reaction mixture was filtered through celite to remove Pd/C. Excess methanol was evaporated from the reaction mixture to afford tert-butyl 4-(4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indol-5-yl) piperidine-1-carboxylate (654 mg, 1.271 mmol, 100% yield, 30% purity) a clear, pale yellow oil. Product was checked by ^1H NMR and was approximately 30% reduced and 70% starting material alkene. LCMS MH^+: 517.5. HPLC Ret. Time 1.53 min. Method G.

Intermediate 991F: tert-butyl 4-(4-fluoro-3-isopropyl-1H-indol-5-yl)-3,6-dihydropyridine-1(2H)-carboxylate

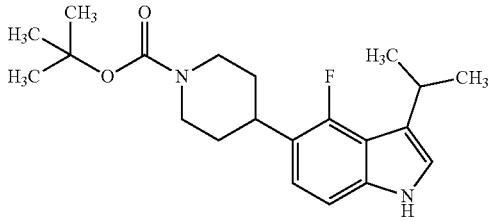
(991F)



Tert-butyl 4-(4-fluoro-3-isopropyl-1-(triisopropylsilyl)-1H-indol-5-yl)-3,6-dihydropyridine-1(2H)-carboxylate (0.650 g, 1.263 mmol) (7:3 mix of piperidine alkene and piperidine alkane) and tetra-n-butylammonium fluoride (0.660 g, 2.53 mmol) were dissolved in THF (6.31 mL) in a 20 mL scintillation vial. The reaction mixture was stirred for 10 min at room temperature. The reaction was complete with 2 peaks corresponding to the product alkene (1.15 min, $M+H^+$=359.3) and alkane (1.16 min, $M+H^+$=359.3, 361.3). The reaction mixture was partitioned between brine and ethyl acetate (1:1, total volume ~16 mL). The phases were separated, and the aqueous phase was extracted with ethyl acetate (2×4 mL). The combined organic phases were washed with brine (2×5 mL), dried over sodium sulfate, and filtered. Excess solvent was evaporated from the organic phase to afford tert-butyl 4-(4-fluoro-3-isopropyl-1H-indol-5-yl)-3,6-dihydropyridine-1(2H)-carboxylate (0.476 g, 1.263 mmol) as a pale yellow oil. LCMS MH^+: 359.3. HPLC Ret. Time 1.15 min. Method G.

Intermediate 991G: tert-butyl 4-(4-fluoro-3-isopropyl-1H-indol-5-yl)-3,6-dihydropyridine-1(2H)-carboxylate

(991G)

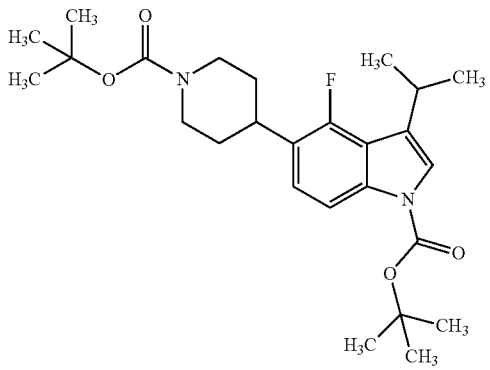


5% Pd on Carbon (150 mg, 1.264 mmol) was weighed into a 20 mL scintillation vial containing a Teflon-coated stir bar with a red pressure-release cap. Tert-butyl 4-(4-fluoro-3-isopropyl-1H-indol-5-yl)-5,6-dihydropyridine-1(2H)-carboxylate (453 mg, 1.264 mmol) was dissolved in MeOH (6.32 mL) and transferred into the vial containing the Pd on C while under a nitrogen atmosphere. Ammonium formate (797 mg, 12.64 mmol) was added to the reaction mixture, and the vial was capped. The reaction mixture was stirred at 60° C. for 30 min. The reaction completed. The reaction mixture was filtered through celite to remove Pd/C. Excess methanol was evaporated from the reaction mixture. The resulting yellow oil was taken up in DCM (3 mL) and purified by flash chromatography on a 24 g silica column, eluting with ethyl acetate and hexanes to afford tert-butyl 4-(4-fluoro-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate as a white crystalline solid (370.3 mg, 1.017 mmol, 80% yield). ^1H NMR (400 MHz, CHLOROFORM-d) δ 7.96 (br s, 1H), 7.10 (d, J=8.4 Hz, 1H), 7.02-6.97 (m, 1H), 6.93 (d, J=2.1 Hz, 1H), 4.28 (br s, 2H), 3.37 (spt, J=6.8 Hz, 1H), 3.17 (tt, J=12.0, 3.6 Hz, 1H), 2.88 (br t, J=11.3 Hz, 2H),

1.89-1.81 (m, 2H), 1.81-1.68 (m, 2H), 1.52 (s, 9H), 1.36 (d, J=6.8 Hz, 6H). LCMS MH⁻: 361.3. HPLC Ret. Time 1.16 min. Method G.

Intermediate 991H: tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-1H-indole-1-carboxylate

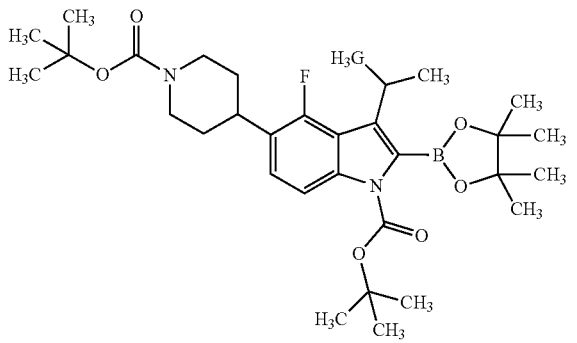
(991H)



Tert-butyl 4-(4-fluoro-3-isopropyl-1H-indol-5-yl)piperidine-1-carboxylate (370 mg, 1.026 mmol) and di-tert-butyl dicarbonate (540 μl, 2.258 mmol) were dissolved in THF (5132 μl) in a 20 mL vial containing a Teflon-covered stir bar. Next, 4-dimethylaminopyridine (12.54 mg, 0.103 mmol) was added. The vial was capped and the clear, pale yellow solution was stirred at room temperature for 2 h. The reaction finished. Excess solvent was evaporated from the reaction mixture. The residue was taken up in DCM (~2 mL) and purified by flash chromatography on a 24 g silica column, eluting with ethyl acetate and hexanes to afford tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-1H-indole-1-carboxylate as a white foam (4.57 g, 0.98 mmol, 99% yield). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.85 (br s, 1H), 7.28 (br s, 1H), 7.12 (dd, J=8.4, 7.2 Hz, 1H), 3.29 (spt, J=6.8 Hz, 1H), 3.14 (tt, J=12.0, 3.5 Hz, 1H), 2.87 (br t, J=11.4 Hz, 2H), 1.88-1.79 (m, 2H), 1.51 (s, 9H), 1.34 (d, J=6.8 Hz, 6H). LCMS MH⁻: 461.4. HPLC Ret. Time 1.36 min. Method G.

Intermediate 9911: tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole-1-carboxylate

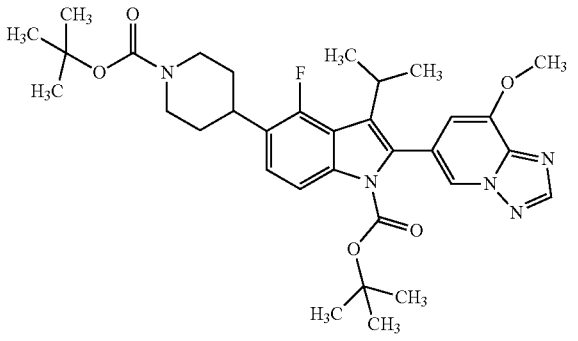
(991I)



Tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-1H-indole-1-carboxylate (456.7 mg, 0.992 mmol) and 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (324 μl, 1.587 mmol) were dissolved in THF (7933 μl) in a 20 mL vial containing a Teflon-covered stir bar. The vial was cooled to −20° C. (dry ice/NMP bath) under a nitrogen atmosphere. Lithium diisopropylamide (992 μl, 1.983 mmol) was added dropwise to the vial (via a syringe through the septum cap) over ~5 min. The reaction mixture was stirred at −20° C. for 1 h, then allowed to slowly warm to 0° C. Most starting material (~75%) converted to product. The reaction mixture was allowed to warm to 10° C., then quenched by addition of 1 M $KHSO_4$-(5 mL). The resulting mixture was extracted with EtOAc (2×3 mL). The combined organic extracts were washed with brine (2×3 mL), and excess solvent was evaporated off. The residue was taken up in DCM (2 mL) and purified by flash chromatography on a 24 g silica column, eluting with ethyl acetate and hexane to afford tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole-1-carboxylate as a white solid (468.9 mg, 0.72 mmol, 72.6% yield, 90% purity). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.61 (d, J=8.6 Hz, 1H), 7.06 (dd, J=8.4, 7.1 Hz, 1H), 4.28 (br s, 2H), 3.35-3.26 (m, 1H), 3.14 (br s, 1H), 2.87 (br t, J=11.9 Hz, 2H), 1.88-1.81 (m, 2H), 1.71 (br s, 2H), 1.67 (s, 9H), 1.44 (s, 12H). LCMS MH⁺-56: 531.4. HPLC Ret. Time 1.39 min. Method G.

Intermediate 991J: tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-2-(8-ethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-4-fluoro-3-isopropyl-1H-indole-1-carboxylate

(991J)



Tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-indole-1-carboxylate (100 mg, 0.170 mmol) and 6-bromo-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (42.8 mg, 0.188 mmol) were weighed into a 1-dram vial with a red pressure-release cap and containing a Teflon-coated stir bar. THF (852 μl) and tripotassium phosphate (170 μl, 0.511 mmol) were added to the vial, and the reaction mixture was degassed by bubbling nitrogen through the

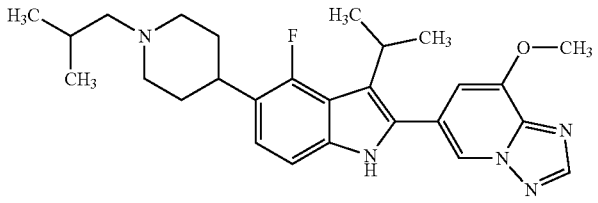
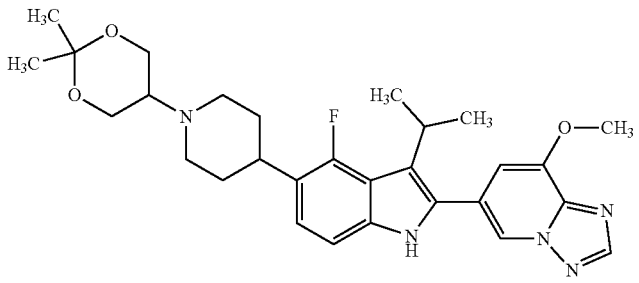
reaction mixture for 3 min. 2ND generation XPhos precatalyst (4.02 mg, 5.11 μmol) was added to the vial, and the reaction mixture was placed under a nitrogen atmosphere and stirred at 60° C. overnight. The reaction was completed. The aqueous phase was removed, and excess solvent was evaporated from the organic phase. The resulting orange residue was taken up in DCM (~3 mL) and purified by flash chromatography on a 12 g silica column, eluting with ethyl acetate and hexanes to afford tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indole-1-carboxylate as a cloudy colorless glass (100.7 mg, 0.124 mmol, 72.9% yield, 75% purity). ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 8.36 (s, 1H), 8.22 (d, J=1.1 Hz, 1H), 8.04 (d, J=8.7 Hz, 1H), 7.28 (s, 1H), 7.23 (dd, J=8.6, 7.2 Hz, 1H), 6.72 (d, J=1.0 Hz, 1H), 4.39-4.22 (m, 2H), 4.04 (s, 3H), 3.19 (tt, J=12.0, 3.3 Hz, 1H), 2.99 (dtd, J=14.1, 7.0, 3.0 Hz, 1H), 2.88 (br t, J=11.2 Hz, 2H), 1.91-1.82 (m, 2H), 1.74 (br dd, J=12.5, 3.8 Hz, 2H), 1.50 (s, 9H), 1.24 (d, J=2.0 Hz, 15H). LCMS MH$^+$: 608.6. HPLC Ret. Time 1.22 min. Method G.

Example 991

Tert-butyl 5-(1-(tert-butoxycarbonyl)piperidin-4-yl)-4-fluoro-3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indole-1-carboxylate (25 mg, 0.041 mmol) was Boc-deprotected by reacting with 2:1 trifluoroacetic acid/dichloromethane (1.2 mL, 0.041 mmol) in a 1-dram vial for 30 min. Toluene (~0.15 mL) was added, and excess solvent was then evaporated from the reaction mixture. The resulting residue was stirred with 2-chloro-N,N-dimethylacetamide (10.00 mg, 0.082 mmol) and potassium carbonate (28.4 mg, 0.206 mmol) in NMP (0.411 mL) at 22° C. for 1.5 h. The reaction did not finish. The reaction mixture was stirred at 22° C. over the weekend. The reaction was completed. The reaction mixture was partitioned between water and ethyl acetate (3 mL total volume), and the aqueous phase was extracted with ethyl acetate (2×1 mL). Excess solvent was evaporated from the combined organic extracts. DMF (~1.5 mL) was added to the resulting residue. The crude material was purified via preparative LC/MS with the following conditions: Column:)(Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 15-55% B over 20 minutes, then a 4-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 2-(4-(4-fluoro-3-isopropyl-2-(8-methoxy-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-N,N-dimethylacetamide (8.5 mg, 0.017 mmol, 42.1% yield). ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 11.44 (br s, 1H), 8.58 (s, 1H), 8.54-8.47 (m, 1H), 7.18 (br d, J=8.5 Hz, 1H), 7.13 (s, 1H), 7.09 (t, J=7.0 Hz, 1H), 4.06 (s, 3H), 3.30 (br s, 1H), 3.17 (s, 2H), 3.07 (s, 3H), 3.01-2.88 (m, 3H), 2.88-2.78 (m, 3H), 2.20 (br t, J=10.5 Hz, 3H), 1.83-1.75 (m, 3H), 1.73 (br s, 4H), 1.36 (br d, J=6.4 Hz, 6H). LCMS MH$^+$: 493. HPLC Ret. Time 1.30 min. Method QC-ACN-AA-XB.

The following examples were prepared in a manner similar to that described in Example 991.

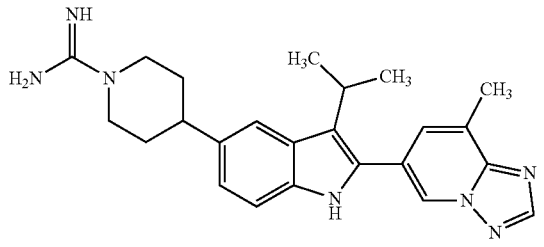
TABLE 26

Ex. No.	Structure	LCMS MH$^+$	R_t (min)	HPLC Method
992		464.5	1.5	QC-ACN-AA-XB
993		522	1.7	QC-ACN-AA-XB

Example 994

4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboximidamide

(994)



6-(3-isopropyl-5-(piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (15.77 mg, 0.042 mmol) was stirred with 1H-pyrazole-1-carboximidamide (5.81 mg, 0.053 mmol) and DIPEA (0.037 mL, 0.211 mmol) in DMF (0.422 mL) at 75° C. for 8 h. DMF (1 mL) was added to the reaction mixture and the reaction mixture was purified via preparative LC/MS with the following conditions: Column:)(Bridge C18, 19×200 mm, 5-μm particles; Mobile Phase A: 5:95 acetonitrile: water with 10-mM ammonium acetate; Mobile Phase B: 95:5 acetonitrile: water with 10-mM ammonium acetate; Gradient: 15-55% B over 19 minutes, then a 5-minute hold at 100% B; Flow: 20 mL/min. Fractions containing the product were combined and dried via centrifugal evaporation to afford 4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidine-1-carboximidamide (8.4 mg, 0.019 mmol, 45.0% yield). LCMS MH^+: 416.2 HPLC Ret. Time 1.23 min. Method QC-ACN-AA-XB. ^1H NMR (500 MHz, DMSO-d_6) δ 9.29 (s, 1H), 8.39 (s, 1H), 7.99 (s, 1H), 7.33-7.33 (m, 1H), 7.31 (d, J=7.9 Hz, 1H), 7.15 (s, 1H), 7.11 (br d, J=8.1 Hz, 1H), 2.99-2.88 (m, 3H), 2.79 (s, 2H), 2.77-2.70 (m, 1H), 2.16-2.06 (m, 1H), 1.74-1.64 (m, 2H), 1.51 (s, 4H), 1.50-1.40 (m, 2H), 1.08-0.98 (m, 6H).

BIOLOGICAL ASSAYS

The pharmacological properties of the compounds of this invention may be confirmed by a number of biological assays. The exemplified biological assays, which follow, have been carried out with compounds of the invention.

TLR7/8/9 Inhibition Reporter Assays

HEK-Blue™-cells (Invivogen) overexpressing human TLR7, TLR8 or TLR9 receptors were used for screening inhibitors of these receptors using an inducible SEAP (secreted embryonic alkaline phosphatase) reporter gene under the control of the IFN-β minimal promoter fused to five NF-κB and AP-1-binding sites. Briefly, cells are seeded into Greiner 384 well plates (15000 cells per well for TLR7, 20,000 for TLR8 and 25,000 for TLR9) and then treated with test compounds in DMSO to yield a final dose response concentration range of 0.05 nM-50 μM. After a 30 minute compound pre-treatment at room temperature, the cells are then stimulated with a TLR7 ligand (gardiquimod at a final concentration of 7.5 μM), TLR8 ligand (R848 at a final concentration of 15.9 μM) or TLR9 ligand (ODN_{2006} at a final concentration of 5 nM) to activate NF-κB and AP-1 which induce the production of SEAP. After a 22 hour incubation at 37° C., 5% CO_2, SEAP levels are determined with the addition of HEK-Blue™ Detection reagent (Invivogen), a cell culture medium that allows for detection of SEAP, according to manufacturer's specifications. The percent inhibition is determined as the % reduction in the HEK-Blue signal present in wells treated with agonist plus DMSO alone compared to wells treated with a known inhibitor.

TABLE 27

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
1	34.5	69	3177
2	3.7	5.1	9015
3	3.9	2.2	1912
4	0.3	0.7	1589
5	0.5	2.7	818
6	1.1	9.8	1193
7	0.7	4.7	6636
8	0.3	2.2	1172
9	—	0.5	21167
10	0.5	1.7	479
11	0.3	2.4	5385
12	0.8	1.9	3063
13	1	2.5	4778
14	2.4	1.5	23273
15	1.4	1.4	5113
16	1	1.6	6321
17	1.9	0.5	2501
18	1.5	1.5	15008
19	1	0.9	4802
20	2.1	0.8	2694
21	0.7	7.6	—
22	—	2	1845
23	0.4	3.3	4811
24	0.4	0.8	2865
25	0.3	3	2425
26	0.9	6.8	11110
27	0.8	3.4	1767
28	0.9	3.7	3052
29	0.3	1.8	1159
30	0.8	1.2	1534
31	0.7	1.5	1998
32	0.5	1.8	2399
33	8.5	22.9	13118
34	18.6	136.1	50000
35	0.5	2.2	1426
36	0.6	3.9	3545
37	0.6	1.2	1907
38	1.8	3.3	29477
39	1.1	0.8	4245
40	0.7	0.5	2462
41	0.5	1.2	4334
42	1.6	0.7	3114
43	2.3	1.1	7816
44	0.8	7	11301
45	0.3	1.1	1757
46	0.5	5.5	3032
47	4.8	45.5	10643
48	2.1	83.7	9585
49	14.2	56.8	50000
50	0.8	6.2	3409
51	12.2	61.4	4680
52	1.8	50.4	44293
53	32.2	210.6	50000
54	0.6	34.6	30085
55	3.1	86.3	6521
56	1.5	23.9	1602
57	4.7	7.4	3749
58	2.7	41.6	2939
59	4.3	65.9	3116
60	1.2	42.5	40436
61	1.6	78.8	42221
62	0.7	4.5	644
63	1.8	46.5	37047

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
64	1.4	61.6	—
65	10.1	175.6	11138
66	0.7	3.7	2659
67	1.1	9.2	5849
68	1.4	29	42823
69	2.1	13.1	3833
70	82.4	558.7	50000
71	1.1	10.7	2476
72	0.4	7.5	1383
73	0.9	6	1270
74	2.9	3.3	6631
75	1	3.9	7158
76	0.8	3.7	2587
77	0.6	2.5	1579
78	0.7	5.8	7303
79	1.4	3.5	6255
80	1	6.1	2209
81	0.8	7	29110
82	0.5	4.7	1654
83	0.9	4	1958
84	0.6	3.8	974
85	0.6	2.9	481
86	1	2.5	2326
87	1	5.7	36053
88	1.2	3.7	2005
89	0.9	6.1	1594
90	0.2	3.4	1388
91	1	1.3	2784
92	1.2	3.3	6613
93	1	5.6	2645
94	0.3	5.7	3200
95	0.4	18.9	1964
96	0.6	19.7	1281
97	3.5	5.2	1549
98	0.8	2.0	1756
99	29.3	33.5	4652
100	8.6	169.4	1721
101	10.9	16.8	11330
102	116.8	3125.0	13829
103	5.3	174.1	2192
104	7.0	10.0	1722
105	0.8	27.1	813
106	126.2	3125.0	12485
107	2.1	5.3	2330
108	79.7	29.0	4236
109	153.0	699.9	427
110	1.5	4.5	1516
111	1.0		1129
112	1.1	16.6	1974
118	0.8	3.3	2382
119	0.2	0.6	2487
120	3.4	47.5	2015
121	20.1	15.5	519
122	9.6	89.5	663
123	28.9	32.0	2091
124	4.6	33.7	5036
125	5.0	67.2	1695
126	18.7	312.9	605
127	81.5	21.6	1339
128	0.4	12.1	2648
131	109.2	16.6	1605
132	2.6	8.2	844
133	1.1	9.5	1436
134	1.0	10.3	1076
135	3.2	30.0	291
136	42.1	189.3	2708
138	0.3	19.6	760
140	0.7	7.2	2512
141	0.9	13.2	1331
142	58.4	1543.0	343
143	5.7	—	424
144	2.0	7.8	779
145	9.9	92.0	2127
146	27.1	178.6	1487

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
147	92.1	730.8	19901
148	12.8	4.2	602
149	47.3	709.4	214
150	142.1	338.2	692
151	0.3	5.0	1567
152	0.8	3.7	1148
153	6.4	144.5	3429
154	10.4	35.4	1064
155	599.7	191.0	862
156	2.8	17.2	2267
157	0.8	3.0	1149
158	0.7	2.9	1927
159	7.0	63.2	8794
160	0.7	5.4	4991
161	1.8	13.4	1402
162	3.2	45.3	1711
163	86.4	73.6	4947
164	9.0	15.0	3664
165	2.1	7.4	1816
166	2.7	17.8	3220
167	0.8	4.3	2471
168	0.4	1.9	3414
169	1.2	12.5	7752
170	1.2	4.4	8087
171	1.3	3.7	11528
172	0.4	4.1	5243
173	2.3	14.6	2860
174	0.5	2.1	3681
175	0.8	5.8	23314
176	0.5	1.9	1708
177	1.0	2.3	10674
178	0.8	3.5	1802
179	1.3	3.9	2038
180	33.6	5.9	12825
181	1.9	2.6	1770
182	12.6	0.8	4939
183	8.4	2.0	5208
184	3.3	2.0	5470
185	7.7	3.3	6266
186	5.2	8.3	14248
187	12.0	3.0	14559
188	6.5	1.9	17971
189	6.5	1.7	2760
190	2.3	11.0	12310
191	14.8	6.8	6359
192	8.7	3.3	9593
193	5.7	44.0	4975
194	5.0	22.3	15692
195	1.6	35.9	3957
196	1.3	25.1	8048
197	2.9	79.6	15694
198	2.7	9.8	4107
199	1.8	12.8	8321
200	8.0	17.1	34036
201	1.8	9.6	1952
202	1.4	16.7	15339
203	2.3	6.9	6028
204	0.7	0.7	2020
205	0.6	0.9	2764
206	0.9	1.5	5737
207	10.8	8.8	4618
208	14.2	4.0	5041
209	3.9	5.9	8219
210	3.4	6.2	4283
211	14.8	211.6	14365
212	10.6	347.6	2855
213	5.0	103.3	7241
214	5.2	111.2	16506
215	15.5	142.8	7579
216	3.2	243.5	19247
217	8.2	238.7	8148
218	5.2	103.9	11257
219	34.0	18.3	10959
220	0.7	3.2	672

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
221	0.4	1.3	5315
222	1.0	6.2	18169
223	0.8	12.0	1074
224	1.5	9.5	6973
225	9.9	249.7	12206
226	8.9	8.9	18002
227	11.6	20.8	5074
228	78.3	962.0	38220
229	2.0	43.5	1047
230	68.1	51.4	7285
231	2.4	6.0	6641
232	2.3	7.0	1099
233	1.0	1.5	15605
234	0.6	6.2	7219
235	1.7	10.4	3087
236	19.6	9.1	1180
237	10.8	588.3	5935
238	8.9	347.5	2625
239	22.5	96.7	—
240	6.6	22.9	6003
241	18.9	4.9	2988
242	2.9	5.6	3600
243	2.8	33.5	44062
244	1.0	10.0	6270
245	1.2	10.5	2648
246	0.2	2.3	2259
247	7.4	48.5	4394
248	4.2	65.7	4582
249	11.5	20.1	1823
250	0.7	8.6	3422
251	0.5	7.8	6316
252	0.5	2.0	2551
253	0.2	13.6	1001
254	0.6	6.1	16008
255	95.0	1125.6	3771
256	178.6	1881.8	2121
257	1703.8	435.7	995
258	1235.5	404.7	5885
259	12.2	137.1	1355
260	0.4	13.9	2603
261	2.1	28.3	8114
262	0.6	5.3	1895
263	1.1	2.8	5301
264	0.5	2.3	3949
265	0.7	9.3	7028
266	560.4	448.9	7984
267	102.9	30.8	7300
268	2.8	15.7	1894
269	4.2	37.1	12314
270	5.2	4.6	1573
271	0.6	12.8	1346
272	0.6	11.7	2416
273	2.1	4.7	973
274	1.1	19.0	3731
275	3.1	25.5	10188
276	5.4	52.0	1824
277	10.4	61.2	2442
278	100.6	70.6	2134
279	61.7	58.7	3164
280	0.6	12.4	4300
281	0.7	15.0	6153
282	1.7	5.9	10082
283	4.9	6.3	2430
284	3.3	8.0	1900
285	1.5	15.1	6012
286	0.5	0.8	3147
287	1.0	0.5	3056
288	0.6	1.4	14105
289	1.0	25.9	6126
290	1.8	35.6	6254
291	8.2	2.1	1568
292	18.3	1.4	1303
293	0.5	15.8	5709
294	0.8	21.1	19539

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
295	1.9	45.6	2449
296	3.1	47.4	10442
297	5.0	26.3	2153
298	10.8	45.7	625
299	26.3	139.7	3432
300	29.0	113.1	2658
301	54.5	252.5	6442
302	4.3	6.1	2971
303	1.6	7.0	17114
304	0.9	3.3	4541
305	2.7	1.8	7034
306	1.2	2.7	16966
307	48.2	103.0	5320
308	40.0	2.1	1533
309	43.1	2.0	709
310	181.4	307.2	112
311	90.5	352.3	155
312	5.7	55.6	4305
313	5.4	80.6	3132
314	11.9	18.3	1640
315	268.6	557.9	1931
316	318.9	491.7	3692
317	19.8	71.8	8575
318	6.8	25.5	2227
319	0.2	7.9	10520
320	0.3	14.2	3024
321	0.7	4.6	6178
322	2.0	7.7	2086
323	2.6	35.3	5189
324	1.6	2.9	1001
325	1.4	12.4	1114
326	1.2	6.7	2187
327	0.9	4.1	1453
328	4.3	4.3	1901
329	3.2	18.5	1051
330	1.0	14.4	1121
331	2.5	6.4	5294
332	3.6	4.1	3165
333	3.3	5.3	3183
334	2.9	1.9	2092
335	1.1	6.3	1501
336	4.9	4.7	2835
337	2.0	5.2	2106
338	1.6	5.8	8874
339	4.1	5.6	14877
340	1.5	6.5	5866
341	1.9	4.2	2860
342	3.7	3.0	1785
343	3.6	19.0	330
344	1.5	13.4	5474
345	5.1	37.6	1412
346	4.2	66.6	4614
347	1511.5	2255.2	8618
348	5.5	—	1145
349	1.5	3.9	1787
350	5.6	12.5	4809
351	39.9	18.4	5322
352	29.5	56.5	11409
353	38.5	44.2	24690
354	18.2	12.5	2258
355	8.3	107.0	6231
358	13.6	29.7	6035
359	6.8	8.9	1819
360	3.5	22.3	3619
361	14.4	9.9	9225
362	325.0	149.2	15799
363	19.4	10.1	822
364	9.2	7.0	1523
365	5.6	10.6	3587
366	29.0	8.7	1917
367	16.3	3.8	4404
368	57.0	19.1	2067
369	19.2	4.7	1839
370	23.4	15.8	2260

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
371	17.0	6.1	1927
372	37.1	21.1	3472
373	21.4	6.5	2329
374	32.2	17.2	10078
375	11.6	10.3	2104
376	9.5	5.2	1996
377	9.0	3.0	—
378	11.1	8.6	5732
379	2.7	1.2	990
380	6.7	12.1	1195
381	7.8	2.4	764
382	19.9	3.8	1894
383	79.8	59.6	18177
384	5.9	7.0	2266
385	7.8	62.9	31598
386	0.9	9.3	5157
387	1.4	6.1	3362
388	1.6	7.1	6145
389	2.8	2.1	7128
390	33.2	151.4	50000
391	0.2	0.9	1904
392	1.7	6.0	50000
393	2.7	1.5	1484
394	1.2	2.7	1379
395	2.3	10.4	44660
396	2.6	8.9	5113
397	0.6	2.9	2183
398	6.3	41.9	12558
399	1.1	3.8	857
400	2.5	13.5	2003
401	5.9	98.5	21445
402	2.5	8.6	6271
403	5.5	12.9	1662
404	1.3	7.2	50000
405	2.1	1.9	2379
406	0.6	1.8	747
407	1.5	1.9	2290
408	2.0	4.9	9828
409	0.5	1.1	658
410	1.5	1.0	1150
411	1.7	7.8	45491
412	0.5	1.8	2865
413	1.2	33.5	632
414	1.4	4.9	3627
415	2.7	4.9	2503
416	5.4	16.4	22305
417	10.1	46.9	26022
418	5.4	11.8	7590
419	1.1	2.6	279
420	1.0	1.5	725
421	2.2	5.2	3405
422	0.6	3.3	7855
423	0.9	3.3	8387
424	1.0	4.3	3152
425	3.7	5.1	1149
426	9.8	877.3	50000
427	1.6	5.9	3650
428	1.3	9.1	9034
429	1.6	5.3	2074
430	0.7	3.1	3572
431	2.6	9.0	5462
432	0.1	1.8	1552
433	6.3	6.6	32563
434	1.4	3.7	5273
435	7.7	11.8	24316
436	3.0	3.3	6254
437	0.8	0.7	1186
438	2.7	5.7	2205
439	7.7	17.3	23290
440	3.4	5.7	24466
441	8.5	10.0	41305
442	9.1	3.9	2823
443	19.7	3.4	5143
444	42.1	5.4	16934

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
445	13.6	1.6	3324
446	41.5	6.3	43852
447	55.8	10.8	50000
448	7.8	0.5	2338
449	13.6	4.4	7125
450	15.8	2.0	11508
451	14.5	2.5	5148
452	11.0	2.8	996
453	20.9	3.4	18886
454	38.9	3.1	10042
455	7.3	1.4	2198
456	98.6	27.6	15101
457	16.4	1.6	6631
458	7.8	8.1	30283
459	14.4	6.4	13406
460	7.3	6.0	50000
461	4.3	1.1	—
462	3.0	2.2	—
463	41.4	3.6	6221
464	3.1	3.8	13473
465	18.5	1.8	4038
466	21.7	3.1	8713
467	14.1	2.2	4589
468	3.7	11.4	2776
469	4.5	37.1	10275
470	8.2	10.0	3881
471	8.5	14.7	5311
472	5.3	2.6	2659
473	6.0	16.9	25227
474	—	13.6	2095
475	0.5	1.8	4172
476	0.4	0.8	1355
477	6.1	49.1	50000
478	1.7	0.7	2435
479	2.9	3.7	3906
480	0.6	1.0	4213
481	0.7	0.8	2203
482	2.1	11.8	4192
483	5.2	1.6	28163
484	6.5	6.3	50000
485	0.8	1.4	3415
486	1.3	1.0	3158
487	7.1	11.2	17398
488	3.6	2.1	4172
489	—	2.7	4570
490	10.3	156.9	9234
491	11.5	49.9	2983
492	5.6	173.4	16217
493	7.1	76.4	3973
494	5.5	82.8	6106
495	14.4	186.5	10106
496	6.4	104.3	8003
497	2.2	97.2	4370
498	6.5	154.2	9516
499	55.0	31.2	50000
500	0.7	6.8	1348
501	1.5	11.4	8063
502	11.9	47.9	3449
503	—	143.5	50000
504	12.4	7.1	47457
505	4.4	2.5	3098
506	4.0	28.4	6661
507	645.6	3125.0	25265
508	51.0	14.0	48633
509	59.8	5.9	2801
510	1.4	4.6	15300
511	5.2	6.2	5624
512	2.8	1.2	2568
513	2.6	2.6	4138
514	3.1	1.9	3749
515	1.5	1.2	1675
516	3.3	1.4	3510
517	5.7	1.5	6413
518	1.9	2.5	11591

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
519	3.0	2.4	3723
520	2.8	3.2	6885
521	2.6	3.9	4828
522	4.5	6.2	25614
523	2.5	3.6	3660
524	1.4	4.3	6234
525	8.3	4.3	13427
526	4.4	1.8	2474
527	4.4	1.5	569
528	30.8	16.5	9591
529	33.7	17.0	10201
530	10.5	7.0	653
532	33.3	435.3	55
533	8.0	281.1	1227
534	27.4	677.0	7557
535	29.9	209.0	1443
536	8.4	15.9	3538
537	2.2	3.3	6503
538	0.5	12.5	1459
539	1.2	15.1	3234
540	0.4	1.5	1836
541	0.3	1.8	1637
542	2.3	56.7	50000
543	1.7	11.0	1632
544	1.8	6.5	5008
545	1.5	4.9	1301
546	71.6	85.3	7699
547	42.4	135.0	6042
548	5.5	30.0	4303
549	1.5	20.7	—
550	1.3	7.7	6413
551	0.8	6.1	2317
552	0.6	3.5	995
553	5.3	29.0	3486
554	1.8	10.9	6093
555	0.3	2.1	2160
556	0.4	5.5	3924
557	0.4	6.5	2730
558	3125.0	3125.0	16753
559	634.2	288.6	483
560	1308.6	149.4	1897
561	1.5	5.8	1327
562	2.2	6.2	6348
563	0.8	2.6	1133
564	0.4	1.8	1234
565	0.4	1.2	549
566	0.3	1.2	1469
567	0.4	3.0	2235
568	0.7	1.8	1451
569	0.4	1.3	1565
570	0.4	0.7	535
571	5.1	1.9	1238
572	20.3	30.5	24538
573	2.6	3.6	1571
574	—	20.5	6570
575	1.1	8.0	1859
576	0.9	6.5	1914
577	2.0	9.7	2237
578	5.4	23.2	7859
579	2.1	18.7	1799
580	4.1	84.8	5087
581	31.5	1.9	2472
582	0.6	3.6	2556
583	1.0	12.2	13615
584	2.1	12.1	3296
585	6.4	95.3	25590
586	34.6	84.5	2111
587	4.4	7.9	7380
588	2.4	10.6	50000
589	2.6	0.7	4122
590	172.6	132.0	6275
591	180.4	2.0	5677
592	384.6	353.6	81
593	0.7	16.1	1785

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
594	10.8	85.1	3928
595	4.1	15.9	14361
596	4.3	12.2	16277
597	8.8	44.3	10928
598	5.2	49.6	6302
599	2.9	10.9	1738
600	6.5	14.1	2652
601	28.7	147.9	50000
602	2.8	41.8	—
603	2.1	50.0	42404
604	4.5	132.1	37270
605	0.8	25.8	40711
606	0.7	36.1	43596
607	0.9	42.6	44356
608	1.8	55.6	50000
609	69.6	243.3	50000
610	1.7	13.7	5711
611	3.2	6.1	3382
612	5.6	174.9	2353
613	48.8	3125.0	50000
614	56.3	3125.0	47110
615	12.8	470.8	1595
616	12.5	607.4	901
617	32.7	3125.0	50000
618	9.1	634.9	2547
619	19.3	310.2	50000
620	0.7	1.3	58
621	16.3	258.0	6809
622	1.3	21.6	1590
623	2.7	9.1	1106
624	1.6	12.1	1490
625	0.9	11.2	554
626	0.5	6.7	3181
627	0.4	11.3	5872
628	—	231.9	50000
629	0.7	7.4	3171
630	1.1	8.7	1988
631	3.5	66.9	45473
632	2.4	56.5	37917
633	568.1	3125.0	50000
634	8.7	31.5	35483
635	3.1	17.0	1515
636	2.4	16.3	2448
637	34.0	1077.5	42907
638	5.8	152.6	3221
639	5.0	140.1	3028
640	1838.5	3125.0	3723
641	0.3	14.9	1067
642	0.2	14.0	2517
643	0.6	197.5	22162
644	4.8	34.7	5784
645	2.8	240.1	50000
646	5.7	538.0	50000
647	1.3	202.1	50000
648	14.7	1700.8	50000
649	1.6	10.1	7355
650	16.3	931.3	50000
651	3.2	260.9	12737
652	1.5	157.2	36400
653	24.0	3125.0	50000
654	7.9	603.3	50000
655	1.4	115.5	9585
656	131.7	2533.8	707
657	416.4	3125.0	50000
658	385.2	3125.0	50000
659	809.7	3125.0	3750
660	1717.8	268.1	1001
661	868.3	85.9	544
662	1.0	14.0	1349
663	1.6	43.5	50000
664	2.2	56.9	5998
665	4.1	77.9	11847
666	5.8	55.4	12108
667	3.0	8.6	4501

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
668	1.2	36.9	34156
669	311.0	3125.0	50000
670	8.3	59.6	50000
671	2.1	30.3	18365
672	1.0	8.4	2519
673	1.9	29.2	42411
674	1.2	14.4	663
675	0.8	14.5	3586
676	7.8	64.6	1693
677	1.9	43.8	33978
678	3.0	39.3	42260
679	0.4	5.2	1181
680	2.7	25.9	956
681	5.5	47.7	1195
682	1261.1	8.2	778
683	—	1.7	124
684	57.2	338.4	1468
685	12.4	590.1	50000
686	0.6	13.9	2172
687	1.0	15.1	1738
688	—	18.6	4136
689	0.5	3.3	2779
690	9.4	4.9	901
691	50.6	6.2	408
692	10.8	81.2	2415
693	6.6	46.7	893
694	5.8	70.3	1288
695	6.2	23.5	1082
696	0.2	13.4	1547
697	0.2	9.3	1093
698	2.6	41.4	1434
699	1.1	18.1	1215
700	1.8	25.6	1844
701	2.4	8.0	2048
702	2.9	9.9	658
703	2.9	10.7	4601
704	1.1	5.6	2013
705	6.6	217.7	32501
706	2.3	30.3	473
707	5.2	156.8	27366
708	6.0	55.2	2110
709	6.3	357.5	8846
710	16.2	290.8	16893
711	3.6	35.1	989
712	1.6	49.1	3058
713	24.4	177.5	6626
714	0.8	3.7	2537
715	0.2	3.6	3257
716	0.6	117.2	43816
717	5.5	46.3	46627
718	3.4	36.7	44471
719	0.5	3.1	616
720	5.2	35.4	5037
721	3.9	9.9	190
722	3.3	17.5	2973
723	2.9	21.0	7713
724	1.4	4.4	782
725	11.6	55.4	50000
726	10.7	35.8	50000
727	1.7	9.8	4497
728	3.0	15.4	3903
729	2.2	5.4	462
730	27.4	152.8	13740
731	1.7	8.6	3025
732	2.3	7.6	3127
733	10.1	78.2	23792
734	1.4	6.6	2862
735	1.2	7.7	1963
736	1.2	5.9	812
737	1.1	5.9	4342
738	0.4	5.5	4312
739	2.0	11.2	15195
740	1.0	4.7	2044
741	12.2	93.6	50000

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
742	1.0	9.2	5878
743	0.9	5.1	2418
744	3.7	13.4	1387
745	0.7	5.1	1440
746	4.5	12.9	4678
747	3.5	20.0	6211
748	1.8	14.3	3623
749	0.8	3.5	1354
750	1.3	5.4	1632
751	2.7	11.6	2560
752	33.7	144.7	50000
753	0.9	4.3	1923
754	1.4	9.5	3789
755	2.1	7.8	1019
756	0.9	2.7	1275
757	1.8	5.9	782
758	1.0	8.1	2893
759	0.7	12.5	3997
760	1.2	8.0	2950
761	8.9	71.5	50000
762	0.9	8.1	5102
763	2.5	8.1	4756
764	1.4	10.9	4042
765	0.9	3.4	1182
766	1.3	11.4	4842
767	0.2	2.7	2496
768	2.3	12.5	6751
769	1.0	7.3	1769
770	0.7	7.4	1794
771	1.5	12.3	2281
772	1.7	30.2	4855
773	1.0	11.9	3304
774	0.5	5.9	1009
775	0.7	5.6	1735
776	0.4	5.8	1398
777	0.4	22.6	4974
778	0.3	17.0	2934
779	1.1	64.8	7100
780	0.4	8.0	6227
781	—	4.3	368
782	1.6	6.2	5308
783	0.5	4.1	3026
784	2.3	6.3	6602
785	1.0	5.8	—
786	2.0	8.9	5342
787	0.8	4.1	3246
788	2.6	7.5	4575
789	4.2	15.5	4153
790	1.8	6.7	5742
791	1.7	9.7	5028
792	1.3	6.4	3377
793	1.5	5.9	4963
794	2.9	13.9	5588
795	2.2	8.6	3548
796	1.7	7.2	5141
797	1.4	5.4	4075
798	2.1	7.9	3146
799	8.3	18.1	6791
800	8.5	37.4	16645
801	1.8	10.5	2874
802	3.3	5.8	5686
803	7.6	10.0	41531
804	5.1	5.2	5283
805	2.4	6.3	2830
806	1.6	4.3	22288
807	11.5	7.1	16216
808	8.5	5.8	5987
809	17.3	10.3	6047
810	6.6	4.3	3609
811	1.1	13.8	4068
812	1.3	14.4	3769
813	7.8	14.5	5006
814	1.7	19.8	5168
815	9.2	46.0	7886

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
816	4.8	38.1	20361
817	5.3	55.5	5416
818	4.7	18.0	3734
819	6.3	39.7	8031
820	3.8	23.5	6111
821	8.2	61.0	22760
822	9.8	44.2	4011
823	6.7	26.9	3040
824	16.3	76.4	16936
825	11.5	34.3	5468
826	13.4	30.3	6312
827	15.5	23.7	7064
828	16.3	73.1	12747
829	4.8	32.1	1999
830	6.7	37.8	9523
831	9.5	68.3	23615
832	11.3	61.7	50000
833	13.0	43.9	10940
834	20.0	91.8	17529
835	9.9	33.3	3968
836	10.6	33.4	3228
837	10.4	35.7	5202
838	622.3	2352.4	28501
839	6.0	21.0	5577
840	17.0	82.8	50000
841	16.9	112.1	31037
842	58.2	342.0	50000
843	1.3	1.7	3654
844	6.0	9.0	23608
845	1.4	1.1	9868
846	1.1	1.3	14078
847	1.6	1.1	4430
848	0.7	2.1	4492
849	0.9	1.4	5017
850	5.8	206.0	5624
851	1.0	14.3	—
852	3.5	34.6	10807
853	0.5	3.2	2064
854	0.4	4.9	13602
855	2.4	7.6	7042
856	2.0	16.5	8337
857	1.3	13.3	16943
858	0.8	2.4	3330
859	0.7	6.8	3367
860	1.7	24.5	35290
861	0.8	6.0	13098
862	0.3	2.9	1324
863	0.4	2.0	182
864	0.4	3.5	3008
865	0.2	3.4	4108
866	1.1	2.8	312
867	1.1	4.6	1371
868	0.5	5.6	2088
869	2.0	11.8	2042
870	0.5	4.7	3106
871	0.7	6.9	2472
872	0.5	7.2	2838
873	0.8	8.6	3913
874	1.7	10.9	766
875	0.4	6.5	2240
876	4.5	3.9	10992
877	5.3	1.9	16225
878	1.8	2.0	5697
879	2.2	4.9	5146
880	2.0	1.3	6187
881	2.9	5.0	6005
882	4.7	31.3	37052
883	2.7	21.3	12076
884	12.1	71.7	50000
885	20.7	18.5	15041
886	3.4	11.6	467
887	2.5	11.6	1836
888	1.0	4.8	1776
889	2.0	7.6	421

TABLE 27-continued

TLR7/8/9 Reporter Assay Data

Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
890	4.9	24.0	4315
891	0.2	5.2	534
892	1.6	7.5	1379
893	1.3	5.0	1100
894	2.3	1.8	3303
895	1.1	3.3	1000
896	2.4	9.4	2732
897	1.2	2.2	2357
898	2.2	12.0	3608
899	3.8	21.2	2298
900	4.1	19.7	16642
901	2.5	8.7	1286
902	1.4	7.0	707
903	1.6	6.4	724
904	1.1	4.9	1239
905	1.1	4.4	567
906	6.2	22.8	8854
907	1.1	3.9	1053
908	3.8	17.8	2192
909	1.4	4.0	460
910	1.6	7.2	789
911	1.0	5.6	1386
912	3.2	7.4	439
913	9.2	40.7	50000
914	0.9	4.2	1410
915	1.1	4.5	1361
916	1.6	5.5	1958
917	1.1	4.3	1539
918	1.9	11.2	3508
919	3.8	21.0	3197
920	3.9	15.2	1524
921	1.4	10.0	2943
922	3.0	12.4	3234
923	1.6	6.6	652
924	3.0	11.9	1986
925	1.0	7.9	2357
926	5.3	35.2	2859
927	0.9	6.0	3676
928	1.3	10.6	12118
929	0.8	3.1	1289
930	1.1	3.7	2277
931	1.0	3.9	1317
932	1.7	10.7	2686
933	1.5	3.9	1814
934	0.5	1.3	1715
935	0.4	3.9	875
936	6.2	13.8	1601
937	1.4	3.1	1532
938	1.2	5.6	1698
939	2.1	7.0	1962
940	0.7	2.6	1912
941	0.4	1.5	1520
942	2.5	14.7	7172
943	1.0	6.2	9610
944	2.0	17.2	7735
945	1.3	6.9	1954
946	9.5	38.9	30228
947	2.6	12.4	2448
948	24.3	125.9	18223
949	18.6	128.9	18701
950	2.3	40.7	5688
951	0.9	10.1	3767
952	3.4	35.9	27912
953	2.3	13.4	5808
954	1.2	4.0	2148
955	1.8	10.0	13172
956	1.3	8.5	1629
957	1.1	21.0	50000
958	1.3	9.4	4557
959	69.8	186.9	24350
960	2.5	12.3	5034
961	16.3	37.7	5021
962	6.0	12.7	2523
963	4.2	30.9	50000

TABLE 27-continued

TLR7/8/9 Reporter Assay Data			
Ex. No.	TLR7 IC_{50} (nM)	TLR8 IC_{50} (nM)	TLR9 IC_{50} (nM)
964	3.7	7.7	1522
965	1.6	11.5	5622
966	14.8	31.8	3080
967	0.8	5.8	3780
968	12.1	24.4	3588
969	0.7	2.4	542
970	11.4	28.9	3387
971	20.9	22.3	2635
972	3.9	15.5	2311
973	32.8	134.2	50000
974	2.6	4.9	2241
975	2.9	5.2	2223
976	1.5	6.8	6155
977	1.0	1.6	604
978	2.0	3.4	3040
979	8.1	12.4	11509
980	1.9	3.6	868
981	16.9	249.7	7530
982	1.4	—	3106
983	69.2	258.9	6108
984	0.9	8.4	4750
985	2.4	59.6	4832
986	50.5	335.8	1256
987	196.7	384.6	160
988	1835.0	3125.0	413
989	74.2	302.1	50000
990	1.9	12.1	2592
991	0.5	1.8	5591
992	2.2	1.7	1461
993	2.0	5.4	6521
994	9.1	85.4	13067

Inhibition Data

In Vivo mouse TLR7 PD model:

Adult male C_{57}BL/6 mice were used for the experiments. Mice (7 to 10 per group) were randomized into different treatment groups based on body weight. Mice from the respective treatment groups were administered orally with vehicle or test compound. Thirty min after the oral administration of vehicle or test compound, mice were challenged with intraperitoneal injection of gardiquimod for TLR7 PD model. Ninety minutes after gardiquimod injection, mice were bled under isoflurane anaesthesia and plasma IL-6 and IFN-alpha levels were estimated by using commercially available ELISA kit (BD Biosciences, PBL Life Sciences). At the end of experiment, mean cytokine data was plotted and one way ANOVA with Dunnett's test was performed to calculate the significance of test compound treated group vs. vehicle control group. Percent inhibition of cytokine induction was calculated for test compound treated group vs vehicle control group. Data from multiple studies with different test compounds is shown in Table 28.

TABLE 28

Percent inhibition of IL-6 and IFN-alpha in mouse TLR7 PD model			
Ex. No.	Dose (mg/kg)	% inhibition of IL6	% inhibition of IFN-alpha
6	0.0000375	10	9
	0.0001875	30	31
	0.00075	56	55
	0.003	64	66
	0.015	86	96
15	0.000625	18	11
	0.0025	49	27
	0.01	65	62
	0.04	84	88
	0.16	91	99
18	0.00055	9	7
	0.0022	22	10
	0.0088	50	44
	0.0352	60	66
	0.1408	80	99
25	0.00096	22	2
	0.00385	39	44
	0.01540	62	62
	0.06160	89	98
	0.24640	95	100
26	0.000655	20	1
	0.003276	40	33
	0.01638	56	68
	0.0819	91	99
	0.4095	98	100

NZB/W Model of Systemic Lupus Erythematosus (SLE):

Female NZB/W mice of were screened and randomized based on the titers of anti-dsDNA antibodies and urinary NGAL (Neutrophil Gelatinase Associated Lipocalin). Mice were treated orally, once daily for 24 weeks with vehicle or test compound. The effect of test compound on disease severity was assessed by measuring end points including proteinuria, urinary-NGAL, urinary TIMP1, blood urea nitrogen (BUN), anti-dsDNA Ab titer, anti-smRNP Ab titer, and plasma levels of IL10 and IL12p40. In case of BUN the absolute increase was measured by subtracting the BUN values estimated before the initiation of treatment, from BUN values estimated after the completion of treatment. At the end of experiment, all mice were euthanized by CO_2 asphyxiation and kidney samples were subjected for histology. To calculate the significance of test compound treated group vs. vehicle control group, one way ANOVA with Dunnett's test was performed. Percent reduction in disease severity was calculated for each parameter, for test compound treated group vs vehicle control group. A cumulative disease score and the percent reduction in cumulative disease score was calculated by considering the average inhibition in proteinuria, urinary-NGAL, anti-dsDNA Ab titer and anti-sm Ab titer to reflect the impact on the overall severity of disease progression. Data from multiple studies with different test compounds is shown in Table 30.

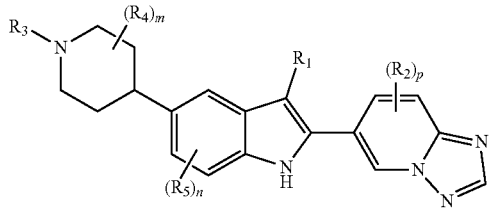
TABLE 30

Inhibition of Disease Development by TLR7/8 Inhibitors in NZB/W Model of Lupus

		% inhibition								
Ex No	Dose (mg/kg)	Proteinuria	Urinary NGAL	Urinary TIMP1	BUN	Anti-SmR NP Ab titer	Anti-ds DNA Ab titer	IL-12p 40	IL-10	Cumulative score
15	0.06	96	79	66	100	28	20	68	98	56
	0.25	96	84	73	100	48	34	78	93	66
	0.75	98	86	72	100	51	45	81	93	70
	2.5	97	93	80	100	55	55	83	97	75
18	0.1	98	78	94	100	40	23	75	100	60
	0.5	98	93	94	100	52	33	88	98	69
	1.5	99	93	95	100	61	43	87	100	74
	5	98	93	92	100	66	57	89	100	79
25	0.5	99	77	71	97	41	4	91	97	65
	3	99	80	73	100	51	51	93	98	70
	9	99	83	81	98	65	54	92	100	75
	30	98	84	82	100	68	62	93	97	78

The invention claimed is:

1. A compound of Formula (I)



(I)

or a salt thereof, wherein:

R_1 is H, Cl, —CN, C_{1-4} alkyl, C_{1-3} fluoroalkyl, C_{1-3} hydroxy-fluoroalkyl, $—CR_z=CH_2$, C_{3-6} cycloalkyl, $—CH_2(C_{3-6}$ cycloalkyl), $—C(O)O(C_{1-3}$ alkyl), or tetrahydropyranyl;

each R_2 is independently halo, —CN, —OH, $—NO_2^+$, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-2} cyanoalkyl, C_{1-3} hydroxyalkyl, C_{1-3} aminoalkyl, $—O(CH_2)_{1-2}OH$, $—(CH_2)_{0-4}O(C_{1-4}$ alkyl), C_{1-3} fluoroalkoxy, $—(CH_2)_{1-4}O(C_{1-3}$ alkyl), $—O(CH_2)_{1-2}OC(O)(C_{1-3}$ alkyl), $—O(CH_2)_{1-2}NR_xR_x$, $—C(O)O(C_{1-3}$ alkyl), $—C(O)NR_yR_y$, $—NR_yR_y$, $—NR_y(C_{1-3}$ fluoroalkyl), $—NR_y(C_{1-4}$ hydroxyalkyl), $—NR_xCH_2$(phenyl), $—NR_xS(O)_2(C_{3-6}$ cycloalkyl), $—NR_xC(O)(C_{1-3}$ alkyl), $—NR_x(CH_2$-cyclopropyl), C_{3-6} cycloalkyl, morpholinyl, dioxothiomorpholinyl, methylpiperidinyl, methylpiperazinyl, amino-oxadiazolyl, imidazolyl, triazolyl, or —C(O)(thiazolyl);

R_3 is $-L_1$-A;

L_1 is bond;

A is 2-oxa-6-azaspiro[3,3]heptanyl, 4-oxaspiro[2.5]octanyl, 7-azaspiro[3.5]nonanyl, 8-azabicyclo[3.2.1]octanyl, 8-oxa-3-azabicyclo[3.2.1]octanyl, 9-azabicyclo[3.3.1]nonanyl, adamantanyl, azepanyl, azetidinyl, C_{3-6} cycloalkyl, diazepanyl, dihydroinonyl, dihydropyrimidinonyl, dioxanyl, dioxidothiadiazinanyl, dioxidothiazolidinyl, dioxidothiomorpholinyl, dioxoisothiazolidinyl, dioxidothiazinanyl, dioxotetrahydrothiophenyl, dioxotetrahydrothiopyranyl, dioxothiomorpholinyl, furanyl, imidazolyl, imidazolidinonyl, indolyl, isoquinolinyl, isoxazolyl, morpholinyl, morpholinonyl, naphthalenyl, octahydrocyclopenta[b]pyranyl, octahydropyrrolo[3,4-b]pyridinyl, oxazolidinonyl, oxadiazolyl, oxazolyl, oxetanyl, phenyl, piperidinyl, piperidinonyl, piperazinyl, piperazinonyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridazinonyl, pyridinonyl, pyridinyl, pyrimidinyl, pyrrolidinonyl, pyrrolidinyl, pyrrolyl, quinolinyl, quinolizinonyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrazolyl, thiadiazolyl, thiazolyl, triazolonyl, or triazolyl, each substituted with $-L_2-R_a$ and zero to 4 R_b;

L_2 is a bond or $—CR_xR_x—$;

R_a is:

(a) H, F, Cl, —CN, —OH, C_{1-6} alkyl, C_{1-3} fluoroalkyl, C_{1-5} hydroxyalkyl, $—(CH_2)_{0-4}O(C_{1-3}$ alkyl), $—(CR_xR_x)_{1-3}S(C_{1-3}$ alkyl), $—NHC(O)OC(CH_3)_3$, $—(CR_xR_x)_{1-3}NHC(O)O(C_{1-4}$ alkyl), $—(CR_xR_x)_{1-3}NR_yR_y$, $—(CR_xR_x)_{1-3}C(O)NR_yR_y$, $—O(C_{1-3}$ fluoroalkyl), $—S(O)_2NR_xR_x$, $—O(CR_xR_x)_{1-3}NR_xR_x$, $—NHS(O)_2(C_{1-3}$ alkyl), $—NR_xR_x$, $—NR_x(C_{1-4}$ alkyl), $—NR_xC(O)(C_{1-4}$ alkyl), $—(CR_xR_x)_{0-3}C(O)OH$, $—C(O)(C_{1-5}$ alkyl), $—C(O)(C_{1-3}$ fluoroalkyl), $—C(O)O(C_{1-4}$ alkyl), $—C(O)NH(C_{1-3}$ cyanoalkyl), $—C(O)NR_yR_y$, $—C(O)NR_xCH_2C(O)NR_xR_x$, or $—C(O)NR_xCH_2CH_2NHC(O)(C_{1-3}$ alkyl);

(b) C_{3-6} cycloalkyl or $—C(O)NH(C_{3-6}$ cycloalkyl), wherein each cycloalkyl is substituted with zero to 2 substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, and $—C(O)O(C_{1-3}$ alkyl); or

(c) A_1, $—CH_2A_1$, $—C(O)A_1$, $—NR_xA_1$, or $—C(O)NR_xA_1$, wherein A_1 is furanyl, imidazolyl, indolyl, isoxazolyl, morpholinyl, octahydropyrrolo[3,4-c]pyrrolyl, oxazolyl, oxetanyl, phenyl, piperazinonyl, piperazinyl, piperidinyl, pyrazinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolidinonyl, pyrrolidinyl, pyrrolyl, tetrahydrofuranyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophenyl, or triazolyl, each substituted with zero to three substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, $—C(O)(C_{1-2}$ alkyl), $—C(O)O(C_{1-3}$ alkyl), $—NR_xR_x$, phenyl, trifluoromethyl-phenyl, $—CH_2$(bromophenyl), and $—CH_2CH_2$(pyrrolidinyl);

each R_b is independently F, —OH, $—CH_3$, $—CF_3$, or $—OCH_3$;

each R_x is independently H or $—CH_3$;

each R_y is independently H or C_{1-6} alkyl;

R_z is H, C_{1-2} alkyl, or C_{1-2} fluoroalkyl;

each R_4 is independently F, —OH, C_{1-2} alkyl, or —OCH_3; or two R_4 attached to the same carbon atom form =O; or wherein when m is at least 2, two R_4, each attached to a different carbon atom adjacent to the nitrogen atom in the piperidinyl ring, can form a —CH_2CH_2— bridge;

each R_5 is independently F, Cl, —CN, C_{1-2} alkyl, C_{1-2} fluoroalkyl, or —OCH_3;

m is zero, 1, 2, 3, or 4;

n is zero, 1, or 2; and

p is zero, 1, 2, 3, or 4.

2. The compound according to claim **1** or salt thereof, wherein:

R_1 is H, Cl, —CN, C_{1-4} alkyl, or C_{1-2} fluoroalkyl;

each R_2 is independently F, Cl, —CN, —OH, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-2} cyanoalkyl, C_{1-3} hydroxyalkyl, C_{1-3} aminoalkyl, —$O(CH_2)_{1-2}OH$, —$O(C_{1-4}$ alkyl), C_{1-2} fluoroalkoxy, —$(CH_2)_{1-4}O(C_{1-3}$ alkyl), —$O(CH_2)_{1-2}OC(O)(C_{1-3}$ alkyl), —$O(CH_2)_{1-2}NR_xR_x$, —$C(O)O(C_{1-3}$ alkyl), —$C(O)NR_yR_y$, —NR_yR_y, —$NR_y(C_{1-3}$ fluoroalkyl), —$NR_y(C_{1-4}$ hydroxyalkyl), —NR_xCH_2(phenyl), —$NR_xS(O)_2(C_{3-6}$ cycloalkyl), —$NR_xC(O)(C_{1-3}$ alkyl), —$NR_x(CH_2$-cyclopropyl), C_{3-6} cycloalkyl, morpholinyl, dioxothiomorpholinyl, methylpiperidinyl, methylpiperazinyl, amino-oxadiazolyl, imidazolyl, triazolyl, or —C(O)(thiazolyl);

A is azetidinyl, C_{3-6} cycloalkyl, dioxotetrahydrothiopyranyl, dioxidothiadiazinanyl, dioxidothiomorpholinyl, furanyl, imidazolyl, isoquinolinyl, morpholinyl, oxazolyl, 2-oxa-6-azaspiro[3.3]heptanyl, octahydropyrrolo[3,4-b]pyridinyl, oxetanyl, phenyl, piperazinonyl, piperazinyl, piperidinyl, pyrazinyl, pyrazolyl, pyridinyl, pyrrolidinonyl, pyrrolidinyl, pyrrolyl, quinolinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrazolyl, thiadiazolyl, thiazolyl, or triazolyl, each substituted with -L_2-R_a and zero to 4 R_b;

R_a is:

(a) H, F, —CN, —OH, C_{1-3} alkyl, C_{1-2} fluoroalkyl, C_{1-3} hydroxyalkyl, —$(CH_2)_{0-2}O(C_{1-3}$ alkyl), —NHC(O)$OC(CH_3)_3$, —$(CR_xR_x)_{1-3}NHC(O)O(C_{1-4}$ alkyl), —$(CR_xR_x)_{1-3}NH_2$, —$(CR_xR_x)_{1-3}NR_x(C_{1-4}$ alkyl), —$O(C_{1-2}$ fluoroalkyl), —$S(O)_2NR_xR_x$, —$NHS(O)_2(C_{1-3}$ alkyl), —NR_xR_x, —$NR_x(C_{1-4}$ alkyl), —$(CR_xR_x)_{1-2}C(O)OH$, —C(O)OH, —$C(O)(C_{1-3}$ alkyl), —$C(O)O(C_{1-4}$ alkyl), —$C(O)NR_x(C_{1-2}$ alkyl), —$C(O)N(C_{1-3}$ alkyl)$_2$, —$C(O)NR_xCH_2C(O)NR_xR_x$, or —$C(O)NR_xCH_2CH_2NHC(O)(C_{1-3}$ alkyl);

(b) C_{3-6} cycloalkyl or —$C(O)NH(C_{3-6}$ cycloalkyl), wherein each cycloalkyl is substituted with zero to 2 substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, C_{1-3} fluoroalkyl, and —$C(O)O(C_{1-3}$ alkyl); or

(c) A_1, —CH_2A_1, —$C(O)A_1$, or —$C(O)NHA_1$, wherein A_1 is furanyl, imidazolyl, indolyl, isoxazolyl, octahydropyrrolo[3,4-c]pyrrolyl, oxazolyl, oxetanyl, phenyl, piperazinyl, piperidinyl, pyrazinyl, pyrazolyl, pyridinyl, pyrimidinyl, pyrrolidinyl, pyrrolyl, tetrahydrofuranyl, tetrahydropyranyl, thiadiazolyl, thiazolyl, thiophenyl, or triazolyl, each substituted with zero to three substituents independently selected from —OH, C_{1-3} alkyl, C_{1-3} hydroxyalkyl, —$C(O)(C_{1-2}$ alkyl), —$C(O)O(C_{1-3}$ alkyl), —NR_xR_x, phenyl, trifluoromethylphenyl, —CH_2(bromophenyl), and —CH_2CH_2(pyrrolidinyl);

each R_4 is independently F, —OH, C_{1-2} alkyl, or —OCH_3; or two R_4 attached to the same carbon atom form =O;

R_5 is F, Cl, —CN, —CH_3, —CF_3, or —OCH_3;

each R_b is independently —OH, —CH_3, or —CF_3;

each R_x is independently H or —CH_3;

each R_y is independently H or C_{1-5} alkyl;

m is zero, 1, or 2;

n is zero or 1; and

p is zero, 1, or 2.

3. The compound according to claim **1** or salt thereof, wherein:

R_1 is —CH_2CH_3, —$CH(CH_3)_2$, or —CH_2CHF_2;

each R_2 is independently F, Cl, —CN, —CH_3, —CD_3, —CH_2CH_3, —$CH(CH_3)_2$, —CF_3, —CH_2CN, —CH_2OH, —CH_2CH_2OH, —$CH(CH_3)OH$, —$C(CH_3)_2OH$, —OCH_2CH_2OH, —OCH_3, —OCH_2CH_3, —CH_2OCH_3, —$OCH_2CH_2OC(O)CH_3$, —$NH(CH_2CF_3)$, —$NHS(O)_2$(cyclopropyl), cyclopropyl, morpholinyl, dioxothiomorpholinyl, or methylpiperazinyl;

A is C_{4-6} cycloalkyl, dioxanyl, dioxotetrahydrothiophenyl, dioxotetrahydrothiopyranyl, oxetanyl, pyridinyl, pyrimidinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydrothiopyranyl, or triazolyl, each substituted with -L_2-R_a and zero to 1 R_b;

L_2 is a bond;

R_a is —CN, —OH, —CH_3, —$NHC(O)OC(CH_3)_3$, or —$C(O)OCH_2CH_3$;

R_b is —CH_3;

m is zero;

n is zero; and

p is zero, 1 or 2.

4. The compound according to claim **1** or salt thereof, wherein:

R_1 is —CH_2CH_3, —$CH(CH_3)_2$, or —CH_2CHF_2;

A is oxetanyl, tetrahydrofuranyl, or tetrahydropyranyl, each substituted with -L_2-R_a and zero to 2 R_b;

L_2 is a bond;

m is zero or 1;

n is zero; and

p is zero, 1 or 2.

5. The compound according to claim **1** or salt thereof, wherein:

R_1 is —CH_2CH_3, —$CH(CH_3)_2$, or —CH_2CHF_2;

A is cyclobutyl, cyclopentyl, or dioxotetrahydrothiopyranyl, each substituted with -L_2-R_a and zero to 2 R_b;

L_2 is a bond;

m is zero or 1;

n is zero; and

p is zero, 1 or 2.

6. The compound according to claim **1** or a salt thereof, wherein said compound is:

4-(4-(2-(7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (20);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (26);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (35);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (37);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (38);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (40);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (44);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (45);

3-(4-(2-(8-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)oxetane-3-carbonitrile (235);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (351);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (352);

6-(3-isopropyl-5-(1-((1-methyl-1H-1,2,4-triazol-3-yl)methyl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (353);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (354);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (355);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trideuteromethyl)-[1,2,4]triazolo[1,5-a]pyridine (357);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (393);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (394);

3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydrothiophene 1,1-dioxide (395);

4-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)cyclohexan-1-ol (403);

2-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)-1-methylcyclopentane-1-carbonitrile (416-417);

6-(3-isopropyl-5-(1-(tetrahydro-2H-thiopyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (425);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (441);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (443);

3-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydrothiophene 1,1-dioxide (460);

8-fluoro-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (469);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-[1,2,4]triazolo[1,5-a]pyridine (473);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (487);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (488);

4-(4-(2-(5,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (489);

2-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (492);

2-(6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)propan-2-ol (493);

4-(4-(2-(8-(2-hydroxypropan-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (496);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(methoxymethyl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (499);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile (500);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine-8-carbonitrile (501);

1-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-ol (503);

(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (504);

2-(6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)acetonitrile (506);

8-fluoro-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (507);

(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-7-yl)methanol (508);

(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (510);

4-(4-(2-(8-(hydroxymethyl)-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (514);

(6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)methanol (521);

2-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)ethan-1-ol (525);

2-((6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)oxy)ethyl acetate (528);

2-((6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)oxy)ethan-1-ol (529-530);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (534);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (535);

tert-butyl (3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)cyclobutyl)carbamate (538);

ethyl 3-(4-(3-isopropyl-2-(8-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)cyclobutane-1-carboxylate (539);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (540-541);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (542);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (543);

4-(4-(2-(2,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (545);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (546);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2,7-dimethyl-[1,2,4]triazolo [1,5-a]pyridine (547);

4-(4-(2-(2,7-dimethyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (548);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a] pyridine (549);

4-(4-(3-isopropyl-2-(8-(trifluoromethyl)-[1,2,4]triazolo [1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-ioxide (550);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (552);

6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo[1,5-a]pyridine (554);

4-(4-(3-isopropyl-2-(7-methyl-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (455);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(trifluoromethyl)-[1,2,4]triazolo [1,5-a]pyridine (556-557);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2,5-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (558);

4-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (561);

6-(5-(1-(2,2-dimethyltetrahydro-2H-pyran-4-yl)piperidin-4-yl)-3-isopropyl-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (562-564);

3-(4-(3-isopropyl-2-(8-methoxy-[1,2,4]triazolo[1,5-a] pyridin-6-yl)-1H-indol-5-yl)piperidin-1-yl)cyclobutane-1-carbonitrile (567);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a] pyridine (568-569);

8-ethoxy-6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl) piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a] pyridine (571);

8-ethoxy-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (572);

4-(4-(2-(8-ethoxy-[1,2,4]triazolo[1,5-a]pyridin-6-yl)-3-isopropyl-1H-indol-5-yl)piperidin-1-yl)tetrahydro-2H-thiopyran 1,1-dioxide (573);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-2-methyl-[1,2,4]triazolo[1,5-a] pyridine (574);

6-(3-isopropyl-5-(1-(tetrahydrofuran-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-2-methyl-[1,2,4]triazolo [1,5-a]pyridine (575-576);

8-ethyl-6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl) piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (577);

8-ethyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (578);

8-chloro-6-(3-isopropyl-5-(1-(tetrahydro-2H-pyran-4-yl) piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (579);

8-chloro-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (580);

4-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)morpholine (581);

8-ethyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (583);

8-isopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (585);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-N-(2,2,2-trifluoroethyl)-[1,2,4]triazolo[1,5-a]pyridin-8-amine (586);

8-ethyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (587);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-7-methyl-[1,2,4]triazolo[1,5-a] pyridine (588);

N-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)cyclopropanesulfonamide (590);

4-(6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridin-8-yl)thiomorpholine 1,1-dioxide (591);

6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-(4-methylpiperazin-1-yl)-[1,2,4]triazolo[1,5-a]pyridine (592);

8-cyclopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-[1,2,4]triazolo[1,5-a]pyridine (593);

8-cyclopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-2-methyl-[1,2,4]triazolo[1,5-a]pyridine (594);

8-cyclopropyl-6-(3-isopropyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-7-methyl-[1,2,4]triazolo[1,5-a]pyridine (595);

6-(3-ethyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (596);

6-(3-(2,2-difluoroethyl)-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methyl-[1,2,4]triazolo[1,5-a]pyridine (597);

6-(3-(2,2-difluoroethyl)-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a] pyridine (598);

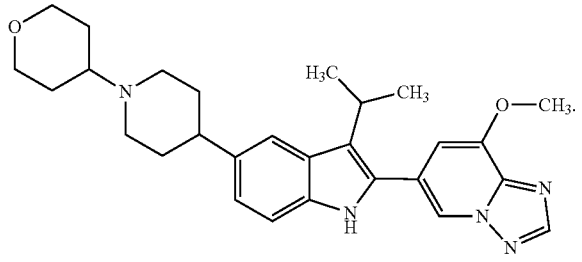
6-(3-ethyl-5-(1-(oxetan-3-yl)piperidin-4-yl)-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (600);

6-(3-isopropyl-5-(1-(pyridin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (986);

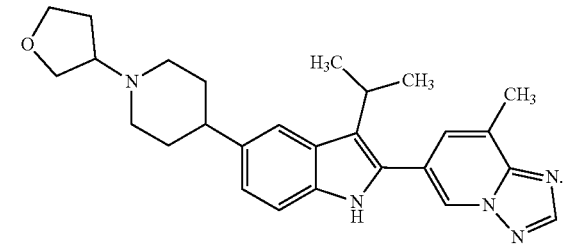
6-(3-isopropyl-5-(1-(pyrimidin-2-yl)piperidin-4-yl)-1H-indol-2-yl)-7,8-dimethyl-[1,2,4]triazolo[1,5-a]pyridine (989); or

6-(5-(1-(2,2-dimethyl-1,3-dioxan-5-yl)piperidin-4-yl)-4-fluoro-3-isopropyl-1H-indol-2-yl)-8-methoxy-[1,2,4]triazolo[1,5-a]pyridine (993).

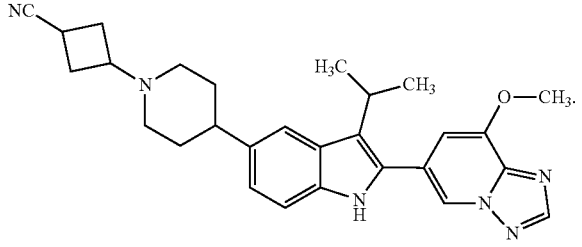
7. The compound according to claim **1** or a salt thereof, wherein said compound is:



8. The compound according to claim **1** or a salt thereof, wherein said compound is:



9. The compound according to claim **1** or a salt thereof, wherein said compound is:



10. A pharmaceutical composition comprising a compound according to claim **1** or a pharmaceutically-acceptable salt thereof; and a pharmaceutically acceptable carrier.

11. A pharmaceutical composition comprising a compound according to claim **7** or a pharmaceutically-acceptable salt thereof; and a pharmaceutically acceptable carrier.

12. A pharmaceutical composition comprising a compound according to claim **8** or a pharmaceutically-acceptable salt thereof; and a pharmaceutically acceptable carrier.

13. A pharmaceutical composition comprising a compound according to claim **9** or a pharmaceutically-acceptable salt thereof; and a pharmaceutically acceptable carrier.

14. A method of treating an autoimmune disease or a chronic inflammatory disease, comprising administering to a mammalian [patent] *patient* a compound according to claim **1** or a pharmaceutically acceptable salt thereof, wherein said autoimmune disease or chronic inflammatory disease is systemic lupus erythematosus.

15. A method of treating an autoimmune disease or a chronic inflammatory disease, comprising administering to a mammalian [patent] *patient* a compound according to claim **7** or a pharmaceutically acceptable salt thereof, wherein said autoimmune disease or chronic inflammatory disease is systemic lupus erythematosus.

16. A method of treating an autoimmune disease or a chronic inflammatory disease, comprising administering to a mammalian [patent] *patient* a compound according to claim **8** or a pharmaceutically acceptable salt thereof, wherein said autoimmune disease or chronic inflammatory disease is systemic lupus erythematosus.

17. A method of treating an autoimmune disease or a chronic inflammatory disease, comprising administering to a mammalian [patent] *patient* a compound according to claim **9** or a pharmaceutically acceptable salt thereof, wherein said autoimmune disease or chronic inflammatory disease is systemic lupus erythematosus.

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