US 20200048223A1

(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2020/0048223 A1**

Zhang (43) **Pub. Date: Feb. 13, 2020**

(54) **WNT SIGNALING PATHWAY INHIBITORS AND THERAPEUTIC APPLICATIONS THEREOF**

(71) Applicant: **Suzhou Yunxuan Yiyao Keji Youxian Gongsi**, Suzhou (CN)

(72) Inventor: **Xiaohu Zhang**, Suzhou (CN)

(73) Assignee: **Suzhou Yunxuan Yiyao Keji Youxian Gongsi**, Suzhou (CN)

(21) Appl. No.: **16/653,217**

(22) Filed: **Oct. 15, 2019**

Related U.S. Application Data

(63) Continuation of application No. 15/766,799, filed on Apr. 6, 2018, now Pat. No. 10,450,300, filed as application No. PCT/US2016/055851 on Oct. 6, 2016.

(30) **Foreign Application Priority Data**

Oct. 8, 2015	(CN)	201510645986.2
Mar. 31, 2016	(CN)	201610195731.5
Mar. 31, 2016	(CN)	201610195733.4
Aug. 16, 2016	(CN)	201610670828.7
Sep. 26, 2016	(CN)	201610850357.8
Sep. 26, 2016	(CN)	201610850358.2
Sep. 26, 2016	(CN)	201610850360.X

Publication Classification

(51) **Int. Cl.**

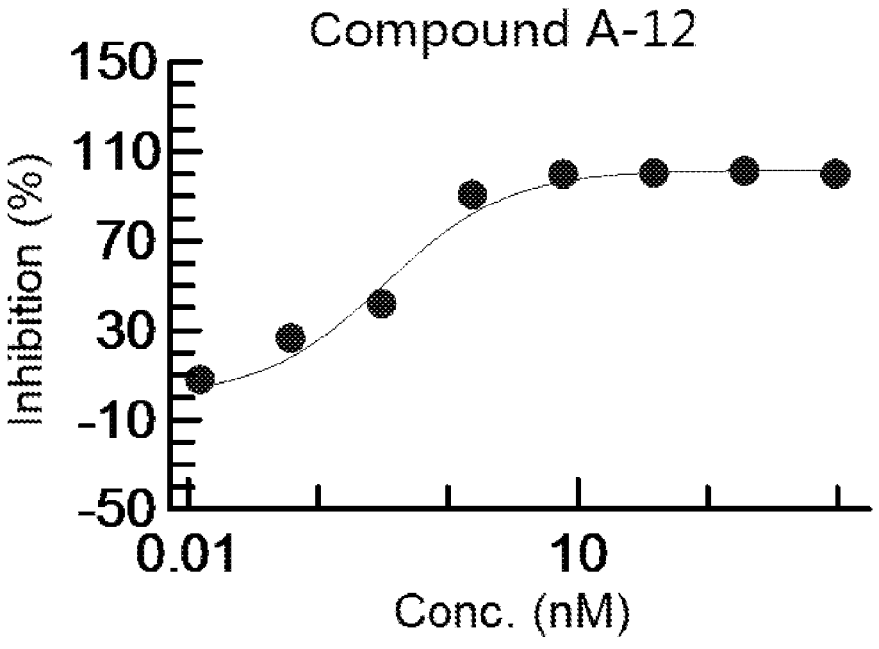
C07D 401/14	(2006.01)
C07D 513/04	(2006.01)
C07D 498/04	(2006.01)
C07D 487/04	(2006.01)
C07D 471/04	(2006.01)
C07D 417/14	(2006.01)
C07D 409/14	(2006.01)
C07D 403/12	(2006.01)
C07D 401/12	(2006.01)
C07D 401/04	(2006.01)
A61P 35/02	(2006.01)
A61K 31/4709	(2006.01)
A61K 31/541	(2006.01)
A61K 31/53	(2006.01)
A61K 31/4725	(2006.01)
A61K 31/517	(2006.01)
A61K 31/444	(2006.01)
A61K 31/506	(2006.01)
A61K 45/06	(2006.01)

(52) **U.S. Cl.**

CPC ***C07D 401/14*** (2013.01); ***A61K 45/06*** (2013.01); ***C07D 498/04*** (2013.01); ***C07D 487/04*** (2013.01); ***C07D 471/04*** (2013.01); ***C07D 417/14*** (2013.01); ***C07D 409/14*** (2013.01); ***C07D 403/12*** (2013.01); ***C07D 401/12*** (2013.01); ***C07D 401/04*** (2013.01); ***A61P 35/02*** (2018.01); ***A61K 31/4709*** (2013.01); ***A61K 31/541*** (2013.01); ***A61K 31/53*** (2013.01); ***A61K 31/4725*** (2013.01); ***A61K 31/517*** (2013.01); ***A61K 31/444*** (2013.01); ***A61K 31/506*** (2013.01); ***C07D 513/04*** (2013.01)

(57) **ABSTRACT**

Inhibitors of Wnt signaling pathway with structures of Formula I are disclosed, together with their pharmaceutical salts. Applications of compounds of Formula I in inhibiting or modulating the Wnt signaling pathway are also disclosed. Compounds of Formula I can treat disorders caused by aberrant activation of the Wnt signaling pathway.



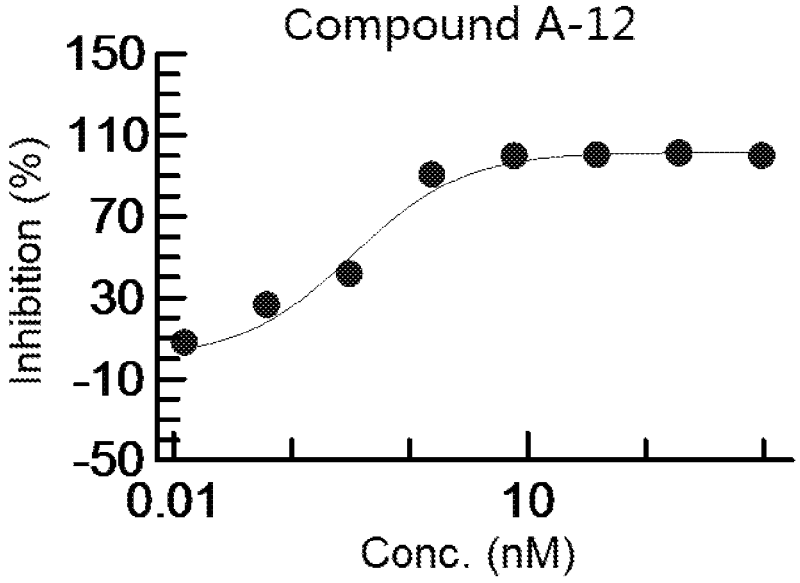

Compound A-12
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 1

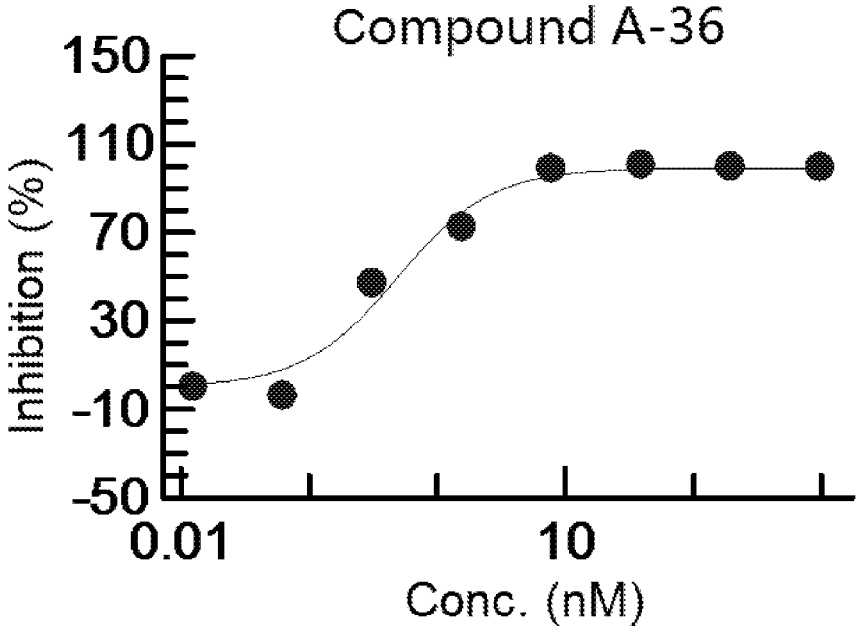

Compound A-36
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 2

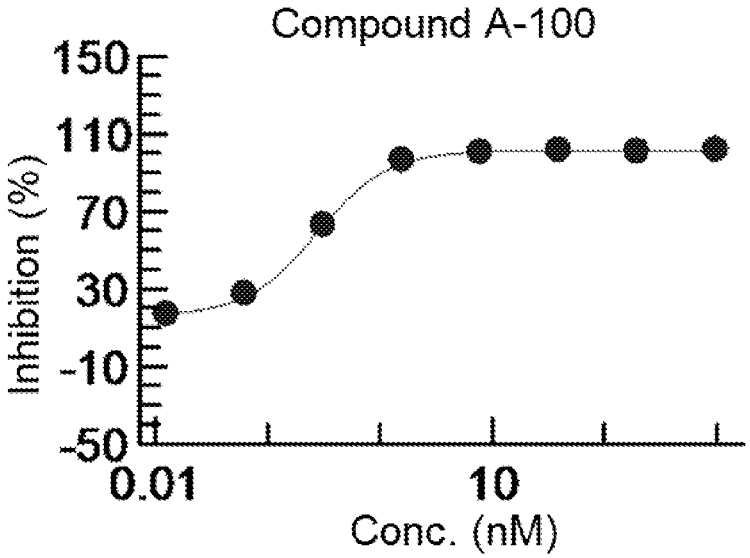

Compound A-100
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 3

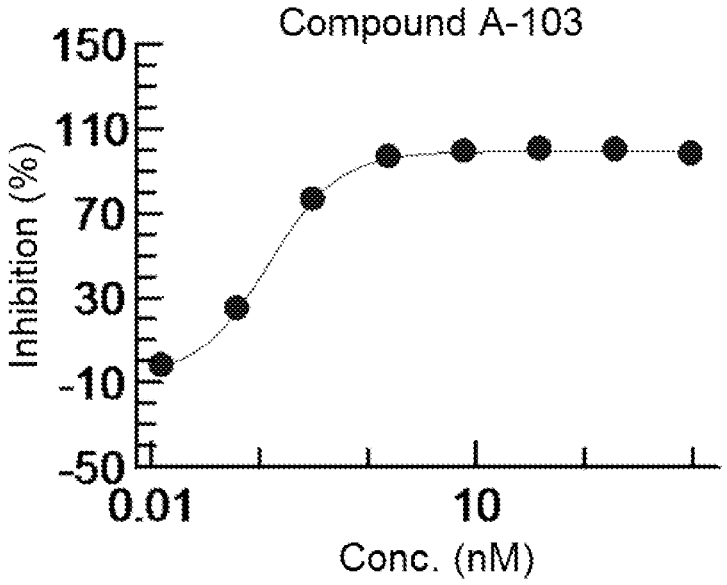

Compound A-103
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 4

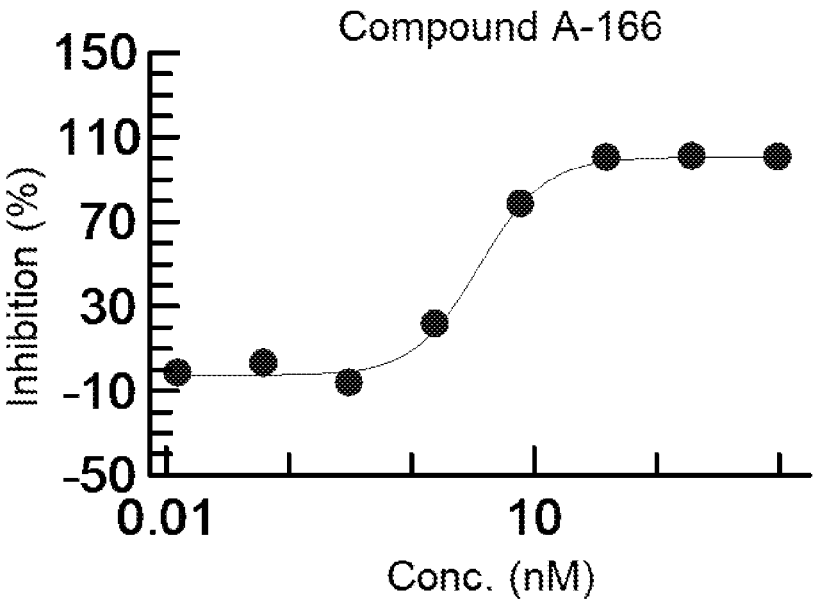

Compound A-166
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 5

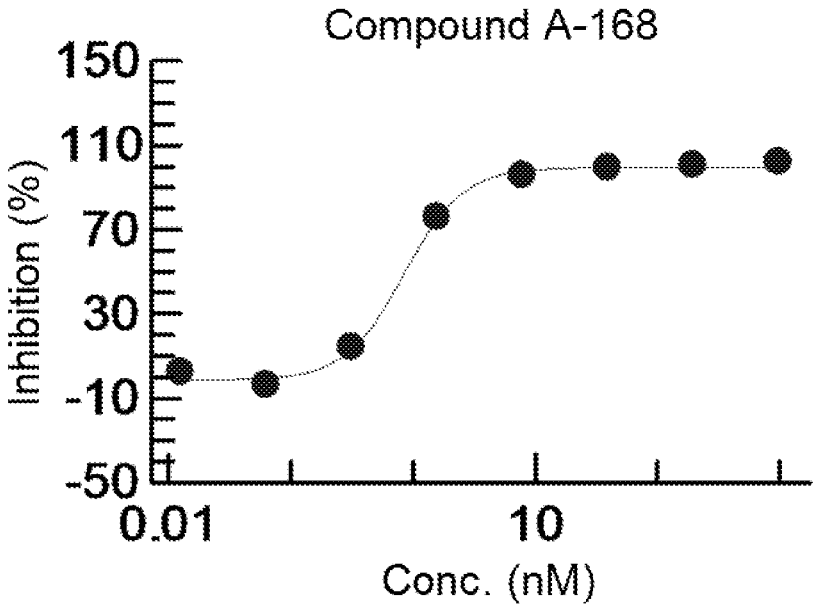

Compound A-168
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 6

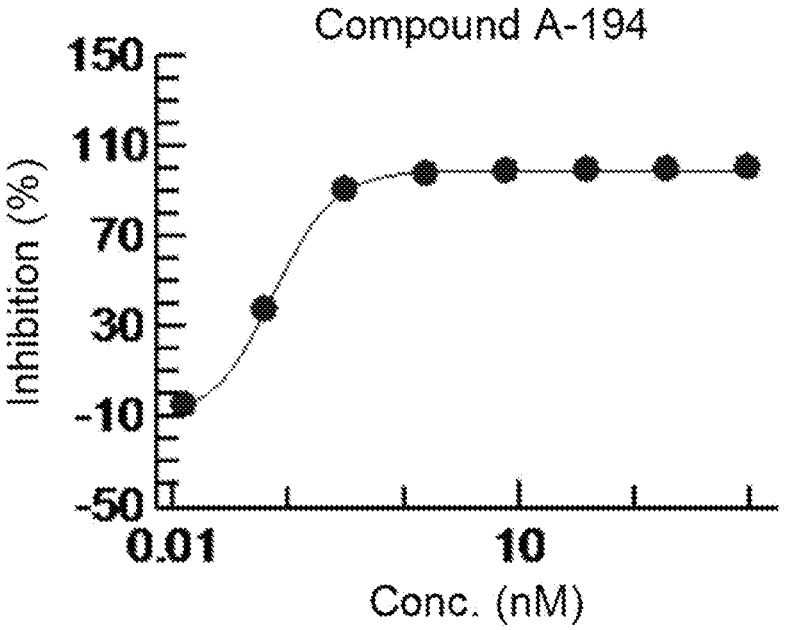

Compound A-194
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 7

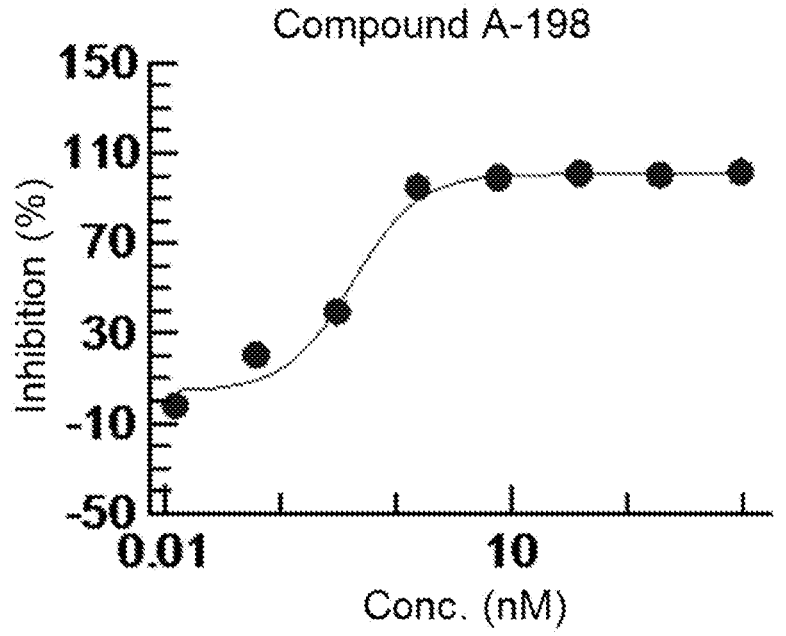

Compound A-198
150
110
70
30
-10
-50
Inhibition (%)
0.01
10
Conc. (nM)

FIG. 8

WNT SIGNALING PATHWAY INHIBITORS AND THERAPEUTIC APPLICATIONS THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application is a Continuation of U.S. patent application Ser. No. 15/766,799, filed on Apr. 6, 2018, which is the U.S. National Phase of International Application No. PCT/US2016/055851, filed on Oct. 6, 2016, which claims the benefit of Chinese Patent Applications 201510645986.2, filed on Oct. 8, 2015; 201610195733.4, filed on Mar. 31, 2016; 201610195731.5, filed on Mar. 31, 2016; 201610670828.7, filed on Aug. 16, 2016; 201610850360.X, filed on Sep. 26, 2016; 201610850358.2, filed on Sep. 26, 2016; and 201610850357.8, filed on Sep. 26, 2016; all of which are hereby incorporated by reference.

FIELD OF INVENTION

[0002] The present invention generally relates to heterocyclic compounds and, more particularly, relates to novel heterocyclic compounds that are useful in therapies targeting the Wnt signaling pathway mediated diseases, such as cancer, in mammals.

BACKGROUND OF THE INVENTION

[0003] The Wnt signaling pathway has critical roles in developmental pathways, including regulatory roles in cell proliferation, tissue patterning, and cell fate, migration, morphogenesis and function, as well as cell survival and degeneration (Logan and Nusse, *Annu. Rev. Cell Dev. Biol.* (2004) 20:781-810). Recently during research on stem cells, Wnt signaling pathway has been found to regulate the maintenance of epidermal stem cells, intestinal stem cells, hematopoietic stem cells, neural stem cells, embryonic stem cells and tumor stem cells (Reya and Clevers, *Nature* (2005) 434:843-850).

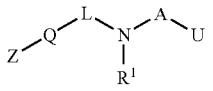
[0004] The canonical Wnt signaling pathway is activated by Wnt proteins that interact with seven-pass transmembrane receptors of the Frizzled (Fzd) family and single-pass transmembrane co-receptors, such as lipoprotein receptor-related protein 5/6 (LRP5/6). Such interaction activates the Wnt signaling pathway by recruiting and activating the Dishevelled (Dvl) protein, which, in turn, silences glycogen synthase kinase 3β (GSK3β) within a destructive complex formed by adenomatous polyposis coli (APC) protein, GSK3β, Axin, and a priming kinase for β-catenin called casein kinase 1α (CK1α). The destructive complex can phosphorylate β-catenin for its degradation. By inhibiting the destructive complex, cytoplasmic β-catenin can be stabilized and accumulated in the presence of lymphoid enhancing factor/T-cell factor (LEF/TCF) transcription factors so that β-catenin can be translocated into the nucleus to activate β-catenin mediated gene expressions of disease-causing products, including c-Myc、cyclin-D1、survivin、gastrin、VEGF、ASEF, etc., to increase cell proliferation (Boutros and Mlodzik, *Mech. Dev.* (1999) 83:27-37; and Perrimon, *Cell* (1994) 76:781-4).

[0005] Mutations or deregulated expression of components of the Wnt signaling pathway have been linked to the formation and metastasis of numerous tumors. For example, in patients with colon cancer, gene mutations have been observed in regulators of the Wnt cascade, including APC, β-catenin, Axin and TCF, leading to over-expression of genes associated with cell proliferation (Klaus and Birchmeier, *Nat. Rev. Cancer* (2008) 8:387-98). Aberrant activation of the Wnt signaling pathway is associated with a variety of diseases including various cancers (Hoang et al., *Int. J. Cancer* (2004) 109:106-111), decrease of neural precursor cells (Chenn and Walsh, *Science* (2002) 297:365-9), pathogenesis of sporadic medulloblastoma (Dahmen et al., *Cancer Res.* (2001) 61:7039-43), malignant proliferation of cancer cells due to disruption of Wnt signaling pathway in stem and progenitor cells (Reya and Clevers, *Nature* (2005) 434:843-850).

[0006] Thus, there is a need for agents and methods that modulate the Wnt signaling pathway, thereby treating, and/or ameliorating Wnt signaling-related disorders.

SUMMARY OF THE INVENTION

[0007] In one aspect, the present invention provides compounds of Formula I:



I

or a pharmaceutically acceptable salt, solvate, stereoisomer or a tautomer thereof, wherein

[0008] A is A1, A2, A3 or A4;

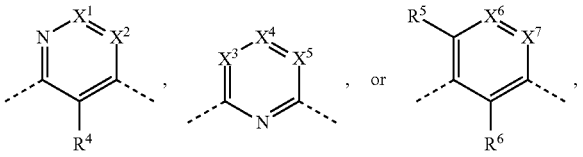
[0009] U is U1, U2, U3 or U4;

[0010] L is L1, L2, or L3;

[0011] Q is Q1, Q2, Q3 or Q4;

[0012] Z is Z1, Z2, Z3 or Z4;

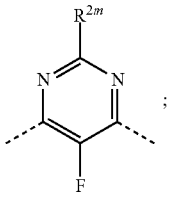
[0013] A1 is



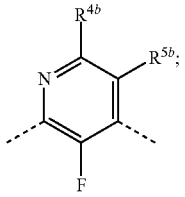
wherein

[0014] X^1 to X^7 are independently selected from N and C—$R^{1.3}$;

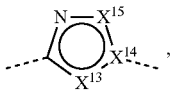
[0015] A2 is



[0016] A3 is

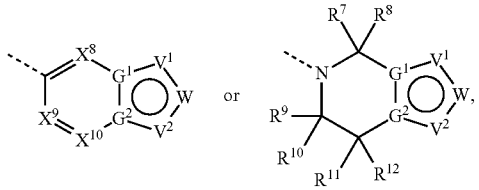


[0017] A4 is



wherein X^{13} and X^{15} are independently O, N, S or C—R^{4c}, and X^{14} is N or C;

[0018] U1 is



wherein X^8 to X^{10} are independently selected from N and C—R^{14};

[0019] G^1 and G^2 are independently selected from N and C;

[0020] V^1 and V^2 are independently selected from N, O, S and C—R^{15};

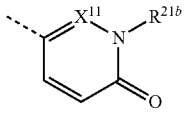
[0021] W is V^3, V^4—V^5 or V^4═V^5, wherein V^3 to V^5 are independently selected from N, O, S and C—R^{16}, wherein V^4 connects with V^1; and

[0022] V^5 connects with V^2;

[0023] U2 is C_6-C_{10} aryl, 5-12 membered heteroaryl, 11-13 membered heterocyclophenyl or 10-13 membered heterocycloheteroaryl, wherein heterocyclo and heteroaryl comprises 1 to 4 heteroatoms independently selected from N, O and S; and

[0024] C_6-C_{10} aryl, 5-12 membered heteroaryl, 11-13 membered heterocyclophenyl and 10-13 membered heterocycloheteroaryl are unsubstituted or substituted with 1 to 4 R^{6a} groups;

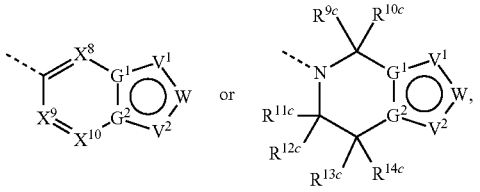
[0025] U3 is —OR^{14b}, —$NR^{14b}R^{15b}$, C_6-C_{12} aryl unsubstituted or substituted with 1-6 R^{13b} group, 5-14 membered heteroaryl unsubstituted or substituted with 1-6 R^{13b} group, 11-13 membered heterocyclophenyl unsubstituted or substituted with 1-6 R^{13b} group, 10-13 membered heterocycloheteroaryl unsubstituted or substituted with 1-6 R^{13b} group, C_2-C_8 alkenyl substituted with 5-6 membered aryl or heteroaryl, C_2-C_8 alkynyl substituted with 5-6 membered aryl or heteroaryl, or



unsubstituted or substituted with 1 to 2 R^{13b} groups, wherein heterocyclo and heteroaryl comprises 1 to 4 heteroatoms independently selected from N, O and S; and

[0026] X^{11} is N or C—R^{13b};

[0027] U4 is



wherein X^8 to X^{10} are independently selected from N and C—R^{15c};

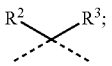
[0028] G^1 and G^2 are independently selected from N and C;

[0029] V^1 and V^2 are independently selected from N, O, S and C—R^{16c};

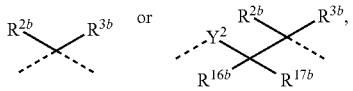
[0030] W is V^3, V^4—V^5 or V^4═V^5, wherein V^3 to V^5 are independently selected from N, O, S and C—R^{17c}, wherein V^4 connects with V^1; and

[0031] V^5 connects with V^2;

[0032] L1 is



[0033] L2 is



wherein Y^2 is blank, —O—, —S—, —$N(R^{18b})$— or —$C(R^{18b})(R^{19b})$—;

[0034] L3 is —$C(R^{2c})(R^{3c})$— or —$NHCH_2CH_2$—;

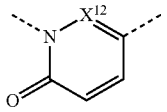
[0035] Q1 is C_6-C_{10} arylene or 5-12 membered heteroarylene, wherein 5-12 membered heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

[0036] C_6-C_{10} aryl and 5-12 membered heteroarylene are unsubstituted or substituted with 1 to 4 R^{17} groups;

[0037] Q2 is C_6-C_{10} arylene or 5-10 membered heteroarylene, wherein 5-10 membered heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

[0038] C_6-C_{10} arylene and 5-10 membered heteroarylene are unsubstituted or substituted with 1 to 4 R^{4a} groups;

[0039] Q3 is C_6-C_{12} arylene unsubstituted or substituted with 1-6 R^{6b} group, 5-14 membered heteroarylene unsubstituted or substituted with 1-6 R^{6b} group, C_3-C_6 cycloalkylene unsubstituted or substituted with 1-6 R^{6b} group, C_3-C_6 heterocylene unsubstituted or substituted with 1-6 R^{6b} group, or



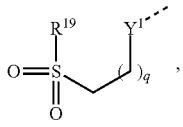
unsubstituted or substituted with 1 to 2 R^{6b} groups, wherein heterocyclene and heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

[0040] X^{12} is N or C—R^{6b};

[0041] Q4 is C_6-C_{10} arylene or 5-12 membered heteroarylene, wherein 5-12 membered heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

[0042] C_6-C_{10} arylene and 5-12 membered heteroarylene are unsubstituted or substituted with 1 to 4 R^{5c} groups;

[0043] Z1 is —CN, C_6 aryl, 5-6 membered heteroaryl, or



wherein 5-6 membered heteroaryl comprises 1 to 3 heteroatoms independently selected from N, O and S;

[0044] C_6 aryl and 5-6 membered heteroaryl are unsubstituted or substituted with 1 to 3 R^{18} groups;

[0045] Y^1 is O or NR^{20}; and

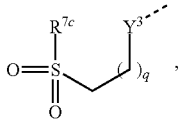
[0046] q is 0, 1, 2, or 3;

[0047] Z2 is H, —CN, halide, —OH, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkylsulfonyl, C_1-C_8 acyl, aminoacyl, C_1-C_8 acylamino, C_1-C_8 alkylcarbamoylamino, C_1-C_8 alkoxycarbamoyl, C_1-C_8 alkylsulfonamido, C_1-C_8 alkylaminosulphonyl, C_1-C_8 alkoxy, C_2-C_8 alkoxyacyl, phenyl, 5-6 membered heteroaryl, or 5-7 membered heterocyclo, wherein 5-6 membered heteroaryl and 5-7 membered heterocyclo comprise one or more hetero atoms independently selected from N, O and S; and

[0048] phenyl, 5-6 membered heteroaryl and 5-7 membered heterocycle are unsubstituted or substituted with 1 to 3 R^{5a} groups;

[0049] Z3 is H, —CN, halide, —OH, C_1-C_8 alkyl unsubstituted or substituted with 1 to 3 R^{12b} groups, C_3-C_8 cycloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkylsulfonyl, C_1-C_8 acyl, aminoacyl, C_1-C_8 acylamino, C_1-C_8 alkylcarbamoylamino, C_1-C_8 alkoxycarbamoyl, C_1-C_8 alkylsulfonamido, C_1-C_8 alkylaminosulphonyl, C_1-C_8 alkoxy, C_2-C_8 alkoxyacyl, —$N(R^{7b})(R^{8b})$ unsubstituted or substituted with 1 to 3 R^{12b} groups, phenyl unsubstituted or substituted with 1 to 3 R^{9b} groups, 5-6 membered heteroaryl unsubstituted or substituted with 1 to 3 R^{10b} groups, or 5-7 membered heterocyclo unsubstituted or substituted with 1 to 3 R^{11b} groups, wherein 5-6 membered heteroaryl and 5-7 membered heterocyclo comprises 1-3 hetero atoms independently selected from N, O and S;

[0050] Z4 is —CN, C_6 aryl, 5-6 membered heteroaryl, or



wherein 5-6 membered heteroaryl comprises 1 to 3 heteroatoms independently selected from N, O and S;

[0051] C_6 aryl and 5-6 membered heteroaryl are unsubstituted or substituted with 1 to 3 R^{6c} groups;

[0052] Y^3 is O or NR^{8c}; and

[0053] q is 0, 1, 2, or 3;

[0054] R^1 to R^3 are independently selected from H and C_1-C_6 alkyl, wherein C_1-C_6 alkyl is unsubstituted or substituted with 1 to 3 halide, —CN, —OH, C_1-C_3 alkyl, C_3-C_5 cycloalkyl, or C_1-C_3 alkoxy groups;

[0055] R^4 is H, halide, —CN, —OH, —NO_2, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, or C_1-C_6 alkoxy, wherein C_1-C_6 alkyl, C_3-C_8 cycloalkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide;

[0056] R^5 and R^6 are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl and C_1-C_6 alkoxy, wherein C_1-C_6 alkyl, C_3-C_6 cycloalkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide;

[0057] R^7 and R^8 are independently selected from H and C_1-C_6 alkyl, or R^7 and R^8 together are oxo (=O);

[0058] R^9 to R^{12} are independently selected from H, C_1-C_6 alkyl;

[0059] R^{13} is H, halide, —CN, —OH, amino, —NO_2, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 alkylthio or 1-pyrrolidino, wherein amino, C_1-C_6 alkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide, C_1-C_3 alkyl or C_3-C_6 cycloalkyl groups;

[0060] R^{14} to R^{17} are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy and C_1-C_6 alkylthio, wherein amino, C_1-C_6 alkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide, C_1-C_3 alkyl or C_3-C_6 cycloalkyl groups;

[0061] R^{18} is H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl or C_1-C_6 alkoxy, wherein amino, C_1-C_6 alkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide, C_1-C_3 alkyl or C_3-C_6 cycloalkyl groups;

[0062] R^{19} and R^{20} are independently selected from H and C_1-C_3 alkyl, or R^{19} and R^{20} together, with adjacent atoms they attached to, form a cyclic structure;

[0063] R^{4a}, R^{5a} and R^{6a} are independently selected from halide, —CN, and —OH, or R^{4a}, R^{5a} and R^{6a} are independently selected from C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_1-C_8 alkoxy, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkylsulfonyl, C_1-C_8 acyl, aminoacyl, C_1-C_8 acylamino, C_1-C_8 alkylcarbamoylamino, C_1-C_8 alkoxycarbamoyl, C_1-C_8 alkylsulfonamido, C_1-C_8

alkylaminosulphonyl, C_2-C_8 alkoxyacyl, and 3-8 membered heterocycle, all of which are unsubstituted or substituted with 1-3 halide, —OH, —CN, C_1-C_3 alkyl, C_1-C_3 alkoxyl or C_3-C_8 cycloalkyl groups, wherein 3-8 membered heterocycle comprises one or more hetero atoms from N, O or S;

[0064] R^{2m} is H, deuterium, tritium, halide, —OH, —CN, C_1-C_8 alkyl, C_3-C_8 cycloalkyl or C_1-C_8 alkoxy;

[0065] R^{2b} and R^{3b} are independently selected from H, C_1-C_6 alkyl unsubstituted or substituted with 1-3 groups selected from halide, —CN, —OH, C_1-C_6 alkyl, C_3-C_5 cycloalkyl and C_1-C_3 alkoxy;

[0066] R^{4b} and R^{5b} are independently selected from H, halide, —CN, amino, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_1-C_8 alkoxy, and C_1-C_3 alkylamino;

[0067] R^{6b} is H, halide, —CN or —OH, or R^{6b} is selected from amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, and C_1-C_3 alkylamino, all of which are unsubstituted or substituted with 1-3 halide, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl groups;

[0068] R^{7b} and R^{8b} are independently selected from H, C_1-C_8 alkyl and C_3-C_8 cycloalkyl, the latter two of which are unsubstituted or substituted with 1-3 R^{12b}, or R^7 and R^8 together, with adjacent atoms they attached to, form a cyclic structure;

[0069] R^{9b} and R^{10b} are independently selected from H, halide, —CN and —OH, or R^{9b} and R^{10b} are independently selected from amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and C_1-C_6 alkoxy, all of which are unsubstituted or substituted with 1-3 halide, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl groups;

[0070] R^{11b} is H, halide, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with halide, C_3-C_6 cycloalkyl, oxo, or C_1-C_6 alkoxy;

[0071] R^{12b} is H, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with halide, C_3-C_6 cycloalkyl, oxo, or C_1-C_6 alkoxy;

[0072] R^{13b} is H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_2-C_6 alkylcarbamoylamino, C_2-C_6 alkoxycarbamoyl, C_1-C_3 alkylsulphonyl, —$N(R^{16b})S(O)_2$—C_1-C_3 alkyl, or —$N(R^{16b})C(O)$—C_1-C_3 alkyl;

[0073] R^{14b} and R^{15b} are independently selected from H, C_3-C_6 cycloalkyl unsubstituted or substituted with 1 to 3 R^{20b} groups, C_1-C_6 alkyl unsubstituted or substituted with 1 to 3 R^{20b} groups, 5-6 membered aryl unsubstituted or substituted with 1 to 3 R^{20b} groups, 5-6 membered heteroaryl unsubstituted or substituted with 1 to 3 R^{20b} groups, and 5-6 membered heterocyclo unsubstituted or substituted with 1 to 3 R^{20b} groups, wherein 5-6 membered heteroaryl and 5-7 membered heterocyclo comprise 1 to 3 hetero atoms independently selected from N, O and S, or R^{14b} and R^{15b} together, with adjacent atoms they attached to, form a cyclic structure;

[0074] R^{16b} to R^{19b} are independently selected from H and C_1-C_6 alkyl unsubstituted or substituted with halide;

[0075] R^{20b} is H, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5-6 membered aryl, or 5-6 membered heteroaryl, wherein 5-6 membered heteroaryl comprises 1 to 3 hetero atoms independently selected from N, O and S;

[0076] R^{21b} is H or C_1-C_6 alkyl;

[0077] R^{2c} and R^{3c} are independently selected from H and C_1-C_6 alkyl unsubstituted or substituted with 1-3 halide;

[0078] R^{4c} is H, halide, C_1-C_3 alkyl, C_3-C_5 cycloalkyl, or C_1-C_3 alkoxy;

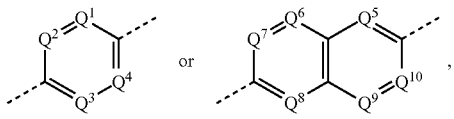
[0079] R^{5c} and R^{6c} are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with 1-3 halide, C_3-C_5 cycloalkyl, and C_1-C_6 alkoxy;

[0080] R^{7c} and R^{8c} are independently selected from H and C_1-C_6 alkyl, or R^{7c} and R^{8c} together, with adjacent atoms they attached to, form a cyclic structure;

[0081] R^{9c} to R^{14c} are independently selected from H, C_1-C_6 alkyl and —CF_3;

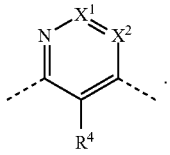
[0082] R^{15c} to R^{17c} are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with 1-3 halide, C_3-C_5 cycloalkyl, and C_1-C_6 alkoxy.

[0083] In one embodiment, the compound of Formula I comprises Q which is

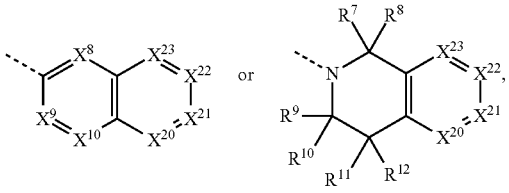


wherein Q^1 to Q^{10} are independently N or C—R^{17}.

[0084] In another embodiment, the compound of Formula I comprises A which is

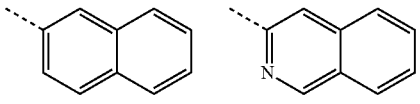


[0085] In one embodiment, the compound of Formula I comprises U which is

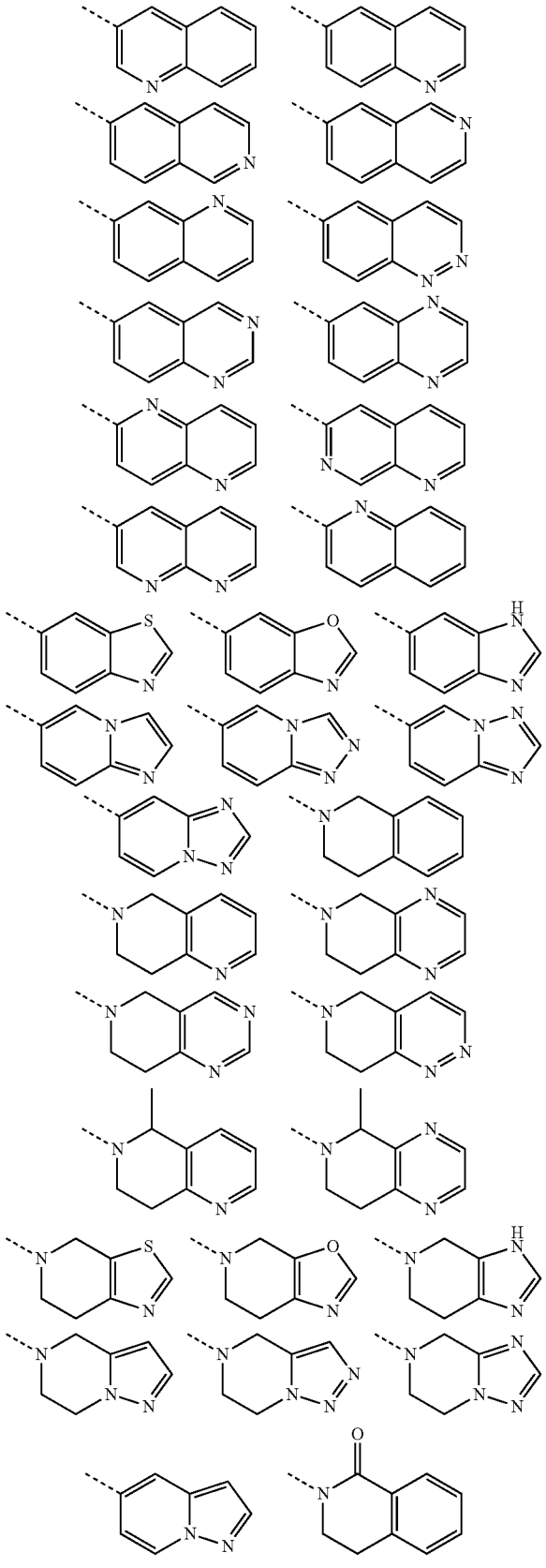


wherein X^{20} to X^{23} are independently N or C—R^{15}.

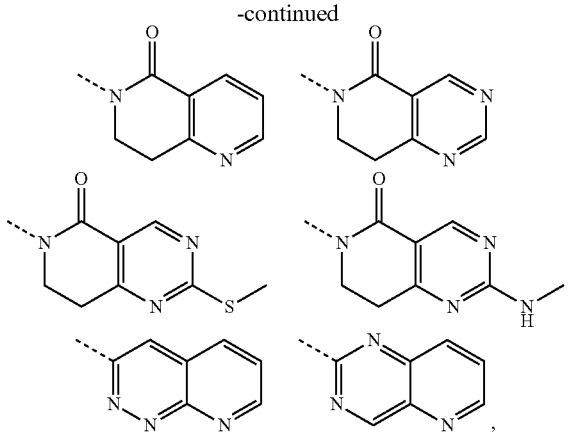
[0086] In another embodiment, the compound of Formula I comprises U which is selected from:



-continued

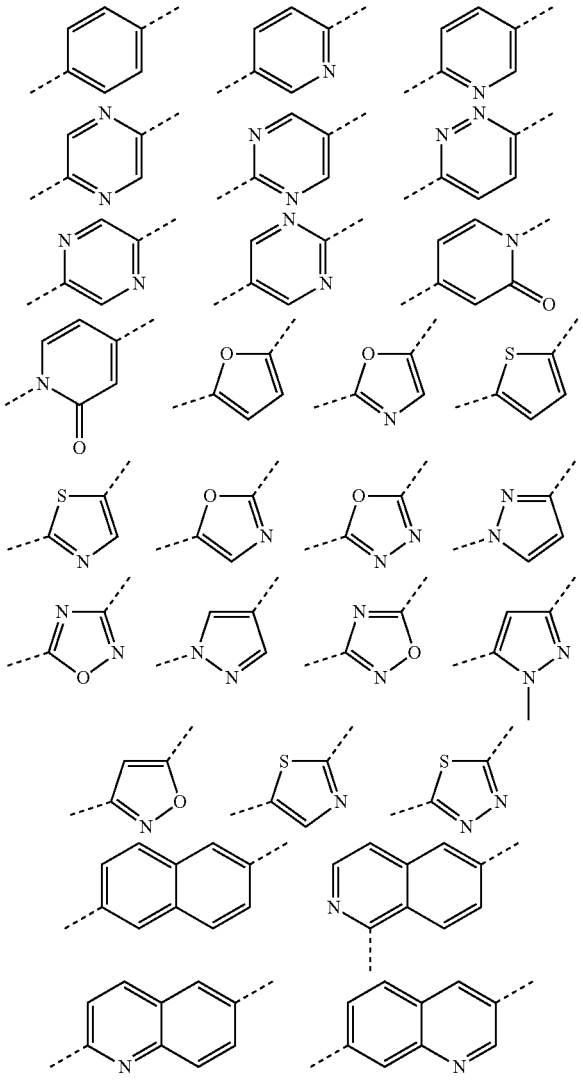


-continued

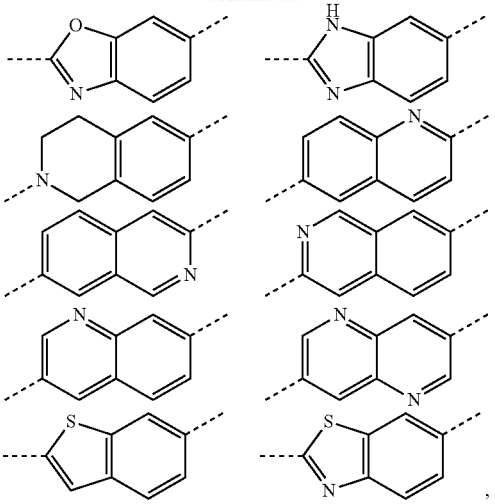


unsubstituted or substituted with 1 to 3 R^{15} groups.

[0087] In one embodiment, the compound of Formula I comprises Q which is selected from:

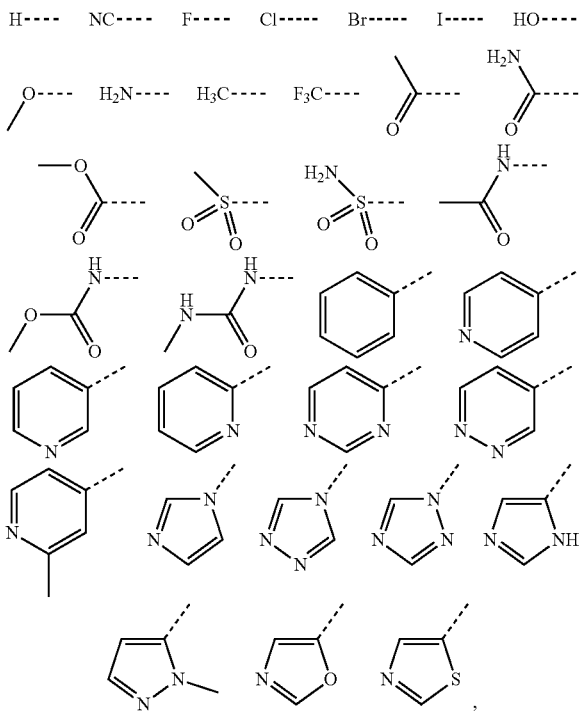


-continued



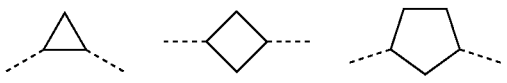
unsubstituted or substituted with 1 to 3 R^{4a} groups.

[0088] In one embodiment, the compound of Formula I comprises Z which is selected from:

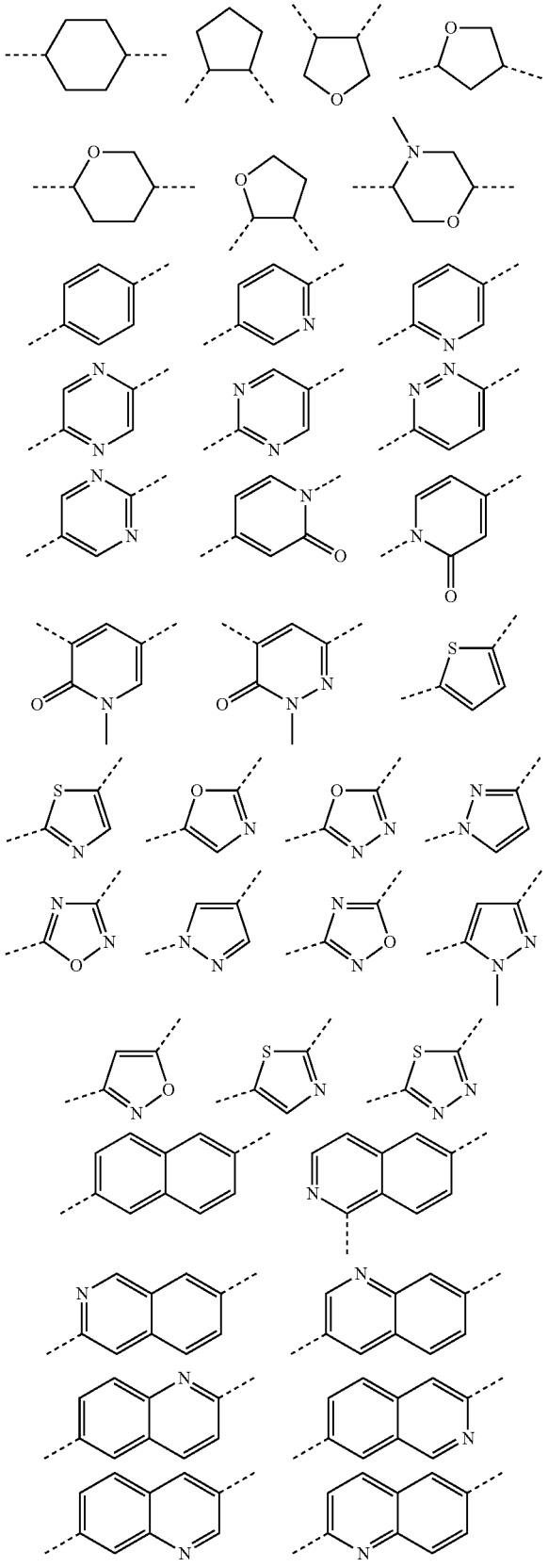


unsubstituted or substituted with 1 to 3 R^{5a} groups.

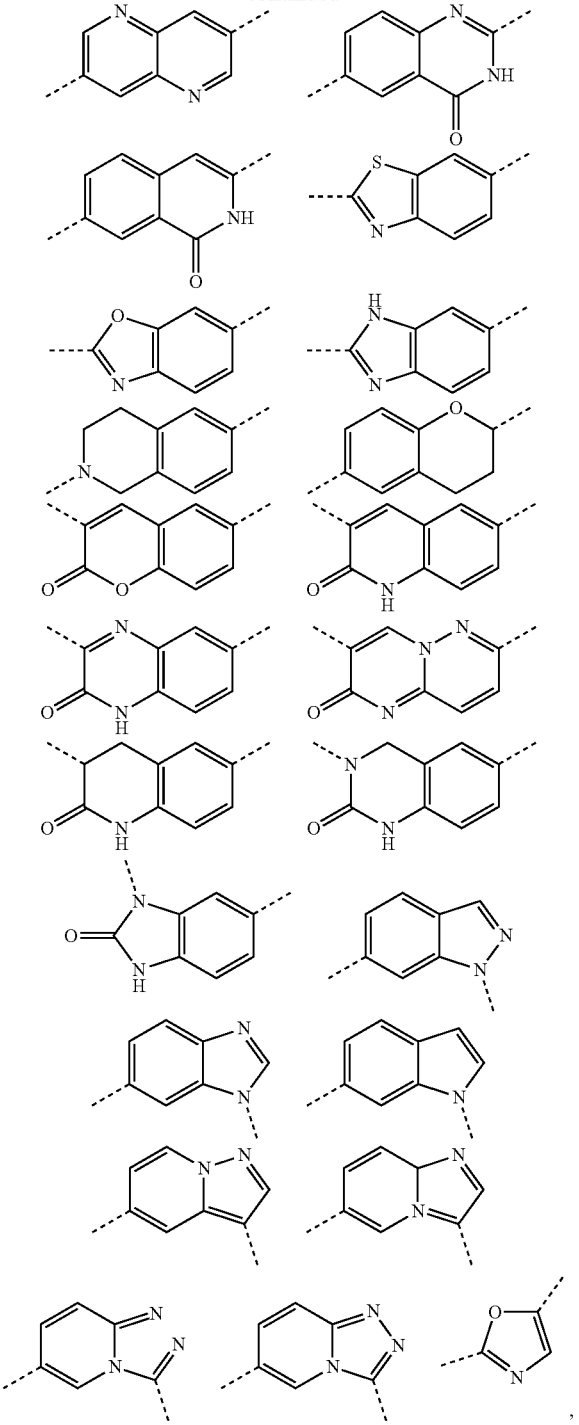
[0089] In another embodiment, the compound of Formula I comprises Q which is selected from:



-continued

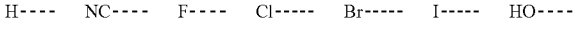


-continued

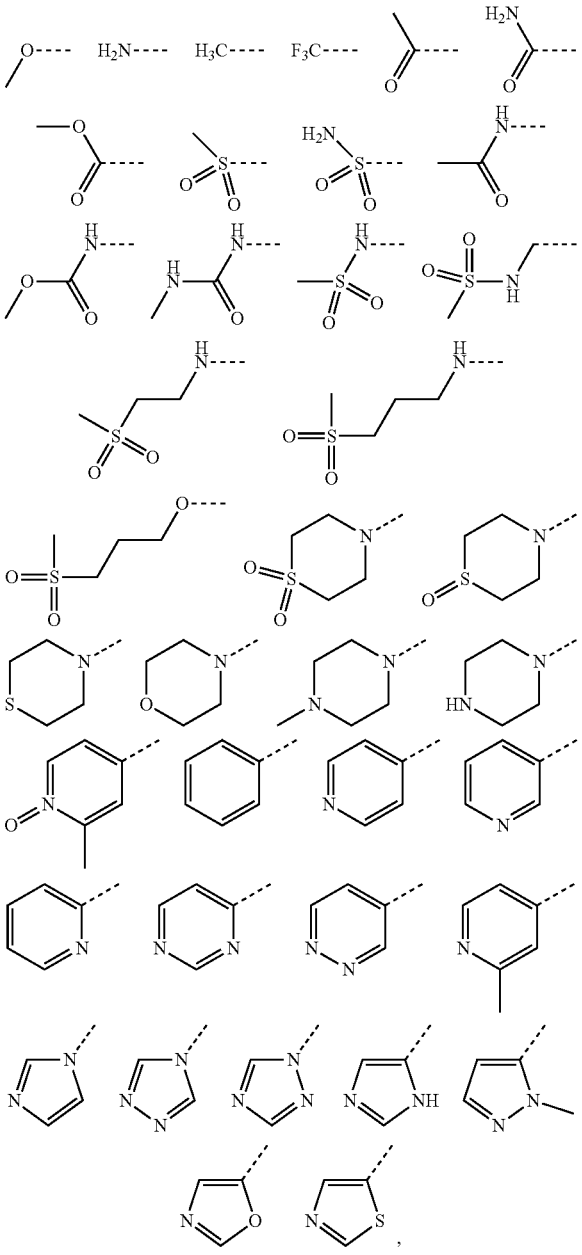


unsubstituted or substituted with 1 to 6 R^{6b} groups.

[0090] In one embodiment, the compound of Formula I comprises Z which is selected from:

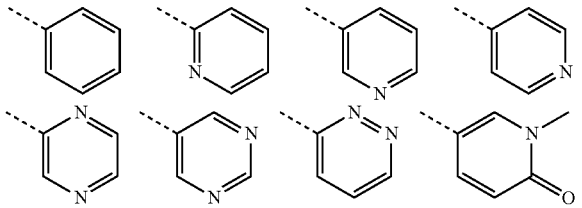


-continued

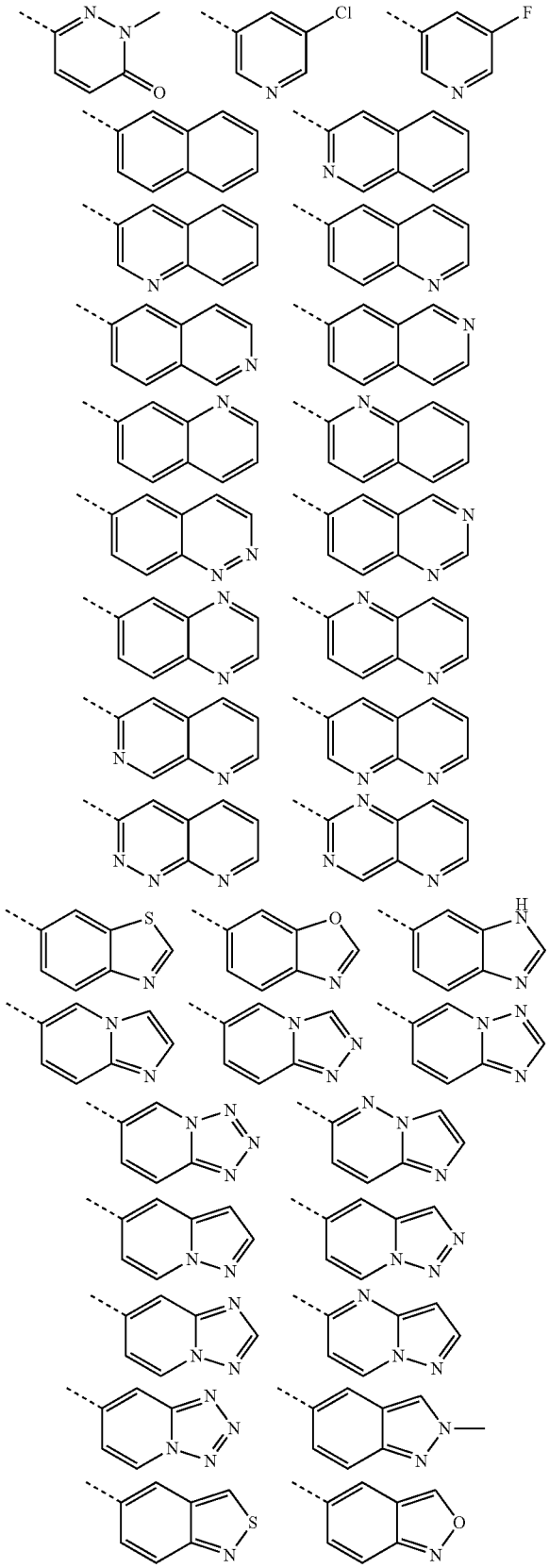


unsubstituted or substituted with 1-2 R^{10b} groups.

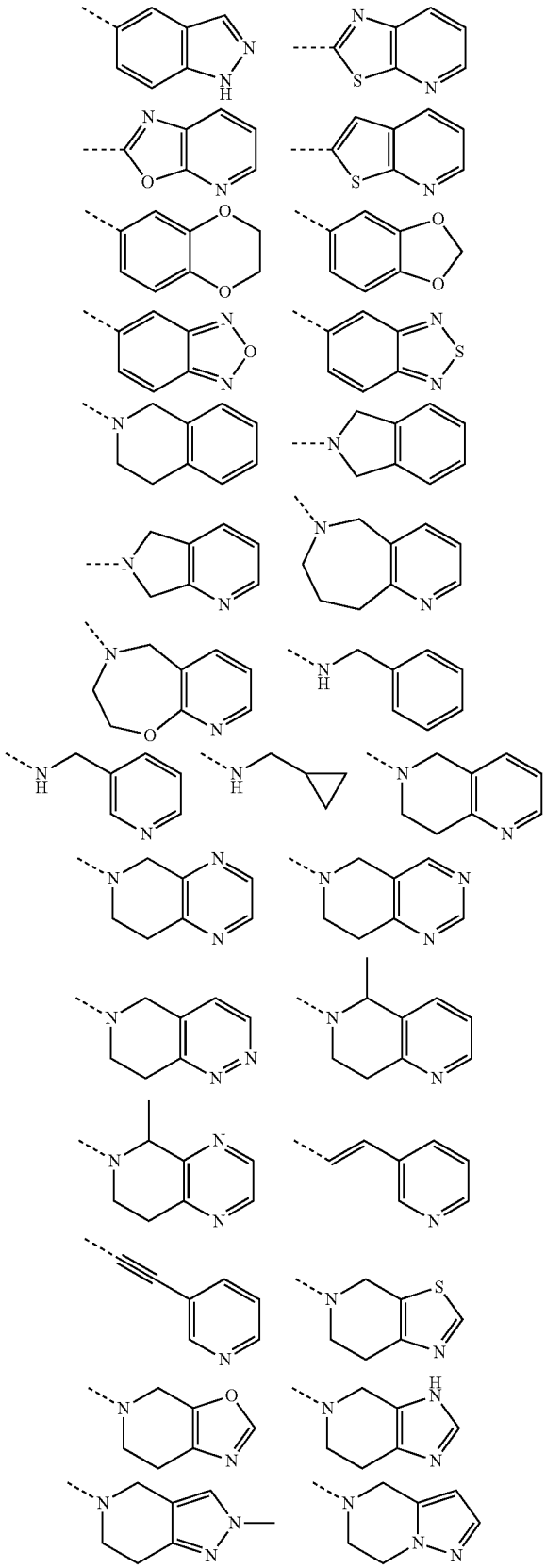
[0091] In another embodiment, the compound of Formula I comprises U which is selected from:



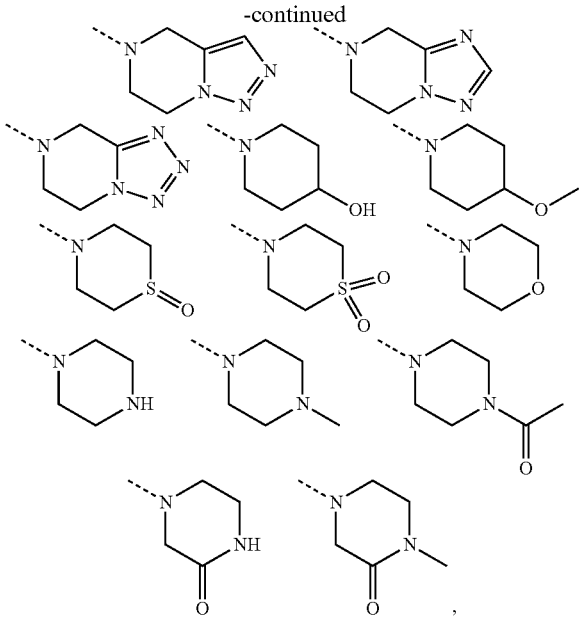
-continued



-continued

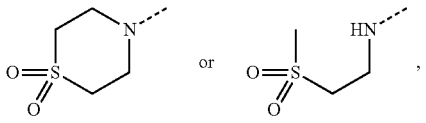


-continued

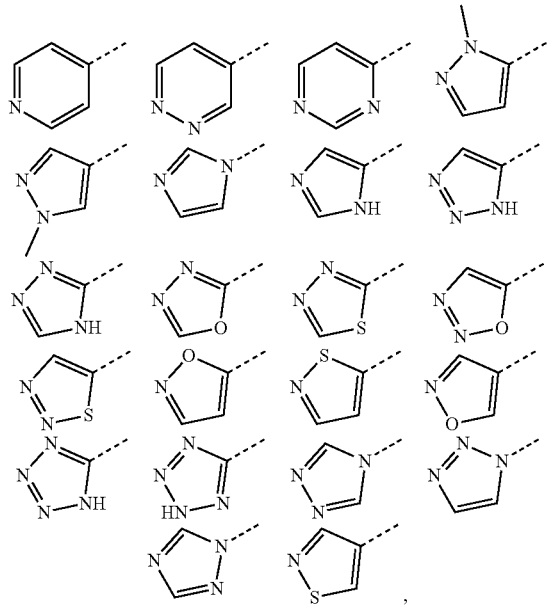


unsubstituted or substituted with 1-6 R^{13c} groups.

[0092] In another embodiment, the compound of Formula I comprises Z which is

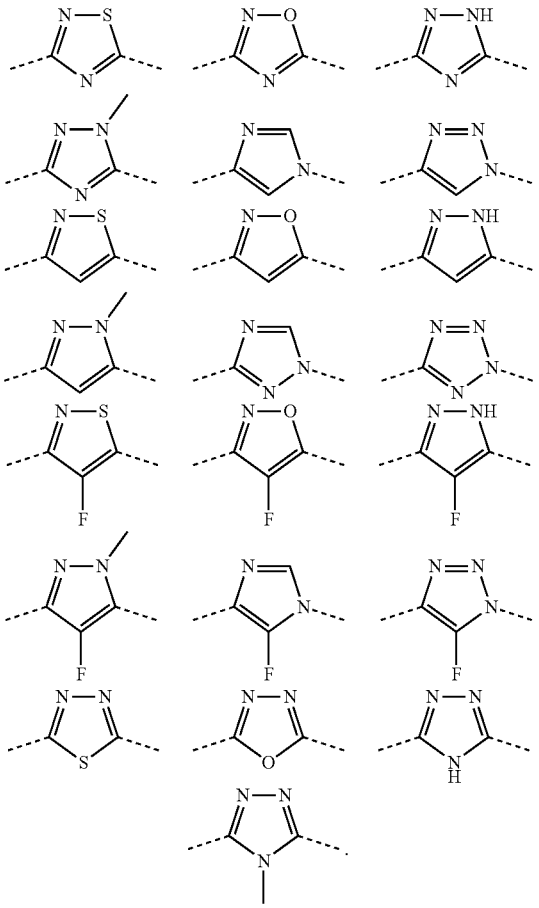


or Z is selected from:



unsubstituted or substituted with 1-3 R^{6c} groups.

[0093] In one embodiment, the compound of Formula I comprises A which is selected from:



[0094] In another aspect, herein provides a pharmaceutical composition comprising a therapeutically effective amount of a compound of claim **1** and a pharmaceutically acceptable carrier.

[0095] In another aspect, herein provides a method for regulating the Wnt signaling pathway and/or treating a Wnt-mediated disorder in a mammal suffering therefrom. The method comprises administrating to a mammalian subject a therapeutically effective amount of at least one compound of formula I, or a pharmaceutical composition thereof, and optionally in combination with a second therapeutic agent.

[0096] In one embodiment, the method can treat a cell proliferative disorder selected from the group consisting of systemic sclerosis, skin fibrosis, idiopathic pulmonary fibrosis, renal fibrosis, liver fibrosis, drug-induced fibrosis, radiation-induced fibrosis, colorectal cancer, breast cancer, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, non-small cell lung cancer, gastric cancer, pancreatic cancer, leukemia, lymphoma, neuroblastoma, retinoblastoma, sarcoma, osteosarcoma, chondosarcoma, Ewing's sarcoma, rhabdomysarcoma, brain tumor, Wilms' tumor, basal cell carcinoma, melanoma, head and neck cancer, cervical cancer and prostate cancer.

[0097] In another aspect, herein provides compounds of formula I, wherein the compounds are the molecules shown in Table 1:

TABLE 1

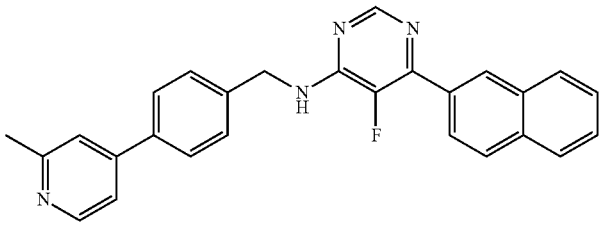
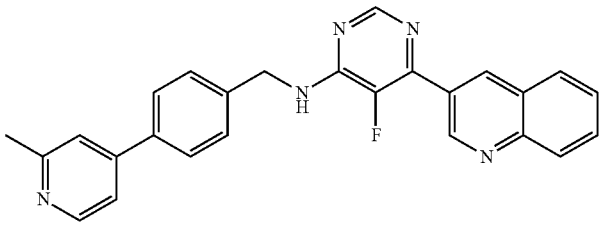
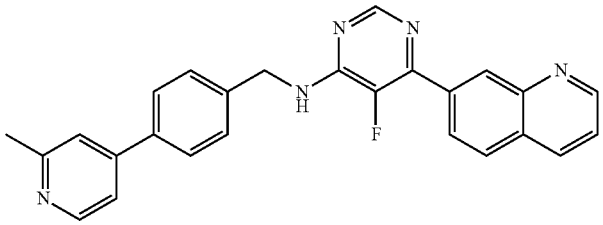
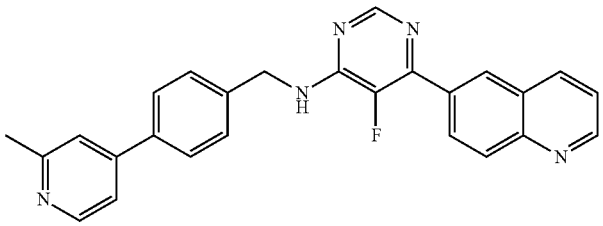
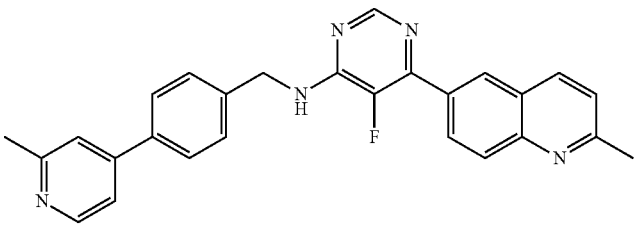
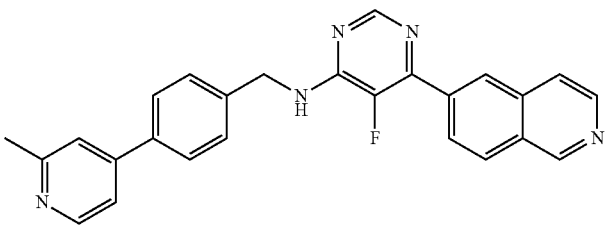
Compounds of Formula I	
A-1	
A-2	
A-3	
A-4	
A-5	
A-6	

TABLE 1-continued

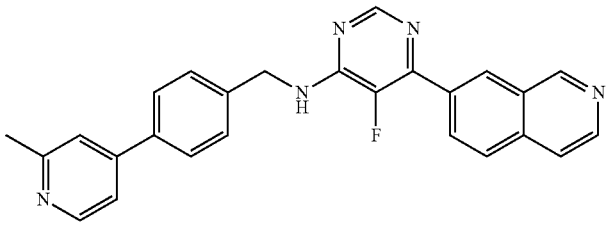
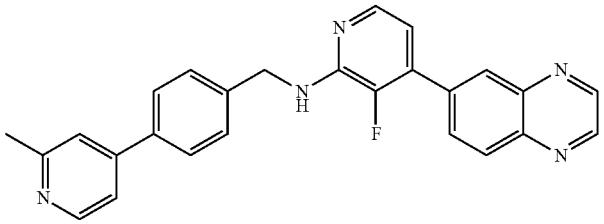
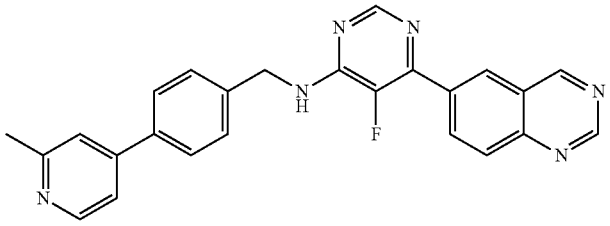
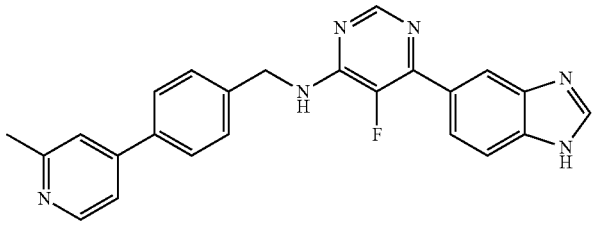
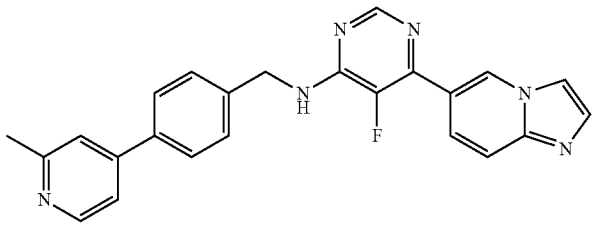
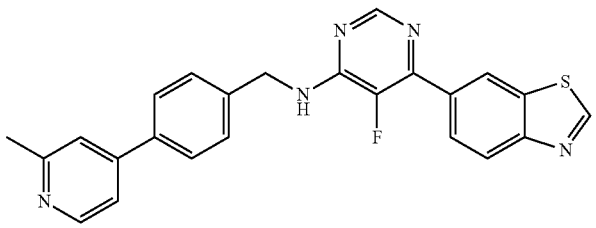
Compounds of Formula I	
A-7	
A-8	
A-9	
A-10	
A-11	
A-12	

TABLE 1-continued

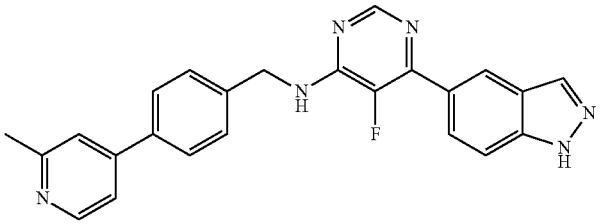
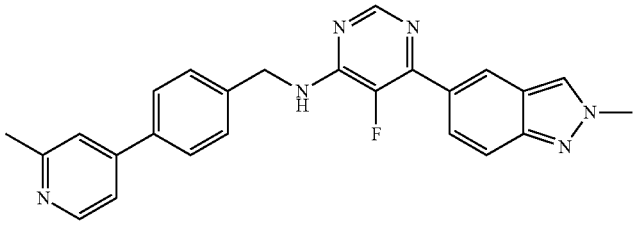
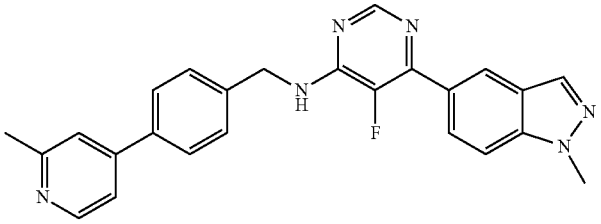
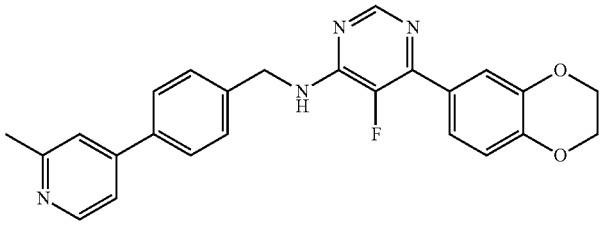
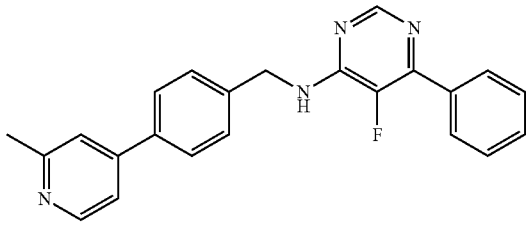
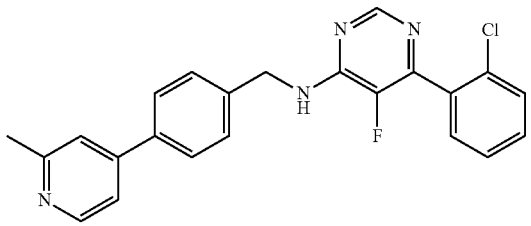
Compounds of Formula I	
A-13	
A-14	
A-15	
A-16	
A-17	
A-18	

TABLE 1-continued

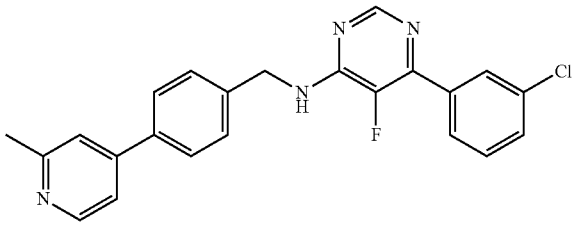
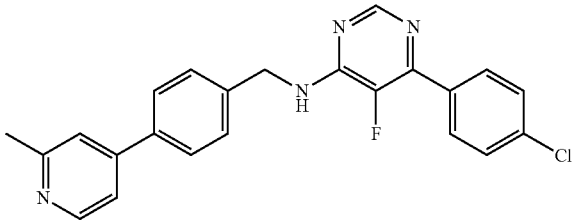
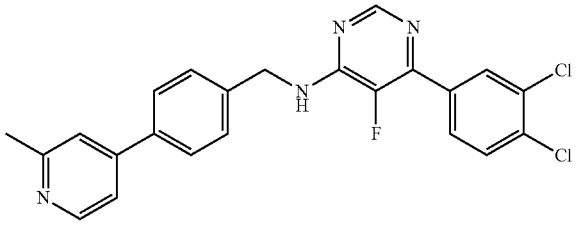
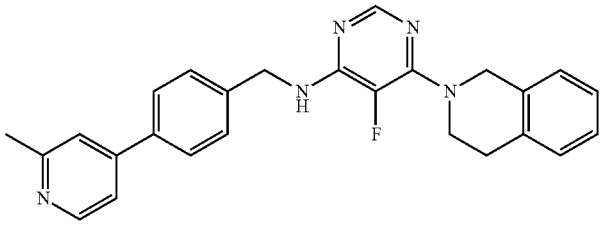
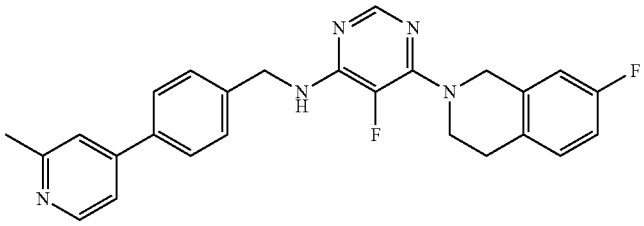
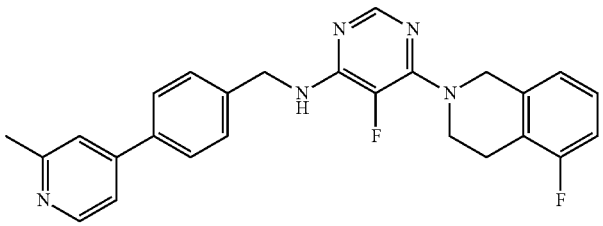
Compounds of Formula I	
A-19	
A-20	
A-21	
A-22	
A-23	
A-24	

TABLE 1-continued

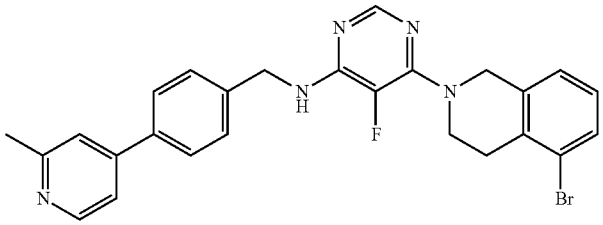
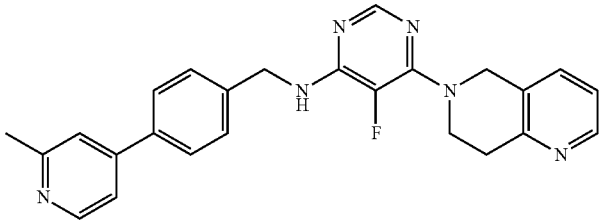
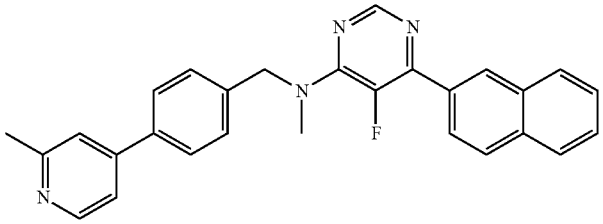
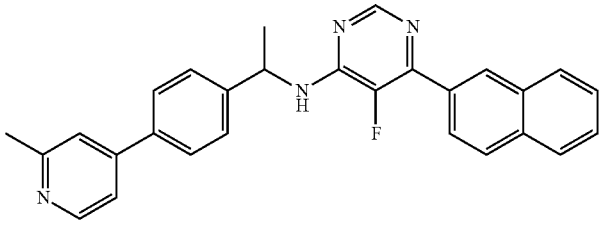
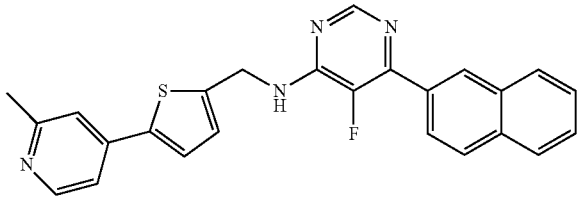
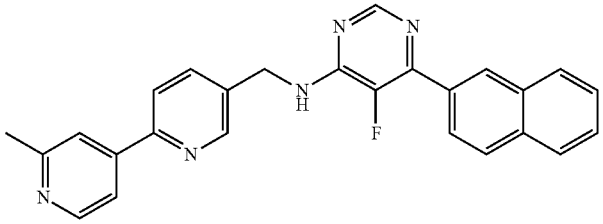
Compounds of Formula I	
A-25	
A-26	
A-27	
A-28	
A-29	
A-30	

TABLE 1-continued

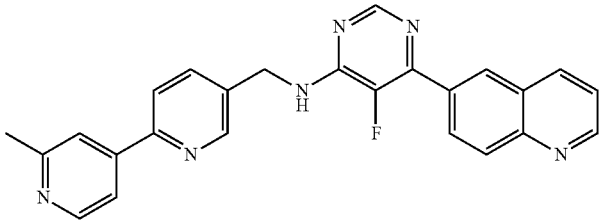
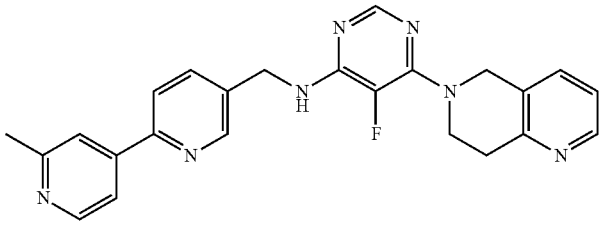
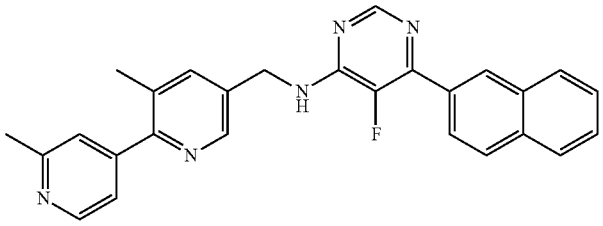
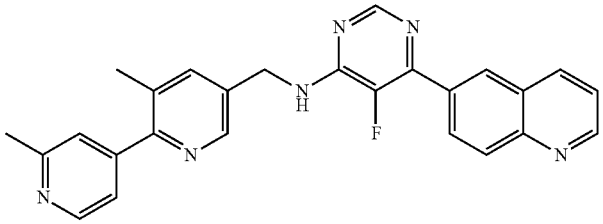
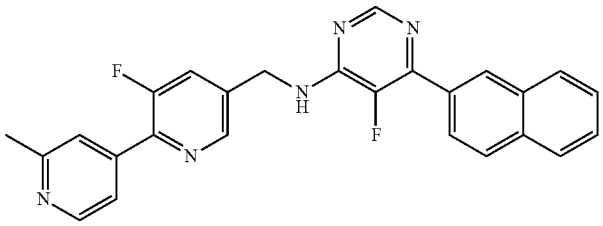
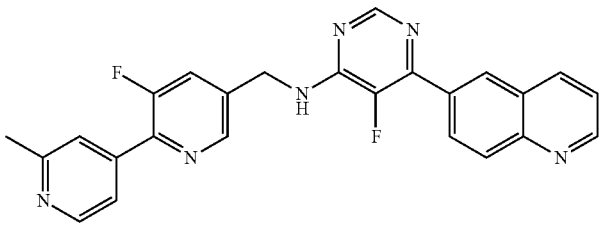
Compounds of Formula I	
A-31	
A-32	
A-33	
A-34	
A-35	
A-36	

TABLE 1-continued

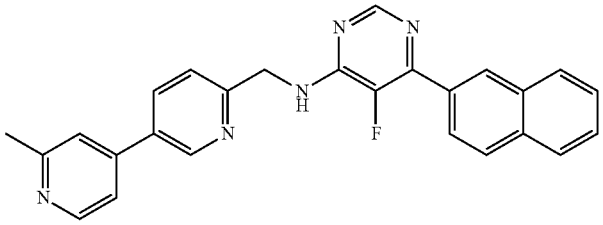
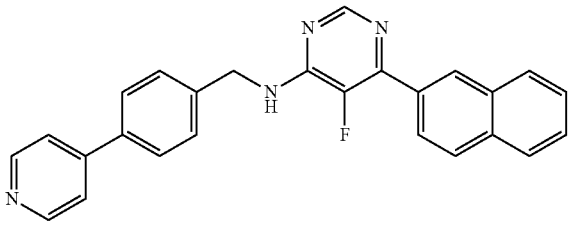
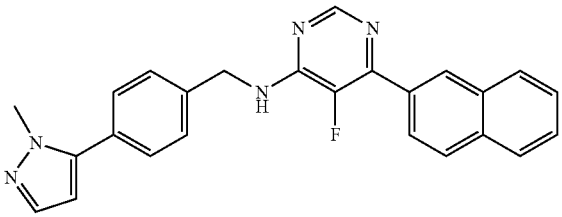
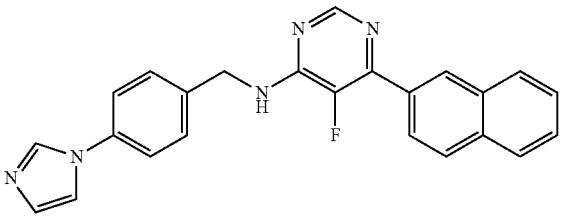
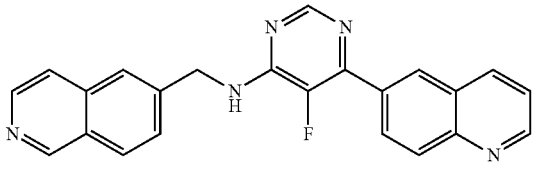
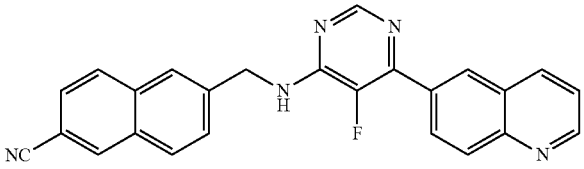
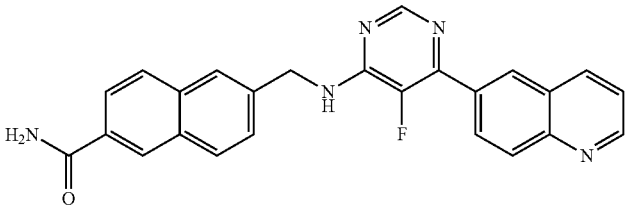
Compounds of Formula I	
A-37	
A-38	
A-39	
A-40	
A-41	
A-42	
A-43	

TABLE 1-continued

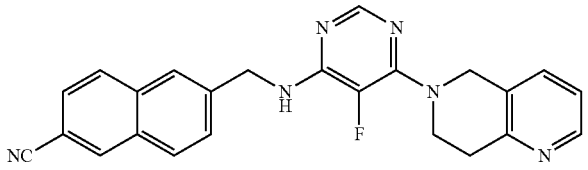
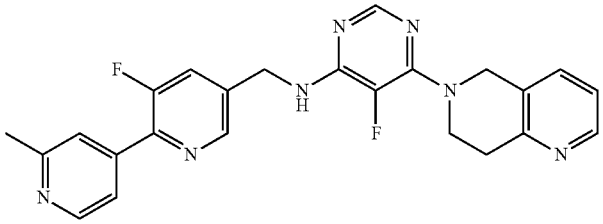
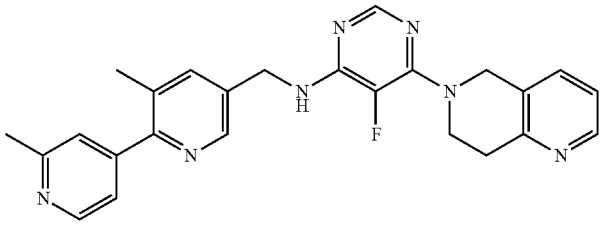
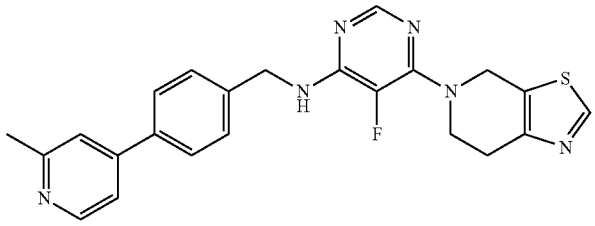
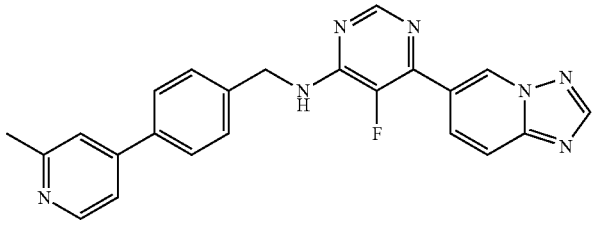
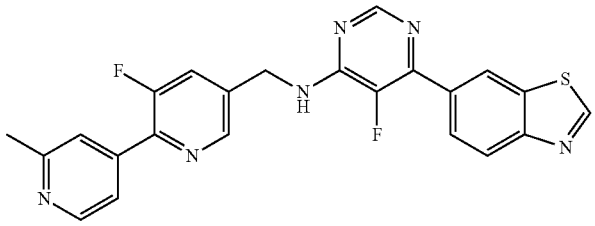
Compounds of Formula I	
A-44	
A-45	
A-46	
A-47	
A-48	
A-49	

TABLE 1-continued

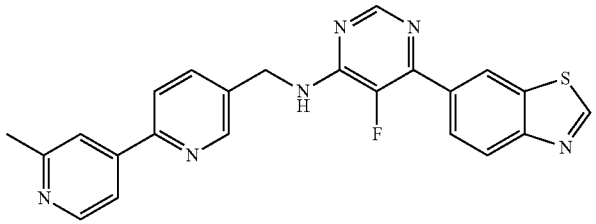
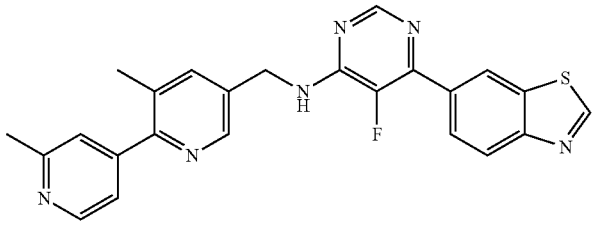
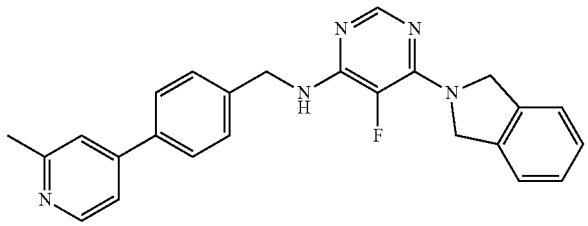
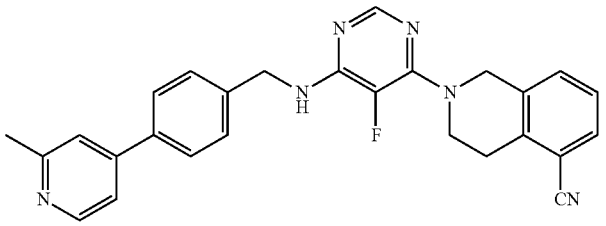
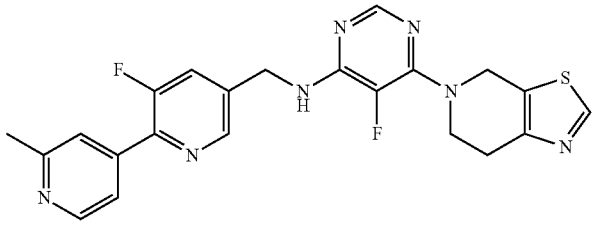
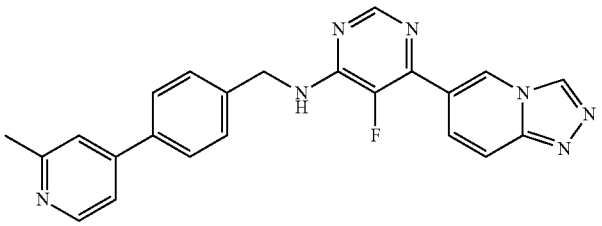
Compounds of Formula I	
A-50	
A-51	
A-52	
A-53	
A-54	
A-55	

TABLE 1-continued

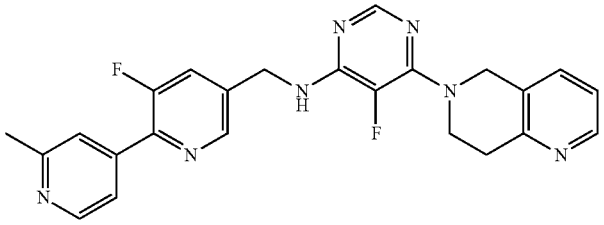
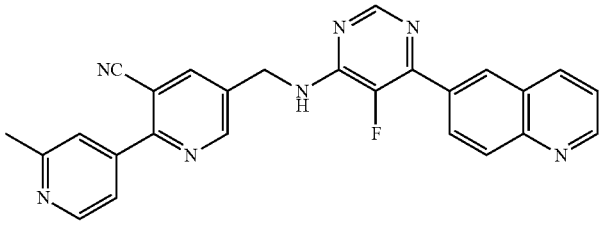
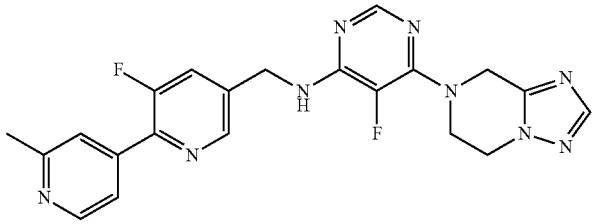
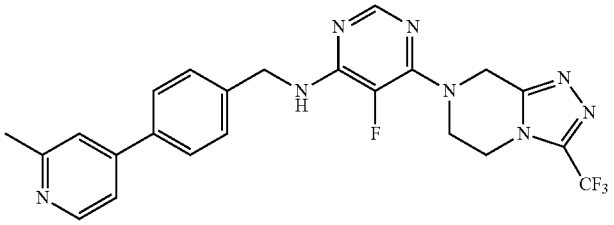
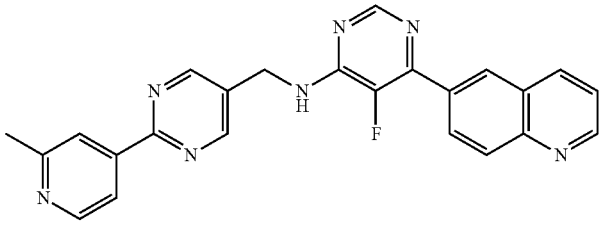
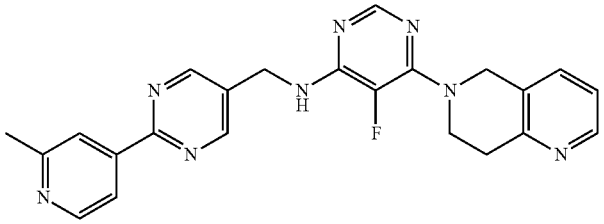
Compounds of Formula I	
A-56	
A-57	
A-58	
A-59	
A-60	
A-61	

TABLE 1-continued

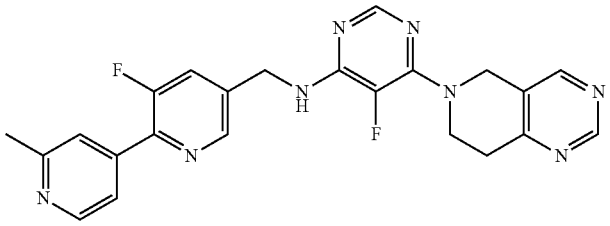
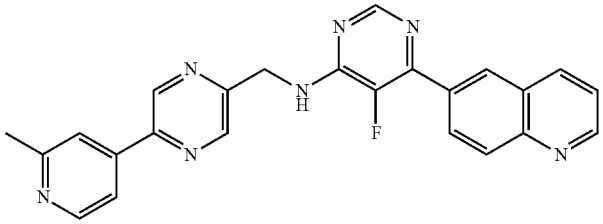
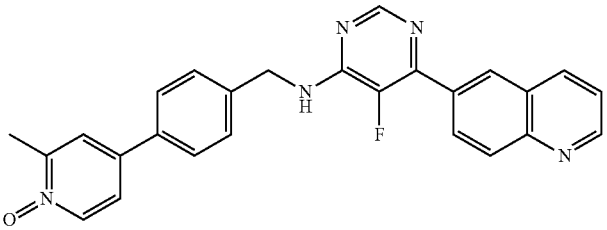
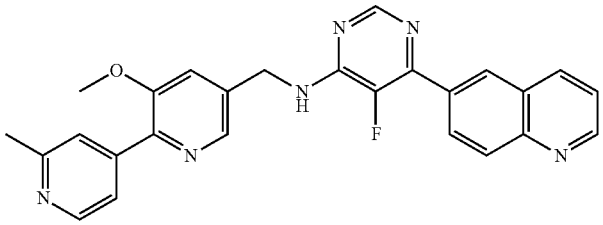
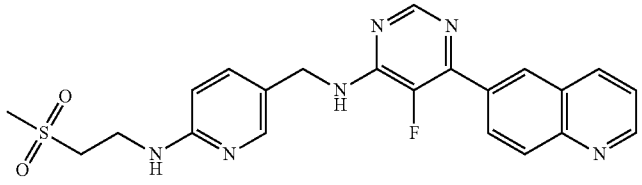
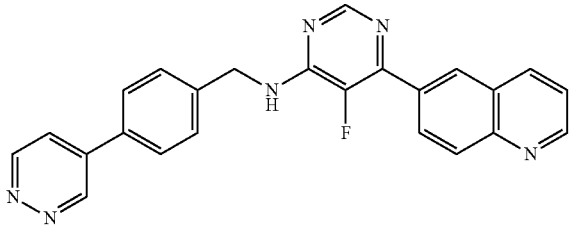
Compounds of Formula I	
A-62	
A-63	
A-64	
A-65	
A-66	
A-67	

TABLE 1-continued

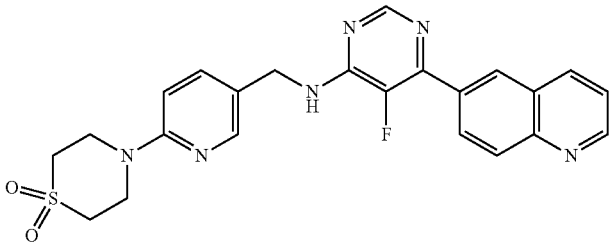
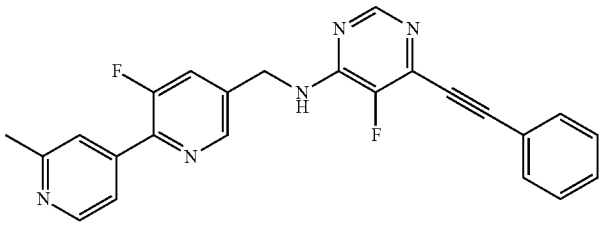
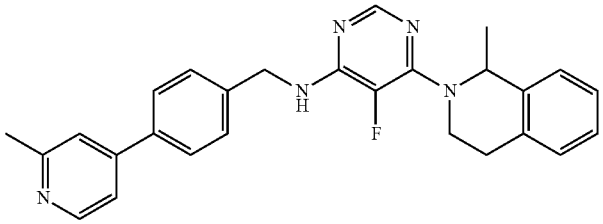
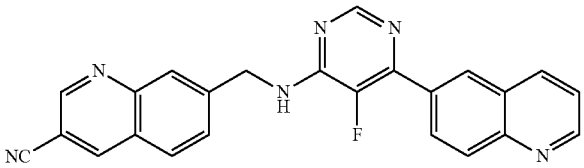
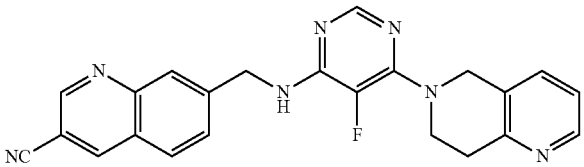
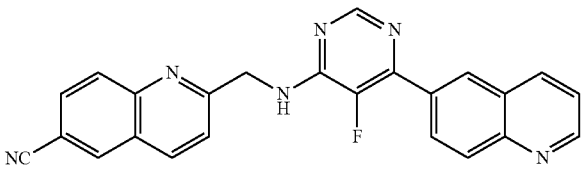
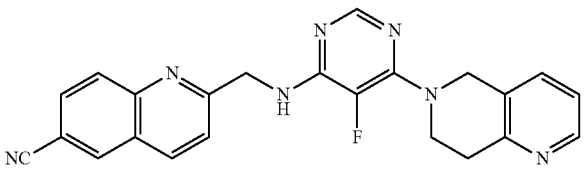
Compounds of Formula I	
A-68	
A-69	
A-70	
A-71	
A-72	
A-73	
A-74	

TABLE 1-continued

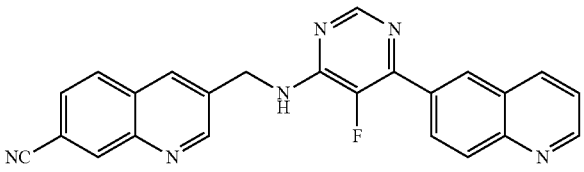
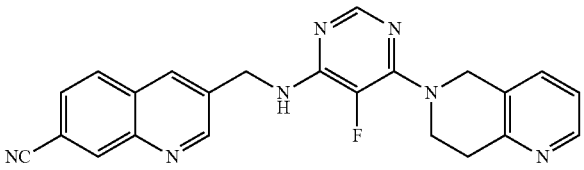
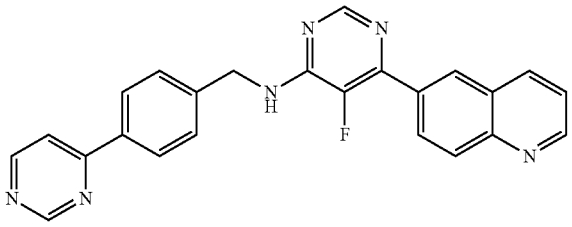
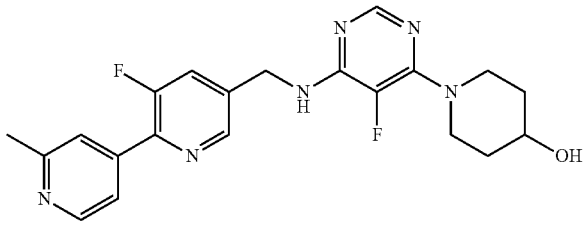
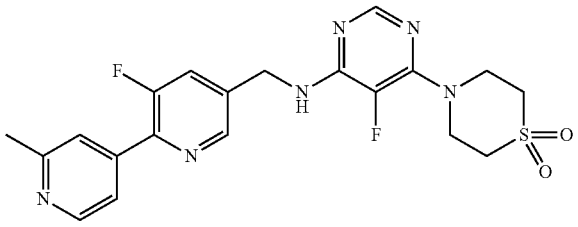
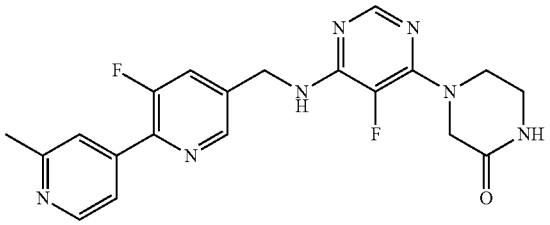
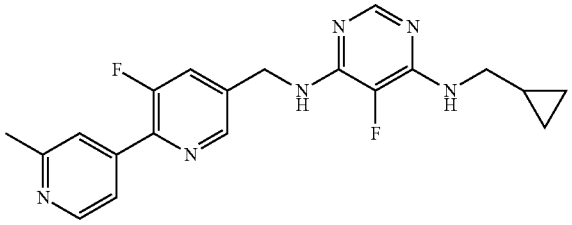
Compounds of Formula I	
A-75	
A-76	
A-77	
A-78	
A-79	
A-80	
A-81	

TABLE 1-continued

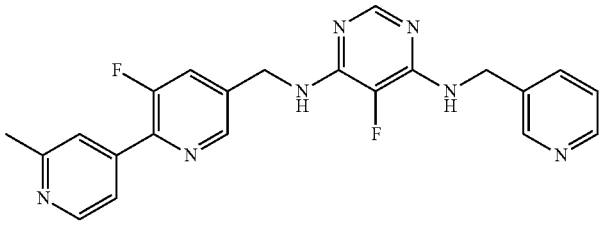
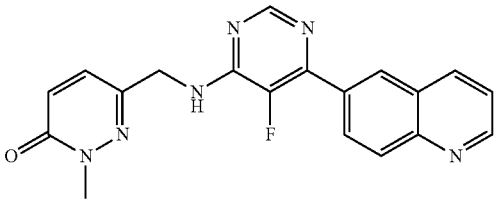
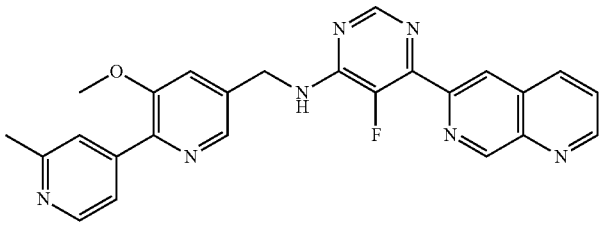
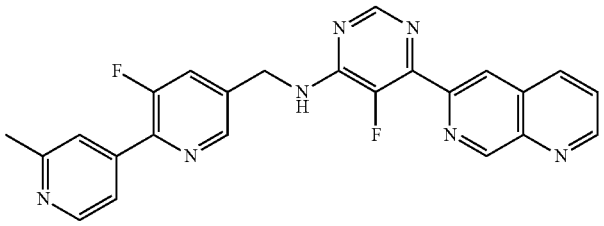
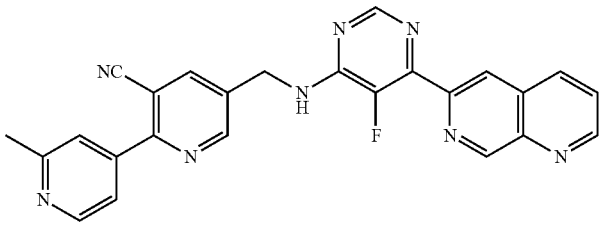
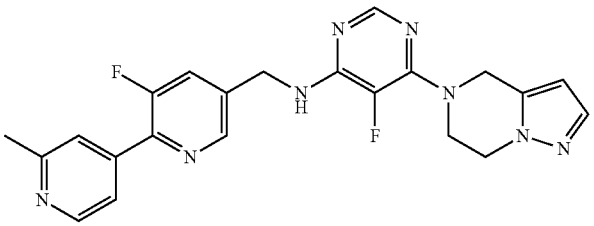
Compounds of Formula I
A-82 
A-83 
A-84 
A-85 
A-86 
A-87 

TABLE 1-continued

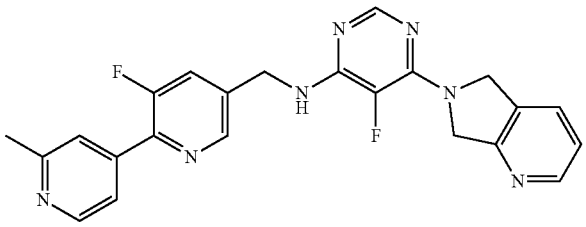
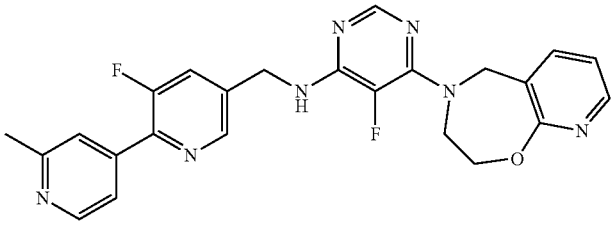
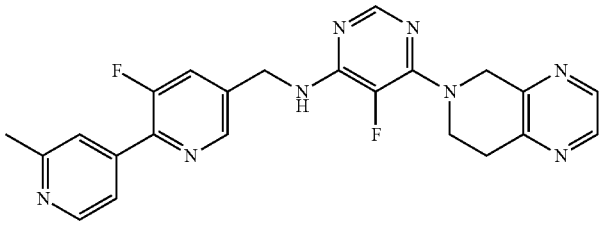
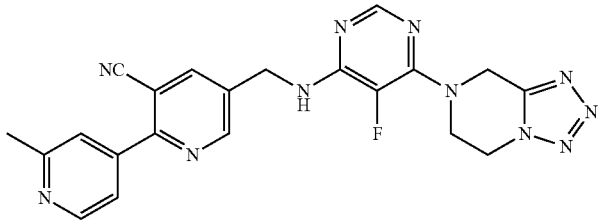
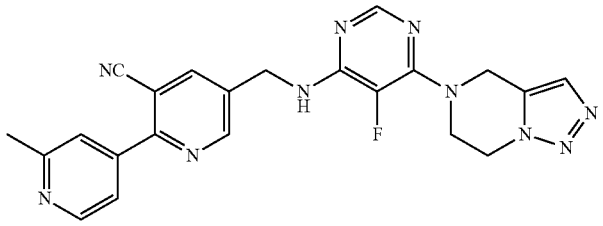
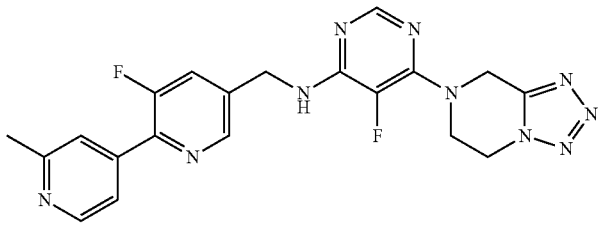
Compounds of Formula I	
A-88	
A-89	
A-90	
A-91	
A-92	
A-93	

TABLE 1-continued

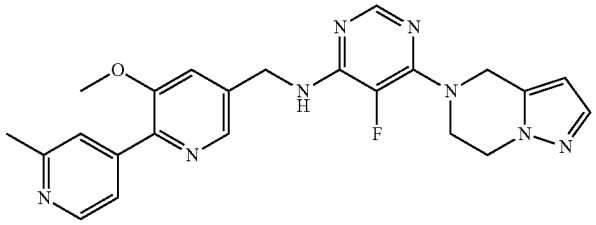
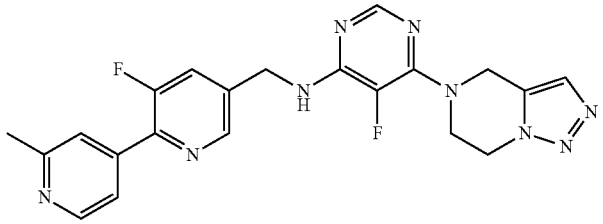
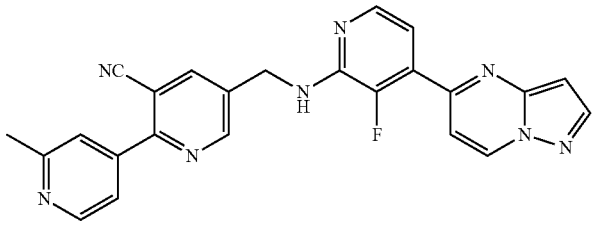
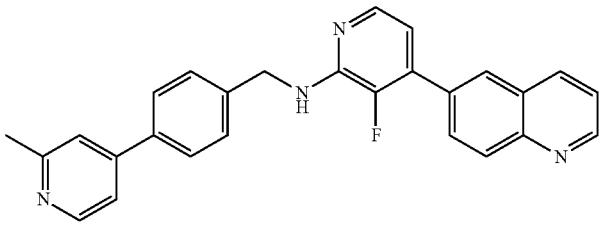
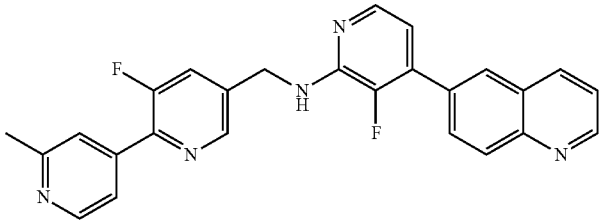
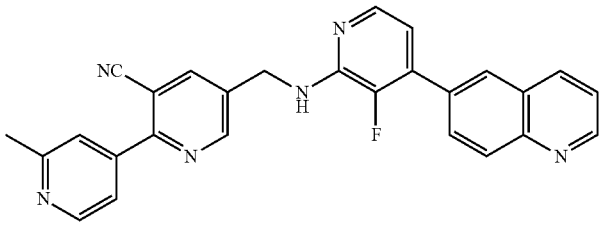
Compounds of Formula I
A-94 
A-95 
A-96 
A-97 
A-98 
A-99 

TABLE 1-continued

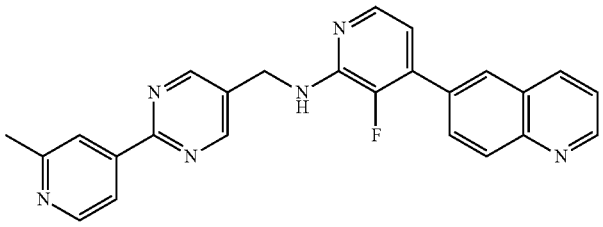
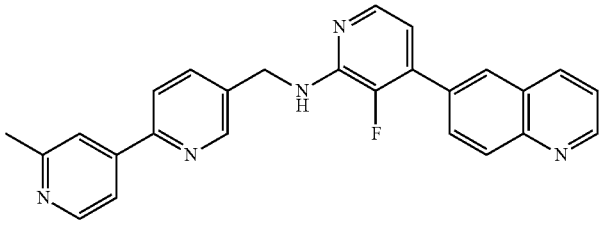
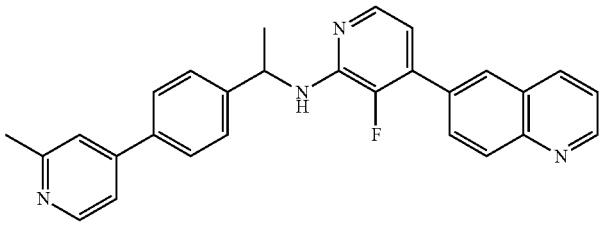
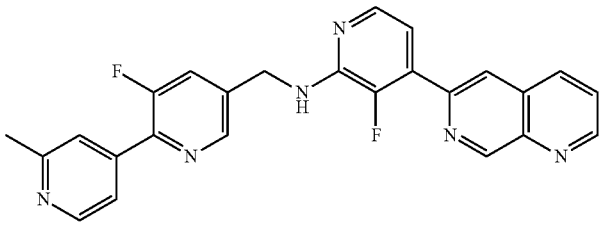
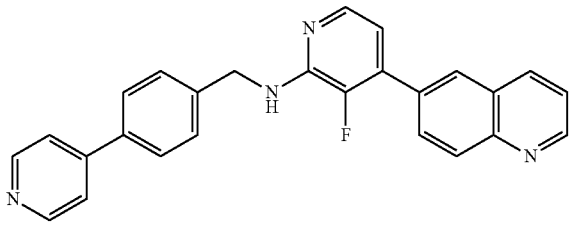
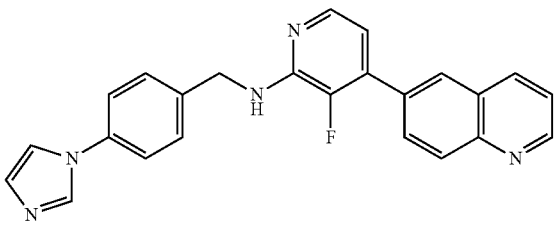
Compounds of Formula I	
A-100	
A-101	
A-102	
A-103	
A-104	
A-105	

TABLE 1-continued

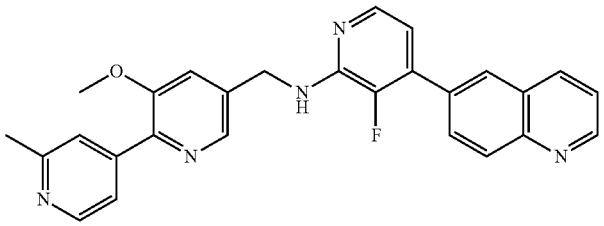
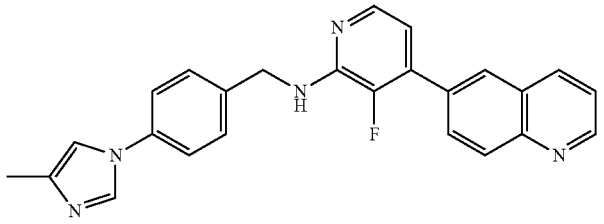
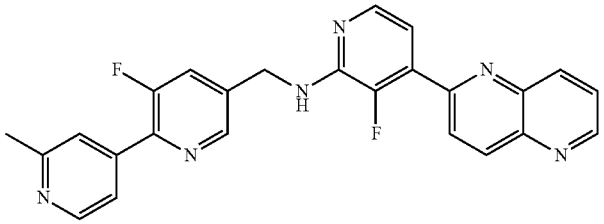
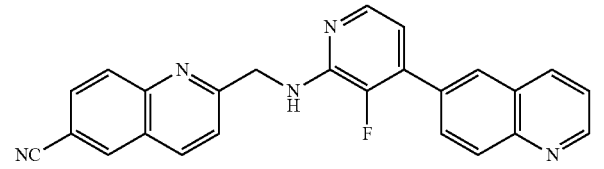
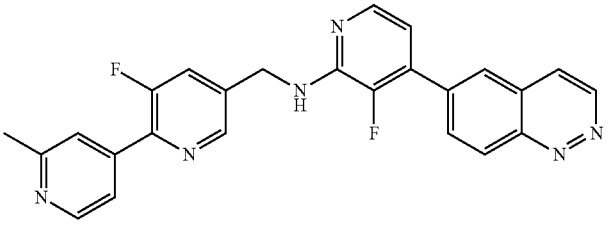
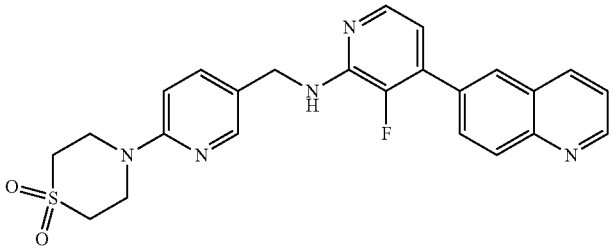
Compounds of Formula I	
A-106	
A-107	
A-108	
A-109	
A-110	
A-111	

TABLE 1-continued

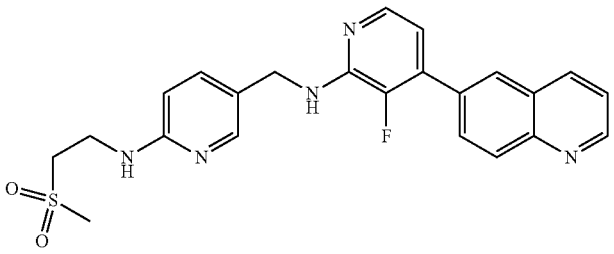
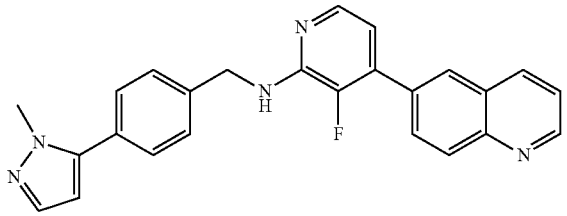
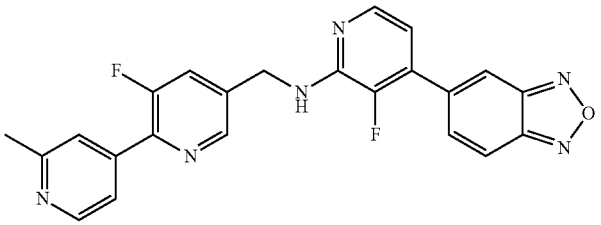
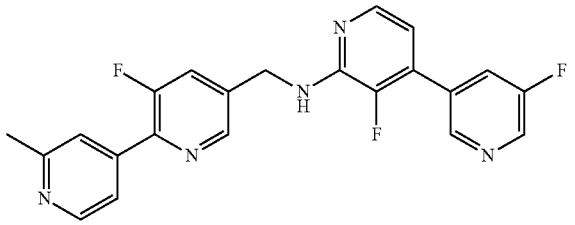
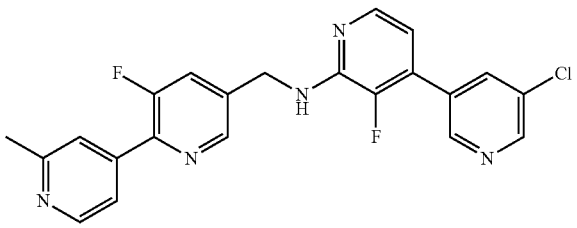
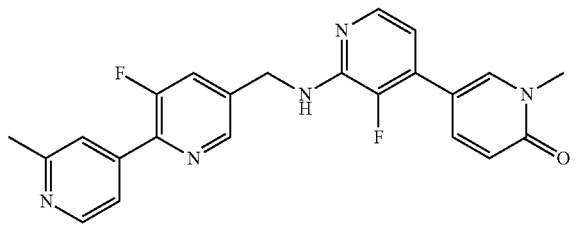
Compounds of Formula I	
A-112	
A-113	
A-114	
A-115	
A-116	
A-117	

TABLE 1-continued

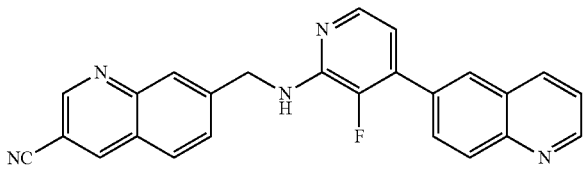
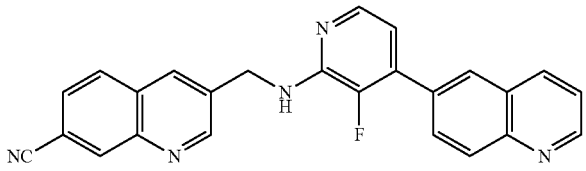
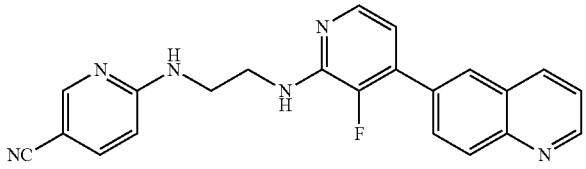
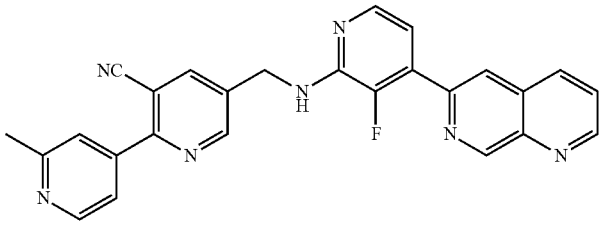
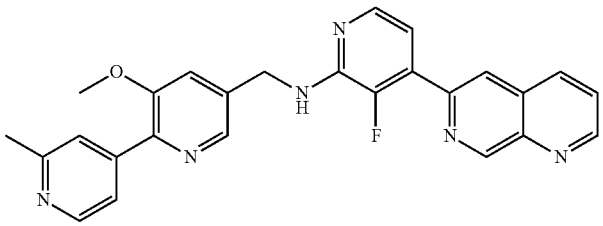
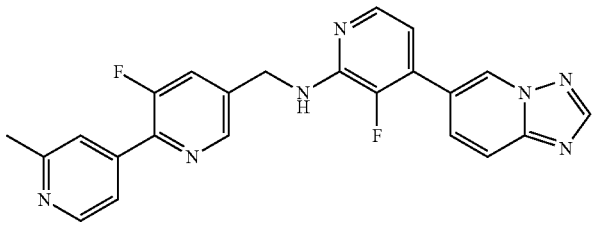
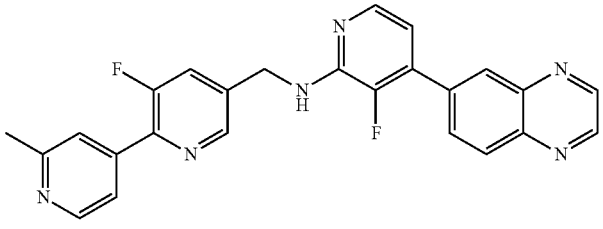
Compounds of Formula I	
A-118	
A-119	
A-120	
A-121	
A-122	
A-123	
A-124	

TABLE 1-continued

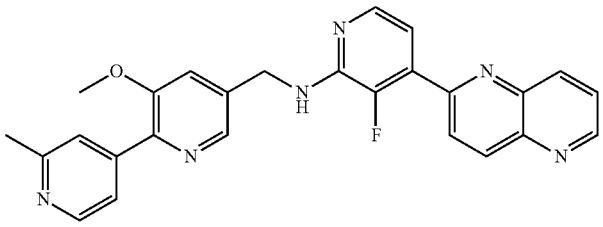
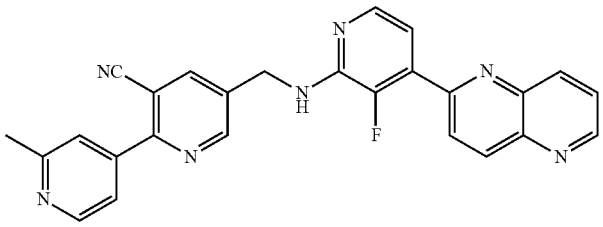
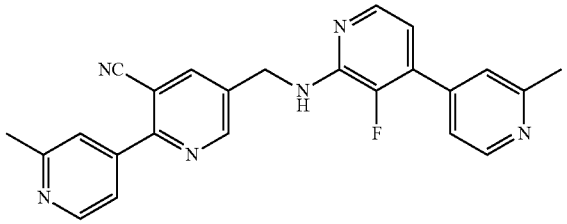
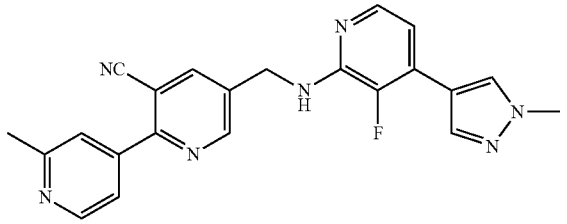
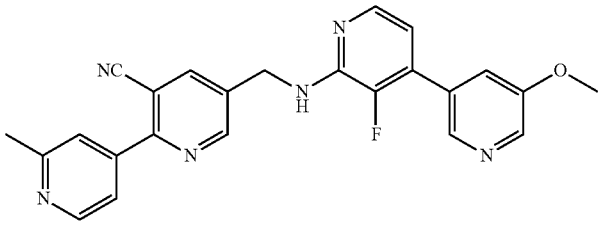
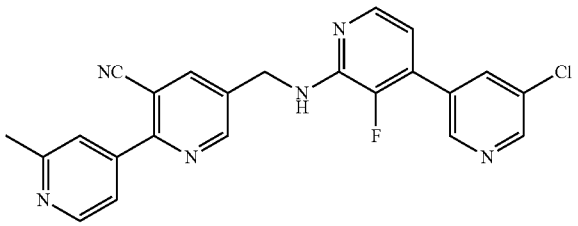
Compounds of Formula I	
A-125	
A-126	
A-127	
A-128	
A-129	
A-130	

TABLE 1-continued

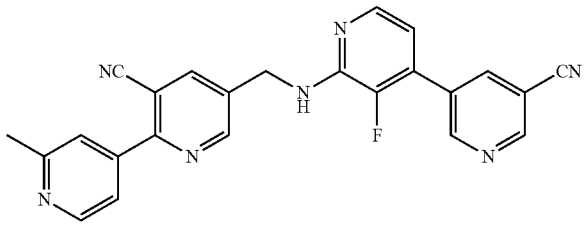
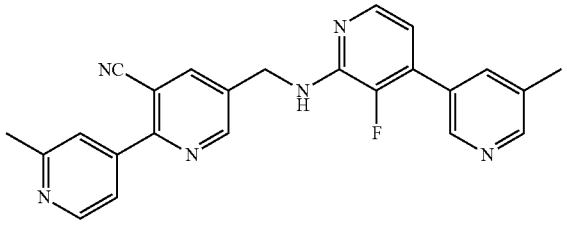
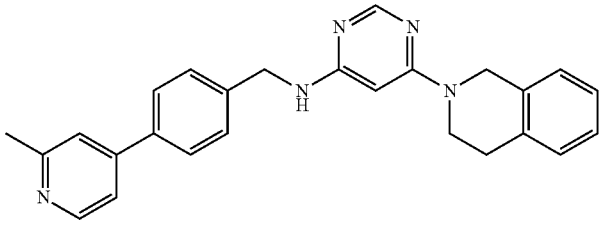
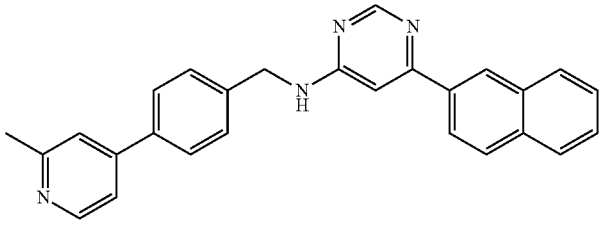
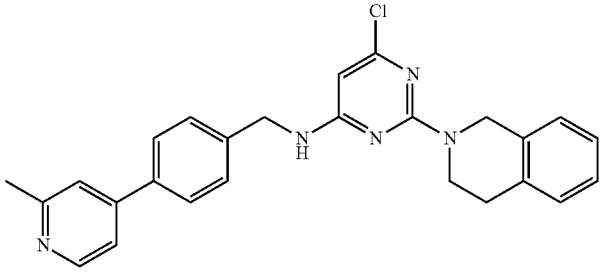
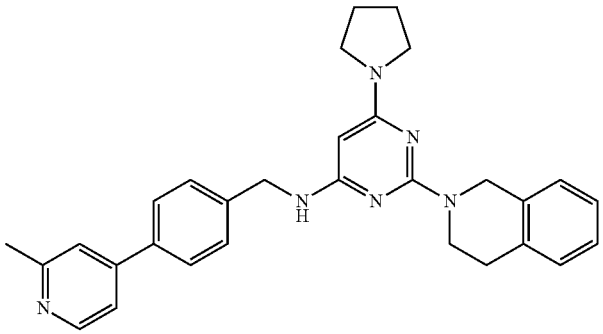
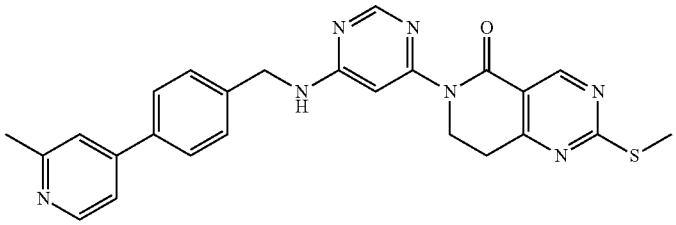
Compounds of Formula I	
A-131	
A-132	
A-133	
A-134	
A-135	
A-136	

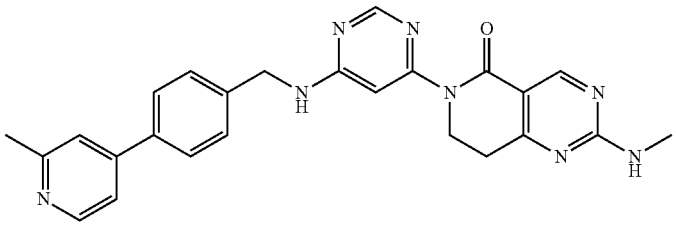
TABLE 1-continued

Compounds of Formula I

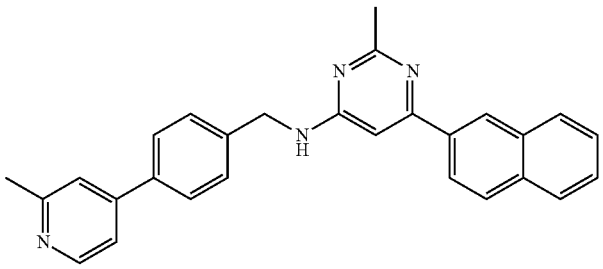
A-137



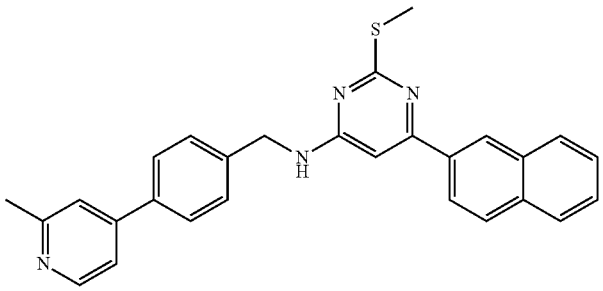
A-138



A-139



A-140



A-141

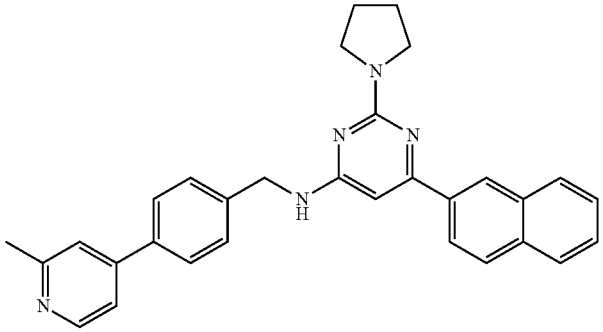


TABLE 1-continued

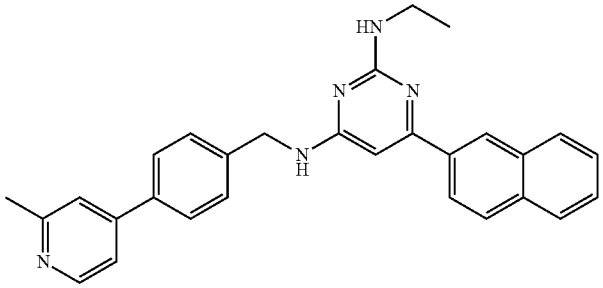
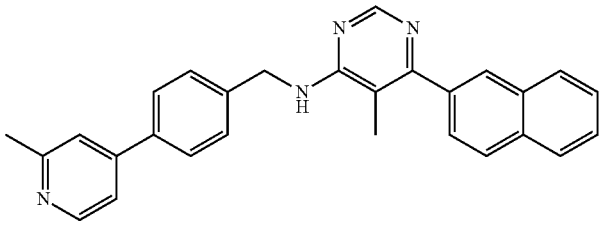
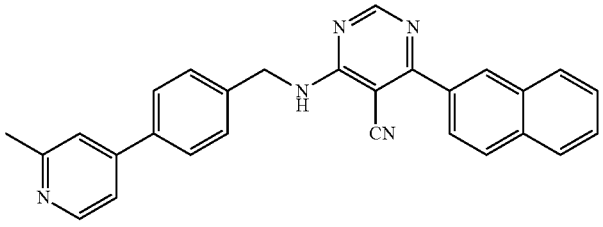
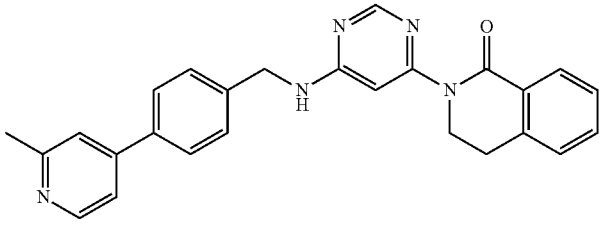
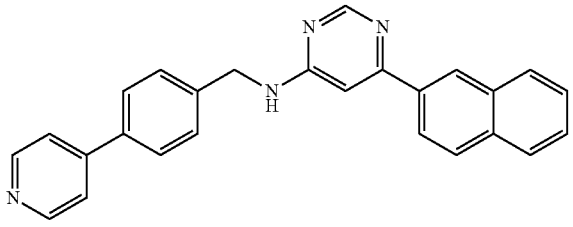
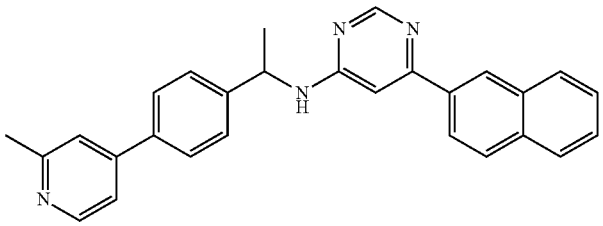
Compounds of Formula I	
A-142	
A-143	
A-144	
A-145	
A-146	
A-147	

TABLE 1-continued

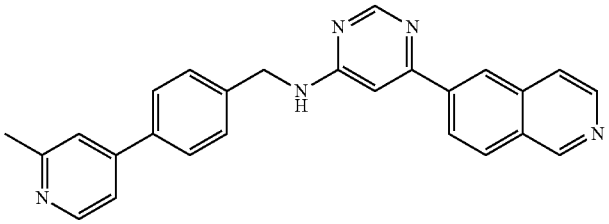
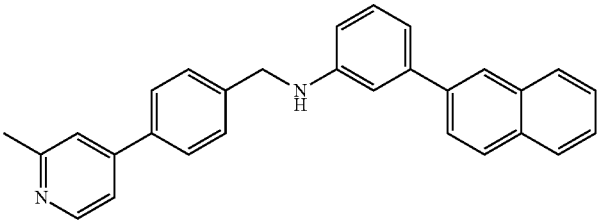
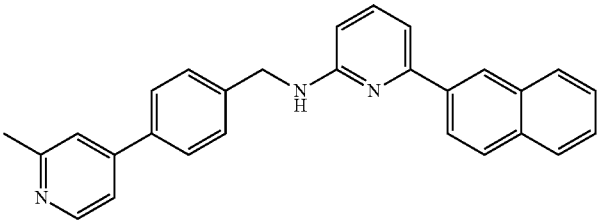
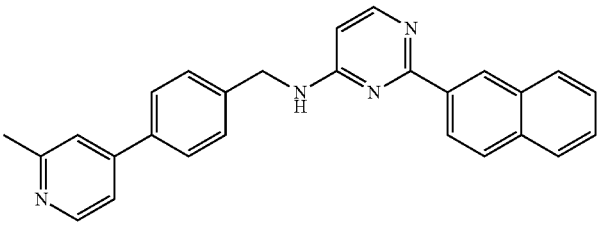
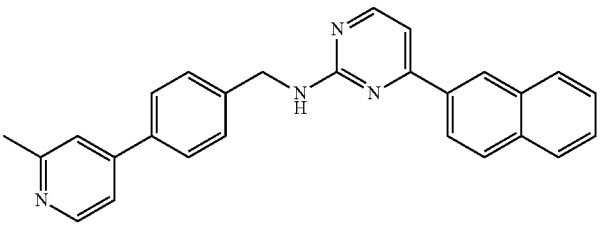
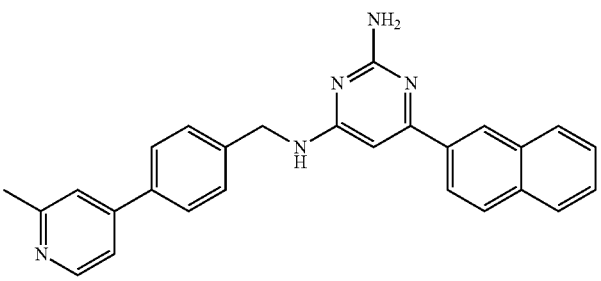
Compounds of Formula I	
A-148	
A-149	
A-150	
A-151	
A-152	
A-153	

TABLE 1-continued

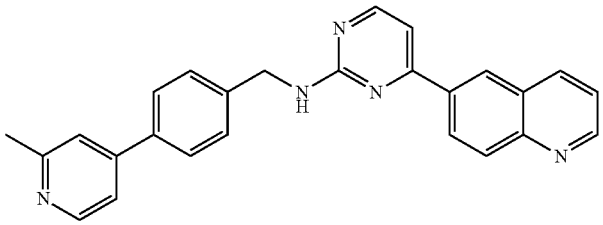
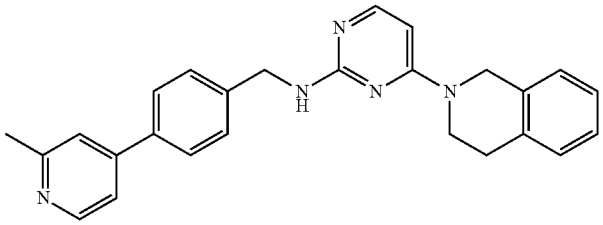
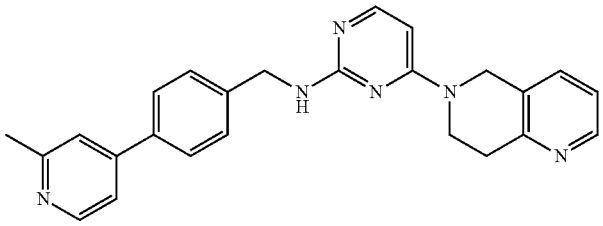
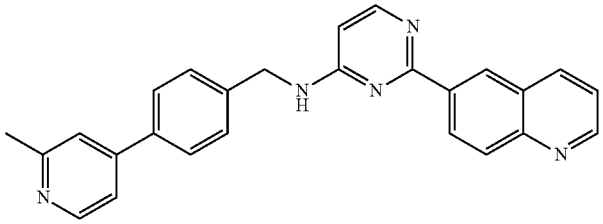
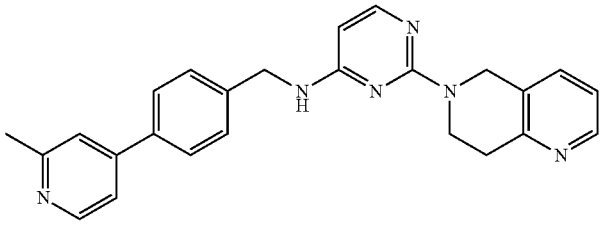
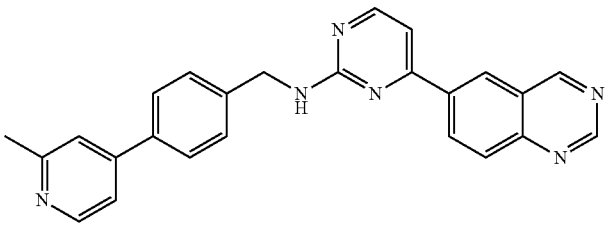
Compounds of Formula I	
A-154	
A-155	
A-156	
A-157	
A-158	
A-159	

TABLE 1-continued

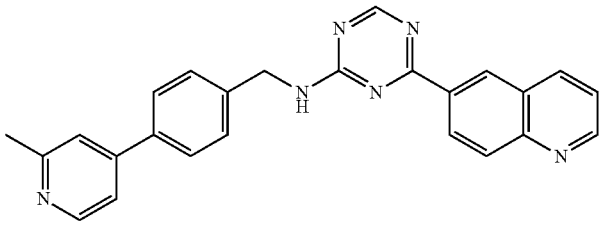
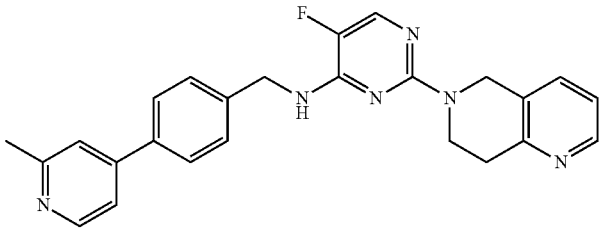
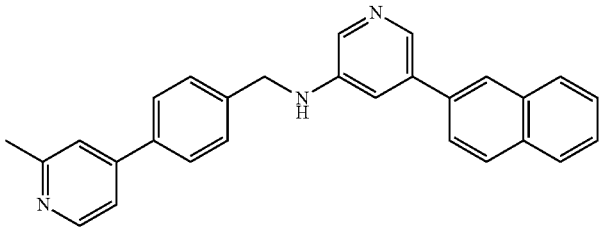
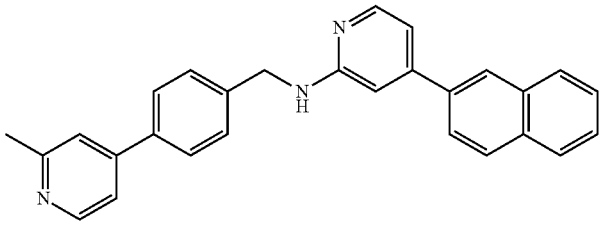
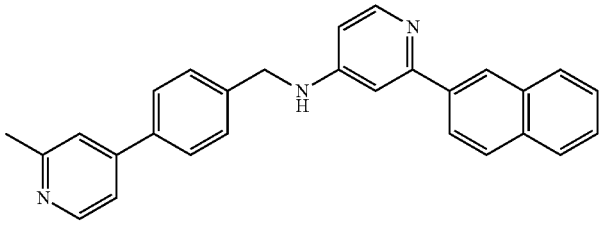
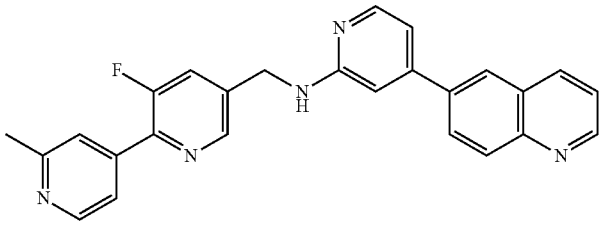
Compounds of Formula I	
A-160	
A-161	
A-162	
A-163	
A-164	
A-165	

TABLE 1-continued

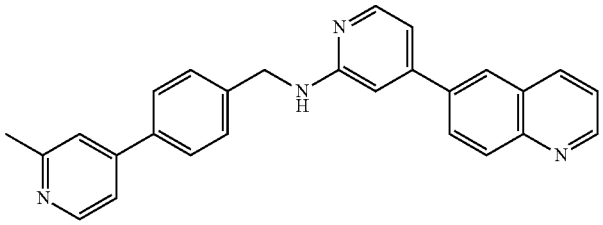
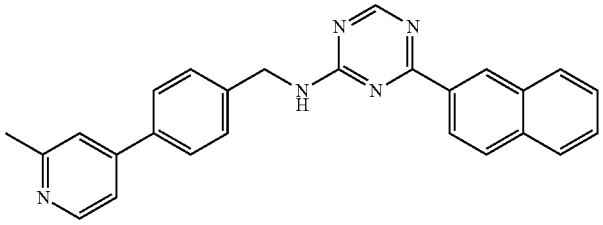
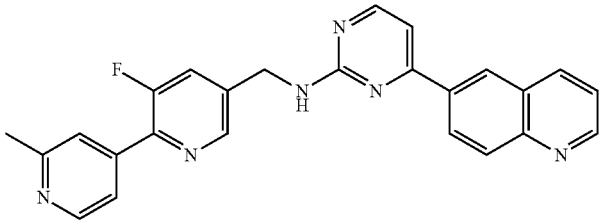
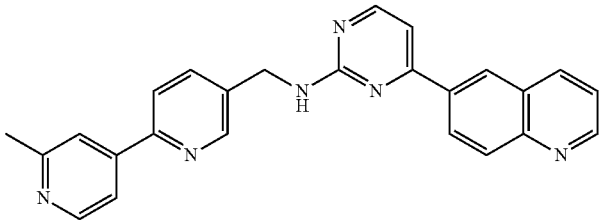
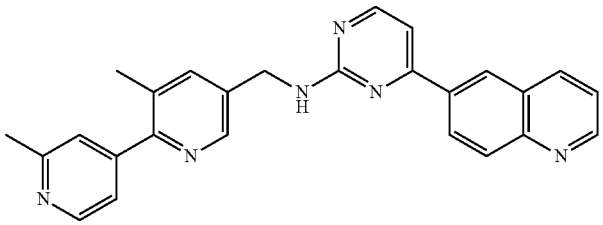
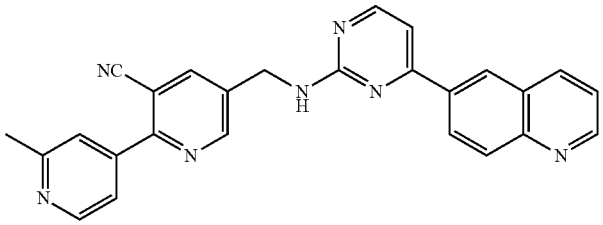
Compounds of Formula I	
A-166	
A-167	
A-168	
A-169	
A-170	
A-171	

TABLE 1-continued

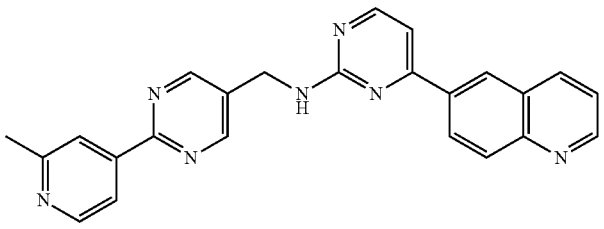
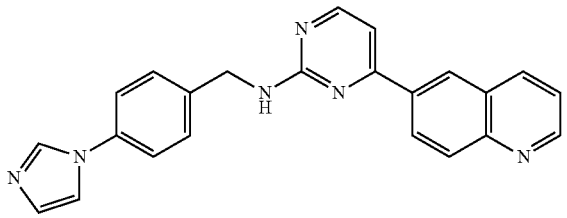
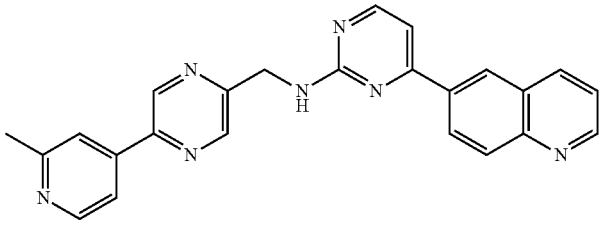
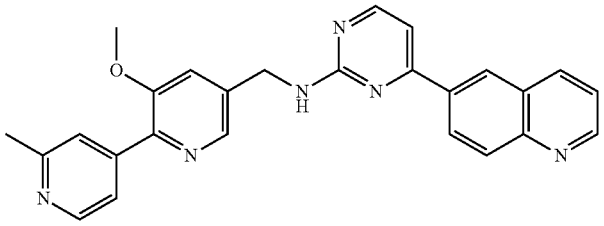
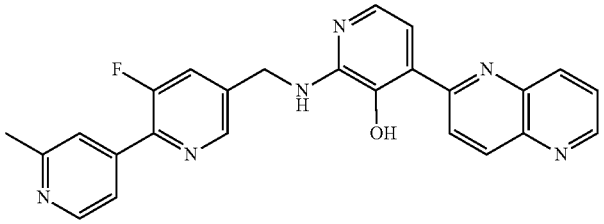
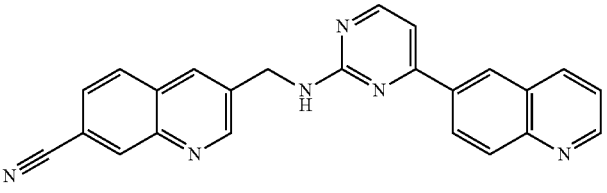
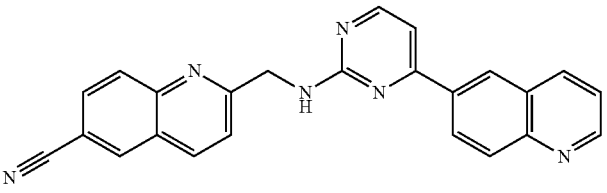
Compounds of Formula I	
A-172	
A-173	
A-174	
A-175	
A-176	
A-177	
A-178	

TABLE 1-continued

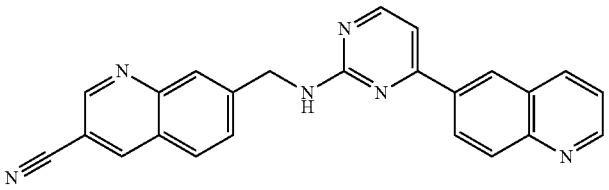
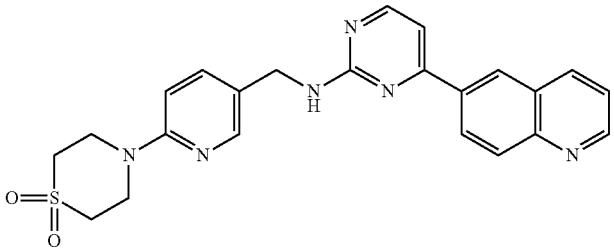
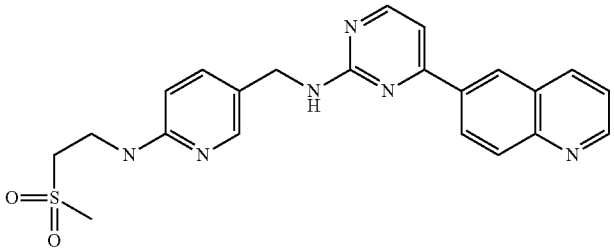
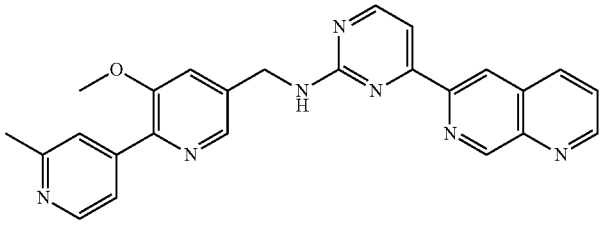
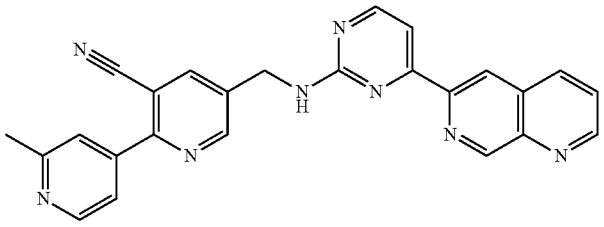
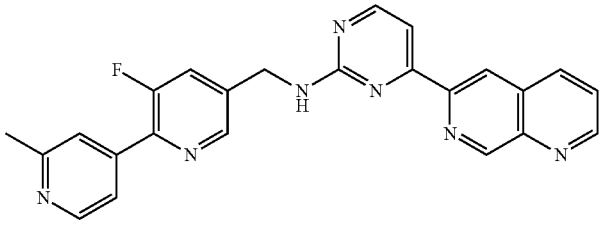
Compounds of Formula I	
A-179	
A-180	
A-181	
A-182	
A-183	
A-184	

TABLE 1-continued

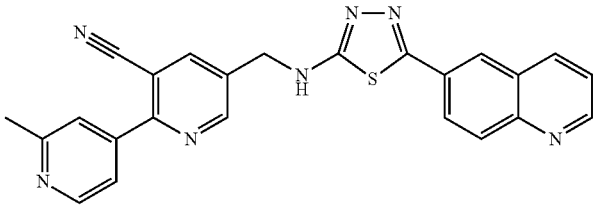
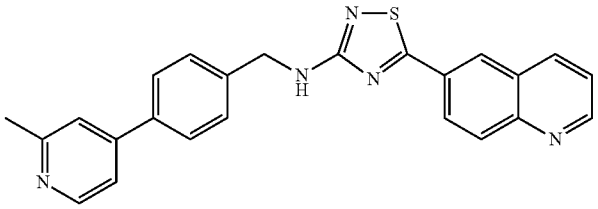
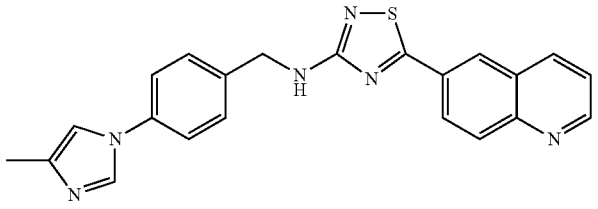
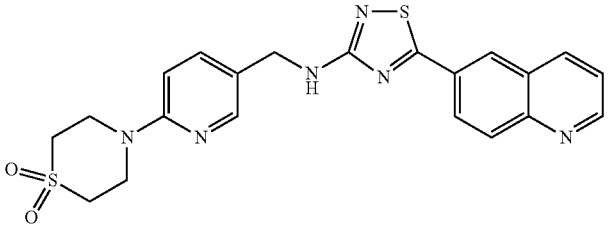
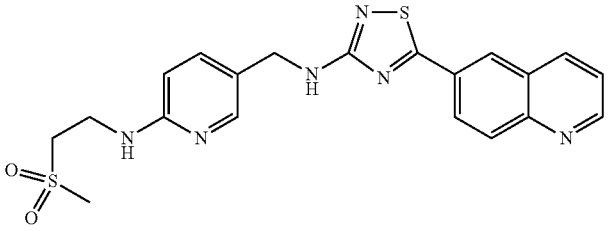
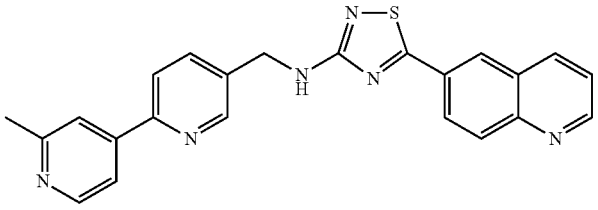
Compounds of Formula I	
A-185	
A-186	
A-187	
A-188	
A-189	
A-190	

TABLE 1-continued

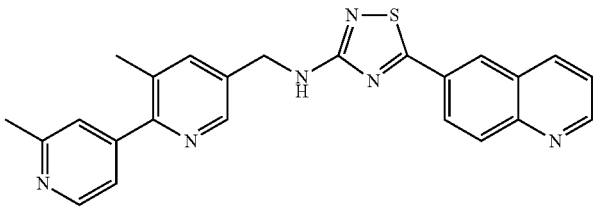
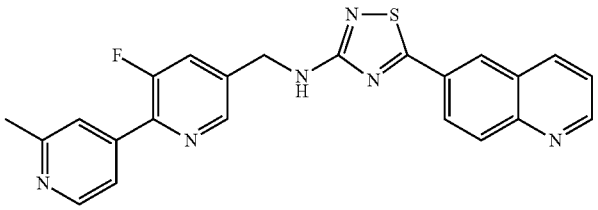
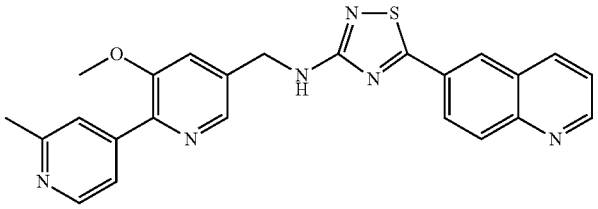
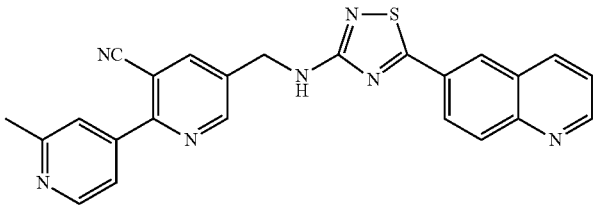
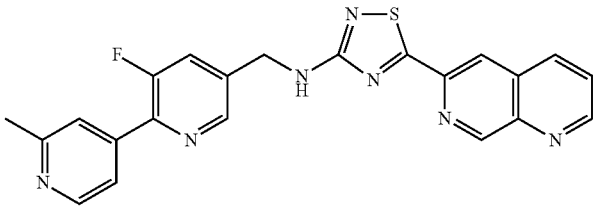
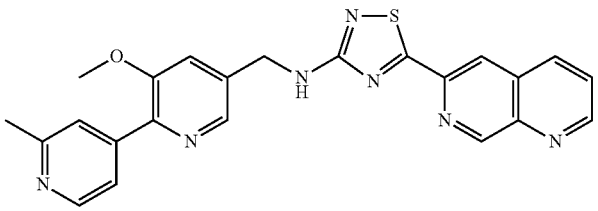
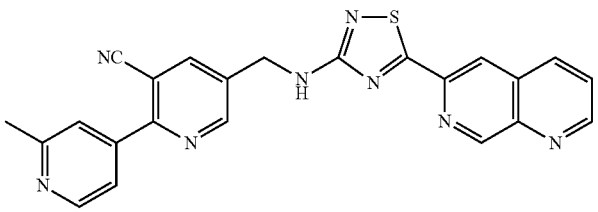
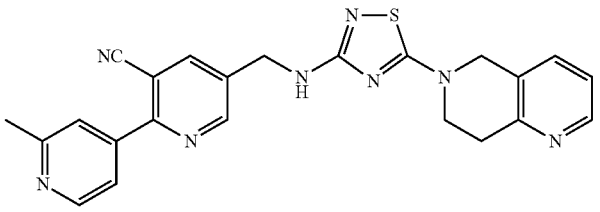
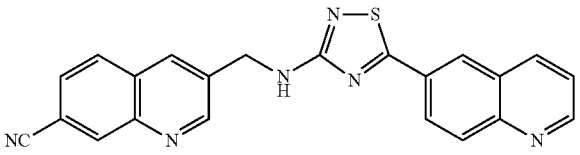
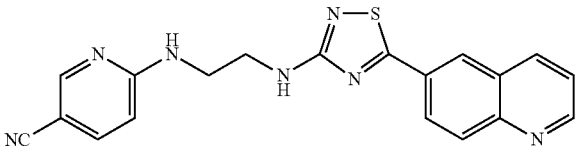
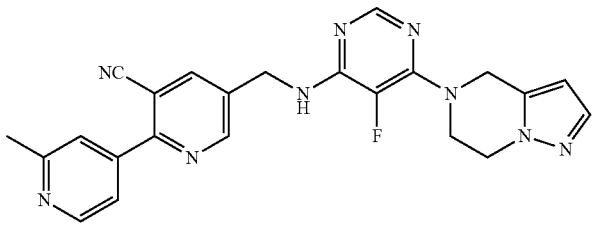
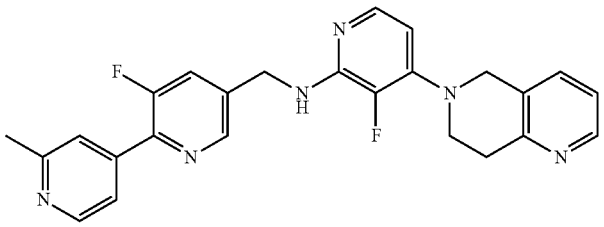
Compounds of Formula I	
A-191	
A-192	
A-193	
A-194	
A-195	
A-196	
A-197	

TABLE 1-continued

Compounds of Formula I

A-198	
A-199	
A-200	
A-201	
A-202	

BRIEF DESCRIPTION OF THE DRAWINGS

[0098] FIG. **1** depicts the IC50 curve of compound A-12 of the present invention in the primary assay;

[0099] FIG. **2** depicts the IC50 curve of compound A-36 of the present invention in the primary assay;

[0100] FIG. **3** depicts the IC50 curve of compound A-100 of the present invention in the primary assay;

[0101] FIG. **4** depicts the IC50 curve of compound A-103 of the present invention in the primary assay;

[0102] FIG. **5** depicts the IC50 curve of compound A-166 of the present invention in the primary assay;

[0103] FIG. **6** depicts the IC50 curve of compound A-168 of the present invention in the primary assay;

[0104] FIG. **7** depicts the IC50 curve of compound A-194 of the present invention in the primary assay; and

[0105] FIG. **8** depicts the IC50 curve of compound A-198 of the present invention in the primary assay.

[0106] Before proceeding with the detailed description, it is to be appreciated that the following detailed description is merely exemplary in nature and is not intended to limit the invention or the application and uses thereof. Hence, although the present disclosure is, for convenience of explanation, depicted and described as shown in certain illustrative embodiments, it will be appreciated that it can be implemented in various other types of embodiments and equivalents, and in various other systems and environments. Furthermore, there is no intention to be bound by any theory presented in the preceding background or the following detailed description.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

[0107] Compounds are generally described herein using standard nomenclature. For compounds having asymmetric centers, it should be understood that (unless otherwise specified) all of the optical isomers and mixtures thereof are

encompassed. In addition, compounds with carbon-carbon double bonds may occur in Z- and E-forms, with all isomeric forms of the compounds being included in the present invention unless otherwise specified. Where a compound exists in various tautomeric forms, a recited compound is not limited to any one specific tautomer, but rather is intended to encompass all tautomeric forms.

[0108] As used herein, the term "alkyl" refers to a straight or branched chain saturated aliphatic hydrocarbon. Alkyl groups include groups having from 1 to 8 carbon atoms (C_{1-8} alkyl), from 1 to 6 carbon atoms (C_{1-6} alkyl) and from 1 to 4 carbon atoms (C_{1-4} alkyl), including, for example, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, pentyl, 2-pentyl, isopentyl, neopentyl, hexyl, 2-hexyl, 3-hexyl and 3-methylpentyl. In some instances, a substituent of an alkyl group is specifically indicated. For example, "cyanoalkyl" refers to an alkyl group substituted with at least one cyano substituent.

[0109] "Alkenyl" refers to straight or branched chain alkene groups, which comprise at least one unsaturated carbon-carbon double bond. Alkenyl groups include C_{2-8} alkenyl, C_{2-6} alkenyl and C_{2-4} alkenyl groups, which have from 2 to 8, 2 to 6 or 2 to 4 carbon atoms, respectively, including, for example, ethenyl, allyl or isopropenyl. "Alkynyl" refers to straight or branched chain alkyne groups, which have one or more unsaturated carbon-carbon bonds, at least one of which is a triple bond. Alkynyl groups include C_{2-8} alkynyl, C_{2-6} alkynyl and C_{2-4} alkynyl groups, which have from 2 to 8, 2 to 6 or 2 to 4 carbon atoms, respectively.

[0110] A "cycloalkyl" is a group that comprises one or more saturated rings in which all ring members are carbon, including, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, adamantyl. Cycloalkyl groups do not comprise an aromatic ring or a heterocyclic ring. Certain cycloalkyl groups are C_{3-7} cycloalkyl, in which the cycloalkyl group contains a single ring having from 3 to 7 ring members, all of which are carbon. A "cycloalkenyl" is a group that comprises one or more unsaturated rings in which all ring members are carbon.

[0111] "Alkoxy" is meant an alkyl group as described above attached via an oxygen bridge. Alkoxy groups include C_{1-6} alkoxy and C_{1-4} groups, which have from 1 to 6 or from 1 to 4 carbon atoms, respectively. Methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy, n-pentoxy, 2-pentoxy, 3-pentoxy, isopentoxy, neopentoxy, hexoxy, 2-hexoxy, 3-hexoxy, and 3-methylpentoxy are representative alkoxy groups.

[0112] "Alkylamino" refers to a secondary or tertiary amine that has the general structure —NH-alkyl or —N(alkyl)(alkyl), wherein each alkyl is selected independently from alkyl, cycloalkyl and (cycloalkyl)alkyl groups. Such groups include, for example, mono- and di-(C_{1-6} alkyl)amino groups, in which each C_{1-6} alkyl may be the same or different. It will be apparent that the definition of "alkyl" as used in the term "alkylamino" differs from the definition of "alkyl" used for all other alkyl-containing groups, in the inclusion of cycloalkyl and (cycloalkyl)alkyl groups.

[0113] "Halogen" means fluorine, chlorine, bromine, and iodine. A "haloalkyl" is an alkyl group that is substituted with 1 or more independently chosen halogens (e.g., "C_{1-6} haloalkyl" groups have from 1 to 6 carbon atoms and at least one halogen). Examples of haloalkyl groups include, but are not limited to, mono-, di- or tri-fluoromethyl; mono-, di- or tri-chloromethyl; mono-, di-, tri-, tetra- or penta-fluoroethyl; mono-, di-, tri-, tetra- or penta-chloroethyl; and 1,2,2,2-tetrafluoro-1-trifluoromethyl-ethyl.

[0114] A "heteroaryl" is an aromatic group in which at least one aromatic ring comprises at least one heteroatom selected from N, O and S. Heteroaryls include, for example, 5-12 membered heteroaryls. Examples included but are not limited to imidazole, furan, furazan, isothiazole, isoxazole, oxadiazole, oxazole, pyrazine, pyrazole, pyridazine, pyridine, pyrimidine, tetrazole, thiazole and thiophene.

[0115] The term "heterocyclic" refers to a ring structure containing 3-12 ring atoms, in which at least one ring atom is carbon and at least one ring atom is heteroatom selected from N, O, and S. A heterocyclic group may be aromatic or non-aromatic. Piperidine and oxetane are non-limiting examples of non-aromatic heterocycles. Thiazole and pyridine are non-limiting examples of aromatic heterocycles.

[0116] A "substituent" and "substituted," as used herein, denote that a molecular moiety is covalently bonded to an atom within a molecule of interest. For example, a ring substituent may be a moiety such as a halogen, alkyl group, haloalkyl group or other group that is covalently bonded to an atom (preferably a carbon or nitrogen atom) that is a ring member. Substituents of aromatic groups are generally covalently bonded to a ring carbon atom.

[0117] The term "pharmaceutically acceptable" when used with reference to a compound of formula I is intended to refer to a form of the compound that is safe for administration to a subject. For example, a free base, a salt form, a solvate, a hydrate, a prodrug or derivative form of a compound of formula I, which has been approved for mammalian use, via oral ingestion or any other route of administration, by a governing authority or regulatory agency, such as the Food and Drug Administration (FDA) of the United States, is pharmaceutically acceptable.

[0118] Included in the compounds of formula I are the pharmaceutically acceptable salt forms of the free-base compounds. The term "pharmaceutically-acceptable salts" embraces salts, commonly used to form alkali metal salts and to form addition salts of free acids or free bases, which have been approved by a regulatory agency. Salts are formed from ionic associations, charge-charge interactions, covalent bonding, complexation, coordination, etc. The nature of the salt is not critical, provided that it is pharmaceutically acceptable.

[0119] In some embodiments, the compound(s) of formula I is used to treat a subject by administering the compound(s) as a pharmaceutical composition. To this end, the compound (s), in one embodiment, is combined with one or more pharmaceutically acceptable excipients, including carriers, diluents or adjuvants, to form a suitable composition, which is described in more detail herein.

[0120] The term "excipient", as used herein, denotes any pharmaceutically acceptable additive, carrier, adjuvant, or other suitable ingredient, other than the active pharmaceutical ingredient (API), which is typically included for formulation and/or administration purposes. "Diluent" and "adjuvant" are defined hereinafter.

[0121] The terms "treat", "treating," "treatment," and "therapy" as used herein refer to therapy, including without limitation, curative therapy, prophylactic therapy, and preventative therapy. Prophylactic treatment generally consti-

tutes either preventing the onset of disorders altogether or delaying the onset of a pre-clinically evident stage of disorders in individuals.

[0122] The phrase "effective amount" is intended to quantify the amount of each agent, which will achieve the goal of improvement in disorder severity and the frequency of incidence over treatment of each agent by itself, while avoiding adverse side effects typically associated with alternative therapies. The effective amount, in one embodiment, is administered in a single dosage form or in multiple dosage forms.

[0123] Regardless of the route of administration selected, the compounds of the present invention, which may be used in a suitable hydrated form, and/or the pharmaceutical compositions of the present invention, are formulated into pharmaceutically acceptable dosage forms or by other conventional methods known to those of skill in the art.

[0124] Actual dosage levels of the active ingredients in the pharmaceutical compositions of the present invention may be varied so as to obtain an effective amount of the active ingredient to achieve the desired therapeutic response for a particular patient, composition, and mode of administration, without being toxic to the patient.

[0125] The selected dosage level will depend upon a variety of factors including the activity of the particular compound of the present invention employed, the route of administration, the time of administration, the rate of excretion of the particular compound being employed, the duration of the treatment, other drugs, compounds and/or materials used in combination with the particular hedgehog inhibitor employed, the age, sex, weight, condition, general health and prior medical history of the patient being treated, and like factors well known in the medical arts.

[0126] A physician or veterinarian having ordinary skill in the art can readily determine and prescribe the effective amount of the pharmaceutical composition required. For example, the physician or veterinarian could start doses of the compounds of the invention employed in the pharmaceutical composition at levels lower than that required in order to achieve the desired therapeutic effect and gradually increase the dosage until the desired effect is achieved.

[0127] In general, a suitable daily dose of a compound of the invention will be that amount of the compound which is the lowest dose effective to produce a therapeutic effect. Such an effective dose will generally depend upon the factors described above. Generally, intravenous, intracerebroventricular and subcutaneous doses of the compounds of this invention for a patient will range from about 0.0001 to about 100 mg per kilogram of body weight per day. The mode of administration can have a large effect on dosage. Higher doses may be used for localized routes of delivery.

[0128] If desired, the effective daily dose of the active compound may be administered as two, three, four, five, six or more sub-doses administered separately at appropriate intervals throughout the day, optionally, in unit dosage forms. Those of skill in the art will readily appreciate that dose levels can vary as a function of the specific compound, the severity of the symptoms and the susceptibility of the subject to side effects. Dosages for a given compound disclosed herein are readily determinable by those of skill in the art by a variety of means.

Pharmaceutical Compositions/Formulations

[0129] One embodiment provides a pharmaceutical composition comprising a compound of formula I, or a stereoisomer, tautomer, hydrate, solvate or pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

[0130] In some embodiments, the present invention provides methods for regulating the Wnt signaling pathway and/or treating a Wnt-mediated disorder in a mammal suffering therefrom. The method comprises administrating to a mammalian subject a therapeutically effective amount of at least one compound of formula I, or a pharmaceutical composition thereof, and optionally in combination with a second therapeutic agent. The method comprises treating or preventing disorder is a cell proliferative disorder selected from the group consisting of systemic sclerosis, skin fibrosis, idiopathic pulmonary fibrosis, renal fibrosis, liver fibrosis, drug-induced fibrosis, radiation-induced fibrosis, colorectal cancer, breast cancer, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, non-small cell lung cancer, gastric cancer, pancreatic cancer, leukemia, lymphoma, neuroblastoma, retinoblastoma, sarcoma, osteosarcoma, chondosarcoma, Ewing's sarcoma, rhabdomysarcoma, brain tumor, Wilm's tumor, basal cell carcinoma, melanoma, head and neck cancer, cervical cancer and prostate cancer.

[0131] In some embodiments, the compounds described herein are formulated into pharmaceutical compositions. Pharmaceutical compositions are formulated in a conventional manner using one or more pharmaceutically acceptable inactive ingredients that facilitate processing of the active compounds into preparations that can be used pharmaceutically. Proper formulation is dependent upon the route of administration chosen. A summary of pharmaceutical compositions described herein can be found, for example, in Remington: *The Science and Practice of Pharmacy*, Nineteenth Ed., Easton, Pa.: Mack Publishing Company (1995); Hoover, John E., *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, Pa. (1975); Liberman, H. A. and Lachman, L., Eds., *Pharmaceutical Dosage Forms*, Marcel Decker, New York, N.Y. (1980); and *Pharmaceutical Dosage Forms and Drug Delivery Systems*, Seventh Ed., Lippincott Williams & Wilkins (1999), herein incorporated by reference for such disclosure.

[0132] A pharmaceutical composition, as used herein, refers to a mixture of a compound of formula I with other chemical components (i.e. pharmaceutically acceptable inactive ingredients), such as carriers, excipients, binders, filling agents, suspending agents, flavoring agents, sweetening agents, disintegrating agents, dispersing agents, surfactants, lubricants, colorants, diluents, solubilizers, moistening agents, plasticizers, stabilizers, penetration enhancers, wetting agents, anti-foaming agents, antioxidants, preservatives, or one or more combination thereof. The pharmaceutical composition facilitates administration of the compound to an organism. In practicing the methods of treatment or use provided herein, therapeutically effective amounts of compounds described herein are administered in a pharmaceutical composition to a mammal having a disease, disorder, or condition to be treated. In some embodiments, the mammal is a human. A therapeutically effective amount can vary widely depending on the severity of the disease, the age and relative health of the subject, the potency of the compound

used and other factors. The compounds can be used singly or in combination with one or more therapeutic agents as components of mixtures.

[0133] The pharmaceutical formulations described herein are administered to a subject by appropriate administration routes, including but not limited to, oral, parenteral (e.g., intravenous, subcutaneous, intramuscular), intranasal, buccal, topical, rectal, or transdermal administration routes. The pharmaceutical formulations described herein include, but are not limited to, aqueous liquid dispersions, self-emulsifying dispersions, solid solutions, liposomal dispersions, aerosols, solid dosage forms, powders, immediate release formulations, controlled release formulations, fast melt formulations, tablets, capsules, pills, delayed release formulations, extended release formulations, pulsatile release formulations, multiparticulate formulations, and mixed immediate and controlled release formulations.

[0134] All formulations for oral administration are in dosages suitable for such administration. Examples of such dosage units are tablets or capsules. In some embodiments, these contain an amount of active ingredient from about 1 to 2000 mg, advantageously from about 1 to 500 mg, and typically from about 5 to 150 mg. A suitable daily dose for a human or other mammal vary widely depending on the condition of the patient and other factors, but, once again, can be determined using routine methods and practices.

[0135] Conventional formulation techniques include, e.g., one or a combination of methods: (1) dry mixing, (2) direct compression, (3) milling, (4) dry or non-aqueous granulation, (5) wet granulation, or (6) fusion. Other methods include, e.g., spray drying, pan coating, melt granulation, granulation, fluidized bed spray drying or coating (e.g., wurster coating), tangential coating, top spraying, tableting, extruding and the like.

Synthetic Methods

[0136] Methods of the present invention include the use of at least one compound of formula I, which inhibits hedgehog signaling in the regulation of repair and/or functional performance of a wide range of cells, tissues and organs, and have therapeutic and cosmetic applications ranging from regulation of neural tissues, bone and cartilage formation and repair, regulation of spermatogenesis, regulation of smooth muscle, regulation of lung, liver and other organs arising from the primitive gut, regulation of hematopoietic function, regulation of skin and hair growth, etc. Accordingly, the methods and compositions of the present invention include the use of the subject inhibitors for all such uses as inhibitors of hedgehog proteins may be implicated. Moreover, the subject methods can be performed on cells which are provided in culture (in vitro), or on cells in a whole animal (in vivo).

[0137] The examples and preparations provided below illustrated and exemplify the compounds described herein and methods of preparing such compounds. In general, the compounds described herein may be prepared by processes known in the general chemical arts.

[0138] The compounds of the present invention can be prepared using various synthetic routes, including those described below, starting from commercially available materials. Starting materials of the invention, are either known, commercially available, or can be synthesized in analogy to or according to methods that are known in the art. Many starting materials may be prepared according to known processes and, in particular, can be prepared using processes described in the examples. In synthesizing starting materials, functional groups in some cases are protected with suitable protecting groups when necessary. Functional groups may be removed according to known procedures in the art.

[0139] The protection of functional groups by protecting groups, the protecting groups themselves, and their removal reactions (commonly referred to as "deprotection") are described, for example, in standard reference works, such as J. F. W. McOmie, Protective Groups in Organic Chemistry, Plenum Press, London and New York (1973), in T. W. Greene, Protective Groups in Organic Synthesis, Wiley, New York (1981), in The Peptides, Volume 3, E. Gross and J. Meienhofer editors, Academic Press, London and New York (1981).

[0140] All synthetic procedures described herein can be carried out under known reaction conditions, advantageously under those described herein, either in the absence or in the presence (usually) of solvents or diluents.

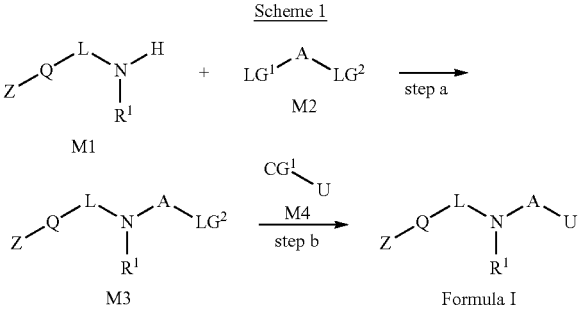
[0141] The invention further encompasses "intermediate" compounds, including structures produced from the synthetic procedures described, whether isolated or not, prior to obtaining the finally desired compound. Structures resulting from carrying out steps from a transient starting material, structures resulting from divergence from the described method(s) at any stage, and structures forming starting materials under the reaction conditions are all "intermediates" included in the invention. Further, structures produced by using starting materials in the form of a reactive derivative or salt, or produced by a compound obtainable by means of the process according to the invention and structures resulting from processing the compounds of the invention in situ are also within the scope of the invention.

[0142] New starting materials and/or intermediates, as well as processes for the preparation thereof, are likewise the subject of this invention. In select embodiments, such starting materials are used and reaction conditions so selected as to obtain the desired compound(s).

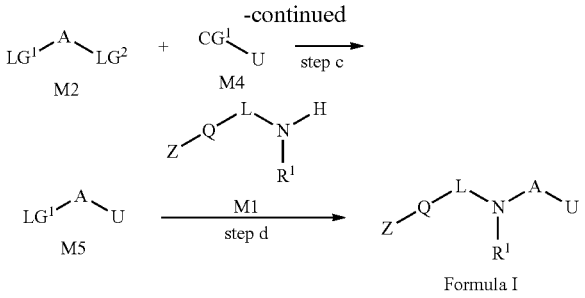
[0143] Starting materials of the invention, are either known, commercially available, or can be synthesized in analogy to or according to methods that are known in the art. Many starting materials may be prepared according to known processes and, in particular, can be prepared using processes described in the examples. In synthesizing starting materials, functional groups in some cases are protected with suitable protecting groups when necessary. Protecting groups, their introduction and removal are described above.

[0144] General Method A:

Scheme 1



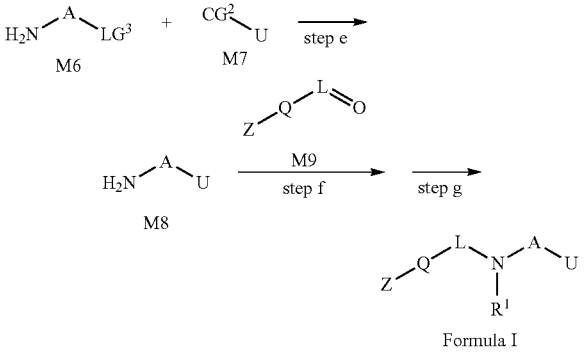
-continued



[0145] Scheme 1 depicts a general synthetic route leading to the synthesis of compounds of Formula I. Compounds of Formula I can be assembled from three components: M1, M2, and M4. Component M1 can be formed from other precursors, as shown in examples vide infra. Component M2 has two leaving groups (LG^1 and LG^2) which can undergo reactions with an amino group in component M1 and a chemical group (CG^1) in component M4 to form compounds of Formula I. LG^1 and LG^2 can be selected from halide, $CH_3S(O)_2$—, triflate, tosylate, and mesylate. CG^1 can be selected from borate, organotin, alkyne, amino, and amide groups. Palladium catalyzed reactions of borate, organotin, alkyne, amide, or amino in CG^1, or treating amino group in CG^1 with a base can form a covalent bond between A and U in M. Further modifications of A or U may be needed to complete the syntheses of compounds of Formula I. Alternatively, LG^2 can be converted to borate and CG^1 can be selected from Br, I, and triflate so that a palladium catalyzed reaction may form the covalent bond between A and U. Further, M1 may only contains shorter tails, such as Q-L- or L- to start with, and Z or Z-Q may be added later to complete the synthesis of compounds of Formula I. Conditions for steps a and d can be: DIPEA, t-BuOH, 50-60° C., overnight; DIPEA, i-PrOH, 60-80° C. overnight; Et_3N, THF, rt, overnight; DIPEA, cyclohexanol, $ZnCl_2$, 120° C., 40 h; K_2CO_3, DMSO, 120-135° C., 10 h; $Pd(AcO)_2$, BINAP, t-BuONa, dioxane, 100° C., 12 h; and DIPEA, THF, 50° C., overnight. Conditions for steps b and c can be: DIPEA, NMP, 120-130° C., overnight; DIPEA, THF, reflux, overnight; DIPEA, t-BuOH, 50° C.; NMP, 130° C., 24 h; $Pd(PPh_3)_4$, K_2CO_3, dioxane/H_2O, 100-120° C., overnight; Cs_2CO_3, $Pd(PPh_3)_4$, dioxane/H_2O, 100° C., 12 h; $Pd(dppf)Cl_2$, dppf, K_3PO_4, dioxane, H_2O, 100° C., 12 h; $Pd(dppf)Cl_2$, dioxane/H_2O, 100° C., 10 h; and $Pd(PPh_3)_4$, xantphos, Cs_2CO_3, dioxane, reflux, overnight.

[0146] General Method B:

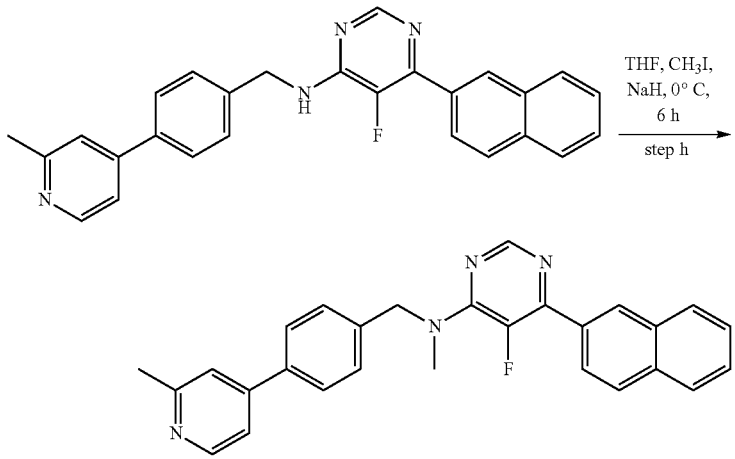
Scheme 2



[0147] Scheme 2 illustrates another general synthetic route leading the synthesis of compounds of Formula I. LG^3 can be selected from halide, triflate, tosylate, and mesylate, while CG^2 can be a borate group. Alternatively, LG^3 can be selected from halide, triflate, tosylate, and mesylate; and CG^2 can be a borate group. Palladium catalyzed reaction can lead to the covalent bond formation between A and U in M8. An ensuing reductive amination between M8 and M9 form the covalent bond between L and the amino group on A. Further alkylation of the amino group, if needed, may lead to compounds of Formula I. Step e can be Na_2CO_3, $Pd(PPh_3)_4$, EtOH, toluene, H_2O, 90° C., 12 h; and K_2CO_3, $Pd(PPh_3)_4$, dioxane/H_2O, 80° C., 10-12 h. Step f can be 1) EtOH, 90° C., 12 h, 2) $NaBH_4$; and TFA, Et_3SiH, MeCN, 80° C.

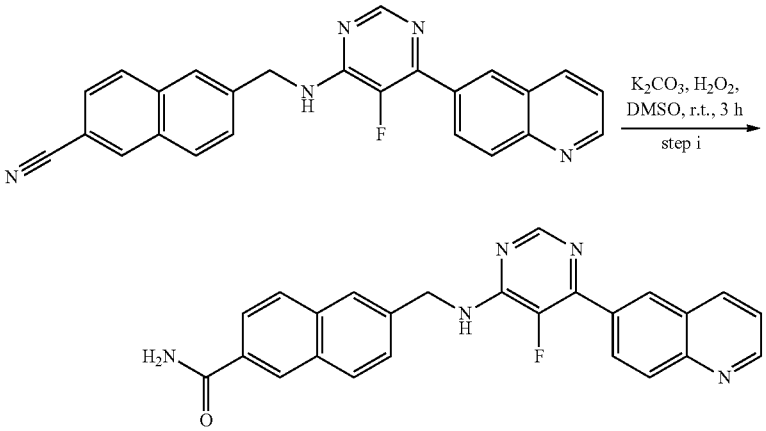
Scheme 3

Method C:

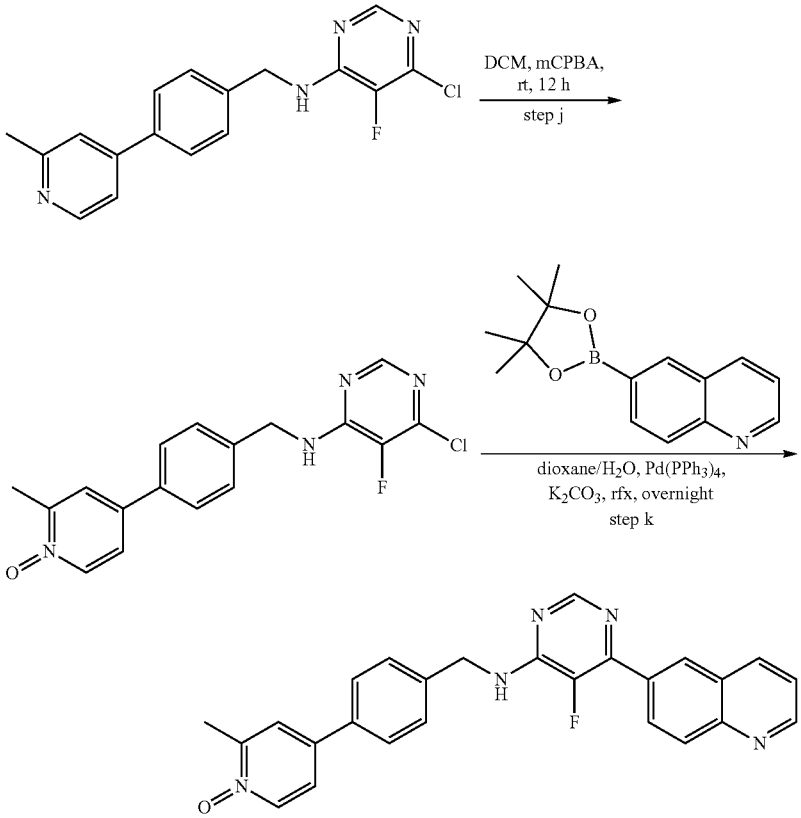


-continued

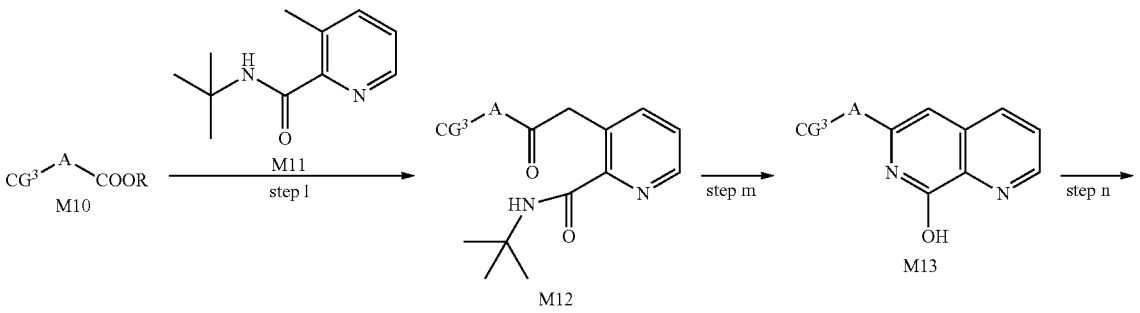
Method D:



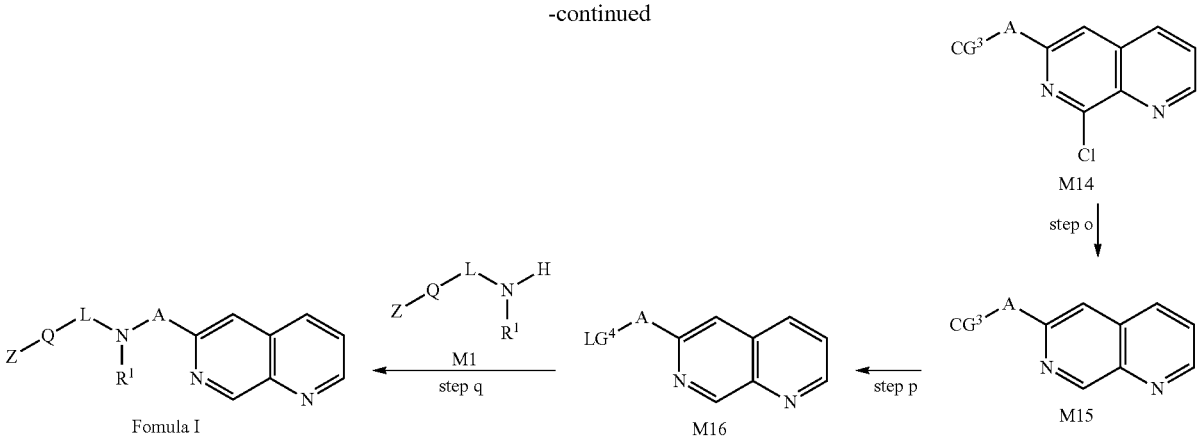
Method E:



Method F:

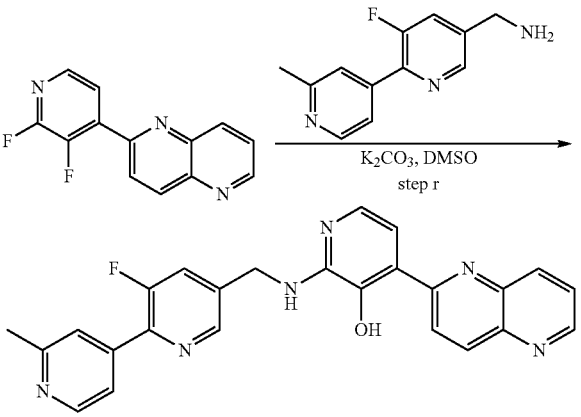


-continued



[0148] Scheme 3 depicts a general synthetic route leading to the synthesis of compounds of Formula I. Compounds of Formula I can be assembled from three components: M1, M10, and M11. Component M10 can be formed from other precursors, as shown in examples vide infra. Component M10 has a ester group (R=Me or Et) which can undergo reaction with the methyl group in component M11 to afford M12. Ring closure of M12 with loss of tert-butylamine afforded M13. The OH group of M13 was converted to hydrogen in two steps to give M14. The CG^3 group of M14 was converted to leaving group (LG^4) which can undergo reactions with an amino group in component M1 to form compounds of Formula I. CG^3 can be selected from CH_3S— and CH_3O— groups. LG^4 can be selected from $CH_3S(O)_2$— and HO— groups. Conditions for steps 1 can be: LDA, THF, −60° C., 1 h. Conditions for steps m can be: NH_4OAc, AcOH, 108° C., 8 h. Conditions for steps n can be: $POCl_3$, 100° C., 1 h. Conditions for steps o can be: $Pd(PPh_3)_4$, HCOOH, Et_3N, DMSO, 100° C., 1-3 h. Conditions for steps p can be: HBr, H_2O, 100° C., 1 h; and Oxone, THF, H_2O, r.t., 10 h. Conditions for steps q can be: PyBOP, DIPEA, DMF, r.t., 12 h; and DIPEA, NMP, 135° C., 16 h.

[0149] Method G:



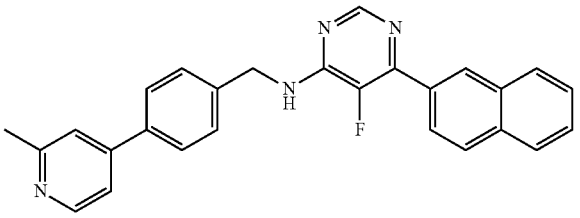
Materials and Methods

[0150] All reagents and solvents were obtained commercially. When required, all reagents and solvents were purified by standard techniques: tetrahydrofuran was purified by distillation from sodium. All thin-layer chromatography (TLC, GF254) analyses and column purification (100-200 mesh) were performed on silica gel (Qingdao Haiyang Chemical Co.Ltd. or Yantai Chemical Co. Ltd.) and spots revealed by UV visualization at 254 nm and I_2 vapor or phosphomolybdic acid. All nuclear magnetic resonance spectra were recorded using a Varian unity INOVA 400NB spectrometer at 400 MHz or a Varian Vnmrs spectrometer at 300 MHz as indicated. LC-MS was run using an Agilent 1100 system using an Agela Durashell C18 3.5 μm 4.6×50 mm column. Gradients were run using 0.1 NH_4HCO_3 aqueous solution and acetonitrile with gradient 5/95 to 95/5 in the run time indicated (for example, 5 min), flow rate at 1.8 mL/min.

Synthesis

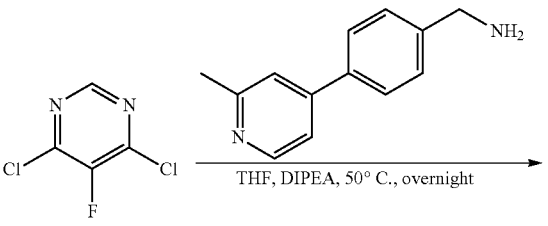
Example 1: Preparation of 5-fluoro-N-(4-(2-methylpyridin-4-yl)benzyl)-6-(naphthalen-2-yl)pyrimidin-4-amine (A-1)

[0151]

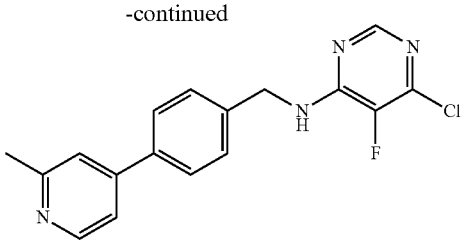


Method A—Step a: 6-chloro-5-fluoro-N-(4-(2-methylpyridin-4-yl)benzyl)pyrimidin-4-amine

[0152]



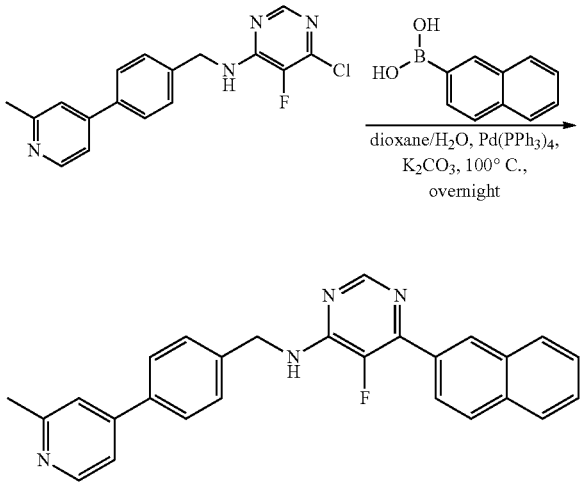
-continued



[0153] To a solution of (4-(2-methylpyridin-4-yl)phenyl) methanamine (100 mg, 0.51 mmol) in THF (10 mL), was added 4,6-dichloro-5-fluoropyrimidine (101 mg, 0.61 mmol) and N,N-diisopropylethylamine (260 mg, 2.0 mmol), and the reaction mixture was stirred at 50° C. overnight. After cooling to room temperature, the mixture was concentrated and the resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=100:1) to give the title compound (140 mg, 84%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J=5.2 Hz, 1H), 8.23 (s, 1H), 7.62 (d, J=8.4 Hz, 2H), 7.45 (d, J=8.4 Hz, 2H), 7.36 (s, 1H), 7.30 (d, J=5.2 Hz, 1H), 5.60 (s, 1H), 4.79 (d, J=6.0 Hz, 2H), 2.62 (s, 3H).

Method A—Step b: 5-fluoro-N-(4-(2-methylpyridin-4-yl)benzyl)-6-(naphthalen-2-yl)pyrimidin-4-amine

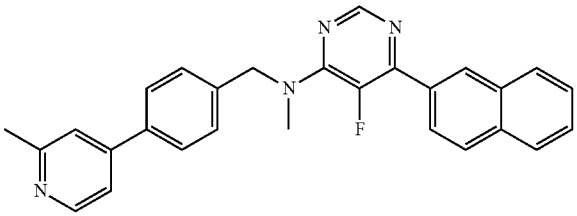
[0154]



[0155] To a solution of 6-chloro-5-fluoro-N-(4-(2-methylpyridin-4-yl)benzyl)pyrimidin-4-amine (66 mg, 0.20 mmol), naphthalen-2-ylboronic acid (52 mg, 0.30 mmol) in dioxane (5 mL) and H_2O (1 mL), was added K_2CO_3 (116 mg, 0.84 mmol) and $Pd(PPh_3)_4$ (12 mg, 0.01 mmol). The mixture was stirred at 100° C. overnight under N_2 atmosphere. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with EtOAc (15 mL), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=200:1-50:1) to give the title compound (45 mg, 54%) as a white solid.

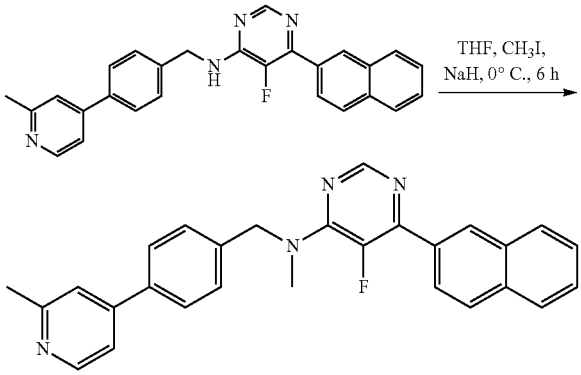
Example 2: Preparation of 5-fluoro-N-methyl-N-(4-(2-methylpyridin-4-yl)benzyl)-6-(naphthalen-2-yl) pyrimidin-4-amine (A-27)

[0156]



Method C—Step h: 5-fluoro-N-methyl-N-(4-(2-methylpyridin-4-yl)benzyl)-6-(naphthalen-2-yl) pyrimidin-4-amine

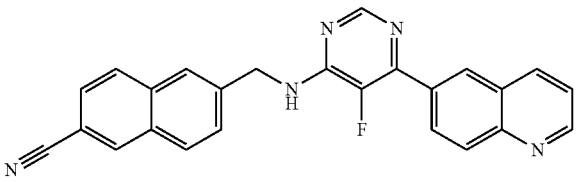
[0157]



[0158] To a solution of 5-fluoro-N-(4-(2-methylpyridin-4-yl)benzyl)-6-(naphthalen-2-yl)pyrimidin-4-amine (30 mg, 0.07 mmol) in THF (3 mL) at 0° C., was added NaH (6 mg, 80%, 0.20 mmol). The mixture was stirred for 30 min before MeI (20 mg, 0.14 mmol) was added. After stirring for further 6 h, the mixture was concentrated and the resulting residue was purified by silica gel column chromatography (CH_2Cl_2: MeOH=100:1) to give the title compound (30 mg, 97%) as a pale yellow oil.

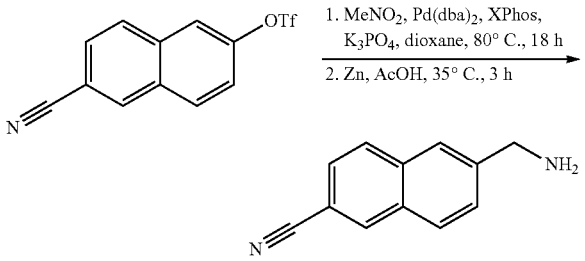
Example 3: Preparation of 6-((5-fluoro-6-(quinolin-6-yl)pyrimidin-4-ylamino)methyl)-2-naphthonitrile (A-42)

[0159]



Preparation of 6-(aminomethyl)-2-naphthonitrile

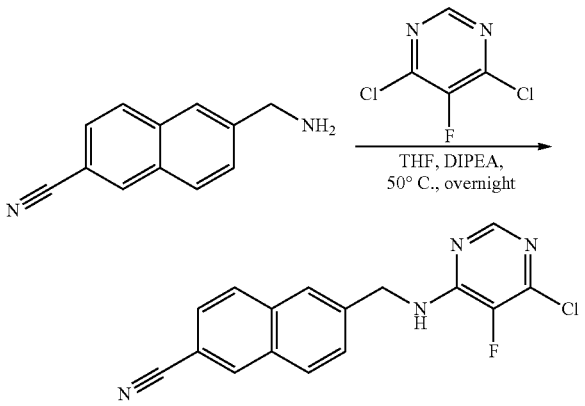
[0160]



[0161] A mixture of 6-cyanonaphthalen-2-yl trifluoromethanesulfonate (1.35 g, 4.49 mmol), K_3PO_4 (1.27 g, 5.99 mmol), $Pd(dba)_2$ (114 mg, 0.20 mmol), and XPhos (143 mg, 0.30 mmol) in $MeNO_2$ (4 mL) and 1,4-dioxane (25 mL) was heated to 80° C. under N_2 atmosphere for 18 h. After cooling to room temperature, AcOH (8 mL) was added, followed by Zn power (2.93 g, 45 mmol). The mixture was stirred at 35° C. for another 3 h. After filtration, the filtrate was diluted with H_2O (30 mL) and washed with EtOAc (20 mL×2). The aqueous phase was treated with 1 N NaOH to adjust PH=10, and extracted with EtOAc (50 mL×3). The combined organic layers was washed with brine, dried over Na2SO4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether: EtOAc=3:1-0:1) to give the title compound (280 mg, 34%) as a yellow solid.

Method A—Step a: 6-((6-chloro-5-fluoropyrimidin-4-ylamino)methyl)-2-naphthonitrile

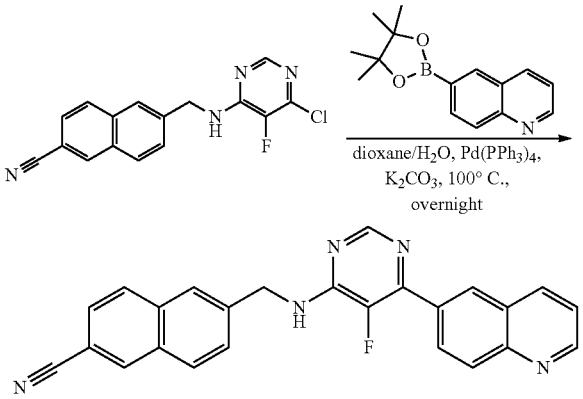
[0162]



[0163] To a solution of 6-(aminomethyl)-2-naphthonitrile (182 mg, 1.0 mmol) in THF (1 mL), was added 4,6-dichloro-5-fluoropyrimidine (167 mg, 1.0 mmol) and N,N-diisopropylethylamine (260 mg, 2.0 mmol), and the reaction mixture was stirred at 50° C. overnight. After cooling to room temperature, the mixture was concentrated and the resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=5:1-3:1) to give the title compound (120 mg, 38%) as a pale yellow solid.

Method A—Step b: 6-((5-fluoro-6-(quinolin-6-yl) pyrimidin-4-ylamino)methyl)-2-naphthonitrile

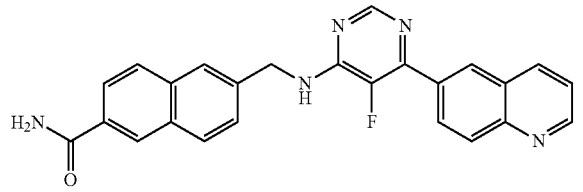
[0164]



[0165] To a solution of 6-((6-chloro-5-fluoropyrimidin-4-ylamino)methyl)-2-naphthonitrile (53 mg, 0.17 mmol), 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (66 mg, 0.26 mmol) in dioxane (5 mL) and H_2O (1 mL), was added K_2CO_3 (96 mg, 0.69 mmol) and $Pd(PPh_3)_4$ (20 mg, 0.017 mmol). The mixture was stirred at 100° C. overnight under N_2 atmosphere. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with EtOAc (15 mL), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=100:1-50:1) to give the title compound (35 mg, 66%) as a pale yellow solid.

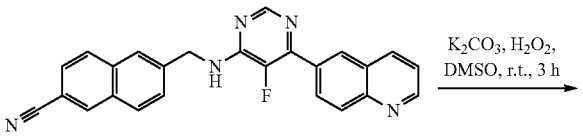
Example 4: Preparation of 6-((5-fluoro-6-(quinolin-6-yl)pyrimidin-4-ylamino)methyl)-2-naphthamide (A-43)

[0166]

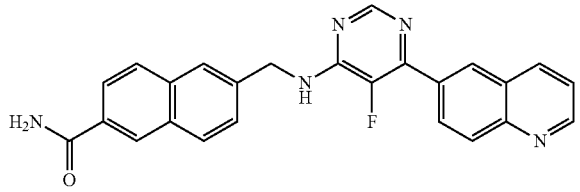


Method D—Step i: 6-((5-fluoro-6-(quinolin-6-yl) pyrimidin-4-ylamino)methyl)-2-naphthamide

[0167]



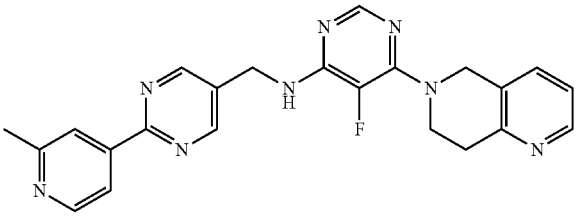
-continued



[0168] To a suspension of 6-((5-fluoro-6-(quinolin-6-yl) pyrimidin-4-ylamino)methyl)-2-naphthonitrile (17 mg, 0.04 mmol) and K_2CO_3 (2.8 mg, 0.02 mmol) in DMSO (1 mL), was added 30% H_2O_2 (6 mg, 0.05 mmol). The mixture was stirred at room temperature for 3 h, and then poured into H_2O (5 mL). The resulting precipitate was filtered, washed with water followed by hexane, and dried in vacuum to give the title compound (14 mg, 83%) as a pale yellow solid.

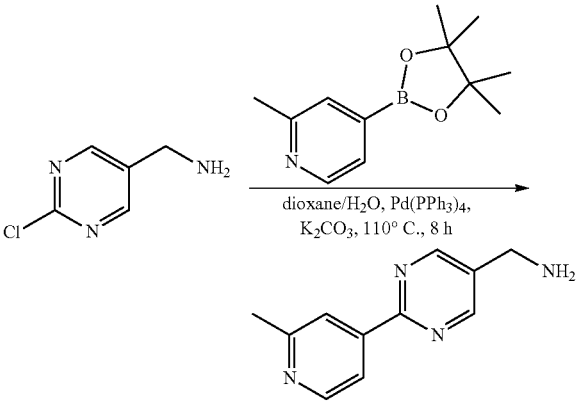
Example 5: Preparation of 6-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-5-fluoro-N-((2-(2-methylpyridin-4-yl)pyrimidin-5-yl)methyl)pyrimidin-4-amine (A-61)

[0169]



Preparation of (2-(2-methylpyridin-4-yl)pyrimidin-5-yl)methanamine

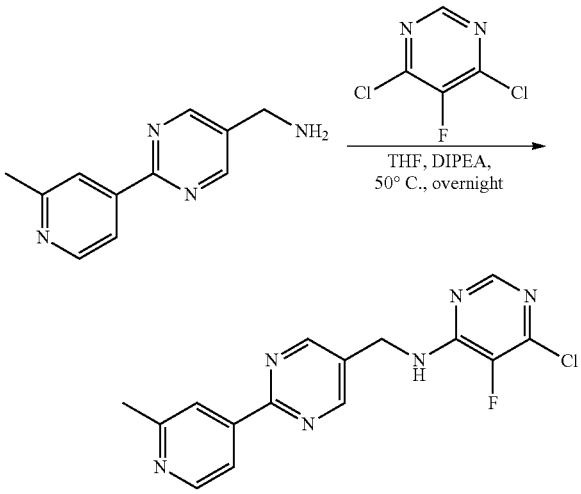
[0170]



[0171] To a solution of (2-chloropyrimidin-5-yl)methanamine (1.0 g, 7.0 mmol) in dioxane (30 mL) and H_2O (6 mL) was added 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine (45%, 3.7 g, 7.7 mmol), K_2CO_3 (2.9 g, 21 mmol) and $Pd(PPh_3)_4$ (809 mg, 0.7 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 8 h. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with H_2O (10 mL), and extracted with EtOAc (50 mL×3). The combined organic layers was washed with brine (15 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether: EtOAc=2:1-1:1) to give the title compound (1.3 g, 93%) as a gray solid.

Method A—Step a: 6-chloro-5-fluoro-N-((2-(2-methylpyridin-4-yl)pyrimidin-5-yl)methyl) pyrimidin-4-amine

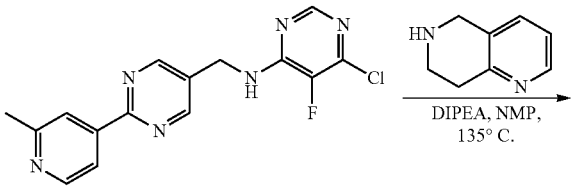
[0172]



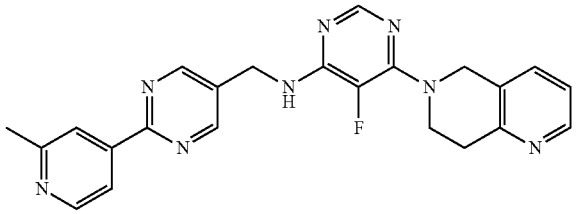
[0173] To a solution of (2-(2-methylpyridin-4-yl)pyrimidin-5-yl)methanamine (300 mg, 1.51 mmol) in THF (6 mL) was added 4,6-dichloro-5-fluoropyrimidine (278 mg, 1.51 mmol) and N,N-diisopropylethylamine (580 mg, 4.53 mmol), and the reaction mixture was stirred at 50° C. overnight. After cooling to room temperature, the mixture was concentrated and the resulting residue was purified by silica gel column chromatography (petroleum ether: EtOAc=1:1-0:1) to give the title compound (200 mg, 40%) as a yellow solid.

Method A—Step b: 6-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-5-fluoro-N-((2-(2-methylpyridin-4-yl) pyrimidin-5-yl)methyl)pyrimidin-4-amine

[0174]



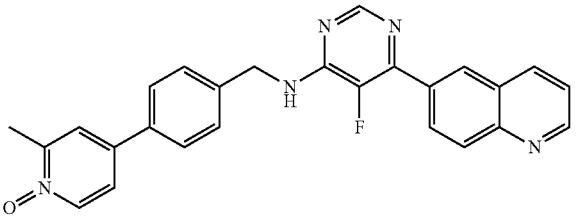
-continued



[0175] A mixture of 6-chloro-5-fluoro-N-((2-(2-methylpyridin-4-yl)pyrimidin-5-yl)methyl)pyrimidin-4-amine (80 mg, 0.24 mmol), 5,6,7,8-tetrahydro-1,6-naphthyridine (129 mg, 0.97 mmol) and N,N-diisopropylethylamine (467 mg, 3.6 mmol) in NMP (2 mL) was stirred at 135° C. for 8 h. After cooling to room temperature, the mixture was diluted with H_2O (5 mL), and extracted with EtOAc (5 mL×3). The combined organic layers was washed with brine (5 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=5:1-1:1) to give the title compound (30 mg, 50%) as a brown solid.

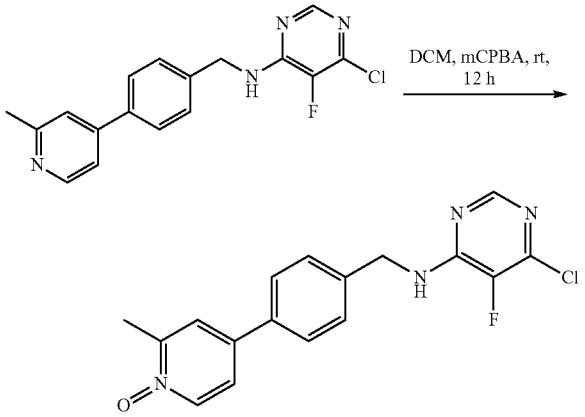
Example 6: Preparation of 4-(4-((5-fluoro-6-(quinolin-6-yl)pyrimidin-4-ylamino)methyl)phenyl)-2-methylpyridine 1-oxide (A-64)

[0176]



Method E—Step j: 4-(4-((6-chloro-5-fluoropyrimidin-4-ylamino)methyl)phenyl)-2-methylpyridine 1-oxide

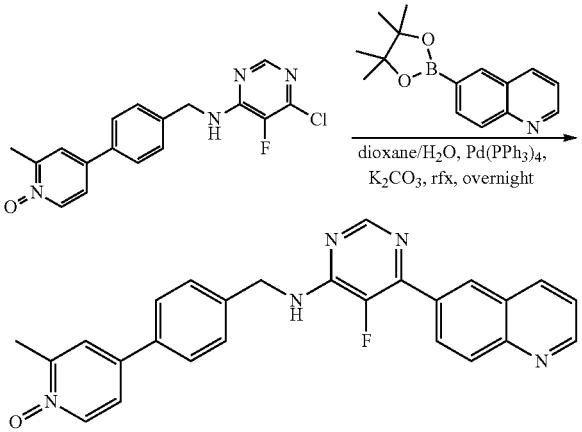
[0177]



[0178] To a solution of 6-chloro-5-fluoro-N-(4-(2-methylpyridin-4-yl)benzyl)pyrimidin-4-amine (133 mg, 0.404 mmol) in CH_2Cl_2 (5 mL) at room temperature, was added m-CPBA (174 mg, 1.01 mmol). The mixture was stirred at room temperature overnight, and then diluted with CH_2Cl_2 (15 mL). A mixture of sat. $Na_2S_2O_3$ (5 mL) and sat. $NaHCO_3$ (5 mL) was added, and the mixture was stirred for another 30 min. The organic layer was separated, washed with brine (5 mL), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=100:1-50:1) to give the title compound (130 mg, 96%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J=6.8 Hz, 1H), 8.22 (s, 1H), 7.54 (d, J=8.0 Hz, 2H), 7.43 (d, J=8.0 Hz, 3H), 7.35-7.29 (m, 1H), 5.91 (s, 1H), 4.79 (d, J=6.0 Hz, 2H), 2.57 (s, 3H).

Method E—Step k: 4-(4-((5-fluoro-6-(quinolin-6-yl)pyrimidin-4-ylamino)methyl)phenyl)-2-methylpyridine 1-oxide

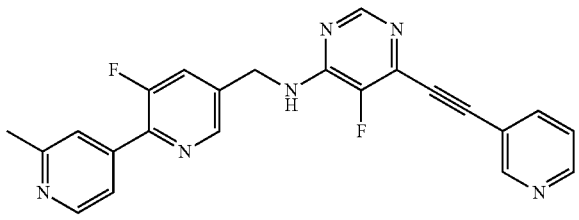
[0179]



[0180] To a solution of 4-(4-((6-chloro-5-fluoropyrimidin-4-ylamino)methyl)phenyl)-2-methylpyridine 1-oxide (67 mg, 0.19 mmol), 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (74 mg, 0.29 mmol) in dioxane (5 mL) and H_2O (1 mL), was added K_2CO_3 (107 mg, 0.78 mmol) and $Pd(PPh_3)_4$ (22 mg, 0.02 mmol). The mixture was stirred at reflux overnight under N_2 atmosphere. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with EtOAc (15 mL), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=50:1-30:1) to give the title compound (65 mg, 77%) as a white solid.

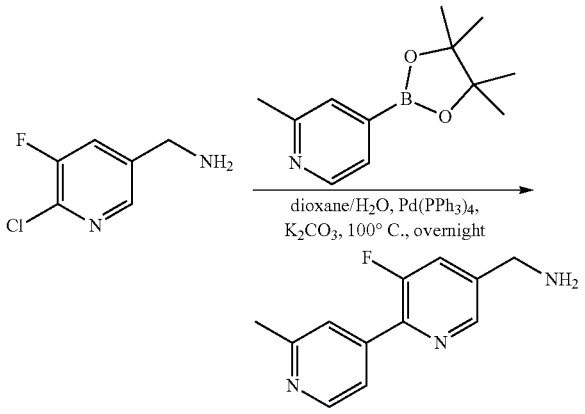
Example 7: Preparation of 5-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)-6-(pyridin-3-ylethynyl)pyrimidin-4-amine (A-69)

[0181]



Preparation of (3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methanamine

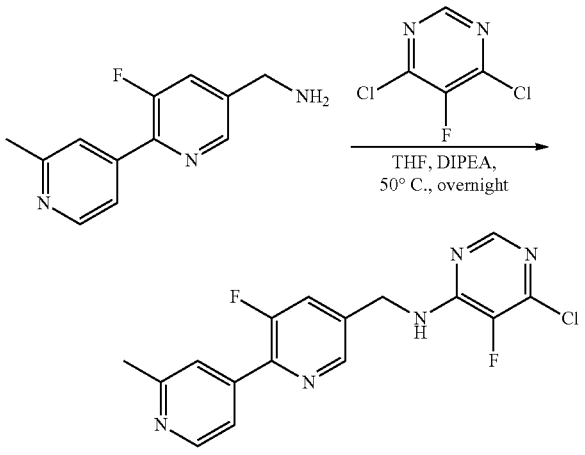
[0182]



[0183] To a solution of (6-chloro-5-fluoropyridin-3-yl) methanamine (2.36 g, 14.6 mmol) in dioxane (50 mL) and H_2O (10 mL) was added 2-methyl-4-(4,4,5,5-tetramethyl-1, 3,2-dioxaborolan-2-yl)pyridine (1.7 g, 16.1 mmol), K_2CO_3 (8.09 g, 58.6 mmol) and $Pd(PPh_3)_4$ (847 mg, 0.73 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 8 h. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with H_2O (100 mL), and extracted with CH_2Cl_2 (100 mL×6). The combined organic layers was dried over Na_2SO_4 and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH:NH_4OH=50:1:0. 1-20:1:0.1) to give the title compound (2.5 g, 79%) as a brown solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J=4.8 Hz, 1H), 8.50 (s, 1H), 7.77 (s, 1H), 7.69 (d, J=4.0 Hz, 1H), 7.58 (d, J=12.0 Hz, 1H), 4.01 (s, 2H), 2.65 (s, 3H).

Method A—Step a: 6-chloro-5-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)pyrimidin-4-amine

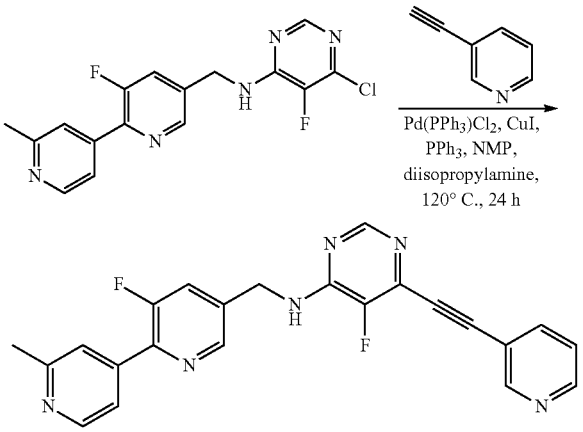
[0184]



[0185] To a solution of (3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methanamine (200 mg, 0.92 mmol) in THF (10 mL), was added 4,6-dichloro-5-fluoropyrimidine (154 mg, 0.92 mmol) and N,N-diisopropylethylamine (357 mg, 2.77 mmol), and the reaction mixture was stirred at 50° C. overnight. After cooling to room temperature, the mixture was concentrated and the resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=50:1) to give the title compound (200 mg, 62%) as a gray solid. ^1HNMR (400 MHz, $CDCl_3$) δ 8.61 (d, J=4.8 Hz, 1H), 8.56 (s, 1H), 8.24 (s, 1H), 7.76 (s, 1H), 7.69 (s, 1H), 7.55 (d, J=11.6 Hz, 1H), 5.78 (s, 1H), 4.84 (d, J=6.0 Hz, 2H), 2.65 (s, 3H).

Method A—Step b: 5-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)-6-(pyridin-3-ylethynyl)pyrimidin-4-amine

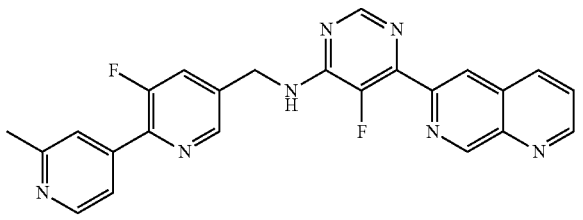
[0186]



[0187] A mixture of 6-chloro-5-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)pyrimidin-4-amine (100 mg, 0.29 mmol), 3-ethynylpyridine (92 mg, 0.87 mmol), $Pd(PPh_3)_2Cl_{12}$ (9 mg, 0.012 mmol), PPh_3 (6.1 mg, 0.023 mmol), and CuI (0.55 mg, 0.023 mmol) in diisopropylanmine (2 mL) and NMP (2 mL) was heated at 100° C. under N_2 atmosphere for 24 h. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with H_2O (10 mL), and extracted with EtOAc (10 mL×3). The combined organic layers was washed with brine (5 mL×2), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=2:1-1:1) to give the title compound (17 mg, 14%) as a white solid.

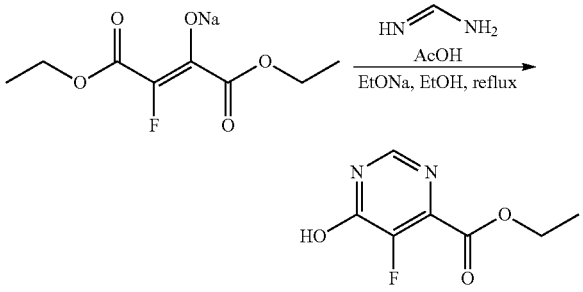
Example 8: Preparation of 5-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)-6-(1,7-naphthyridin-6-yl)pyrimidin-4-amine (A-85)

[0188]



Preparation of ethyl 5-fluoro-6-hydroxypyrimidine-4-carboxylate

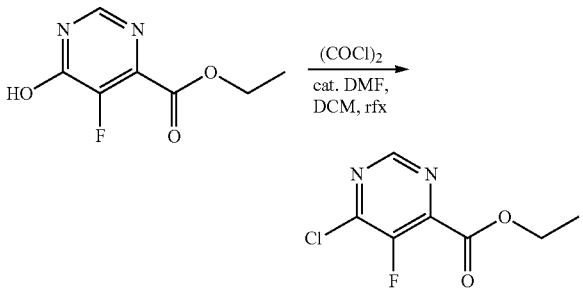
[0189]



[0190] A solution of sodium (E)-1,4-diethoxy-3-fluoro-1,4-dioxobut-2-en-2-olate (45.6 g, 200 mmol), formamidine acetate (20.8 g, 200 mmol) and EtONa (13.6 g, 200 mmol) in anhydrous EtOH (200 mL) was heated at reflux overnight. After cooling to room temperature, the solvent was removed by vacuum. The residue was neutralized with 2 N HCl and extracted with ethyl acetate (100 mL×3). The combined organic layers was dried over Na_2SO_4, and concentrated to give the title compound (22 g, 59%) as a brown solid, which was used directly in the next step without further purification.

Preparation of ethyl 6-chloro-5-fluoropyrimidine-4-carboxylate

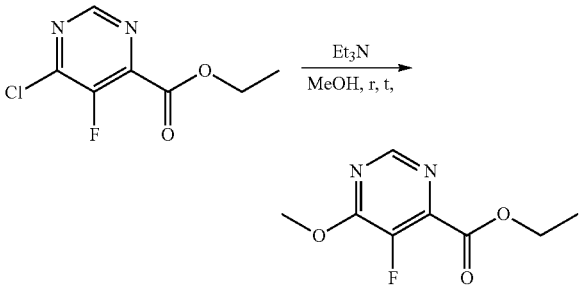
[0191]



[0192] To a stirred solution of ethyl 5-fluoro-6-hydroxypyrimidine-4-carboxylate (21.0 g, 113 mmol) and DMF (0.5 mL) in CH_2Cl_2 (200 mL) at room temperature, was added $(COCl)_2$ (43.0 g, 339 mmol) dropwise. The reaction was heated at reflux overnight. After cooling to room temperature, the solvent was removed by vacuum. The residue was dissolved in ethyl acetate (300 mL) and washed with sat. $NaHCO_3$ and brine successively. The organic layer was dried over Na_2SO_4, and concentrated. The resulting residue was purified by column chromatography (petroleum ether: ethyl acetate=10:1) to give the title compound (17.8 g, 77%) as a colerless oil. ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 4.52 (q, J=7.1 Hz, 2H), 1.44 (t, J=7.2 Hz, 3H).

Preparation of ethyl 5-fluoro-6-methoxypyrimidine-4-carboxylate

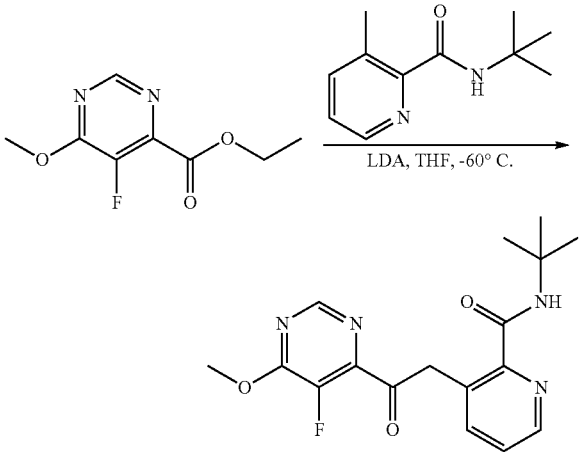
[0193]



[0194] A mixture of ethyl 6-chloro-5-fluoropyrimidine-4-carboxylate (6.14 g, 30.0 mmol) and triethylamine (3.03 g, 30.0 mmol) in methanol (50 mL) was stirred at room temperature overnight. After concentration, the residue was purified by column chromatography (petroleum ether:ethyl acetate=10:1) to give the title compound (4.14 g, 74%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 4.11 (s, 3H), 4.01 (s, 3H).

Method F—Step 1: N-(tert-butyl)-3-(2-(5-fluoro-6-methoxypyrimidin-4-yl)-2-oxoethyl) picolinamide

[0195]

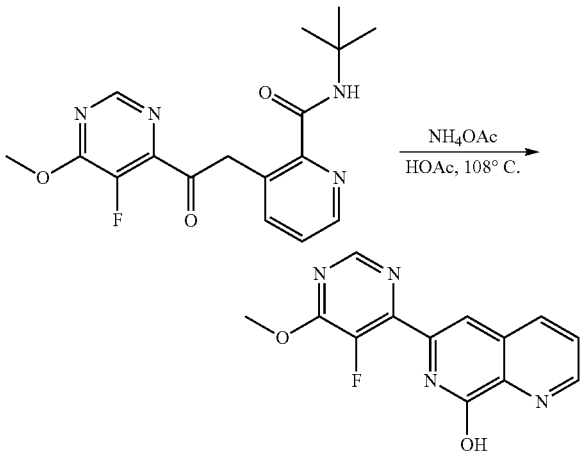


[0196] To a stirred solution of N-(tert-butyl)-3-methylpicolinamide (2.69 g, 14 mmol) in anhydrous tetrahydrofuran (50 mL) at −40° C., was added lithium diisopropylamide (2 M in THF, 28 mL, 56 mmol) dropwise. The mixture was stirred at this temperature for 30 min and then cooled to −60° C. Ethyl 5-fluoro-6-methoxypyrimidine-4-carboxylate (2.60 g, 14.0 mmol) in 5 mL anhydrous tetrahydrofuran was added and the reaction mixture was stirred at −60° C. for another 1 h. The reaction was quenched with sat. NH_4Cl (50 mL) and extracted with ethyl acetate (50 mL×3). The combined organic layers dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:ethyl acetate=3:1) to give the title

compound (1.36 g, 28%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.48 (d, J=4.4 Hz, 1H), 8.08 (s, 1H), 7.60 (d, J=7.6 Hz, 1H), 7.41-7.37 (m, 1H), 4.86 (s, 2H), 4.13 (s, 3H), 1.40 (s, 9H).

Method F—Step m: 6-(5-fluoro-6-methoxypyrimidin-4-yl)-1,7-naphthyridin-8-ol

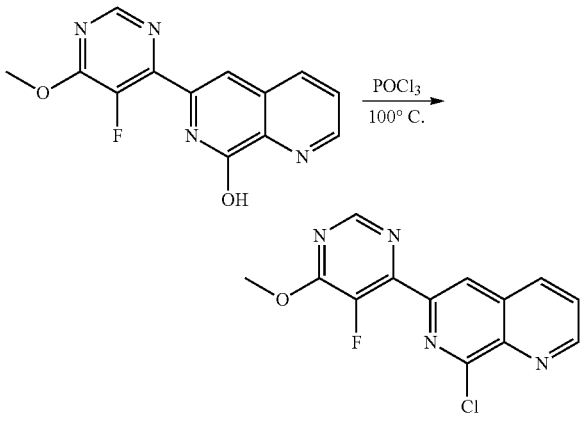
[0197]



[0198] A mixture of N-(tert-butyl)-3-(2-(5-fluoro-6-methoxypyrimidin-4-yl)-2-oxoethyl)picolinamide (1.36 g, 3.93 mmol) and NH_4OAc (3.03 g, 39.3 mmol) in HOAc (20 mL) was heated to 108° C. for 8 h. After concentration, the resulting residue was dissolved in ethyl acetate (30 mL) and washed with sat. $NaHCO_3$ (5 mL). The organic layer was dried over Na_2SO_4 and concentrated to give the title compound (880 mg, 82%) as a yellow solid without further purification.

Method F—Step n: 8-chloro-6-(5-fluoro-6-methoxypyrimidin-4-yl)-1,7-naphthyridine

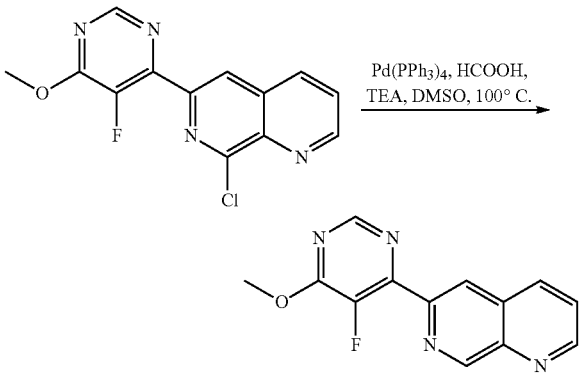
[0199]



[0200] A mixture of 6-(5-fluoro-6-methoxypyrimidin-4-yl)-1,7-naphthyridin-8-ol (440 mg, 1.62 mmol) and triethylamine (327 mg, 3.24 mmol) in $POCl_3$ (7.5 mL) and toluene (2.5 mL) was heated to 100° C. for 1 h. After concentration, the residue was dissolved in ethyl acetate (20 mL) and washed with sat. $NaHCO_3$ (5 mL). The organic layer was dried over Na_2SO_4 and concentrated. The resulting residue was purified by column chromatography (petroleum ether:ethyl acetate=2:1) to give the title compound (440 mg, 100%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 8.68 (s, 1H), 8.47 (s, 1H), 8.34 (d, J=8.2 Hz, 1H), 7.78-7.74 (m, 1H), 4.16 (s, 3H).

Method F—Step o: 6-(5-fluoro-6-methoxypyrimidin-4-yl)-1,7-naphthyridine

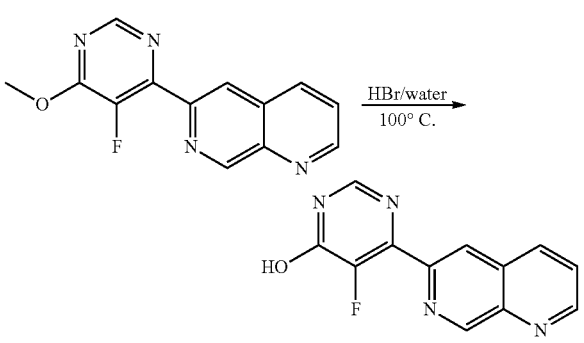
[0201]



[0202] A mixture of 8-chloro-6-(5-fluoro-6-methoxypyrimidin-4-yl)-1,7-naphthyridine (440 mg, 1.62 mmol), triethylamine (924 mg, 9.15 mmol), formic acid (253 mg, 5.50 mmol) and $Pd(PPh_3)_4$ (200 mg, 0.173 mmol) in DMSO (10 mL) was stirred at 100° C. under N_2 atmosphere for 1 h. After cooling to room temperature, the mixture was diluted with ethyl acetate (40 mL) and filtered. The filtrate was washed with brine (10 mL×3), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (petroleum ether:ethyl acetate=3:1) to give the title compound (400 mg, 96%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H), 9.12 (d, J=3.6 Hz, 1H), 8.70 (s, 1H), 8.52 (s, 1H), 8.30 (d, J=8.4 Hz, 1H), 7.56-7.53 (m, 1H), 4.16 (s, 3H).

Method F—Step p: 5-fluoro-6-(1,7-naphthyridin-6-yl)pyrimidin-4-ol

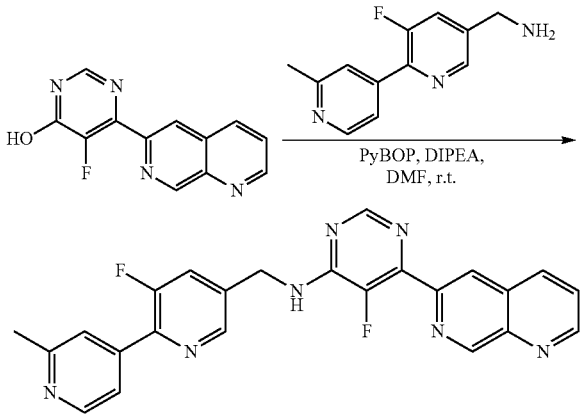
[0203]



[0204] A mixture of 6-(5-fluoro-6-methoxypyrimidin-4-yl)-1,7-naphthyridine (400 mg, 1.56 mmol) in 37% HBr (10 mL) was heated at reflux for 1 h. After concentration, the resulting residue was suspended in isopropanol (10 mL). The precipitate was filtered and washed with ether (3 mL) to give the title compound (400 mg, quantitative) as a yellow solid.

Method F—Step q: 5-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)-6-(1,7-naphthyridin-6-yl) pyrimidin-4-amine

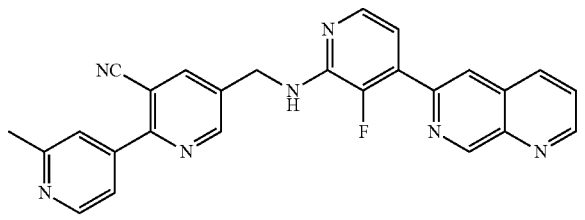
[0205]



[0206] To a stirred solution of 5-fluoro-6-(1,7-naphthyridin-6-yl)pyrimidin-4-ol (25 mg, 0.1 mmol), (3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methanamine (22 mg, 0.1 mmol), and N,N-diisopropylethylamine (26 mg, 0.2 mmol) in N,N-Dimethylformamide (1 mL) at room temperature, was added PyBOP (78 mg, 0.15 mmol) in portions. The mixture was stirred at room temperature for 12 h and then diluted with ethyl acetate (5 mL). The organic phase was washed with brine (2 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (CH_2Cl_2:MeOH=100:4) to give the title compound (30 mg, 68%) as a white solid.

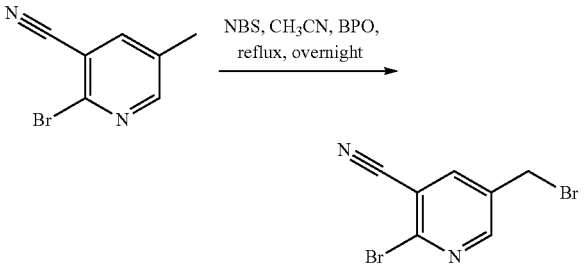
Example 9: Preparation of 5-((3-fluoro-4-(1,7-naphthyridin-6-yl)pyridin-2-ylamino)methyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile (A-121)

[0207]



Preparation of 2-bromo-5-(bromomethyl)nicotinonitrile

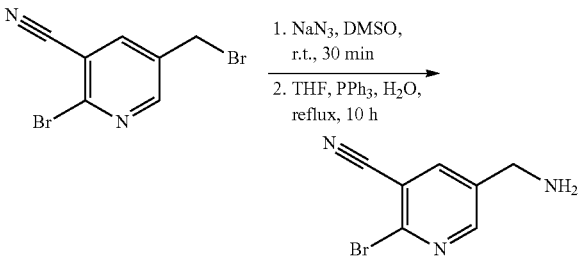
[0208]



[0209] To a solution of 2-bromo-5-methylnicotinonitrile (5 g, 25.4 mmol) in MeCN (100 mL) was added NBS (6.8 g, 38 mmol) and BPO (100 mg, 0.41 mmol). The mixture was heated at reflux overnight, and then BPO (50 mg, 0.21 mmol) was added. The mixture was heated at reflux for another 12 h. After cooling to room temperature, the mixture was concentrated and purified by column chromatography (petroleum ether:ethyl acetate=100:1-50:1) to give the title compound (4.3 g, 61%) as a brown solid.

Preparation of 5-(aminomethyl)-2-bromonicotinonitrile

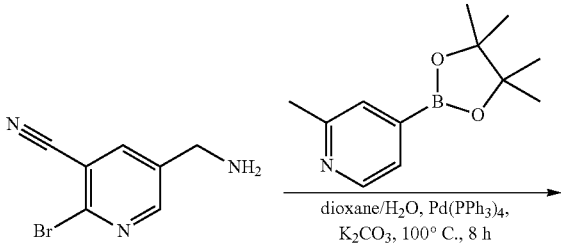
[0210]



[0211] To a solution of 2-bromo-5-(bromomethyl)nicotinonitrile (2.3 g, 8.2 mmol) in DMSO (40 mL) in ice bath, was added NaN_3 (637 mg, 9.8 mmol). The mixture was stirred at room temperature for 30 min before H_2O (100 mL) was added. The mixture was extracted with EtOAc (100 mL×3). The combined organic layers was washed with brine (50 mL×3), dried over Na_2SO_4 and concentrated to give a white solid (940 mg). THF (15 mL) was added followed by PPh_3 (1.14 g, 4.34 mmol) and H_2O (3 mL) and the mixture was heated at reflux 10 h. After cooling to room temperature, the mixture was diluted with EtOAc (100 mL), and extracted with 0.2 N HCl (20 mL×2). The combined aqueous layers was washed with EtOAc (20 mL) before sat. Na_2CO_3 was added to adjust PH=9. The aqueous layer was extracted with CH_2Cl_2 (40 mL×5). The combined organic layers was washed with brine (20 mL), dried over Na_2SO_4 and concentrated to give a yellow solid (570 mg, 33%).

Preparation of
5-(aminomethyl)-2-bromonicotinonitrile

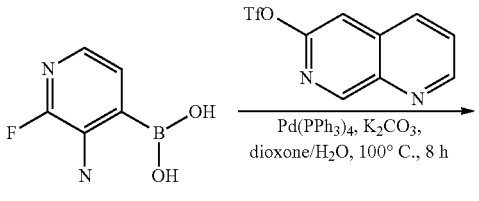
[0212]



[0213] To a solution of (6-chloro-5-fluoropyridin-3-yl) methanamine (570 mg, 2.69 mmol) in dioxane (15 mL) and H_2O (3 mL) was added 2-methyl-4-(4,4,5,5-tetramethyl-1, 3,2-dioxaborolan-2-yl)pyridine (1.43 g, 45%, 2.96 mmol), K_2CO_3 (1.12 g, 8.07 mmol) and $Pd(PPh_3)_4$ (310 mg, 0.27 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 8 h. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with H_2O (10 mL), and extracted with EtOAc (50 mL×6). The combined organic layers was dried over Na_2SO_4 and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:ethyl acetate=2: 1-1:1) to give the title compound (570 mg, 95%) as a gray solid.

Method A—Step c:
6-(2,3-difluoropyridin-4-yl)-1,7-naphthyridine

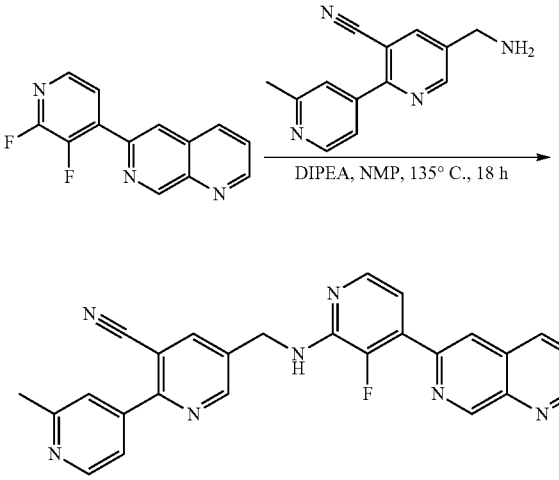
[0214]



[0215] To a solution of 2,3-difluoropyridin-4-ylboronic acid (105 mg, 0.66 mmol) and 1,7-naphthyridin-6-yl trifluoromethanesulfonate (167 mg, 0.6 mmol) in dioxane (4 mL) and H_2O (1 mL), was added $Pd(dppf)Cl_2$ (39 mg, 0.048 mmol), dppf (26 mg, 0.048 mmol) and K_3PO_4 (254 mg, 1.2 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 8 h. After cooling to room temperature, the mixture was concentrated and purified by silica gel column chromatography (petroleum ether:EtOAc=1:1) to give the title compound (80 mg, 47%) as a white solid.

Method A—Step d: 5-((3-fluoro-4-(1,7-naphthyridin-6-yl)pyridin-2-ylamino)methyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile

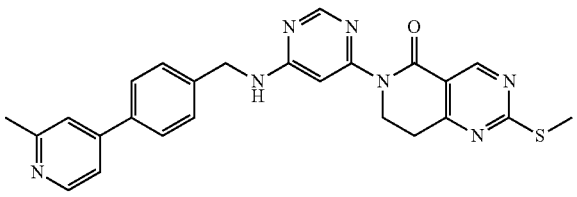
[0216]



[0217] To a solution of 5-(aminomethyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile (89 mg, 0.4 mmol) and N,N-diisopropylethylamine (206 mg, 1.6 mmol) in NMP (1 mL), was added 6-(2,3-difluoropyridin-4-yl)-1,7-naphthyridine (49 mg, 0.2 mmol). The mixture was stirred at 135° C. under N_2 atmosphere for 18 h. After cooling to room temperature, the mixture was diluted with H_2O (10 mL), and extracted with EtOAc (20 mL×3). The combined organic layers was washed with brine (10 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=50:1) to give the title compound (42 mg, 48%) as a yellow solid.

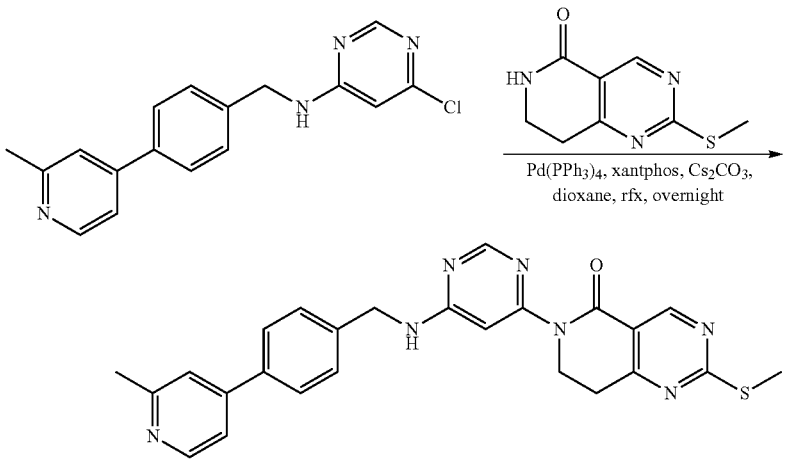
Example 10: Preparation of 6-(6-(4-(2-methylpyridin-4-yl)benzylamino)pyrimidin-4-yl)-2-(methylthio)-7,8-dihydropyrido[4,3-d]pyrimidin-5(6H)-one (A-137)

[0218]



Method A—Step b: 6-(6-(4-(2-methylpyridin-4-yl) benzylamino)pyrimidin-4-yl)-2-(methylthio)-7,8-dihydropyrido[4,3-d]pyrimidin-5 (6H)-one

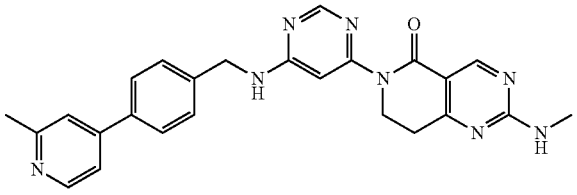
[0219]



[0220] To a solution of 6-chloro-N-(4-(2-methylpyridin-4-yl)benzyl)pyrimidin-4-amine (400 mg, 1.29 mmol) and 2-(methylthio)-7,8-dihydropyrido[4,3-d]pyrimidin-5(6H)-one (305 mg, 1.55 mmol) in dioxane (10 mL) was added $Pd(PPh_3)_4$ (60 mg, 0.05 mmol), Xantphos (60 mg, 0.11 mmol) and Cs_2CO_3 (1.0 g, 3.23 mmol). The mixture was stirred at reflux overnight. After cooling to room temperature, the mixture was diluted with EtOAc (20 mL), and washed with H_2O (6 mL×3). The organic layer was dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=1:2) to give the title compound (180 mg, 31%) as a white solid.

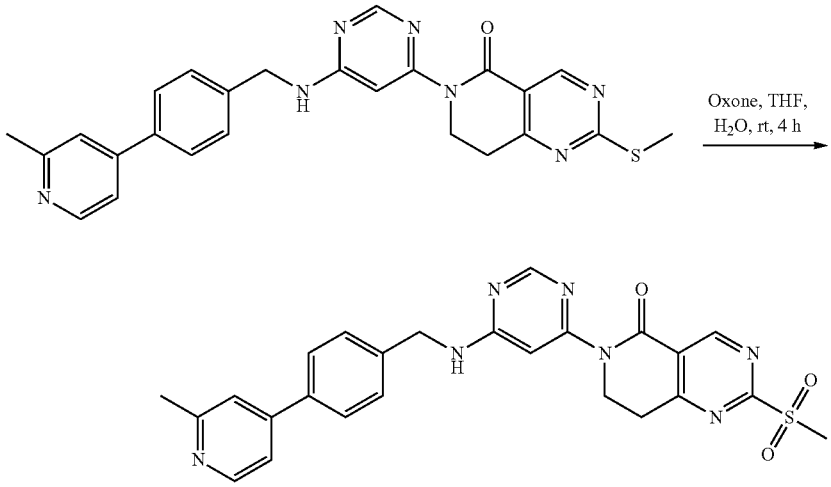
Example 11: Preparation of 2-(methylamino)-6-(6-(4-(2-methylpyridin-4-yl)benzylamino)pyrimidin-4-yl)-7,8-dihydropyrido[4,3-d]pyrimidin-5(6H)-one (A-138)

[0221]



Preparation of 6-(6-(4-(2-methylpyridin-4-yl)benzylamino)pyrimidin-4-yl)-2-(methylthio)-7,8-dihydropyrido[4,3-d]pyrimidin-5 (6H)-one

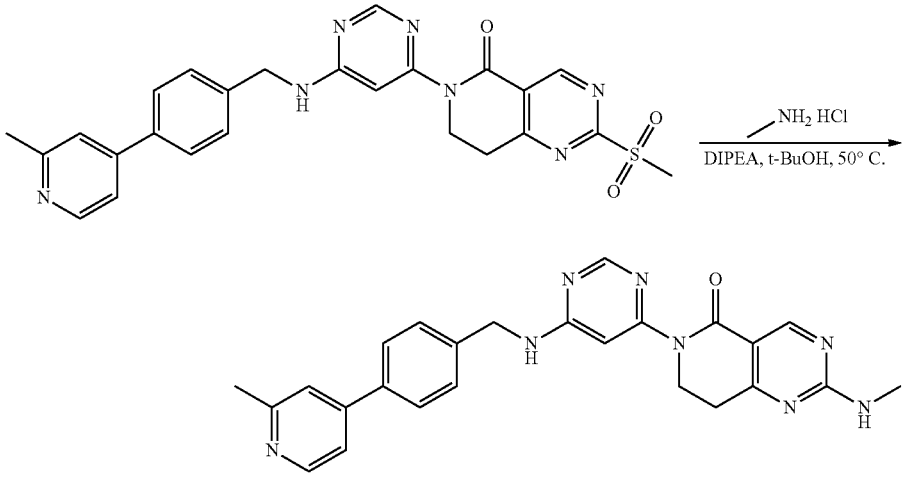
[0222]



[0223] To a solution of 6-(6-(4-(2-methylpyridin-4-yl) benzylamino)pyrimidin-4-yl)-2-(methylthio)-7,8-dihydropyrido[4,3-d]pyrimidin-5(6H)-one (50 mg, 0.11 mmol) in THF (3 mL) and H_2O (1 mL) was added oxone (69 mg, 0.22 mmol), and the mixture was stirred at room temperature for 4 h. After concentration, the title compound (120 mg, crude) was obtained as a yellow solid, which was used directly in the next step without further purification.

Preparation of 2-(methylamino)-6-(6-(4-(2-methylpyridin-4-yl)benzylamino)pyrimidin-4-yl)-7,8-dihydropyrido[4,3-d]pyrimidin-5(6H)-one

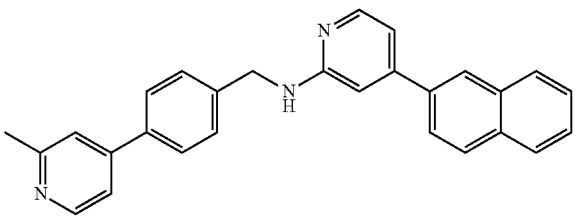
[0224]



[0225] A mixture of 6-(6-(4-(2-methylpyridin-4-yl)benzylamino)pyrimidin-4-yl)-2-(methylthio)-7,8-dihydropyrido [4,3-d]pyrimidin-5(6H)-one (50 mg, 0.1 mmol), methanamine hydrochloride (68 mg, 1.0 mmol), and N,N-diisopropylethylamine (194 mg, 1.5 mmol) in t-BuOH (3 mL) was stirred at 120° C. overnight. After cooling to room temperature, the mixture was diluted with EtOAc (40 mL) and washed with H_2O (8 mL×3). The organic layer was dried over Na_2SO_4 and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2: MeOH=60:1) to give the title compound (31 mg, 68%) as a white solid.

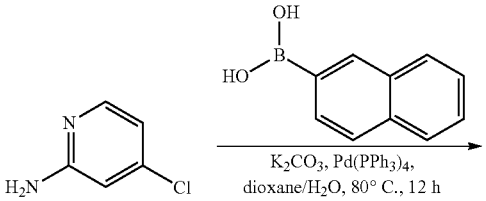
Example 12: Preparation of N-(4-(2-methylpyridin-4-yl)benzyl)-4-(naphthalen-2-yl)pyridin-2-amine (A-163)

[0226]

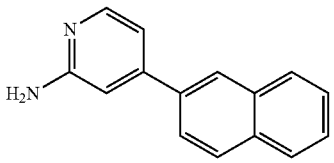


Method B—Step e: 4-(naphthalen-2-yl)pyridin-2-amine

[0227]



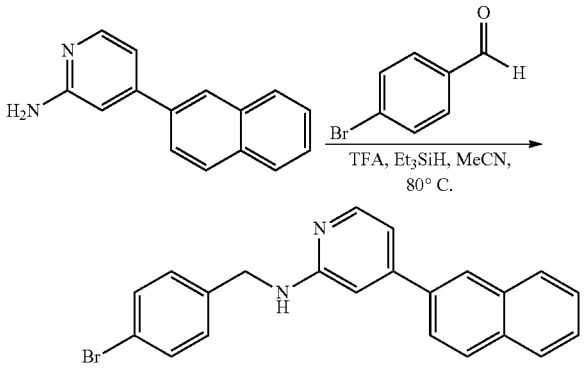
-continued



[0228] To a solution of naphthalen-2-ylboronic acid (206 mg, 1.20 mmol) and 4-chloropyridin-2-amine (128 mg, 1.00 mmol) in dioxane (16 mL) and H_2O (4 mL), was added $Pd(PPh_3)_4$ (115 mg, 0.10 mmol) and K_2CO_3 (276 mg, 2.00 mmol). The mixture was stirred at 80° C. under N_2 atmosphere for 12 h. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with EtOAc (40 mL), washed with brine (20 mL), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2: MeOH=100:3) to give the title compound (120 mg, 55%) as a yellow solid.

Method B—Step f: N-(4-bromobenzyl)-4-(naphthalen-2-yl)pyridin-2-amine

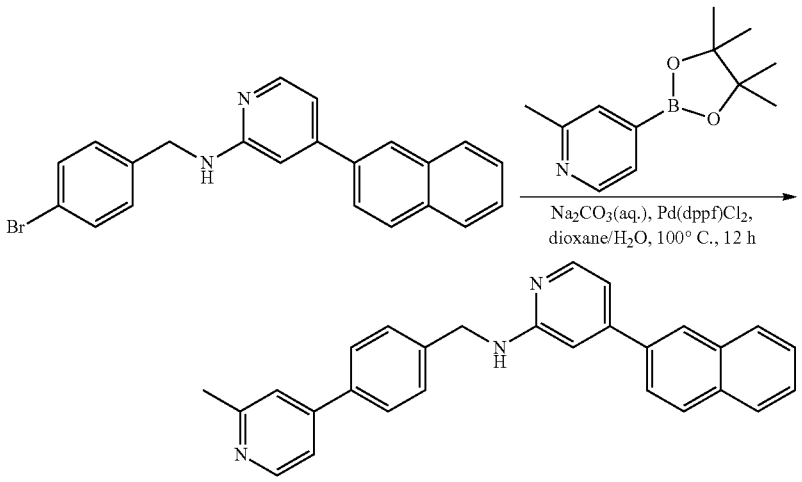
[0229]



[0230] To a solution of 4-(naphthalen-2-yl)pyridin-2-amine (110 mg, 0.50 mmol) and 4-bromobenzaldehyde (95 mg, 0.50 mmol) in MeCN (10 mL), was added trifluoroacetic acid (574 mg, 5.00 mmol) and triethylsilane (580 mg, 5.00 mmol). The mixture was stirred at 80° C. for 12 h. After cooling to room temperature, the mixture was diluted with EtOAc (40 mL), washed with sat. $NaHCO_3$ (10 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=5:1) to give the title compound (80 mg, 41%) as a yellow solid.

Method B—Step g: N-(4-(2-methylpyridin-4-yl)benzyl)-4-(naphthalen-2-yl)pyridin-2-amine

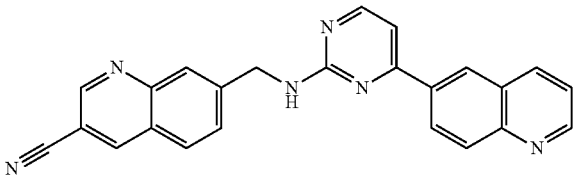
[0231]



[0232] To a solution of N-(4-bromobenzyl)-4-(naphthalen-2-yl)pyridin-2-amine (130 mg, 0.33 mmol) and 2-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) pyridine (27%, 406 mg, 0.50 mmol) in dioxane (20 mL), was added IM aqueous Na_2CO_3 (1 mL) and $Pd(dppf)Cl_2$ (28 mg, 0.034 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 12 h. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with EtOAc (40 mL), washed with brine (10 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2: MeOH=100:3) to give the title compound (50 mg, 37%) as a yellow solid.

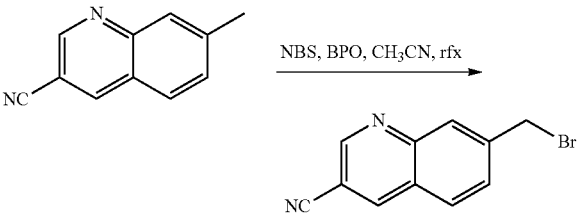
Example 13: Preparation of 7-((4-(quinolin-6-yl)pyrimidin-2-ylamino)methyl)quinoline-3-carbonitrile (A-179)

[0233]



Preparation of 7-(bromomethyl)quinoline-3-carbonitrile

[0234]

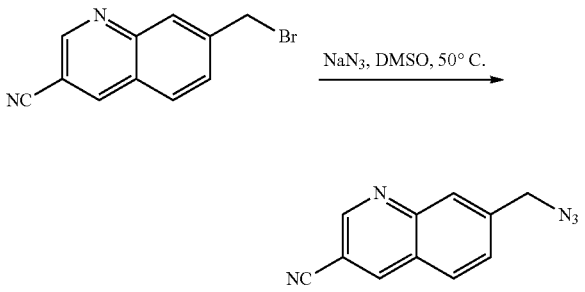


[0235] To a solution of 7-methylquinoline-3-carbonitrile (1.5 g, 8.9 mmol) in MeCN (50 mL) was added NBS (2.1 g, 11.8 mmol) and BPO (216 mg, 0.9 mmol). The mixture was heated at reflux overnight. After cooling to room temperature, H_2O (100 mL) and EtOAc (100 mL) was added. The aqueous layer was extracted with EtOAc (40 mL×3). The combined organic layers was dried over Na_2SO_4, and con-

centrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:petroleum ether=3:2) to give the title compound (743 g, 34%) as a white solid.

Preparation of
7-(azidomethyl)quinoline-3-carbonitrile

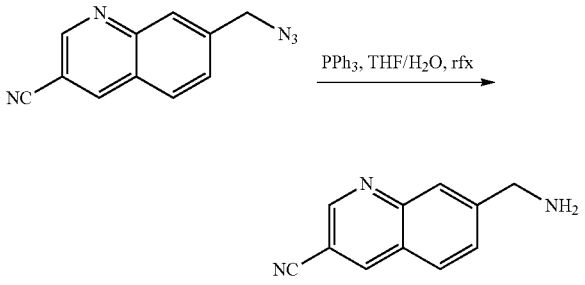
[0236]



[0237] To a solution of 7-(bromomethyl)quinoline-3-carbonitrile (743 mg, 3 mmol) in DMSO (15 mL), was added NaN_3 (293 mg, 4.5 mmol). The mixture was stirred at 50° C. for 1 h. After cooling to room temperature, H_2O (75 mL) and EtOAc (75 mL) was added. The organic layer was dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether: EtOAc=10:1-5:1) to give the title compound (392 mg, 62%) as a white solid.

Preparation of
7-(aminomethyl)quinoline-3-carbonitrile

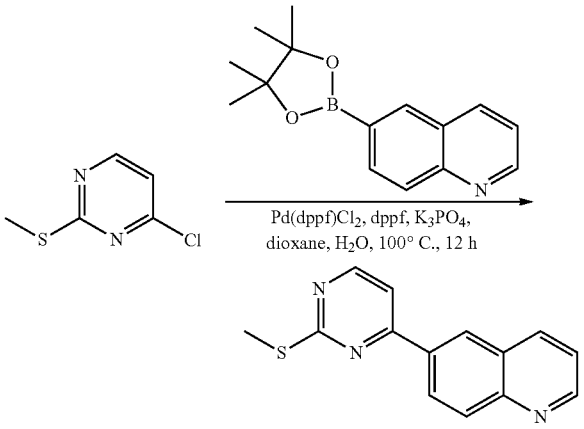
[0238]



[0239] To a solution of 7-(azidomethyl)quinoline-3-carbonitrile (392 mg, 1.87 mmol) in THF (10 mL) was added PPh_3 (541 mg, 2.1 mmol). The mixture was heated at reflux for 5 min before H_2O (1 mL) was added. The mixture was heated at reflux for another 1 h. After cooling to room temperature, the mixture was diluted with EtOAc (100 mL), and extracted with 1 N HCl (100 mL). To the aqueous layer was added NH_4OH to adjust PH=8. The mixture was extracted with EtOAc (100 mL). The organic layer was dried over Na_2SO_4 and concentrated to give the title compound (340 mg, 99%) as a pale yellow solid.

Method A—Step c:
6-(2-(methylthio)pyrimidin-4-yl)quinoline

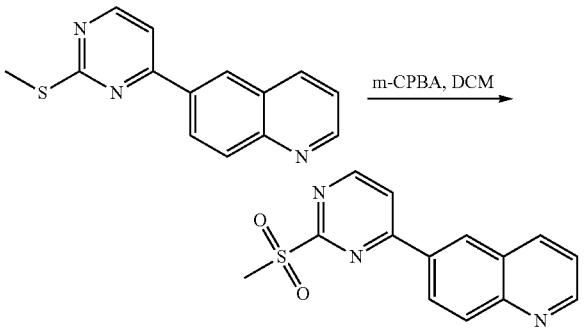
[0240]



[0241] To a solution of 4-chloro-2-(methy thio)pyrimidine (1.6 g, 0 mmol) and 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (3.06 g, 12 mmol) in dioxane (50 mL) and H_2O (12.5 mL), was added $Pd(dppf)Cl_2$ (653 mg, 0.80 mmol), dppf (443 mg, 0.80 mmol) and K_3PO_4 (4.24 g, 20 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 12 h. After cooling to room temperature, the mixture was concentrated and purified by silica gel column chromatography (CH_2Cl_2:MeOH=25:1) to give the title compound (2.0 g, 80%) as a yellow solid.

Preparation of
6-(2-(methylsulfonyl)pyrimidin-4-yl)quinoline

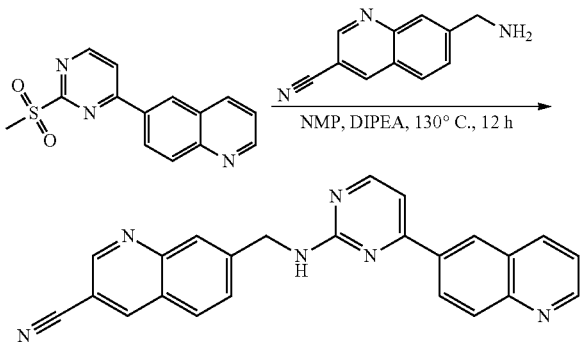
[0242]



[0243] To a solution of 6-(2-(methylthio)pyrimidin-4-yl) quinoline (1.24 g, 4.9 mmol) in CH_2Cl_2 (50 mL) was added m-CPBA (1.79 g, 85%, 8.82 mmol). The mixture was stirred at room temperature for 2 h and sat. $Na_2S_2O_3$ (15 mL) and sat. $NaHCO_3$ (15 mL) was added to quench the reaction. The mixture was extracted with CH_2Cl_2 (100 mL×3), dried over Na_2SO_4, and concentrated to give the title compound (1.1 g, 78%) as a yellow solid.

Method A—Step d: N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)-4-(quinolin-6-yl)pyrimidin-2-amine

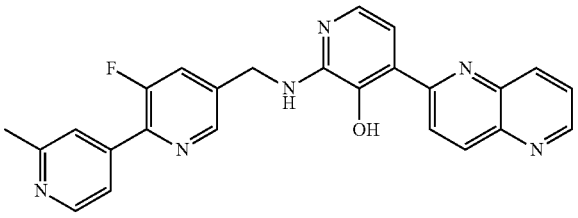
[0244]



[0245] To a solution of 7-(aminomethyl)quinoline-3-carbonitrile (39 mg, 0.21 mmol) in NMP (1.5 mL) was added 6-(2-(methylsulfonyl)pyrimidin-4-yl)quinoline (50 mg, 0.18 mmol) and N,N-diisopropylethylamine (190 mg, 1.4 mmol). The mixture was stirred at 130° C. overnight. After cooling to room temperature, the mixture was diluted with H_2O (50 mL) and EtOAc (50 mL). The aqueous layer was separated and extracted with EtOAc (30 mL×3). The combined organic layers was dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=100:1-20:1) to give the title compound (25 mg, 36%) as a yellow solid.

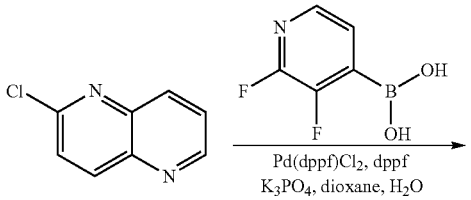
Example 14: Preparation of 2-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methylamino)-4-(1,5-naphthyridin-2-yl)pyridin-3-ol (A-176)

[0246]

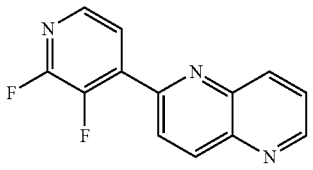


Method A—Step c: 2-(2,3-difluoropyridin-4-yl)-1,5-naphthyridine

[0247]



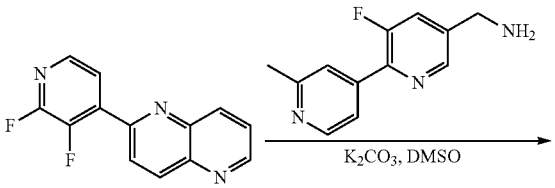
-continued

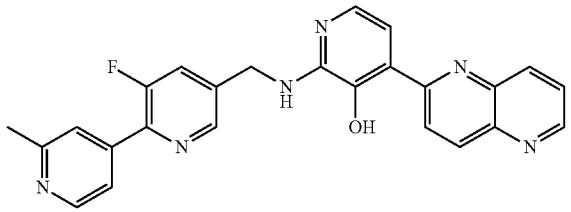


[0248] To a solution of 2,3-difluoropyridin-4-ylboronic acid mg, 1.1 mmol) and 2-chloro-1,5-naphthyridine (164 mg, 1.0 mmol) in dioxane (4 mL) and H_2O (1 mL), was added $Pd(dppf)Cl_2$ (65 mg, 0.08 mmol), dppf (44 mg, 0.08 mmol) and K_3PO_4 (424 mg, 2.0 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 12 h. After cooling to room temperature, the mixture was concentrated and purified by silica gel column chromatography (petroleum ether:EtOAc=1:1) to give the title compound (130 mg, 53%) as a white solid.

Method G—Step r: 2-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methylamino)-4-(1,5-naphthyridin-2-yl)pyridin-3-ol

[0249]

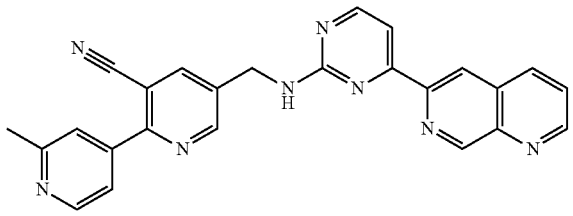




[0250] To a solution of 2-(2,3-difluoropyridin-4-yl)-1,5-naphthyridine (70 mg, 0.29 mmol) in DMSO (2 mL) was added (3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methanamine (93 mg, 0.43 mmol) and K_2CO_3 (80 mg, 0.58 mmol). The mixture was stirred at 135° C. for 18 h. After cooling to room temperature, the mixture was diluted with H_2O (30 mL), and extracted with EtOAc (30 mL×3). The combined organic layers was washed with brine (30 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=30:1) to give the title compound (10 mg, 8%) as a yellow solid.

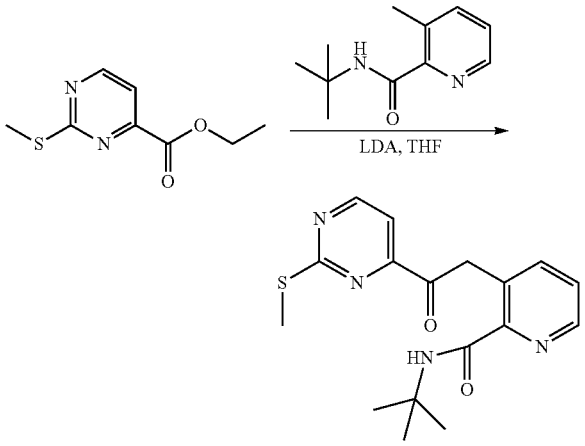
Example 15: Preparation of 5-((4-(1,7-naphthyridin-6-yl)pyrimidin-2-ylamino)methyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile (A-183)

[0251]



Method F—Step 1: N-tert-butyl-3-(2-(2-(methylthio)pyrimidin-4-yl)-2-oxoethyl)picolinamide

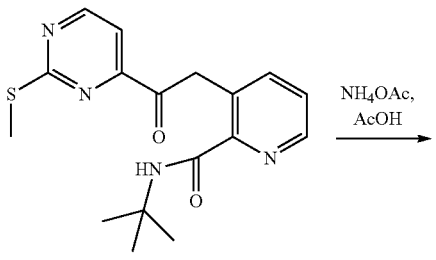
[0252]



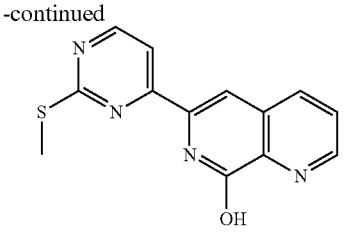
[0253] To a stirred solution of N-(tert-butyl)-3-methylpicolinamide (2.0 g, 10 mmol) in anhydrous tetrahydrofuran (100 mL) at −40° C., was added lithium diisopropylamide (2 M in THF, 12.5 mL, 25 mmol) dropwise. The mixture was stirred at this temperature for 30 min and then cooled to −60° C. Ethyl 2-(methylthio)pyrimidine-4-carboxylate (2.0 g, 10 mmol) in anhydrous THF (10 mL) was added and the reaction mixture was stirred at −60° C. for another 1 h. The reaction was quenched with sat. NH_4Cl (50 mL) and extracted with ethyl acetate (80 mL×3). The combined organic layers dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:ethyl acetate=5:1) to give the title compound (1.2 g, 35%) as a yellow solid.

Method F—Step m: 6-(2-(methylthio)pyrimidin-4-yl)-1,7-naphthyridin-8-ol

[0254]



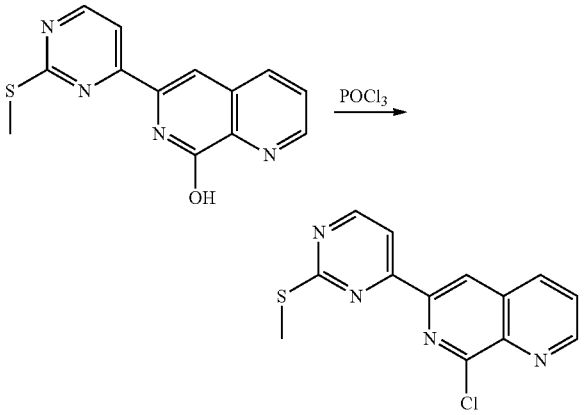
-continued



[0255] A mixture of N-tert-butyl-3-(2-(2-(methylthio)pyrimidin-4-yl)-2-oxoethyl)picolinamide (500 mg, 1.45 mmol) and NH_4OAc (1.11 g, 14.5 mmol) in HOAc (10 mL) was heated to 108° C. for 8 h. After concentration, the resulting residue was dissolved in ethyl acetate (30 mL) and washed with sat. $NaHCO_3$ (5 mL). The organic layer was dried over Na_2SO_4 and concentrated to give the title compound (350 mg, 89%) as a yellow solid without further purification.

Method F—Step n: 8-chloro-6-(2-(methylthio)pyrimidin-4-yl)-1,7-naphthyridine

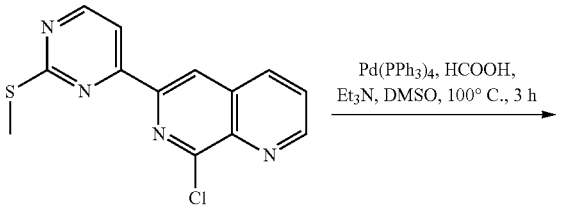
[0256]



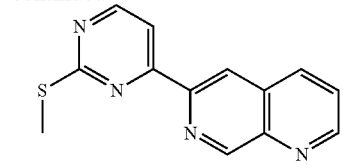
[0257] A solution of 6-(2-(methylthio)pyrimidin-4-yl)-1,7-naphthyridin-8-ol (350 mg, 1.3 mmol) in $POCl_3$ (6 mL) was heated to 100° C. for 1 h. After concentration, the residue was dissolved in ethyl acetate (20 mL) and washed with sat. $NaHCO_3$ (5 mL). The organic layer was dried over Na_2SO_4 and concentrated. The resulting residue was purified by column chromatography (petroleum ether:ethyl acetate=5:1) to give the title compound (350 mg, 93%) as a pale yellow solid.

Method F—Step o: 6-(2-(methylthio)pyrimidin-4-yl)-1,7-naphthyridine

[0258]



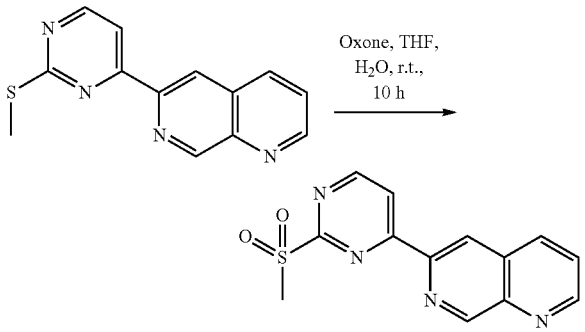
-continued



[0259] A mixture of 8-chloro-6-(2-(methylthio)pyrimidin-4-yl)-1,7-naphthyridine (350 mg, 1.2 mmol), triethylamine (924 mg, 9.15 mmol), formic acid (253 mg, 5.50 mmol) and $Pd(PPh_3)_4$ (138 mg, 0.12 mmol) in DMSO (5 mL) was stirred at 100° C. under N_2 atmosphere for 3 h. After cooling to room temperature, the mixture was diluted with ethyl acetate (40 mL) and filtered. The filtrate was washed with brine (10 mL×3), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (petroleum ether:ethyl acetate=5:1) to give the title compound (180 mg, 59%) as a pale yellow solid.

Method F—Step p: 6-(2-(methylsulfonyl)pyrimidin-4-yl)-1,7-naphthyridine

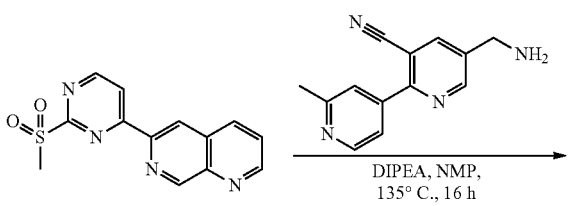
[0260]



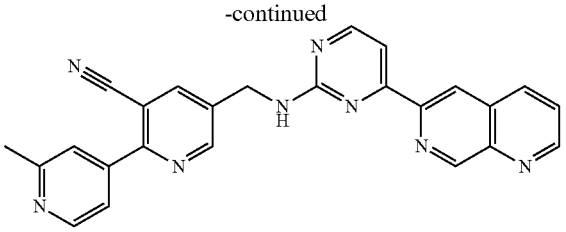
[0261] To a solution of 6-(2-(methylthio)pyrimidin-4-yl)-1,7-naphthyridine (180 mg, 0.71 mmol) in THF (5 mL) and H_2O (0.5 mL) was added oxone (497 mg, 1.56 mmol), and the mixture was stirred at room temperature for 10 h. After concentration, the title compound (680 mg, crude) was obtained as a yellow solid, which was used directly in the next step without further purification.

Method F—Step q: 5-((4-(1,7-naphthyridin-6-yl) pyrimidin-2-ylamino)methyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile

[0262]



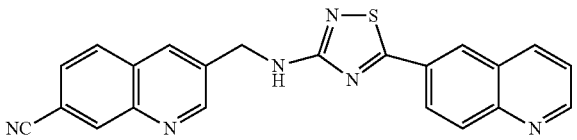
-continued



[0263] To a solution of 5-(aminomethyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile (68 mg, 0.3 mmol) and N,N-diisopropylethylamine (194 mg, 1.5 mmol) in NMP (1 mL), was added 6-(2-(methylsulfonyl)pyrimidin-4-yl)-1,7-naphthyridine (140 mg, 30%, 0.15 mmol). The mixture was stirred at 135° C. under N_2 atmosphere for 16 h. After cooling to room temperature, the mixture was diluted with H_2O (10 mL), and extracted with EtOAc (20 mL×3). The combined organic layers was washed with brine (10 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=50:1) to give the title compound (12 mg, 19%) as a pale yellow solid.

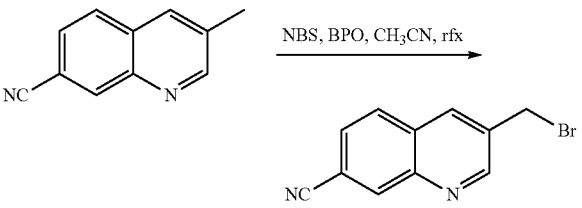
Example 16: Preparation of 3-((5-(quinolin-6-yl)-1,2,4-thiadiazol-3-ylamino)methyl)quinoline-7-carbonitrile (A-199)

[0264]



Preparation of 3-(bromomethyl)quinoline-7-carbonitrile

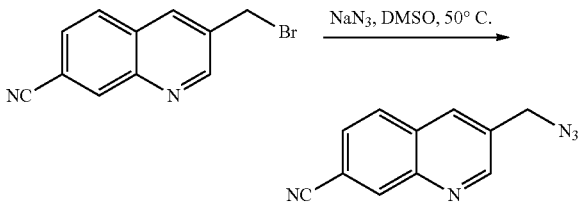
[0265]



[0266] To a solution of 3-methylquinoline-7-carbonitrile (1.5 g, 8.9 mmol) in MeCN (80 mL) was added NBS (1.9 g, 10.7 mmol) and BPO (216 mg, 0.9 mmol). The mixture was heated at reflux overnight. After cooling to room temperature, H_2O (100 mL) and EtOAc (100 mL) was added. The aqueous layer was extracted with EtOAc (40 mL×3). The combined organic layers was dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:petroleum ether=8:1) to give the title compound (1.0 g, 45%) as a pale yellow solid.

Preparation of
3-(azidomethyl)quinoline-7-carbonitrile

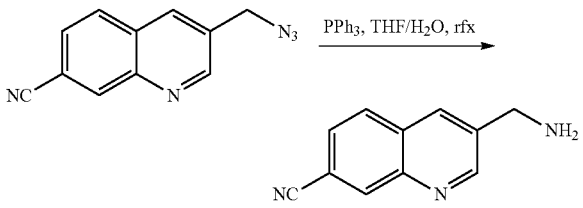
[0267]



[0268] To a solution of 3-(bromomethyl)quinoline-7-carbonitrile (1 g, 4.1 mmol) in DMSO (20 mL), was added NaN_3 (395 mg, 6.2 mmol). The mixture was stirred at 50° C. for 1 h. After cooling to room temperature, H_2O (100 mL) and EtOAc (100 mL) was added. The aqueous layer was extracted with EtOAc (40 mL×3). The combined organic layers was dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=10:1-5:1) to give the title compound (800 mg, 93%) as a yellow solid.

Preparation of
3-(aminomethyl)quinoline-7-carbonitrile

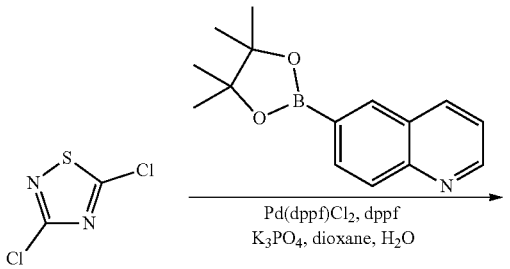
[0269]



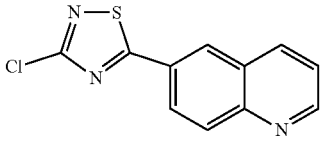
[0270] To a solution of 3-(azidomethyl)quinoline-7-carbonitrile (800 mg, 3.8 mmol) in THF (20 mL) was added PPh_3 (1.1 g, 4.2 mmol). The mixture was heated at reflux for 5 min before H_2O (2 mL) was added. The mixture was heated at reflux for another 1 h. After cooling to room temperature, the mixture was diluted with EtOAc (100 mL), and extracted with 1 N HCl (100 mL). To the aqueous layer was added NH_4OH to adjust PH=8. The mixture was extracted with EtOAc (30 mL×3). The combined organic layers was washed with brine (30 mL×3), dried over Na_2SO_4 and concentrated to give the title compound (400 mg, 56%) as a pale yellow solid.

Method A—Step c:
3-chloro-5-(quinolin-6-yl)-1,2,4-thiadiazole

[0271]



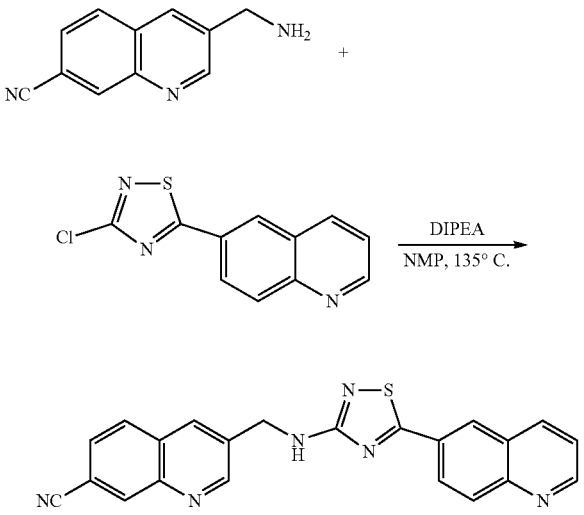
-continued



[0272] To a solution of 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinoline (280 mg, 1.1 mmol) and 3,5-dichloro-1,2,4-thiadiazole (155 mg, 1.0 mmol) in dioxane (6 mL) and H_2O (1.5 mL), was added $Pd(dppf)Cl_2$ (65 mg, 0.08 mmol), dppf (44 mg, 0.08 mmol) and K_3PO_4 (420 mg, 2.0 mmol). The mixture was stirred at 100° C. under N_2 atmosphere for 12 h. After cooling to room temperature, the mixture was concentrated and purified by silica gel column chromatography (petroleum ether:EtOAc=3:1) to give the title compound (200 mg, 81%) as a gray solid. ^1H NMR (400 MHz, $CDCl_3$) δ 9.03 (d, J=3.2 Hz, 1H), 8.53 (s, 1H), 8.29 (d, J=8.0 Hz, 1H), 8.24 (d, J=8.8 Hz, 1H), 8.18 (d, J=8.8 Hz, 1H), 7.53 (dd, J=8.0, 4.0 Hz, 1H).

Method A—Step d: 3-((5-(quinolin-6-yl)-1,2,4-thiadiazol-3-ylamino)methyl)quinoline-7-carbonitrile

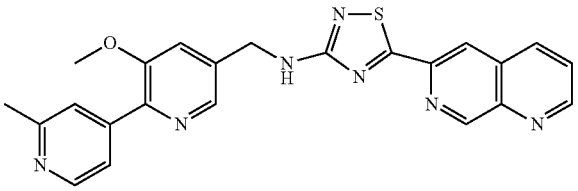
[0273]



[0274] To a solution of 3-(aminomethyl)quinoline-7-carbonitrile (59 mg, 0.32 mmol) in NMP (1.5 mL) was added 3-chloro-5-(quinolin-6-yl)-1,2,4-thiadiazole (40 mg, 0.16 mmol) and N,N-diisopropylethylamine (165 mg, 1.28 mmol). The mixture was stirred at 135° C. for 40 h. After cooling to room temperature, the mixture was diluted with H_2O (30 mL), and extracted with EtOAc (30 mL×3). The combined organic layers was washed with brine (30 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=30:1) to give the title compound (12 mg, 19%) as an orange solid.

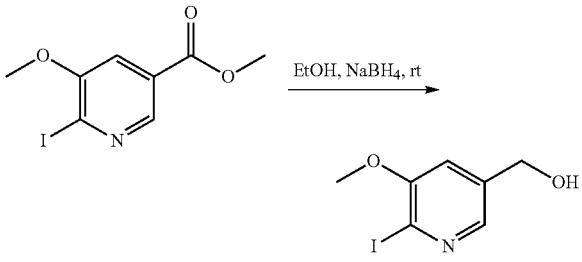
Example 17: Preparation of N-((3-methoxy-2'-methyl-2,4'-bipyridin-5-yl)methyl)-5-(1,7-naphthyridin-6-yl)-1,2,4-thiadiazol-3-amine (A-196)

[0275]



Preparation of 6-iodo-5-methoxypyridin-3-yl)methanol

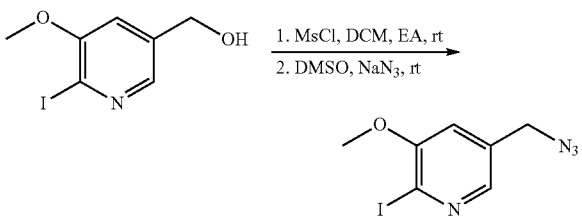
[0276]



[0277] To a suspension of $NaBH_4$ (1.65 g, 43.3 mmol) in EtOH (100 mL) at 0° C. was added a solution of methyl 6-iodo-5-methoxynicotinate (2.54 g, 8.67 mmol) in EtOH (30 mL) dropwise. The mixture was stirred at room temperature for 20 h. After concentration, H_2O (100 mL) was added and the mixture was extracted with CH_2Cl_2 (100 mL×3). The combined organic layers was dried over Na_2SO_4, and concentrated to give the title compound (2.0 g, 87%) as a colorless oil. ^{1}HNMR (400 MHz, $CDCl_3$) δ 8.18 (d, J=2.0 Hz, 1H), 8.13 (s, 1H), 7.94 (s, 1H), 7.09 (s, 1H), 4.71 (s, 2H), 3.92 (s, 3H).

Preparation of 5-(azidomethyl)-2-iodo-3-methoxypyridine

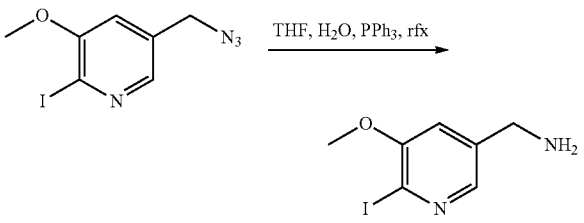
[0278]



[0279] To a solution of (6-iodo-5-methoxypyridin-3-yl) methanol (2.0 g, 7.55 mmol) and Et_3N (3.05 g, 30.2 mmol), was added MsCl (1.72 g, 15.1 mmol). The mixture was stirred at room temperature overnight and then washed with brine (50 mL×2). The combined organic layers was dried over Na_2SO_4, and concentrated. The resulting residue was dissolved in DMSO (40 mL), and NaN_3 (873 mg, 13.4 mmol) was added. After stirring at room temperature for 8 h, H_2O (50 mL) was added and the mixture was extracted with EtOAc (50 mL×3). The combined organic layers was washed with brine (100 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=10:1) to give the title compound (1.35 g, 61%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, J=1.6 Hz, 1H), 6.96 (d, J=1.6 Hz, 1H), 4.38 (s, 2H), 3.94 (s, 3H).

Preparation of (6-iodo-5-methoxypyridin-3-yl)methanamine

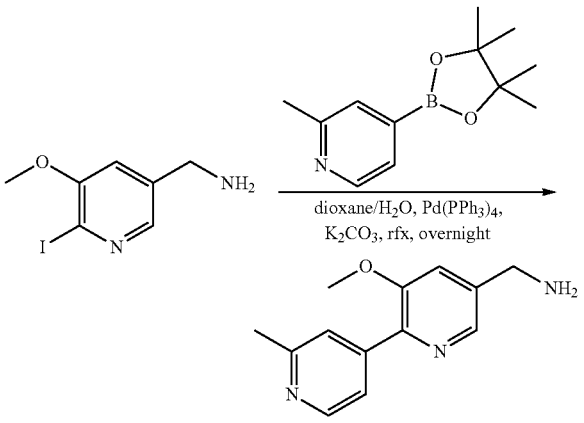
[0280]



[0281] To a solution of 5-(azidomethyl)-2-iodo-3-methoxypyridine (1.35 g, 4.66 mmol) in THF (20 mL) was added PPh_3 (1.14 g, 4.34 mmol). The mixture was heated at reflux and H_2O (3 mL) was added. The mixture was heated at reflux for 8 h. After cooling to room temperature, the mixture was diluted with EtOAc (40 mL), and extracted with 0.2 N HCl (50 mL). The aqueous layer was washed with EtOAc (50 mL) before NaOH was added to adjust PH=10. The aqueous layer was extracted with CH_2Cl_2 (50 mL×6). The combined organic layers was dried over Na_2SO_4 and concentrated to give the title compound (1.18 g, 96%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.07 (s, 1H), 3.92 (s, 3H), 3.89 (s, 2H).

Preparation of (3-methoxy-2'-methyl-2,4'-bipyridin-5-yl)methanamine

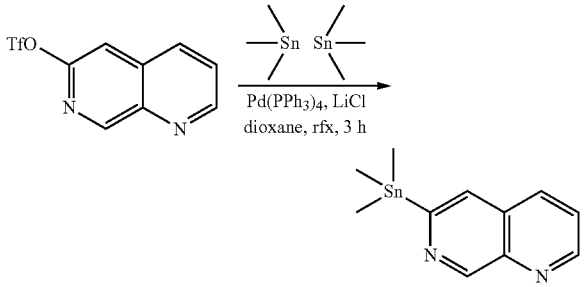
[0282]



[0283] To a solution of (6-iodo-5-methoxypyridin-3-yl) methanamine (1.12 g, 4.24 mmol) in dioxane (20 mL) and H_2O (4 mL) was added 2-methyl-4-(4,4,5,5-tetramethyl-1, 3,2-dioxaborolan-2-yl)pyridine (1.51 g, 50%, 5.52 mmol), K_2CO_3 (2.34 g, 17.0 mmol) and $Pd(PPh_3)_4$ (245 mg, 0.21 mmol). The mixture was stirred at reflux under N_2 atmosphere overnight. After cooling to room temperature, the mixture was filtered through Celite. The filtrate was diluted with EtOAc (100 mL). The organic layer was separated, dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2: MeOH=100:1-50:1) to give the title compound (730 mg, 75%) as a brown oil. ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J=5.2 Hz, 1H), 8.27 (s, 1H), 7.71 (s, 1H), 7.67 (d, J=5.2 Hz, 1H), 7.38 (s, 1H), 3.99 (s, 2H), 3.93 (s, 3H), 2.62 (s, 3H).

Preparation of 6-(trimethylstannyl)-1,7-naphthyridine

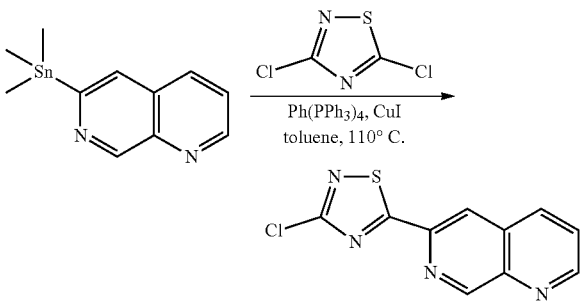
[0284]



[0285] A mixture of 1,7-naphthyridin-6-yl trifluoromethanesulfonate (1.3 g, 4.76 mmol), 1,1,1,2,2,2-hexamethyldistannane (2.3 g, 7.0 mmol), LiCl (590 mg, 14.0 mmol), and $Pd(PPh_3)_4$ (270 mg, 0.23 mmol) in dioxane (20 mL) was heated at reflux under N_2 atmosphere for 3 h. After cooling to room temperature, the mixture was concentrated. The residue was dissolved in EtOAc (30 mL) and washed with brine (30 mL). The organic layer was dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether: EtOAc=10:1) to give the title compound (600 mg, 43%) as an colorless oil.

Method A—Step c: 3-chloro-5-(1,7-naphthyridin-6-yl)-1,2,4-thiadiazole

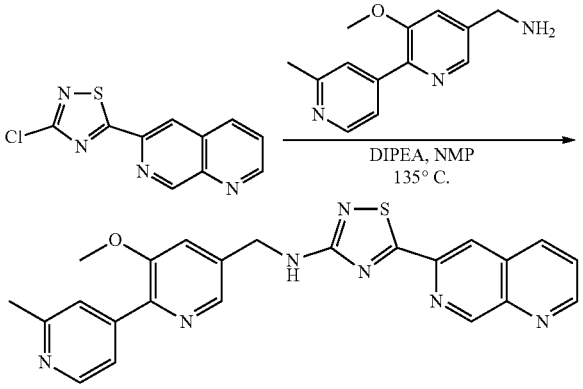
[0286]



[0287] To a solution of 6-(trimethylstannyl)-1,7-naphthyridine (29 mg, 0.1 mmol) and 3,5-dichloro-1,2,4-thiadiazole (21 mg, 0.17 mmol) in toluene (1 mL) was added $Pd(PPh_3)_4$ (12 mg, 0.01 mmol) and CuI (2 mg, 0.01 mmol). The mixture was stirred at 110° C. under N_2 atmosphere overnight. After cooling to room temperature, the mixture was concentrated and purified by silica gel column chromatography (CH_2Cl_2:MeOH=80:1) to give the title compound (17 mg, 70%) as a white solid. ^1H NMR (400 MHz, $CDCl_3$) δ 9.52 (s, 1H), 9.14 (d, J=3.6 Hz, 1H), 8.60 (s, 1H), 8.33 (d, J=8.4 Hz, 1H), 7.73 (dd, J=8.0, 4.0 Hz, 1H).

Method A—Step d: N-((3-methoxy-2'-methyl-2,4'-bipyridin-5-yl)methyl)-5-(1,7-naphthyridin-6-yl)-1, 2,4-thiadiazol-3-amine

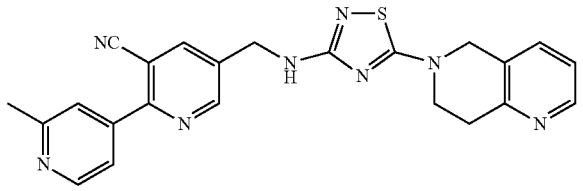
[0288]



[0289] To a solution of (3-methoxy-2'-methyl-2,4'-bipyridin-5-yl)methanamine (37 mg, 0.16 mmol) in NMP (1.5 mL) was added 3-chloro-5-(1,7-naphthyridin-6-yl)-1,2,4-thiadiazole (20 mg, 0.08 mmol) and N,N-diisopropylethylamine (83 mg, 0.64 mmol). The mixture was stirred at 135° C. for 40 h. After cooling to room temperature, the mixture was diluted with H_2O (30 mL), and extracted with EtOAc (30 mL×3). The combined organic layers was washed with brine (30 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (CH_2Cl_2:MeOH=30:1) to give the title compound (8 mg, 23%) as a pale yellow solid.

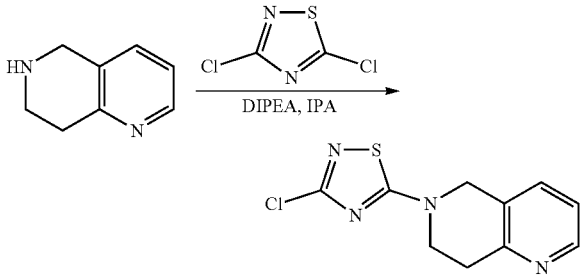
Example 18: Preparation of 5-((5-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-1,2,4-thiadiazol-3-ylamino) methyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile (A-198)

[0290]



Method A—Step c: 3-chloro-5-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-1,2,4-thiadiazole

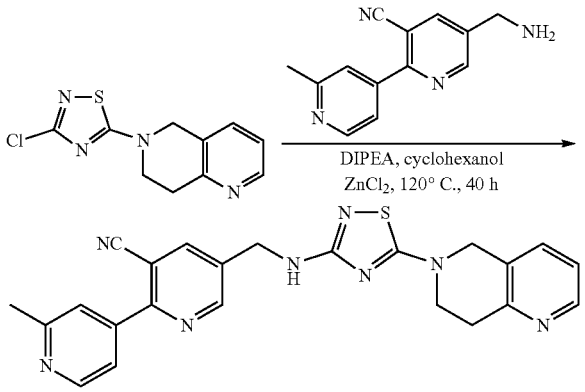
[0291]



[0292] To a solution of 3,5-dichloro-1,2,4-thiadiazole (155 mg, 1.0 mmol) in i-PrOH (10 mL) was added 5,6,7,8-tetrahydro-1,6-naphthyridine (134 mg, 1.0 mmol) and N,N-diisopropylethylamine (645 mg, 5.0 mmol), and the mixture was stirred at room temperature overnight. The mixture was diluted with H_2O (30 mL), and extracted with EtOAc (30 mL×3). The combined organic layers was washed with brine (30 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=2:1) to give the title compound (180 mg, 71%) as a gray solid.

Method A—Step d: 5-((5-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-1,2,4-thiadiazol-3-ylamino) methyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile

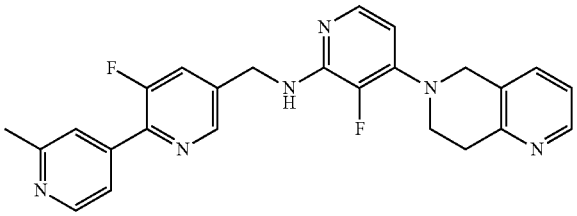
[0293]



[0294] To a solution of 5-(aminomethyl)-2'-methyl-2,4'-bipyridine-3-carbonitrile (185 mg, 0.83 mmol) and N,N-diisopropylethylamine (213 mg, 1.65 mmol) in cyclohexanol (3 mL) in sealed tube was added 3-chloro-5-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-1,2,4-thiadiazole (140 mg, 0.55 mmol) and $ZnCl_2$ (83 mg, 0.61 mmol). The mixture was stirred at 120° C. for 40 h. After cooling to room temperature, the mixture was purified by silica gel column chromatography (petroleum ether:EtOAc=5:1-CH_2Cl_2:MeOH=30:1) to give the title compound (12 mg, 5%) as a yellow solid.

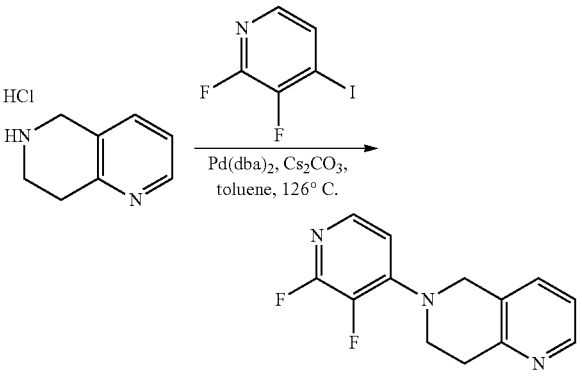
Example 19: Preparation of 4-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-3-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)pyridin-2-amine (A-202)

[0295]



Method A—Step c: 6-(2,3-difluoropyridin-4-yl)-5,6,7,8-tetrahydro-1,6-naphthyridine

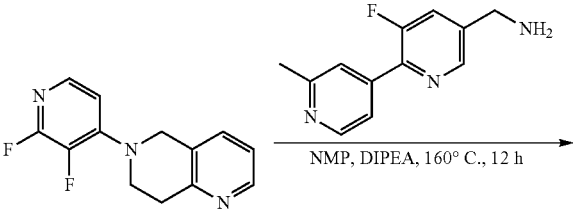
[0296]



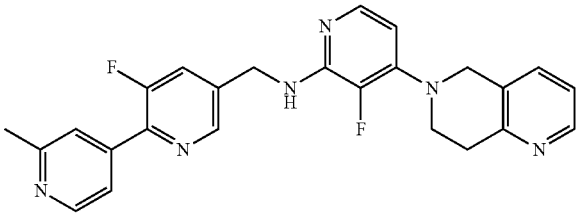
[0297] A mixture of 5,6,7,8-tetrahydro-1,6-naphthyridine hydrochloride (1.7 g, 10 mmol), 2,3-difluoro-4-iodopyridine (4.8 g, 20 mmol), Cs_2CO_3 (16.3 g, 50 mmol), $Pd_2(dba)_3$ (460 mg, 0.5 mmol) in toluene (20 mL) was heated at reflux under N_2 atmosphere for 12 h. After cooling to room temperature, the mixture was filtered through Celite and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=4:1-1:1) to give the title compound (2.3 g, 88%) as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, J=4.2 Hz, 1H), 7.72 (d, J=5.6 Hz, 1H), 7.45 (d, J=7.6 Hz, 1H), 7.17 (m, 1H), 6.69 (m, 1H), 4.57 (s, 2H), 3.81 (m, 2H), 3.18 (m, 2H).

Method A—Step d: 4-(7,8-dihydro-1,6-naphthyridin-6(5H)-yl)-3-fluoro-N-((3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methyl)pyridin-2-amine

[0298]



-continued



[0299] To a solution of 6-(2,3-difluoropyridin-4-yl)-5,6,7,8-tetrahydro-1,6-naphthyridine (50 mg, 0.21 mmol) and (3-fluoro-2'-methyl-2,4'-bipyridin-5-yl)methanamine (66 mg, 0.3 mmol) in NMP (1 mL), was added K_2CO_3 (131 mg, 1.0 mmol). The mixture was stirred at 160° C. for 12 h. After cooling to room temperature, the mixture was diluted with H_2O (5 mL), and extracted with EtOAc (10 mL×3). The combined organic layers was washed with brine (10 mL×3), dried over Na_2SO_4, and concentrated. The resulting residue was purified by silica gel column chromatography (petroleum ether:EtOAc=1:1-0:1) to give the title compound (4 mg, 5%) as a yellow solid.

[0300] Table 2 shows a selection of compounds prepared according to the methods discussed above in detail and indicated in the Third column of the table:

TABLE 2

Selected compounds (A-1 to A-202) of the present invention.

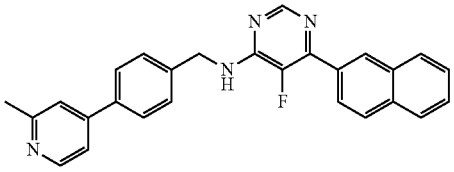
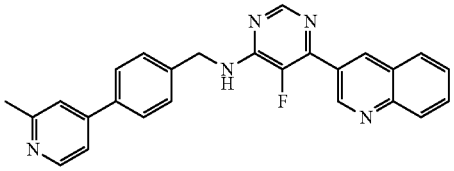
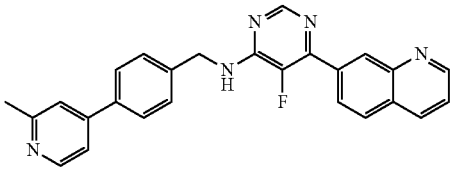
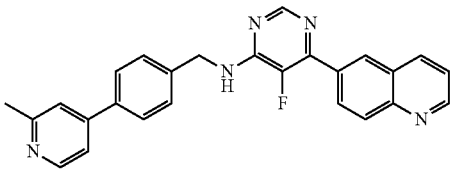
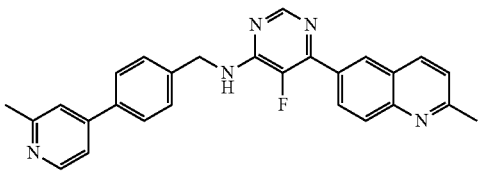
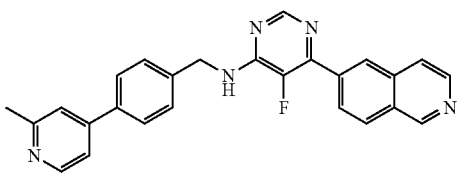
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-1		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 5.0 Hz, 3H), 8.13 (d, J = 8.8 Hz, 1H), 7.95 (d, J = 8.8 Hz, 2H), 7.89(d, J = 7.2 Hz, 1H), 7.64(d, J = 8.0 Hz, 2H), 7.58-7.51(m, 4H), 7.38(s, 1H), 7.32(d, J = 4.0 Hz, 1H), 5.59(s, 1H), 4.86(d, J = 6.0 Hz, 2H), 2.63(s, 3H).	421.0
A-2		A	^{1}HNMR(400 MHz, $CDCl_3$)δ9.55(s, 1H), 8.86(s, 1H), 8.57(d, J = 2.0 Hz, 1H), 8.55(d, J = 5.2 Hz, 1H), 8.17(d, J = 8.8 Hz, 1H), 7.95(d, J = 8.0 Hz, 1H), 7.80(t, J = 7.8 Hz, 1H), 7.66-7.60(m, 3H), 7.52(d, J = 8.4 Hz, 2H), 7.37(s, 1H), 7.31(d, J = 4.0 Hz, 1H), 5.68(s, 1H), 4.87(d, J = 6.0 Hz, 2H), 2.63(s, 3H).	422.0
A-3		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.99-8.98(m, 1H), 8.78(s, 1H), 8.59-8.51(m, 2H), 8.26(d, J = 8.4 Hz, 1H), 8.21(d, J = 8.4 Hz, 1H), 7.95(d, J = 8.4 Hz, 1H), 7.64(d, J = 8.4 Hz, 2H), 7.52(d, J = 8.4 Hz, 2H), 7.48-7.45(m, 1H), 7.37(s, 1H), 7.32(d, J = 4.8 Hz, 1H), 5.70(s, 1H), 4.86(d, J = 6.0 Hz, 2H), 2.63(s, 3H).	422.0
A-4		A	^{1}HNMR (400 MHz, $CDCl_3$)δ8.99-8.98(m, 1H), 8.55-8.54(m, 3H), 8.38(d, J = 9.2 Hz, 1H), 8.27(d, J = 8.0 Hz, 1H), 8.21(d, J = 8.8 Hz, 1H), 7.65(d, J = 8.0 Hz, 2H), 7.52(d, J = 8.0 Hz, 2H), 7.48-7.45(m, 1H), 7.37(s, 1H), 7.31(d, J = 5.2 Hz, 1H), 5.65(s, 1H), 4.87(d, J = 5.6 Hz, 2H), 2.63(s, 3H).	422.0
A-5		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.55-8.54(m, 2H), 8.51(s, 1H), 8.34(d, J = 9.2 Hz, 1H), 8.15(d, J = 8.8 Hz, 1H), 8.11(d, J = 8.8 Hz, 1H), 7.64(d, J = 8.0 Hz, 2H), 7.51(d, J = 7.6 Hz, 2H), 7.37(s, 1H), 7.34(d, J = 8.4 Hz, 1H), 7.31(d, J = 4.8 Hz, 1H), 5.62(s, 1H), 4.86(d, J = 6.0 Hz, 2H), 2.78(s, 3H), 2.63(s, 3H).	436.0
A-6		A	^{1}HNMR(400 MHz, $CDCl_3$)δ9.32(s, 1H), 8.60(d, J = 5.6 Hz, 1H), 8.57(d, J = 2.0 Hz, 1H), 8.55(d, J = 5.6 Hz, 1H), 8.52(s, 1H), 8.25(d, J = 8.4 Hz, 1H), 8.10(d, J = 8.8 Hz, 1H), 7.76(d, J = 5.6 Hz, 1H), 7.65(d, J = 8.0 Hz, 2H), 7.52(d, J = 8.0 Hz, 2H), 7.37(s, 1H), 7.32(d, J = 5.2 Hz, 1H), 5.65(s, 1H), 4.87(d, J = 6.0 Hz, 2H), 2.63(s, 3H).	422.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

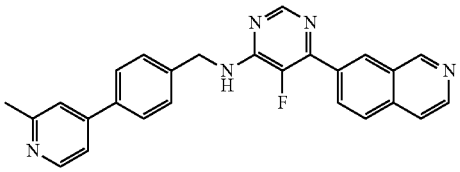
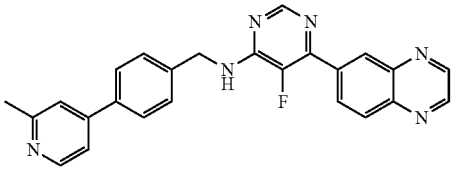
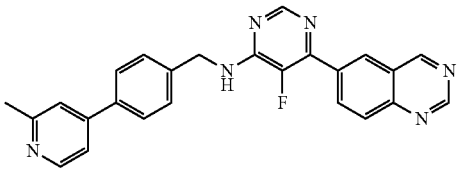
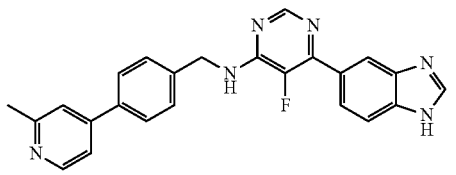
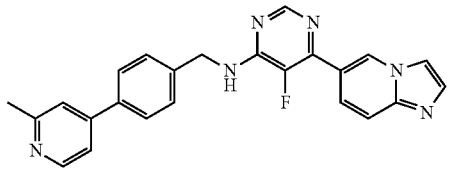
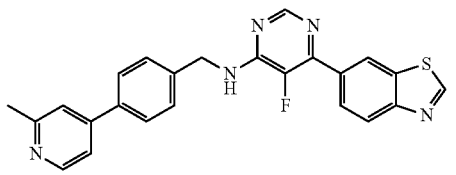
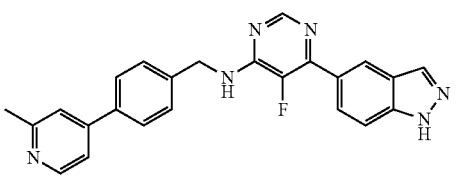
Compd NO.	Structure	Meth-od	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-7		A	^{1}HNMR(400 MHz, $CDCl_3$)δ9.37(s, 1H), 8.70(s, 1H), 8.60(d, J = 5.6 Hz, 1H), 8.56(s, 2H), 8.38(d, J = 8.8 Hz, 1H), 7.95(d, J = 8.4 Hz, 1H), 7.71(d, J = 5.6 Hz, 1H), 7.66(d, J = 8.0 Hz, 2H), 7.53(d, J = 8.0 Hz, 2H), 7.41(s, 1H), 7.36(d, J = 5.6 Hz, 1H), 5.64(s, 1H), 4.88(d, J = 6.0 Hz, 2H), 2.66(s, 3H).	422.0
A-8		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.91(d, J = 2.8 Hz, 2H), 8.79(s, 1H), 8.57(s, 1H), 8.55(d, J = 5.2 Hz, 1H), 8.49(d, J = 8.4 Hz, 1H), 8.23(d, J = 8.8 Hz, 1H), 7.65(d, J = 8.0 Hz, 2H), 7.52(d, J = 8.0 Hz, 2H), 7.37(s, 1H), 7.31(d, J = 4.8 Hz, 1H), 5.68(s, 1H), 4.87(d, J = 5.6 Hz, 2H), 2.63(s, 3H).	423.0
A-9		A	^{1}HNMR(400 MHz, $CDCl_3$)δ9.51(s, 1H), 9.40(s, 1H), 8.67(s, 1H), 8.62(d, J = 8.4 Hz, 1H), 8.56-8.54(m, 2H), 8.17(d, J = 8.4 Hz, 1H), 7.65(d, J = 8.0 Hz, 2H), 7.52(d, J = 8.0 Hz, 2H), 7.38(s, 1H), 7.32(d, J = 5.2 Hz, 1H), 5.69(s, 1H), 4.88(d, J = 5.6 Hz, 2H), 2.64(s, 3H).	423.0
A-10		A	^{1}HNMR(400 MHz, DMSO)δ8.49(d, J = 5.2 Hz, 1H), 8.42-8.34(m, 2H), 8.33(s, 1H), 8.23(s, 1H), 7.88(d, J = 9.2 Hz, 1H), 7.76(d, J = 8.4 Hz, 2H), 7.71(d, J = 8.4 Hz, 1H), 7.59(s, 1H), 7.50(d, J = 7.6 Hz, 3H), 4.71(d, J = 6.0 Hz, 2H), 2.53(s, 3H).	
A-11		A	^{1}HNMR(400 MHz, $CDCl_3$)δ9.00(s, 1H), 8.55(d, J = 4.8 Hz, 1H), 8.46(s, 1H), 7.97(s, 2H), 7.76(s, 1H), 7.69(s, 1H), 7.63(d, J = 7.6 Hz, 2H), 7.51(d, J = 8.0 Hz, 2H), 7.36(s, 1H), 7.31(d, J = 4.8 Hz, 1H), 5.77(s, 1H), 4.85(d, J = 5.6 Hz, 2H), 2.63(s, 3H).	411.0
A-12		A	^{1}HNMR(400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.70 (s, 1H), 8.55-8.52 (m, 2H), 8.27-8.17 (m, 2H), 7.64 (d, J = 8.4 Hz, 2H), 7.51(d, J = 8.0 Hz, 2H), 7.37(s, 1H), 7.31(d, J = 5.2 Hz, 1H), 5.63(s, 1H), 4.86(d, J = 5.6 Hz, 2H), 2.63(s, 3H).	427.9
A-13		A	^{1}HNMR(400 MHz, DMSO)δ13.28(s, 1H), 8.47(d, J = 5.2 Hz, 1H), 8.43(s, 1H), 8.39(t, J = 6.0 Hz, 1H), 8.33(d, J = 2.0 Hz, 1H), 8.22(s, 1H), 8.01(d, J = 9.2 Hz, 1H), 7.75(d, J = 8.0 Hz, 2H), 7.66(d, J = 8.8 Hz, 1H), 7.56(s, 1H), 7.50-7.47(m, 3H), 4.71(d, J = 6.0 Hz, 2H), 2.52(s, 3H).	411.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

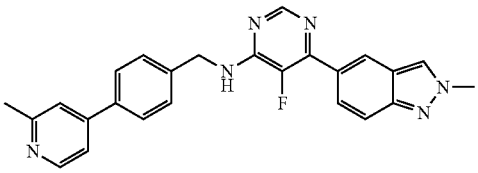
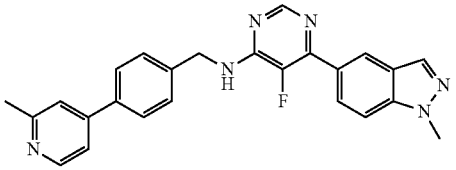
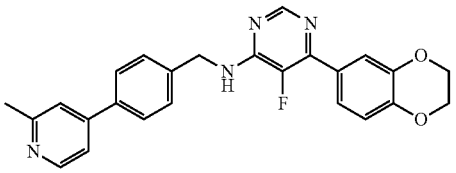
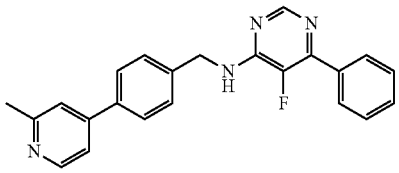
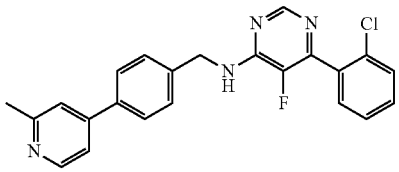
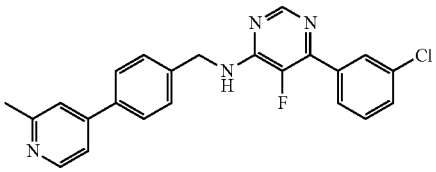
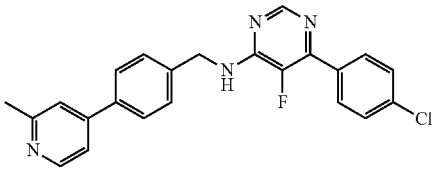
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-14		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.54(d, J = 5.2 Hz, 1H), 8.50(s, 1H), 8.40(s, 1H), 8.01(s, 1H), 7.96(d, J = 9.2 Hz, 1H), 7.78(d, J = 9.2 Hz, 1H), 7.63(d, J = 8.0 Hz, 2H), 7.50(d, J = 8.0 Hz, 2H), 7.36(s, 1H), 7.31(d, J = 5.2 Hz, 1H), 5.56(s, 1H), 4.84(d, J = 5.6 Hz, 2H), 4.25(s, 3H), 2.62(s, 3H).	425.0
A-15		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.55(d, J = 5.2 Hz, 1H), 8.51(d, J = 1.6 Hz, 1H), 8.46(s, 1H), 8.12(d, J = 9.2 Hz, 1H), 8.08(s, 1H), 7.64(d, J = 8.4 Hz, 2H), 7.54-7.47(m, 3H), 7.37(s, 1H), 7.31(d, J = 5.2 Hz, 1H), 5.57(s, 1H), 4.85(d, J = 6.0 Hz, 2H), 4.12(s, 3H), 2.63(s, 3H).	425.0
A-16		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.54(d, J = 4.8 Hz, 1H), 8.45(s, 1H), 7.63(d, J = 8.0 Hz, 3H), 7.58(d, J = 8.8 Hz, 1H), 7.49(d, J = 8.0 Hz, 2H), 7.37(s, 1H), 7.31(d, J = 5.2 Hz, 1H), 6.96(d, J = 8.8 Hz, 1H), 5.52(s, 1H), 4.82(d, J = 5.8 Hz, 2H), 4.31(d, J = 2.4 Hz, 4H), 2.62(s, 3H).	429.0
A-17		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.54(d, J = 5.2 Hz, 1H), 8.50(d, J = 1.6 Hz, 1H), 8.01(d, J = 7.6 Hz, 2H), 7.63(d, J = 8.0 Hz, 2H), 7.51-7.48(m, 5H), 7.36(s, 1H), 7.31(d, J = 4.8 Hz, 1H), 5.54(s, 1H), 4.84(d, J = 5.8 Hz, 2H), 2.62(s, 3H).	371.0
A-18		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.54(d, J = 5.2 Hz, 1H), 8.50(d, J = 1.6 Hz, 1H), 8.01(d, J = 7.6 Hz, 2H), 7.63(d, J = 8.4 Hz, 2H), 7.51-7.48(m, 4H), 7.36(s, 1H), 7.31(d, J = 5.2 Hz, 1H), 5.55(s, 1H), 4.84(d, J = 5.6 Hz, 2H), 2.63(s, 3H).	
A-19		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.54(d, J = 4.8 Hz, 1H), 8.49(d, J = 1.6 Hz, 1H), 8.04(s, 1H), 7.91(d, J = 7.2 Hz, 1H), 7.63(d, J = 8.0 Hz, 2H), 7.49(d, J = 8.0 Hz, 2H), 7.47-7.39(m, 2H), 7.36(s, 1H), 7.30(d, J = 5.2 Hz, 1H), 5.59(s, 1H), 4.83(d, J = 6.0 Hz, 2H), 2.62(s, 3H).	405.0
A-20		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.54(d, J = 5.2 Hz, 1H), 8.48(d, J = 1.6 Hz, 1H), 7.99(d, J = 8.0 Hz, 2H), 7.63(d, J = 8.0 Hz, 2H), 7.50-7.45(m, 4H), 7.36(s, 1H), 7.30(d, J = 4.4 Hz, 1H), 5.54(s, 1H), 4.83(d, J = 6.0 Hz, 2H), 2.62(s, 3H).	405.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

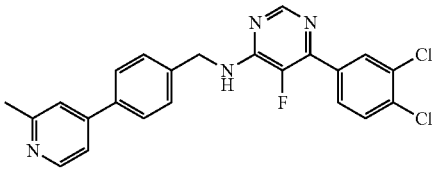
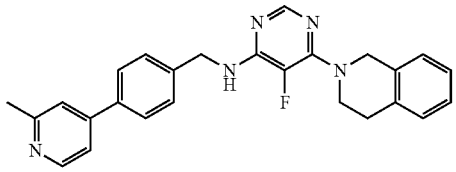
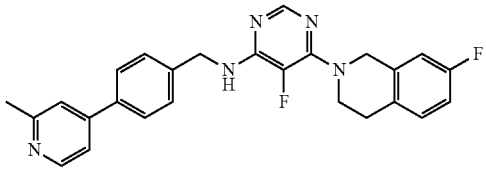
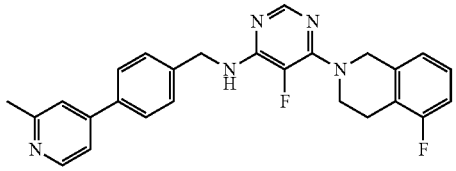
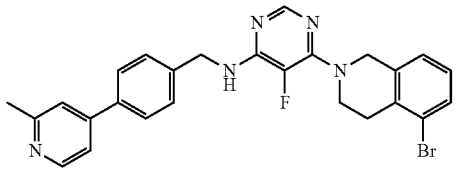
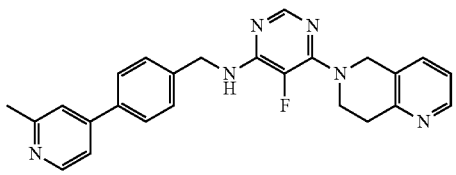
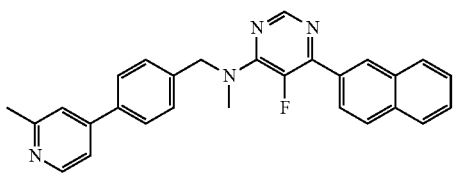
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-21		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.55(d, J = 4.8 Hz, 1H), 8.48(s, 1H), 8.18(s, 1H), 7.90(d, J = 8.4 Hz, 1H), 7.63(d, J = 8.4 Hz, 2H), 7.56(d, J = 8.4 Hz, 1H), 7.49(d, J = 8.0 Hz, 2H), 7.36(s, 1H), 7.30(d, J = 4.8 Hz, 1H), 5.58(s, 1H), 4.83(d, J = 5.6 Hz, 2H), 2.63(s, 3H).	438.9
A-22		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.53(d, J = 5.2 Hz, 1H), 8.06(s, 1H), 7.60(d, J = 8.0 Hz, 2H), 7.45(d, J = 8.0 Hz, 2H), 7.35(s, 1H), 7.29(d, J = 5.2 Hz, 1H), 7.22-7.12(m, 4H), 5.10(s, 1H), 4.85(s, 2H), 4.74(d, J = 6.0 Hz, 2H), 3.94(t, J = 5.8 Hz, 2H), 2.97(t, J = 5.8 Hz, 2H), 2.62(s, 3H).	
A-23		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.53(d, J = 4.8 Hz, 1H), 8.05(s, 1H), 7.60(d, J = 7.6 Hz, 2H), 7.45(d, J = 7.6 Hz, 2H), 7.35(s, 1H), 7.30(d, J = 4.8 Hz, 1H), 7.20-7.08(m, 1H), 6.91(m, 2H), 5.10(s, 1H), 4.85(s, 2H), 4.74(d, J = 8 Hz, 2H), 3.94(m, 2H), 2.93(m, 2H), 2.62(s, 3H).	444.0
A-24		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.53(d, J = 4.8 Hz, 1H), 8.04(s, 1H), 7.60(d, J = 8 Hz, 2H), 7.45(d, J = 8 Hz, 2H), 7.36(s, 1H), 7.31(d, J = 4.8 Hz, 1H), 7.12-7.07(m, 1H), 6.87(m, 2H), 5.09(s, 1H), 4.81(s, 2H), 4.74(d, J = 6 Hz, 2H), 3.92(m, 2H), 2.92(m, 2H), 2.62(s, 3H).	444.0
A-25		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.53(d, J = 4.8 Hz, 1H), 8.05(s, 1H), 7.60(d, J = 8.0 Hz, 2H), 7.45(d, J = 8.0 Hz, 3H), 7.36(s, 1H), 7.30(d, J = 4.8 Hz, 1H), 7.09(m, 2H), 5.09(s, 1H), 4.83(s, 2H), 4.74(d, J = 6 Hz, 2H), 3.95(m, 2H), 2.96(m, 2H), 2.62(s, 3H).	503.9
A-26		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.53(d, J = 5.2 Hz, 1H), 8.44(d, J = 4.4 Hz, 1H), 8.06(s, 1H), 7.60(d, J = 8.0 Hz, 2H), 7.46(d, J = 7.6 Hz, 3H), 7.36(s, 1H), 7.30(d, J = 5.2 Hz, 1H), 7.16-7.13(m, 1H), 5.13(s, 1H), 4.85(s, 2H), 4.75(d, J = 5.6 Hz, 2H), 4.03(t, J = 6.0 Hz, 2H), 3.14(t, J = 5.8 Hz, 2H), 2.62(s, 3H).	427.0
A-27		C	^{1}HNMR(400 MHz, $CDCl_3$)δ8.54-8.53(m, 2H), 8.48(s, 1H), 8.06(d, J = 8.4 Hz, 1H), 7.93(d, J = 8.4 Hz, 2H), 7.87(d, J = 7.6 Hz, 1H), 7.62(d, J = 8.0 Hz, 2H), 7.58-7.48(m, 2H), 7.43(d, J = 8.0 Hz, 2H), 7.36(s, 1H), 7.30(d, J = 4.8 Hz, 1H), 4.98(s, 2H), 3.32(d, J = 3.6 Hz, 3H), 2.62(s, 3H).	435.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

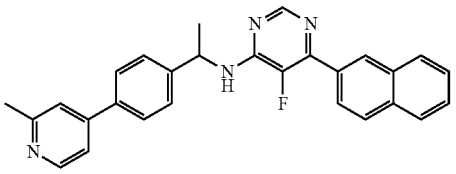
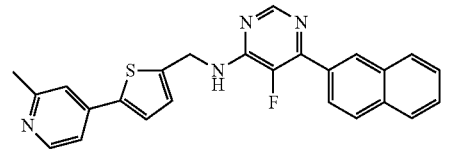
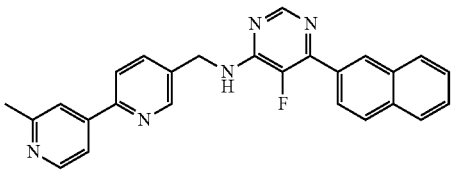
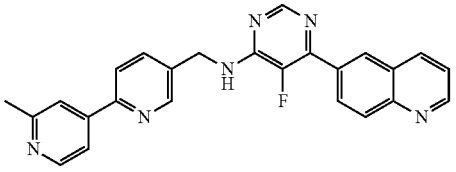
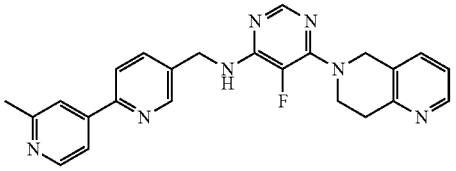
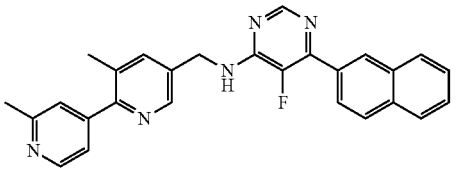
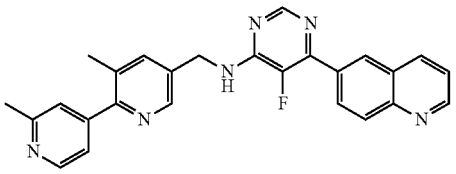
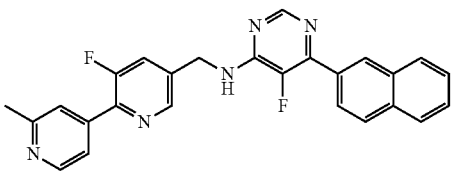
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-28		A	^{1}HNMR(400 MHz, DMSO)δ8.54(s, 1H), 8.48(d, J = 5.2 Hz, 1H), 8.37-8.28(m, 2H), 8.08-8.06(m, 3H), 7.98(d, J = 8.0 Hz, 1H), 7.75(d, J = 8.4 Hz, 2H), 7.64-7.55(m, 5H), 7.48(d, J = 5.2 Hz, 1H), 5.46-5.39(m, 1H), 2.52(s, 3H), 1.59(d, J = 6.8 Hz, 3H).	435.0
A-29		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.59(s, 1H), 8.55(s, 1H), 8.46(d, J = 5.2 Hz, 1H), 8.12(d, J = 8.8 Hz, 1H), 7.95(d, J = 8.8 Hz, 2H), 7.88(d, J = 8.0 Hz, 1H), 7.59-7.50(m, 2H), 7.36(d, J = 3.6 Hz, 1H), 7.30(s, 1H), 7.25(d, J = 3.6 Hz, 1H), 7.10(d, J = 3.6 Hz, 1H), 5.63(s, 1H), 4.98(d, J = 6.0 Hz, 2H), 2.58(s, 3H).	427.0
A-30		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.79(s, 1H), 8.60(d, J = 5.2 Hz, 1H), 8.55(s, 2H), 8.12(d, J = 8.4 Hz, 1H), 7.95(d, J = 8.8 Hz, 2H), 7.89-7.86(m, 2H), 7.82-7.76(m, 2H), 7.66(d, J = 4.8 Hz, 1H), 7.58-7.51(m, 2H), 5.69(s, 1H), 4.88(d, J = 6.0 Hz, 2H), 2.65(s, 3H).	422.0
A-31		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.99-8.98(m, 1H), 8.80(d, J = 1.6 Hz, 1H), 8.61(d, J = 5.2 Hz, 1H), 8.55(d, J = 1.6 Hz, 2H), 8.37(d, J = 8.8 Hz, 1H), 8.28(d, J = 7.6 Hz, 1H), 8.21(d, J = 8.8 Hz, 1H), 7.90-7.87(m, 1H), 7.80(d, J = 8.0 Hz, 2H), 7.66(d, J = 4.4 Hz, 1H), 7.49-7.46(m, 1H), 5.73(s, 1H), 4.89(d, J = 6.0 Hz, 2H), 2.65(s, 3H).	
A-32		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.72(s, 1H), 8.59(d, J = 5.2 Hz, 1H), 8.44(d, J = 4.4 Hz, 1H), 8.04(s, 1H), 7.84-7.71(m, 3H), 7.65(d, J = 5.2 Hz, 1H), 7.46(d, J = 7.6 Hz, 1H), 7.16-7.13(m, 1H), 5.19(s, 1H), 4.85(s, 2H), 4.78(d, J = 6.0 Hz, 2H), 4.03(t, J = 5.8 Hz, 2H), 3.14(t, J = 5.6 Hz, 2H), 2.65(s, 3H).	428.0
A-33		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.60-8.58(m, 2H), 8.56(s, 2H), 8.13(d, J = 8.4 Hz, 1H), 7.96(d, J = 8.0 Hz, 2H), 7.89(d, J = 7.6 Hz, 1H), 7.67(s, 1H), 7.59-7.50(m, 2H), 7.34(s, 1H), 7.24(d, J = 8.4 Hz, 1H), 5.63(s, 1H), 4.85(d, J = 5.6 Hz, 2H), 2.63(s, 3H), 2.38(s, 3H).	436.0
A-34		A	^{1}HNMR (400 MHz, $CDCl_3$) δ 8.99(d, J = 3.6 Hz, 1H), 8.63-8.57(m, 2H), 8.56(s, 2H), 8.38(d, J = 8.8 Hz, 1H), 8.28(d, J = 8.4 Hz, 1H), 8.22(d, J = 9.2 Hz, 1H), 7.68(s, 1H), 7.49-7.46(m, 1H), 7.33(s, 1H), 7.25(d, J = 5.2 Hz, 1H), 5.69(s, 1H), 4.86(d, J = 6.0 Hz, 2H), 2.63(s, 3H), 2.39(s, 3H).	437.0
A-35		A	^{1}HNMR (400 MHz, $CDCl_3$) δ 8.61(s, 2H), 8.58-8.52 (m, 2H), 8.12 (d, J = 8.4 Hz, 1H), 7.96(d, J = 8.4 Hz, 2H), 7.89(d, J = 7.2 Hz, 1H), 7.77(s, 1H), 7.69(s, 1H), 7.61(d, J = 11.2 Hz, 1H), 7.59-7.51(m, 2H), 5.73(s, 1H), 4.90(d, J = 6.0 Hz, 2H), 2.65(s, 3H).	440.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

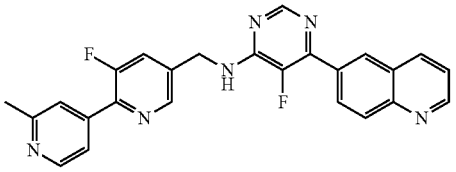
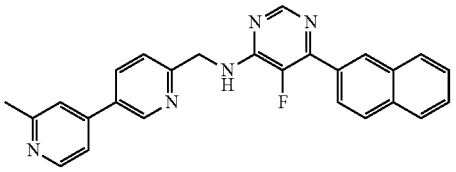
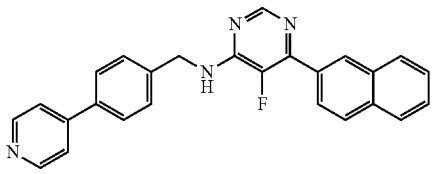
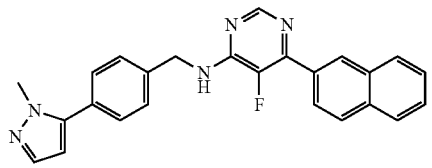
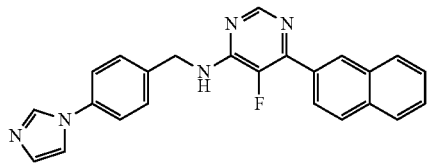
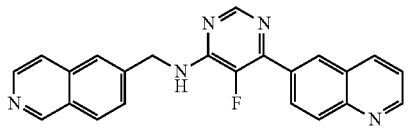
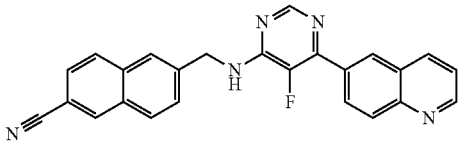
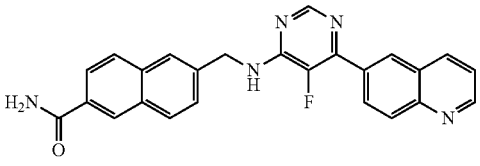
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-36		A	^{1}HNMR(400 MHz, DMSO)δ8.98(d, J = 4.0 Hz, 1H), 8.63(d, J = 4.4 Hz, 2H), 8.58-8.53(m, 3H), 8.42(s, 1H), 8.33(d, J = 8.8 Hz, 1H), 8.15(d, J = 8.8 Hz, 1H), 7.87(d, J = 12.4 Hz, 1H), 7.74(s, 1H), 7.67(d, J = 5.2 Hz, 1H), 7.63-7.60(m, 1H), 4.79(d, J = 6.0 Hz, 2H), 2.55(s, 3H).	
A-37		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.87(s, 1H), 8.61(d, J = 5.2 Hz, 1H), 8.58(s, 1H), 8.54(s, 1H), 8.15(d, J = 8.8 Hz, 1H), 7.97-7.93(m, 3H), 7.89(d, J = 7.6 Hz, 1H), 7.59-7.51(m, 2H), 7.49(d, J = 8.4 Hz, 1H), 7.38(s, 1H), 7.33(d, J = 5.2 Hz, 1H), 6.60(s, 1H), 4.95(d, J = 5.2 Hz, 2H), 2.66(s, 3H).	422.0
A-38		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.68(brs, 2H), 8.55(s, 2H), 8.13(d, J = 8.8 Hz, 1H), 7.95(d, J = 8.8 Hz, 2H), 7.88(d, J = 7.2 Hz, 1H), 7.66(d, J = 8.4 Hz, 2H), 7.57-7.53(m, 6H), 5.63(s, 1H), 4.87(d, J = 5.6 Hz, 2H).	407.0
A-39		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.55(s, 2H), 8.13(d, J = 8.8 Hz, 1H), 7.95(d, J = 8.4 Hz, 2H), 7.88(d, J = 7.2 Hz, 1H), 7.59-7.46(m, 5H), 7.43(d, J = 8.0 Hz, 2H), 6.31(s, 1H), 5.60(s, 1H), 4.86(d, J = 6.0 Hz, 2H), 3.90(s, 3H).	410.0
A-40		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.55(s, 1H), 8.54(s, 1H), 8.12(d, J = 8.8 Hz, 1H), 7.95(d, J = 8.4 Hz, 2H), 7.89(d, J = 7.6 Hz, 1H), 7.86(s, 1H), 7.56-7.52(m, 4H), 7.40(d, J = 8.0 Hz, 2H), 7.29(s, 1H), 7.22(s, 1H), 5.64(s, 1H), 4.85(d, J = 6.0 Hz, 2H).	396.0
A-41		A	^{1}HNMR(400 MHz, $CDCl_3$)δ9.26(s, 1H), 8.99(d, J = 4.0 Hz, 1H), 8.57-8.54(m, 3H), 8.39(d, J = 8.8 Hz, 1H), 8.28(d, J = 8.4 Hz, 1H), 8.22(d, J = 8.8 Hz, 1H), 8.00(d, J = 8.4 Hz, 1H), 7.82(s, 1H), 7.65(d, J = 6.8 Hz, 2H), 7.49-7.46(m, 1H), 5.77(s, 1H), 5.02(d, J = 6.0 Hz, 2H).	382.0
A-42		A	^{1}HNMR(400 MHz, $CDCl_3$)δ8.99(d, J = 4.4 Hz, 1H), 8.67-8.59(m, 2H), 8.58-8.53(m, 2H), 8.39(s, 1H), 8.34(d, J = 8.8 Hz, 1H), 8.16(d, J = 8.8 Hz, 1H), 8.10(d, J = 8.8 Hz, 1H), 8.05(d, J = 8.8 Hz, 1H), 7.98(s, 1H), 7.77(d, J = 8.4 Hz, 1H), 7.72(d, J = 8.4 Hz, 1H), 7.62(dd, J = 8.4, 4.4 Hz, 1H), 4.89(d, J = 6.0 Hz, 2H).	
A-43		D	^{1}HNMR(400 MHz, $CDCl_3$)δ8.96(d, J = 2.8 Hz, 1H), 8.63-8.55(m, 2H), 8.53(d, J = 8.4 Hz, 1H), 8.43(s, 1H), 8.37(s, 1H), 8.32(d, J = 8.8 Hz, 1H), 8.18-8.12(m, 2H), 7.98(d, J = 8.4 Hz, 1H), 7.97-7.91(m, 2H), 7.89(s, 1H), 7.65-7.58(m, 1H), 7.42(s, 1H), 4.86(d, J = 6.0 Hz, 2H).	424.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

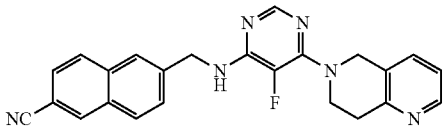
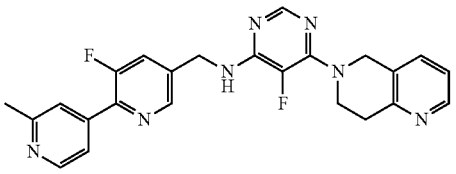
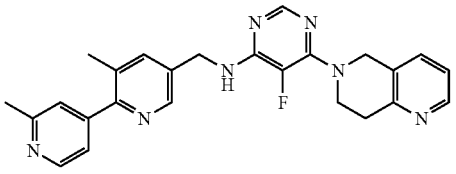
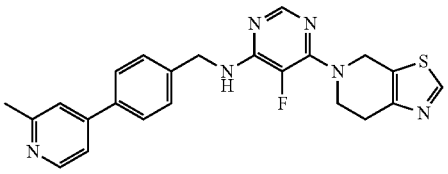
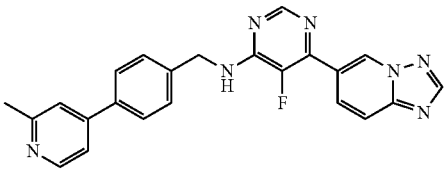
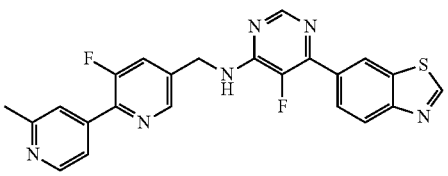
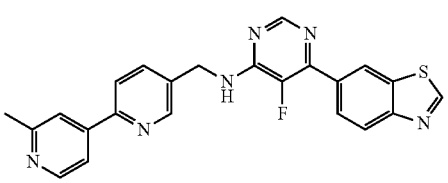
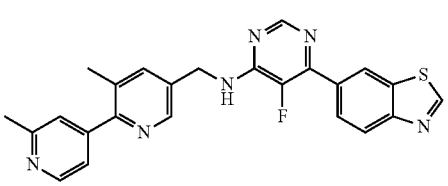
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-44		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 3.6 Hz, 1H), 8.22 (s, 1H), 8.05 (s, 1H), 7.88 (d, J = 8.4 Hz, 2H), 7.82 (s, 1H), 7.60 (m, 2H), 7.47 (d, J = 7.6 Hz, 1H), 7.20 (m, 1H), 5.24 (s, 1H), 4.91 (d, J = 6.0 Hz, 2H), 4.87 (s, 2H), 4.05 (m, 2H), 3.15 (m, 2H).	
A-45		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.53 (s, 1H), 8.44 (s, 1H), 8.02 (s, 1H), 7.75 (s, 1H), 7.67 (s, 1H), 7.54 (d, J = 11.6 Hz, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.14 (s, 1H), 5.27 (s, 1H), 4.85 (s, 2H), 4.79 (d, J = 5.6 Hz, 2H), 4.03 (d, J = 5.6 Hz, 2H), 3.14 (s, 2H), 2.88 (s, 1H), 2.64 (s, 3H).	
A-46		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 2H), 8.45 (s, 1H), 8.05 (s, 1H), 7.61 (s, 1H), 7.46 (d, J = 7.6 Hz, 1H), 7.33 (s, 1H), 7.24 (s, 1H), 7.15 (s, 1H), 5.24 (s, 1H), 4.86 (s, 2H), 4.74 (d, J = 5.6 Hz, 2H), 4.04 (t, J = 5.2 Hz, 2H), 3.14 (s, 2H), 2.62 (s, 3H), 2.35 (s, 3H).	
A-47		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.53 (d, J = 5.2 Hz, 1H), 8.04 (s, 1H), 7.60 (d, J = 7.8 Hz, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.36 (s, 1H), 7.30 (d, J = 4.8 Hz, 1H), 5.13 (s, 1H), 4.94 (s, 2H), 4.75 (d, J = 5.6 Hz, 2H), 4.02 (d, J = 5.2 Hz, 2H), 3.07 (s, 2H), 2.62 (s, 3H).	433.0
A-48		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 (s, 1H), 8.53 (d, J = 15.6 Hz, 2H), 8.42 (s, 1H), 8.33 (d, J = 9.4 Hz, 1H), 7.86 (d, J = 9.4 Hz, 1H), 7.64 (d, J = 6.4 Hz, 2H), 7.51 (d, J = 7.6 Hz, 2H), 7.37 (s, 1H), 7.31 (s, 1H), 5.67 (s, 1H), 4.86 (s, 2H), 2.63 (s, 3H).	451.0
A-49		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 1H), 8.70 (s, 1H), 8.62 (d, J = 5.2 Hz, 2H), 8.52 (s, 1H), 8.22 (m 2H), 7.77 (s, 1H), 7.69 (d, J = 4.8 Hz, 1H), 7.61 (d, J = 11.2 Hz, 1H), 5.74 (s, 1H), 4.90 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	
A-50		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.79 (s, 1H), 8.70 (s, 1H), 8.60 (d, J = 5.2 Hz, 1H), 8.52 (s, 1H), 8.22 (m, 2H), 7.90 (m, 1H), 7.79 (d, J = 7.8 Hz, 2H), 7.66 (d, J = 4.8 Hz, 1H), 5.69 (s, 1H), 4.88 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	
A-51		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.70 (s, 1H), 8.59 (d, J = 5.6 Hz, 2H), 8.53 (s, 1H), 8.22 (q, J = 8.4 Hz, 2H), 7.67 (s, 1H), 7.33 (s, 1H), 7.23 (s, 1H), 5.64 (s, 1H), 4.85 (d, J = 5.6 Hz, 2H), 2.63 (s, 3H), 2.38 (s, 3H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

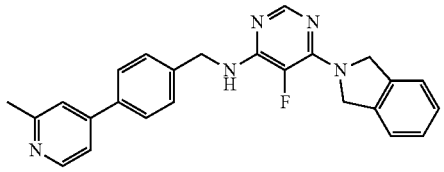
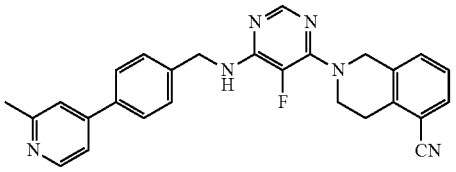
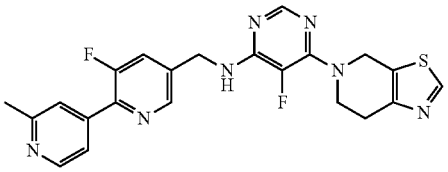
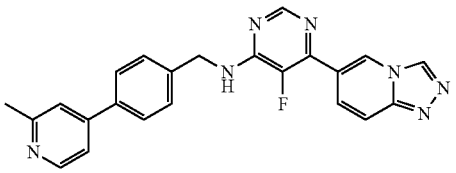
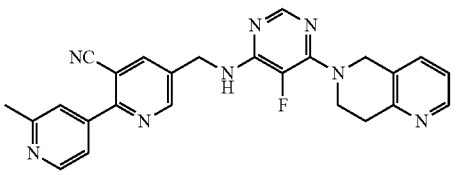
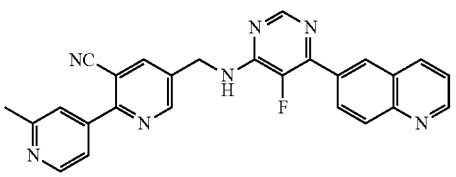
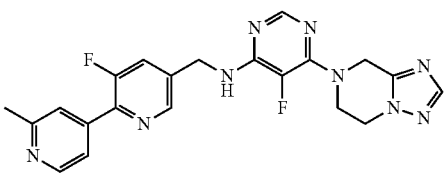
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-52		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.08 (s, 1H), 7.61 (d, J = 7.9 Hz, 2H), 7.48 (d, J = 8 Hz, 2H), 7.36 (s, 1H), 7.31 (s, 5H), 5.03 (d, J = 2.4 Hz, 5H), 4.85 (m, 1H), 4.77 (d, J = 6 Hz, 2H), 4.60 (m, 1H), 2.62 (s, 3H).	412.0
A-53		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.05 (s, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 7.6 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.40 (m, 2H), 7.30 (d, J = 6.8 Hz, 2H), 5.13 (s, 1H), 4.86 (s, 2H), 4.75 (d, J = 6 Hz, 2H), 3.99 (t, J = 5.8 Hz, 2H), 3.16 (t, J = 5.8 Hz, 2H), 2.62 (s, 3H).	
A -54		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.60 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.02 (s, 1H), 7.76 (s, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.54 (d, J = 11.6 Hz, 1H), 5.23 (s, 1H), 4.95 (s, 2H), 4.79 (d, J = 6 Hz, 2H), 4.03 (t, J = 5.6 Hz, 2H), 3.07 (s, 2H), 2.64 (s, 3H).	
A-55		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.91 (s, 1H), 8.55 (d, J = 5.2 Hz, 1H), 8.49 (s, 1H), 8.03 (d, J = 9.6 Hz, 1H), 7.87 (d, J = 9.6 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.36 (s, 1H), 7.31 (d, J = 5.2 Hz, 1H), 5.69 (s, 1H), 4.85 (d, J = 5.8 Hz, 2H), 2.63 (s, 3H).	412.0
A-56		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.67 (d, J = 5.2 Hz, 1H), 8.45 (d, J = 4.4 Hz, 1H), 8.10 (s, 1H), 8.02 (s, 1H), 7.67 (s, 1H), 7.62 (d, J = 5.0 Hz, 1H), 7.46 (d, J = 8 Hz, 1H), 7.15 (m, 1H), 5.28 (s, 1H), 4.87 (s, 2H), 4.81 (d, J = 6.2 Hz, 2H), 4.06 (t, J = 5.8 Hz, 2H), 3.15 (m, 2H), 2.67 (s, 3H).	
A-57		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.0 (m, 2H), 8.69 (d, J = 5.2 Hz, 1H), 8.55 (d, J = 11.2 Hz, 2H), 8.38 (d, J = 9.0 Hz, 1H), 8.29 (d, J = 8.2 Hz, 1H), 8.23 (d, J = 9 Hz, 1H), 8.18 (s, 1H), 7.70 (s, 1H), 7.66 (d, J = 4.6 Hz, 1H), 7.48 (dd, J = 8.2, 4.2 Hz, 1H), 5.86 (s, 1H), 5.3 (m, 1H), 4.93 (d, J = 6 Hz, 2H), 2.68 (s, 3H).	
A-58		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.05 (s, 1H), 7.92 (s, 1H), 7.75 (s, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.54 (d, J = 12.0 Hz, 1H), 5.35 (s, 1H), 5.01 (s, 2H), 4.80 (d, J = 6.2 Hz, 2H), 4.33 (m, 2H), 4.21 (m, 2H), 2.64 (s, 3H).	436.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

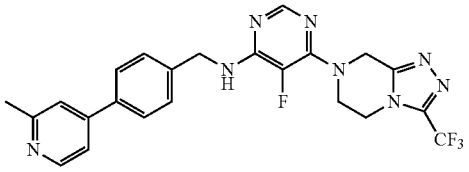
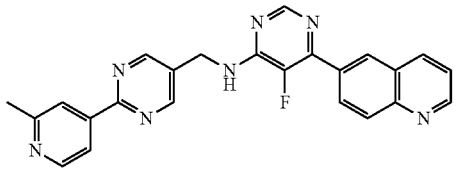
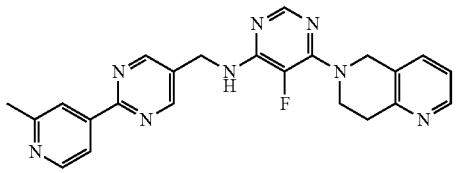
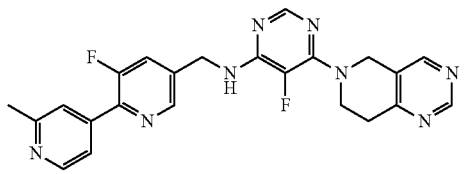
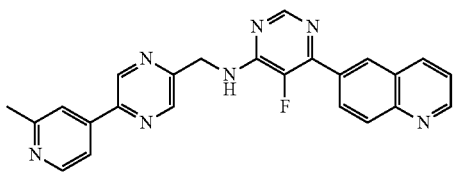
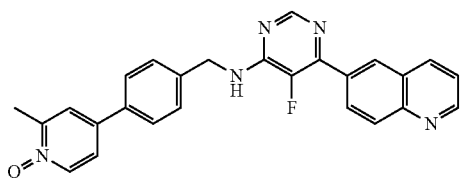
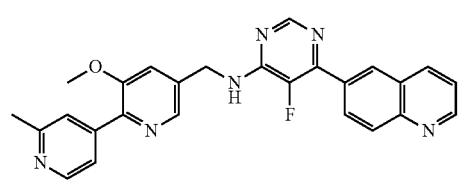
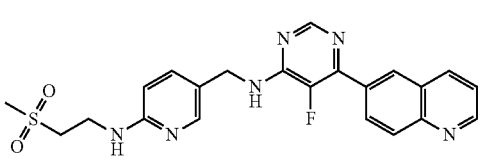
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-59		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.6 Hz, 1H), 8.07 (s, 1H), 7.9 (m, 1H), 7.61 (d, J = 7.6 Hz, 2H), 7.45 (d, J = 7.8 Hz, 2H), 7.35 (s, 1H), 7.28 (s, 1H), 5.24 (s, 1H), 5.12 (s, 2H), 4.76 (d, J = 5.6 Hz, 2H), 4.28 (s, 2H), 4.15 (s, 2H), 2.62 (s, 3H).	485.0
A-60		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.0 (m, 3H), 8.61 (d, J = 5.2 Hz, 2H), 8.54 (d, J = 7.8 Hz, 2H), 8.43 (s, 1H), 8.32 (d, J = 8.6 Hz, 1H), 8.15 (m, 2H), 8.04 (d, J = 5.2 Hz, 1H), 7.61 (m, 1H), 4.76 (d, J = 5.6 Hz, 2H), 2.57 (s, 3H).	424.0
A-61		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (s, 2H), 8.64 (d, J = 5.2 Hz, 1H), 8.44 (d, J = 4 Hz, 1H), 8.14 (s, 1H), 8.06 (d, J = 4.8 Hz, 1H), 8.03 (s, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.16 (m, 1H), 5.23 (s, 1H), 4.85 (s, 2H), 4.76 (d, J = 6 Hz, 2H), 4.03 (m, 2H), 3.13 (m, 2H), 2.66 (s, 3H).	430.9
A-62		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.61 (d, J = 5.2 Hz, 1H), 8.53 (d, J = 7.8 Hz, 2H), 8.04 (s, 1H), 7.76 (s, 1H), 7.68 (d, J = 4.8 Hz, 1H), 7.54 (d, J = 11.0 Hz, 1H), 5.26 (s, 1H), 4.87 (s, 2H), 4.80 (d, J = 6.2 Hz, 2H), 4.04 (t, J = 5.9 Hz, 2H), 3.10 (t, J = 5.8 Hz, 2H), 2.64 (s, 3H).	447.0
A-63		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.99 (d, J = 3.6 Hz, 1H), 8.82 (s, 1H), 8.66 (d, J = 5.2 Hz, 1H), 8.56 (d, J = 9.6 Hz, 2H), 8.39 (d, J = 8.8 Hz, 1H), 8.28 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 9.2 Hz, 1H), 7.81 (s, 1H), 7.71 (d, J = 5.2 Hz, 1H), 7.47 (dd, J = 8.2, 4.2 Hz, 1H), 6.39 (s, 1H), 5.01 (d, J = 5.2 Hz, 2H), 2.68 (s, 3H).	
A-64		E	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 6.8 Hz, 1H), 8.22 (s, 1H), 7.54 (d, J = 8.0 Hz, 2H), 7.43 (d, J = 8.0 Hz, 3H), 7.35-7.29 (m, 1H), 5.91 (s, 1H), 4.79 (d, J = 6.0 Hz, 2H), 2.57 (s, 3H).	
A-65		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, J = 4.0 Hz, 1H), 8.57 (s, 1H), 8.56 (s, 2H), 8.38 (d, J = 9.6 Hz, 2H), 8.28 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 8.8 Hz, 1H), 7.73 (s, 1H), 7.68 (d, J = 5.2 Hz, 1H), 7.47 (dd, J = 8.2, 4.2 Hz, 1H), 7.43 (s, 1H), 5.74 (s, 1H), 4.88 (d, J = 6.0 Hz, 2H), 3.92 (s, 3H), 2.63 (s, 3H).	452.9
A-66		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 3.2 Hz, 1H), 8.53 (s, 2H), 8.35 (d, J = 8.8 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.8 Hz, 1H), 8.16 (s, 1H), 7.52 (d, J = 8.4 Hz, 1H), 7.46 (dd, J = 8.2, 4.2 Hz, 1H), 6.49 (d, J = 8.4 Hz, 1H), 5.46 (s, 1H), 5.04 (s, 1H), 4.65 (d, J = 5.6 Hz, 2H), 3.98-3.94 (m, 2H), 3.39 (t, J = 5.8 Hz, 2H), 2.96 (s, 3H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

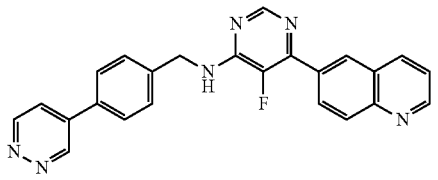
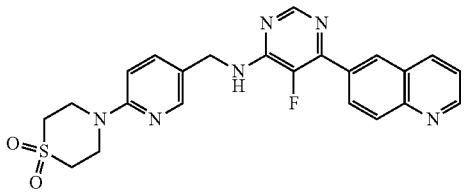
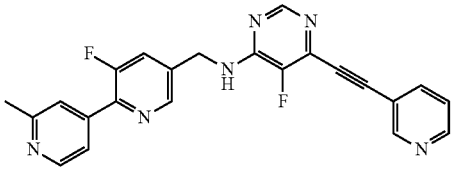
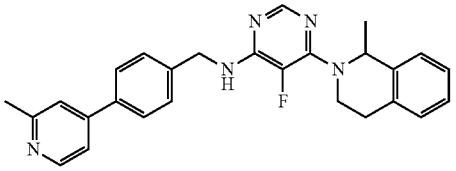
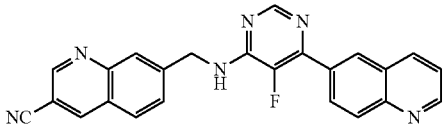
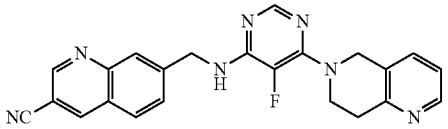
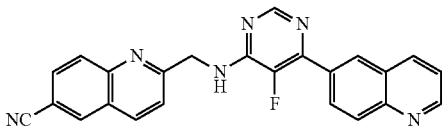
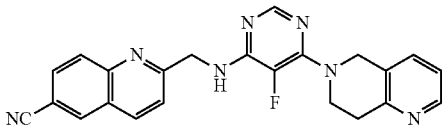
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-67		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.47 (s, 1H), 9.24 (d, J = 5.2 Hz, 1H), 8.99 (d, J = 3.2 Hz, 1H), 8.56 (d, J = 4.0 Hz, 2H), 8.38 (d, J = 8.8 Hz, 1H), 8.28 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 5.2 Hz, 1H), 7.59 (d, J = 7.6 Hz, 2H), 7.48 (dd, J = 8.2, 4.2 Hz, 1H), 5.70 (s, 1H), 4.90 (d, J = 6.0 Hz, 2H).	409.0
A-68		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 3.2 Hz, 1H), 8.54 (d, J = 3.2 Hz, 2H), 8.35 (d, J = 8.8 Hz, 1H), 8.27 (d, J = 7.8 Hz, 2H), 8.20 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 8.8 Hz, 1H), 7.47 (dd, J = 8.2, 4.2 Hz, 1H), 6.76 (d, J = 8.4 Hz, 1H), 5.51 (s, 1H), 4.70 (d, J = 5.6 Hz, 2H), 4.18 (s, 4H), 3.05 (s, 4H).	
A-69		A	^{1}H NMR (400 MHz, DMSO) δ 8.83 (s, 1H), 8.67 (m, 2H), 8.60(m, 2H), 8.29 (s, 1H), 8.08 (d, J = 7.8 Hz, 1H), 7.85 (d, J = 12.2 Hz, 1H), 7.76 (s, 1H), 7.68 (d, J = 4.6 Hz, 1H), 7.53 (m, 1H), 4.75 (d, J = 5.6 Hz, 2H), 2.56 (s, 3H).	414.9
A-70		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.23 (s, 1H), 8.04 (s, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.52 (m, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.35 (s, 1H), 7.30 (d, J = 4.8 Hz, 1H), 7.17 (m, 4H), 5.54 (m, 1H), 5.04 (s, 1H), 4.74 (d, J = 5.6 Hz, 2H), 4.48 (d, J = 10.2 Hz, 1H), 3.48 (m, 1H), 3.16 (m, 1H), 2.80 (d, J = 16.2 Hz, 1H), 2.62 (s, 3H), 1.58 (s, 3H).	
A-71		A	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.14 (d, J = 2.0 Hz, 1H), 9.06 (s, 1H), 8.99 (d, J = 2.8 Hz, 1H), 8.68 (t, J = 5.4 Hz, 1H), 8.65 (s, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.39 (s, 1H), 8.34 (d, J = 9.2 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 8.04 (s, 1H), 7.81 (d, J = 8.4 Hz, 1H), 7.62 (dd, J = 8.4, 4.4 Hz, 1H), 4.94 (d, J = 6.0 Hz, 2H).	
A-72		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (d, J = 2.0 Hz, 1H), 8.52 (s, 1H), 8.45 (d, J = 4.8 Hz, 1H), 8.08 (s, 1H), 8.02 (s, 1H), 7.87 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.15 (dd, J = 8.0, 4.8 Hz, 1H), 5.30 (s, 1H), 4.98 (d, J = 6.0 Hz, 2H), 4.87 (s, 2H), 4.05 (t, J = 5.8 Hz, 2H), 3.15 (t, J = 6.0 Hz, 2H).	
A-73		A	^{1}H NMR (400 MHz, DMSO-d_6) δ 8.99 (d, J = 2.4 Hz, 1H), 8.68-8.62 (m, 3H), 8.56 (d, J = 8.4 Hz, 1H), 8.46 (d, J = 8.8 Hz, 1H), 8.36 (s, 1H), 8.34 (s, 1H), 8.15 (dd, J = 14.8, 8.8 Hz, 2H), 8.05 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 8.8 Hz, 1H), 7.62 (dd, J = 8.4, 4.0 Hz, 1H), 4.98 (d, J = 6.0 Hz, 2H).	447.0
A-74		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 4.8 Hz, 1H), 8.24 (s, 1H), 8.19 (d, J = 8.8 Hz, 2H), 8.06 (s, 1H), 7.90 (d, J = 2.0 Hz, 1H), 7.54 (d, J = 8.8 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.19-7.12 (m, 1H), 6.38 (s, 1H), 4.99 (d, J = 4.8 Hz, 2H), 4.88 (s, 2H), 4.07 (t, J = 5.8 Hz, 2H), 3.16 (t, J = 6.0 Hz, 2H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

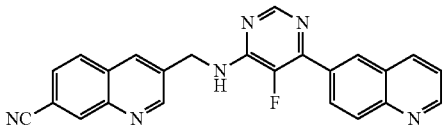
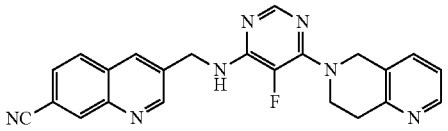
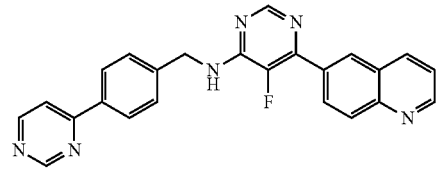
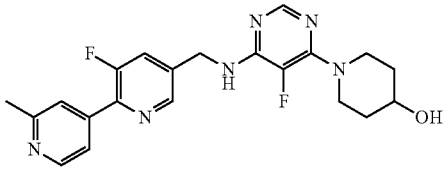
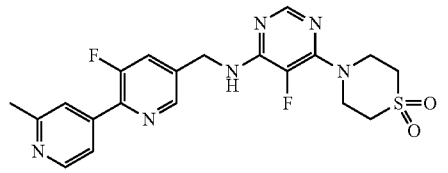
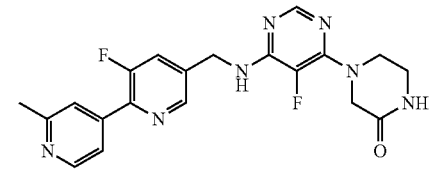
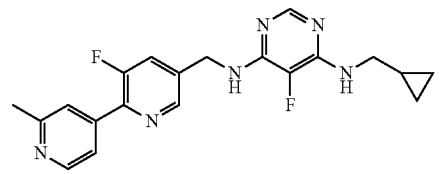
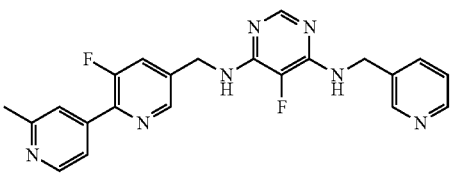
Compd NO.	Structure	Meth-od	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-75		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (d, J = 2.2 Hz, 1H), 8.99 (d, J = 4.2 Hz, 1H), 8.55 (d, J = 8.6 Hz, 2H), 8.49 (s, 1H), 8.38 (d, J = 9.0 Hz, 1H), 8.28 (d, J = 8.3 Hz, 1H), 8.23 (m, 2H), 7.93 (d, J = 8.4 Hz, 1H), 7.72 (d, J = 8..4 Hz, 1H), 7.48 (m, 1H), 5.81 (s, 1H), 5.05 (d, J = 6.1 Hz, −2H).	
A-76		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.45 (d, J = 6.8 Hz, 2H), 8.14 (s, 1H), 8.02 (s, 1H), 7.88 (s, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.46 (d, J = 7.2 Hz, 1H), 7.15 (s, 1H), 5.30 (s, 2H), 4.94 (d, J = 6.2 Hz, 2H), 4.86 (s, 2H), 4.05 (m, 2H), 3.14 (m, 2H).	412.0
A-77		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 8.99 (d, J = 3.2 Hz, 1H), 8.78 (d, J = 5.2 Hz, 1H), 8.56 (s, 2H), 8.38 (d, J = 8.8 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.22 (d, J = 8.8 Hz, 1H), 8.12 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 5.2 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.50-7.44 (m, 1H), 5.67 (s, 1H), 4.89 (d, J = 5.6 Hz, 2H).	409.0
A-78		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.00 (s, 1H), 7.76 (s, 1H), 7.68 (d, J = 4.8 Hz, 1H), 7.55 (d, J = 11.6 Hz, 1H), 5.18 (s, 1H), 4.79 (d, J = 6.0 Hz, 2H), 4.18-4.10 (m, 2H), 3.99-3.90 (m, 1H), 3.34-3.24 (m, 2H), 2.64 (s, 3H), 2.02-1.94 (m, 2H), 1.66-1.58 (m, 2H).	
A-79		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 5.2 Hz, 1H), 8.55 (s, 1H), 8.04 (s, 1H), 7.76 (s, 1H), 7.68 (d, J = 4.4 Hz, 1H), 7.55 (d, J = 11.2 Hz, 1H), 5.34 (s, 1H), 4.81 (d, J = 6.0 Hz, 2H), 4.20 (s, 4H), 3.12 (s, 4H), 2.65 (s, 3H).	
A-80		A	^{1}H NMR (400 MHz, DMSO) δ 8.59-8.54 (m, 2H), 8.07 (s, 1H), 7.90 (s, 1H), 7.80-7.72 (m, 3H), 7.65 (d, J = 4.4 Hz, 1H), 4.66 (d, J = 5.6 Hz, 2H), 4.10 (s, 2H), 3.76 (s, 2H), 3.26 (s, 2H), 2.55 (s, 3H).	
A-81		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.01 (s, 1H), 7.76 (s, 1H), 7.68 (d, J = 4.8 Hz, 1H), 7.55 (d, J = 11.6 Hz, 1H), 5.01 (s, 1H), 4.79 (d, J = 6.0 Hz, 2H), 4.76 (s, 1H), 3.33 (t, J = 6.2 Hz, 2H), 2.65 (s, 3H), 1.13-1.02 (m, 1H), 0.56 (d, J = 7.6 Hz, 2H), 0.27 (d, J = 4.8 Hz, 2H).	
A-82		A	^{1}H NMR (400 MHz, DMSO) δ 8.56 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.51 (s, 1H), 8.41 (d, J = 4.0 Hz, 1H), 7.80 (s, 1H), 7.78-7.71 (m, 2H), 7.69 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 4.8 Hz, 1H), 7.58-7.51 (m, 2H), 7.34-7.29 (m, 1H), 4.62 (d, J = 6.0 Hz, 2H), 4.54 (d, J = 6.0 Hz, 2H), 2.54 (s, 3H).	420.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

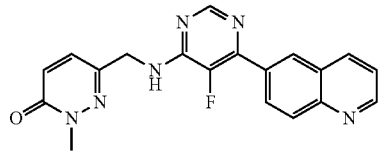
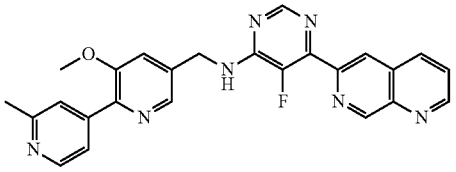
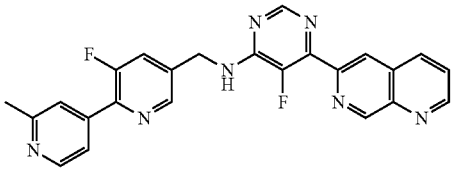
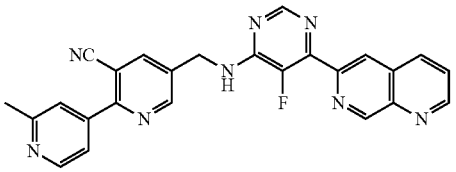
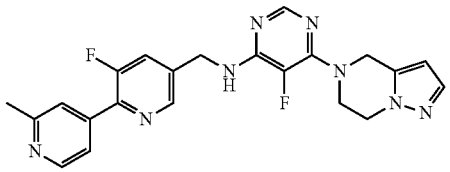
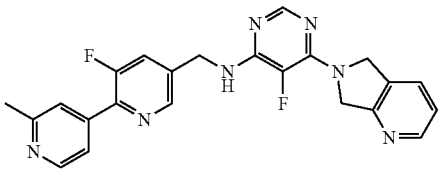
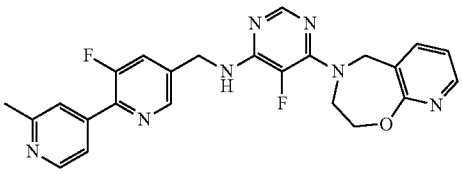
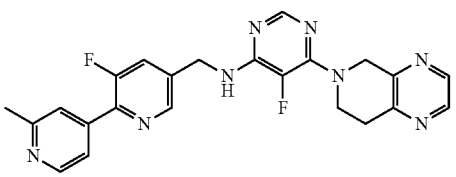
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-83		A	^{1}H NMR (400 MHz, DMSO) δ 8.98 (d, J = 3.2 Hz, 1H), 8.63 (s, 1H), 8.55 (d, J = 8.0 Hz, 1H), 8.43 (s, 2H), 8.32 (d, J = 8.8 Hz, 1H), 8.15 (d, J = 8.8 Hz, 1H), 7.64-7.59 (m, 1H), 7.49 (d, J = 9.6 Hz, 1H), 6.93 (d, J = 9.6 Hz, 1H), 4.58 (d, J = 6.0 Hz, 2H), 3.63 (s, 3H).	
A-84		F	^{1}H NMR (400 MHz, DMSO-d_6) δ 9.52 (s, 1H), 9.14 (d, J = 2.8 Hz, 1H), 8.67 (s, 1H), 8.63 (d, J = 8.4 Hz, 1H), 8.54 (s, 1H), 8.50 (d, J = 5.2 Hz, 1H), 8.43 (s, 1H), 8.36 (s, 1H), 7.87-7.84 (m, 1H), 7.75 (s, 1H), 7.69 (d, J = 4.9 Hz, 1H), 7.67 (s, 1H), 4.77 (d, J = 5.6 Hz, 2H), 3.89 (s, 3H), 2.52 (s, 3H).	454.0
A-85		F	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 9.12 (d, J = 3.2 Hz, 1H), 8.63-8.61 (m, 2H), 8.56 (d, J = 9.6 Hz, 2H), 8.30 (d, J = 8.4 Hz, 1H), 7.78 (s, 1H), 7.71-7.67 (m, 2H), 7.61 (d, J = 11.6 Hz, 1H), 5.87 (br s, 1H), 4.93 (d, J = 6.0 Hz, 2H), 2.66 (s, 3H).	441.9
A-86		F	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 9.12 (d, J = 2.8 Hz, 1H), 8.97 (s, 1H), 8.68 (d, J = 5.2 Hz, 1H), 8.56 (s, 2H), 8.30 (d, J = 8.4 Hz, 1H), 8.17 (s, 1H), 7.71-7.67 (m, 2H), 7.64 (d, J = 4.8 Hz, 1H), 5.94 (br s, 1H), 4.94 (d, J = 6.0 Hz, 2H), 2.67 (s, 3H).	449.0
A-87		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.04 (s, 1H), 7.75 (s, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.54 (d, J = 11.6 Hz, 1H), 7.49 (s, 1H), 6.09 (s, 1H), 5.27 (s, 1H), 4.92 (s, 2H), 4.80 (d, J = 6.2 Hz, 2H), 4.31 (t, J = 5.2 Hz, 2H), 4.16 (t, J = 5.2 Hz, 2H), 2.64 (s, 3H).	435.0
A-88		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.2 Hz, 1H), 8.58-8.50 (m, 2H), 8.07 (s, 1H), 7.76 (s, 1H), 7.66 (dd, J = 12.4, 6.0 Hz, 2H), 7.57 (d, J = 11.6 Hz, 1H), 7.22 (s, 1H), 5.19 (s, 1H), 5.06 (d, J = 8.2 Hz, 4H), 4.82 (d, J = 6.0 Hz, 2H), 2.64 (s, 3H).	
A-89		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 5.2 Hz, 1H), 8.51 (s, 1H), 8.18 (d, J = 3.8 Hz, 1H), 7.95 (s, 1H), 7.74 (s, 1H), 7.68 (d, J = 9.0 Hz, 2H), 7.52 (d, J = 11.6 Hz, 1H), 7.08-6.92 (m, 1H), 5.15 (s, 1H), 4.79 (s, 2H), 4.75 (d, J = 6.2 Hz, 2H), 4.32 (d, J = 4.0 Hz, 2H), 4.21 (d, J = 3.8 Hz, 2H), 2.64 (s, 3H).	
A-90		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 5.2 Hz, 1H), 8.53 (s, 1H), 8.41 (s, 2H), 8.21 (s, 1H), 8.04 (s, 1H), 7.75 (s, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.54 (d, J = 11.6 Hz, 1H), 5.30 (s, 1H), 4.98 (s, 2H), 4.79 (d, J = 6.2 Hz, 2H), 4.09 (t, J = 5.6 Hz, 2H), 3.17 (t, J = 5.6 Hz, 2H), 2.63 (s, 3H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

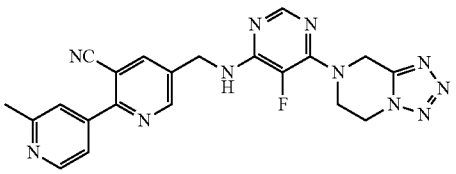
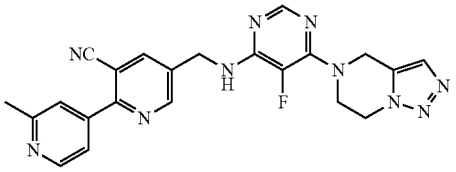
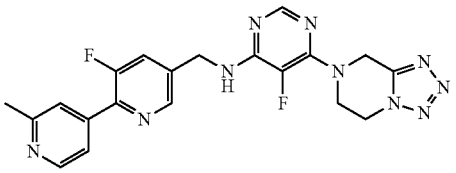
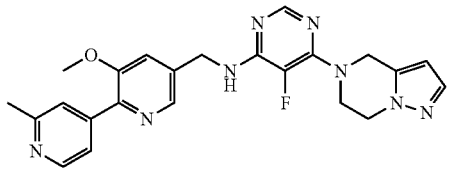
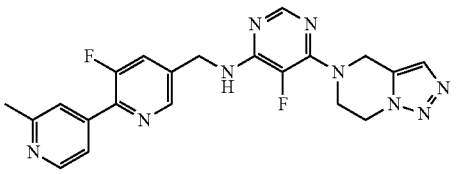
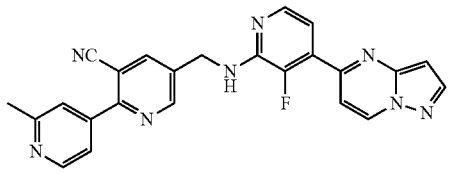
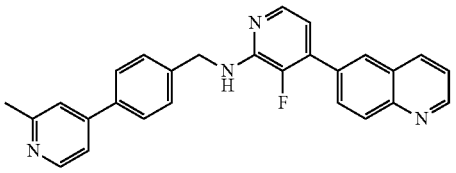
Compd NO.	Structure	Meth-od	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-91		A	^{1}H NMR (400 MHz, DMSO) δ 8.92 (s, 1H), 8.63 (d, J = 5.0 Hz, 1H), 8.34 (s, 1H), 7.95 (s, 2H), 7.67 (s, 1H), 7.61 (d, J = 4.8 Hz, 1H), 5.10 (s, 2H), 4.69 (d, J = 5.8 Hz, 2H), 4.53 (s, 2H), 4.15 (d, J = 4.8 Hz, 2H), 2.56 (s, 3H).	
A-92		A	^{1}H NMR (400 MHz, DMSO) δ 8.92 (s, 1H), 8.63 (d, J = 4.6 Hz, 1H), 8.35 (s, 1H), 7.94 (s, 1H), 7.88 (s, 1H), 7.64 (m, 3H), 4.93 (s, 2H), 4.69 (d, J = 5.6 Hz, 2H), 4.47 (s, 2H), 4.10 (s, 2H), 2.56 (s, 3H)	
A-93		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 5.2 Hz, 1H), 8.55 (s, 1H), 8.06 (s, 1H), 7.75 (s, 1H), 7.67 (d, J = 4.6 Hz, 1H), 7.54 (d, J = 11.6 Hz, 1H), 5.52 (s, 1H), 5.18 (s, 2H), 4.81 (d, J = 6.2 Hz, 2H), 4.58 (m, 2H), 4.22 (m, 2H), 2.64 (s, 3H).	
A-94		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 5.2 Hz, 1H), 8.31 (s, 1H), 8.06 (s, 1H), 7.70 (s, 1H), 7.65 (d, J = 4.8 Hz, 1H), 7.49 (s, 1H), 7.36 (s, 1H), 6.09 (s, 1H), 5.21 (s, 1H), 4.92 (s, 2H), 4.77 (d, J = 6.0 Hz, 2H), 4.31 (m, 2H), 4.16 (m, 2H), 3.88 (s, 3H), 2.62 (s, 3H).	
A-95		A	^{1}H NMR (400 MHz, DMSO) δ 8.92 (s, 1H), 8.63 (d, J = 4.8 Hz, 1H), 8.35 (s, 1H), 7.94 (s, 1H), 7.88 (s, 1H), 7.64 (m, 3H), 4.93 (s, 2H), 4.69 (d, J = 5.6 Hz, 2H), 4.47 (s, 2H), 4.10 (s, 2H), 2.56 (s, 3H).	
A-96		A	^{1}H NMR (400 MHz, DMSO) δ 9.25 (d, J = 7.2 Hz, 1H), 8.85 (s, 1H), 8.63 (d, J = 5.0 Hz, 1H), 8.42 8.20 (m, 3H), 7.65 (m,, 4H), 7.53 (d, J = 7.2 Hz, 1H), 6.81 (s, 1H), 4.68 (s, 2H), 2.57 (s, 3H).	
A-97		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 1H), 8.54 (s, 1H), 8.22 (m, 2H), 8.06 (s, 1H), 8.02 (d, J = 5.2 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 7.8 Hz, 2H), 7.53 (d, J = 7.8 Hz, 2H), 7.47 (m, 4.0 Hz, 1H), 7.38 (s, 1H), 7.32 (s, 1H), 6.79 (m, 1H), 5.14 (s, 1H), 4.83 (d, J = 5.6 Hz, 2H), 2.63 (s, 3H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

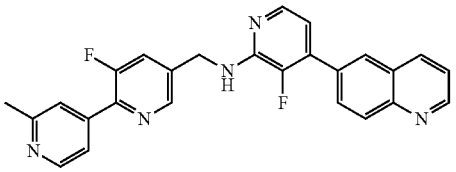
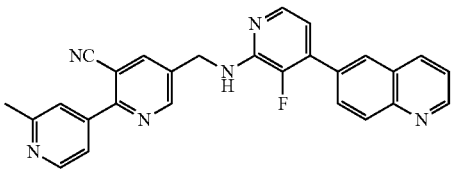
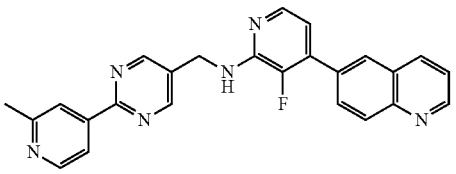
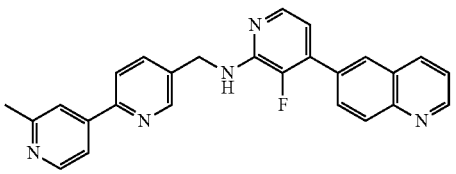
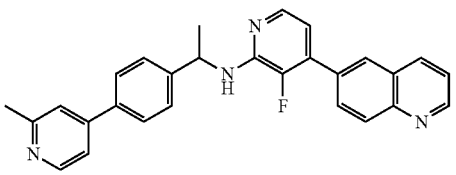
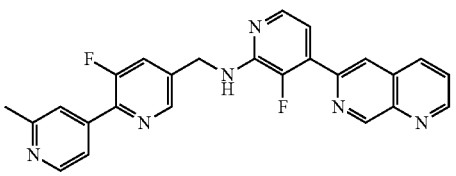
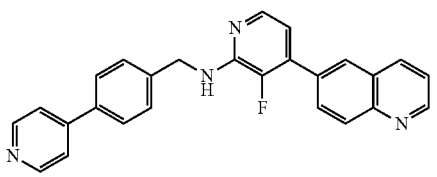
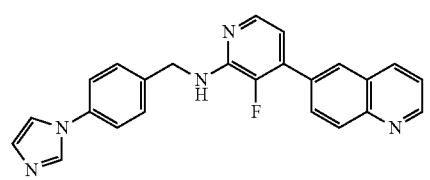
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-98		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 3.2 Hz, 1H), 8.62 (s, 2H), 8.22 (m, 2H), 8.06 (s, 1H), 8.00 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.78 (s, 1H), 7.70 (d, J = 5.0 Hz, 1H), 7.62 (d, J = 12 Hz, 1H), 7.48 (m, 4.2 Hz, 1H), 6.83 (m, 1H), 5.28 (s, 1H), 4.88 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	429.9
A-99		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 9.6 Hz, 2H), 8.68 (d, J = 5.2 Hz, 1H), 8.22 (m, 3H), 8.07 (s, 1H), 7.98 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.69 (s, 1H), 7.64 (d, J = 4 Hz, 1H), 7.48 (m, 1H), 6.86 (m, 1H), 5.35 (s, 1H), 4.89 (d, J = 6.2 Hz, 2H), 2.67 (s, 3H).	
A-100		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 2.6 Hz, 1H), 8.94 (s, 2H), 8.65 (d, J = 5.2 Hz, 1H), 8.20 (m, 3H), 8.07 (d, J = 17.8 Hz, 2H), 7.99 (d, J = 5.2 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.47 (m, 1H), 6.83 (m, 1H), 5.28 (s, 1H), 4.84 (d, J = 6.0 Hz, 2H), 2.68 (s, 3H).	
A-101		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 4 Hz, 1H), 8.80 (s, 1H), 8.60 (d, J = 5.2 Hz, 1H), 8.22 (m, 2H), 8.06 (s, 1H), 8.00 (d, J = 5.2 Hz, 1H), 7.91 (m, 2H), 7.84-7.74 (m, 2H), 7.68 (d, J = 5.0 Hz, 1H), 7.47 (m, 1H), 6.81 (m, 1H), 5.21 (s, 1H), 4.86 (m, 2H), 2.66 (s, 3H).	
A-102		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 2.8 Hz, 1H), 8.53 (d, J = 5.2 Hz, 1H), 8.27-8.15 (m, 2H), 8.04 (s, 1H), 7.95-7.89 (m, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 2H), 7.47 (dd, J = 8.4, 4.4 Hz, 1H), 7.37 (s, 1H), 7.31 (d, J = 4.4 Hz, 1H), 6.76-6.70 (m, 1H), 5.48-5.39 (m, 1H), 5.06 (d, J = 5.6 Hz, 1H), 2.62 (s, 3H), 1.67 (d, J = 6.8 Hz, 3H).	435.0
A-103		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.64 (s, 1H), 9.09 (d, J = 2.4 Hz, 1H), 8.61 (d, J = 4.8 Hz, 2H), 8.26 (d, J = 9.2 Hz, 2H), 8.05 (d, J = 5.2 Hz, 1H), 7.78 (s, 1H), 7.72-7.65 (m, 2H), 7.62 (d, J = 11.6 Hz, 1H), 7.41 (t, J = 5.2 Hz, 1H), 5.28 (s, 1H), 4.89 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	441.0
A-104		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 2.8 Hz, 1H), 8.66 (d, J = 6.0 Hz, 2H), 8.26-8.17 (m, 2H), 8.06 (s, 1H), 8.02 (d, J = 5.2 Hz, 1H),7.94 (d, J = 8.8 Hz, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.58-7.50 (m, 4H), 7.47 (dd, J = 8.4, 4.4 Hz, 1H), 6.81-6.77 (m, 1H), 5.15 (s, 1H), 4.83 (d, J = 6.0 Hz, 2H).	407.0
A-105		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 3.2 Hz, 1H), 8.26-8.18 (m, 2H), 8.06 (s, 2H), 8.00 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.55 (d, J = 8.0 Hz, 2H), 7.47 (dd, J = 8.0, 4.0 Hz, 1H), 7.39 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 10.0 Hz, 2H), 6.83-6.77 (m, 1H), 5.19 (s, 1H), 4.83 (d, J = 6.0 Hz, 2H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

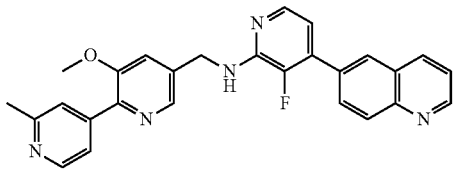
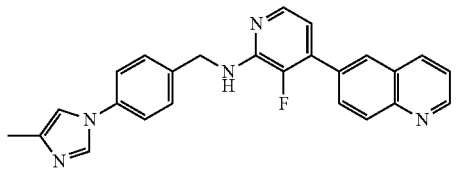
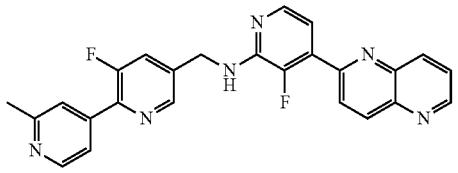
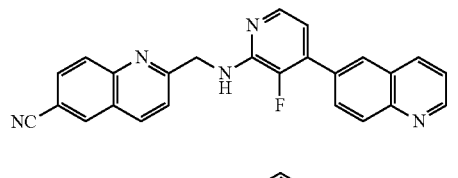
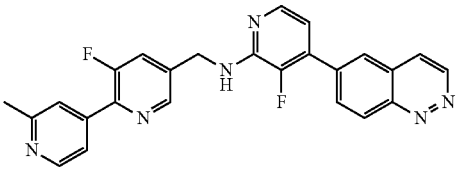
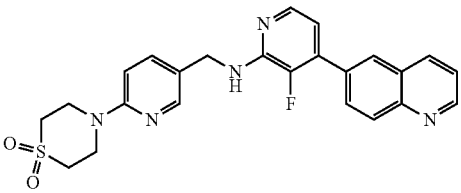
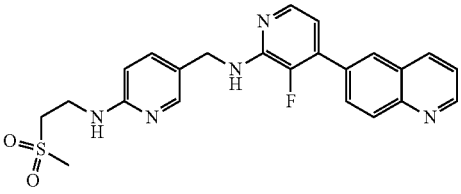
Compd NO.	Structure	Meth-od	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-106		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 3.6 Hz, 1H), 8.56 (d, J = 4.8 Hz, 1H), 8.39 (s, 1H), 8.26-8.18 (m, 2H), 8.06 (s, 1H), 8.02 (d, J = 5.2 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.72 (s, 1H), 7.67 (d, J = 4.8 Hz, 1H), 7.50-7.43 (m, 2H), 6.85-6.80 (m, 1H), 5.20 (s, 1H), 4.84 (d, J = 6.0 Hz, 2H), 3.90 (s, 3H), 2.62 (s, 3H).	452.0
A-107		A	^{1}H NMR (400 MHz, DMSO) δ 8.97 (d, J = 3.2 Hz, 1H), 8.48 (d, J = 8.0 Hz, 1H), 8.27 (s, 1H), 8.17-8.07 (m, 2H), 7.98 (d, J = 8.8 Hz, 1H), 7.90 (d, J = 5.2 Hz, 1H), 7.61 (dd, J = 8.0, 4.0 Hz, 1H), 7.53 (d, J = 8.4 Hz, 3H), 7.47 (d, J = 8.4 Hz, 2H), 7.41 (s, 1H), 6.83-6.77 (m, 1H), 4.65 (d, J = 5.6 Hz, 2H), 2.16 (s, 3H).	
A-108		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.61 (s, 2H), 8.50 (dd, J = 13.2, 8.8 Hz, 2H), 8.13 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 5.2 Hz, 1H), 7.81-7.67 (m, 3H), 7.61 (d, J = 11.6 Hz, 1H), 7.32-7.29 (m, 1H), 5.31 (s, 1H), 4.88 (d, J = 5.6 Hz, 2H), 2.64 (s, 3H).	441.0
A-109		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, J = 4.4 Hz, 1H), 8.19-8.25 (m, 5H), 8.11 (s, 1H), 8.02 (d, J = 5.2 Hz, 1H), 7.97 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 7.52-7.45 (m, 1H), 6.82 (d, J = 5.2 Hz, 1H), 6.38 (s, 1H), 5.08 (d, J = 4.8 Hz, 2H).	
A-110		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.39 (d, J = 5.6 Hz, 1H), 8.65 (d, J = 8.8 Hz, 1H), 8.62 (s, 2H), 8.08-8.01 (m, 3H), 7.93 (d, J = 6.0 Hz, 1H), 7.78 (s, 1H), 7.70 (d, J = 4.0 Hz, 1H), 7.62 (d, J = 11.6 Hz, 1H), 6.84-6.79 (m, 1H), 5.33 (s, 1H), 4.88 (d, J = 6.0 Hz, 2H), 2.66 (s, 3H).	441.0
A-111		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 3.2 Hz, 1H), 8.28 (s, 1H), 8.24-8.16 (m, 2H), 8.04 (s, 1H), 8.01 (d, J = 5.2 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 7.2 Hz, 1H), 7.47 (dd, J = 8.4, 4.4 Hz, 1H), 6.82-6.72 (m, 2H), 5.01 (s, 1H), 4.66 (d, J = 5.6 Hz, 2H), 4.17 (s, 4H), 3.05 (s, 4H).	
A-112		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 3.2 Hz, 1H), 8.24-8.14 (m, 3H), 8.04 (s, 1H), 8.01 (d, J = 5.2 Hz, 1H), 7.91 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 6.8 Hz, 1H), 7.46 (dd, J = 8.4, 4.0 Hz, 1H), 6.80-6.74 (m, 1H), 6.47 (d, J = 8.4 Hz, 1H), 4.94 (d, J = 6.0 Hz, 2H), 4.60 (d, J = 5.6 Hz, 2H), 3.95 (q, J = 6.0 Hz, 2H), 3.39 (t, J = 5.6 Hz, 2H), 2.95 (s, 3H).	452.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

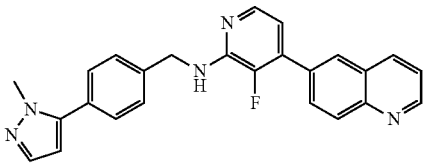
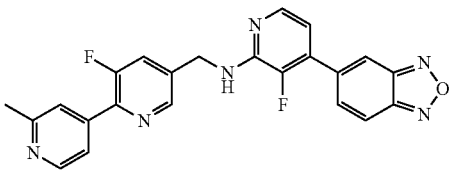
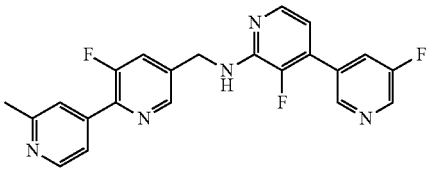
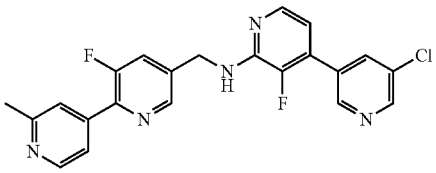
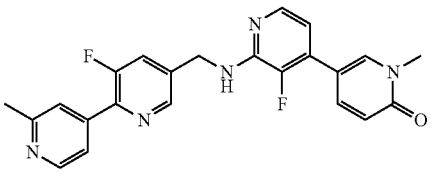
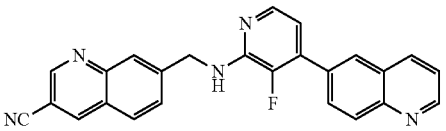
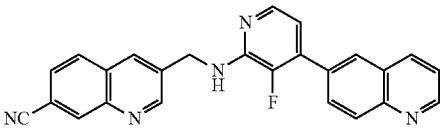
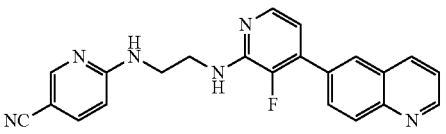
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-113		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 3.2 Hz, 1H), 8.26-8.18 (m, 2H), 8.06 (s, 1H), 8.02 (d, J = 5.2 Hz, 1H), 7.94 (d, J = 8.8 Hz, 1H), 7.51 (d, J = 6.4 Hz, 3H), 7.47 (dd, J = 8.0, 4.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 2H), 6.82-6.77 (m, 1H), 6.31 (s, 1H), 5.15 (s, 1H), 4.83 (d, J = 5.6 Hz, 2H), 3.90 (s, 3H).	
A-114		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.2 Hz, 2H), 8.06 (s, 1H), 8.02 (d, J = 5.2 Hz, 1H), 7.96 (d, J = 9.2 Hz, 1H), 7.77 (s, 1H), 7.69 (d, J = 4.8 Hz, 1H), 7.61 (d, J = 10.8 Hz, 2H), 6.77-6.72 (m, 1H), 5.32 (s, 1H), 4.87 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	
A-115		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.61 (d, J = 6.0 Hz, 2H), 8.55 (s, 1H), 8.00 (d, J = 5.2 Hz, 1H), 7.77 (s, 1H), 7.69 (d, J = 4.0 Hz, 1H), 7.65 (d, J = 9.2 Hz, 1H), 7.60 (d, J = 11.6 Hz, 1H), 6.73-6.68 (m, 1H), 5.30 (s, 1H), 4.85 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	
A-116		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.65-8.57 (m, 3H), 7.99 (d, J = 5.2 Hz, 1H), 7.90 (s, 1H), 7.77 (s, 1H), 7.69 (d, J = 4.4 Hz, 1H), 7.59 (d, J = 11.6 Hz, 1H), 6.71-6.65 (m, 1H), 5.28 (s, 1H), 4.85 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	
A-117		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 5.2 Hz, 1H), 8.58 (s, 1H), 7.91 (d, J = 5.2 Hz, 1H), 7.77 (s, 1H), 7.68 (s, 2H), 7.62-7.55 (m, 2H), 6.68 (d, J = 9.6 Hz, 1H), 6.62-6.58 (m, 1H), 5.20 (s, 1H), 4.83 (d, J = 6.0 Hz, 2H), 3.63 (s, 3H), 2.65 (s, 3H).	
A--118		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.27 (d, J = 2.0 Hz, 1H), 8.98 (d, J = 4.0 Hz, 1H), 8.65 (d, J = 2.0 Hz, 1H), 8.21-8.26 (m, 2H), 8.16 (s, 1H), 8.08 (s, 1H), 7.99 (d, J = 5.2 Hz, 1H), 7.97-7.89 (m, 2H), 7.70 (d, J = 4.8 Hz, 1H), 7.46-7.49 (m, 1H), 6.80 (t, J = 6.8 Hz, 1H), 5.34 (s, 1H), 5.05 (d, J = 6.0 Hz, 2H).	
A-119		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 8.99 (d, J = 2.0 Hz 1H), 8.48 (s, 1H), 8.27-8.18 (m, 3H), 8.07 (s, 1H), 7.99 (d, J = 5.2 Hz, 1H), 7.92 (t, J = 8.6 Hz, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.5-7.46 (m, 1H), 6.83 (t, J = 5.2 Hz, 1H), 5.34 (s, 1H), 5.01 (d, J = 6.0 Hz, 3H).	
A-120		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 2.8 Hz, 1H), 8.39 (s, 1H), 8.24 (d, J = 8.4 Hz, 1H), 8.20 (d, J = 8.8 Hz, 1H), 8.04 (s, 1H), 8.00 (d, J = 5.2 Hz, 1H), 7.90 (d, J = 8.8 Hz, 1H), 7.53 (d, J = 8.8 Hz, 1H), 7.48 (dd, J = 8.2, 4.2 Hz, 1H), 6.79 (t, J = 5.2 Hz, 1H), 6.41 (d, J = 9.2 Hz, 1H), 6.30 (s, 1H), 5.35 (s, 1H), 3.84 (m, 2H), 3.69 (m, 2H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

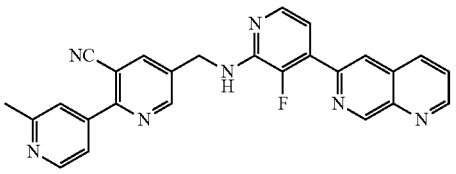
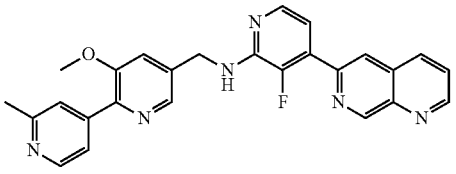
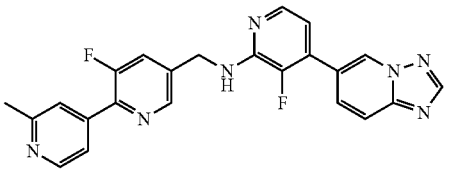
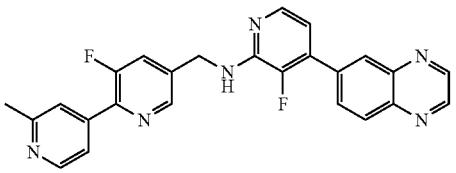
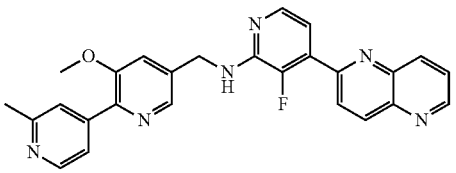
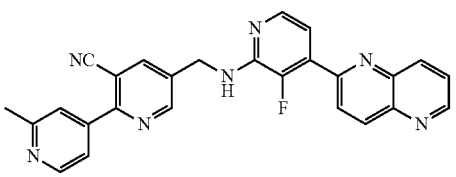
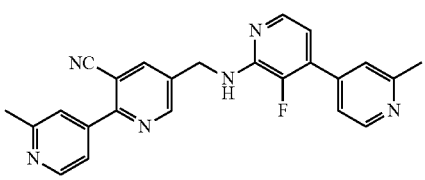
Compd NO.	Structure	Meth-od	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-121		A	^{1}H NMR (400 MHz, DMSO) δ 9.54 (s, 1H), 9.13 (d, J = 3.2 Hz, 1H), 8.99 (s, 1H), 8.64 (d, J = 4.8 Hz, 1H), 8.60 (d, J = 8.4 Hz, 1H), 8.47 (s, 1H), 8.43 (s, 1H), 7.95 (d, J = 5.2 Hz, 1H), 7.86 (dd, J = 8.4, 4.4 Hz, 1H), 7.69 (s, 1H), 7.64 (d, J = 5.2 Hz, 2H), 7.26-7.20 (m, 1H), 4.77 (d, J = 5.6 Hz, 2H), 2.57 (s, 3H).	448.0
A-122		A	^{1}H NMR (400 MHz, DMSO) δ 9.54 (s, 1H), 9.13 (d, J = 3.6 Hz, 1H), 8.60 (d, J = 8.0 Hz, 1H), 8.47 (d, J = 7.2 Hz, 2H), 8.32 (s, 1H), 7.96 (d, J = 5.2 Hz, 1H), 7.86 (dd, J = 8.0, 4.0 Hz, 1H), 7.73 (s, 1H), 7.66 (s, 2H), 7.60-7.54 (m, 1H), 7.23-7.19 (m, 1H), 4.72 (d, J = 5.6 Hz, 2H), 3.88 (s, 3H), 2.51 (s, 3H).	452.9
A--123		A	^{1}H NMR (400 MHz, DMSO) δ 9.30 (s, 1H), 8.61 (d, J = 6.0 Hz, 2H), 8.57 (d, J = 5.2 Hz, 1H), 7.99 (d, J = 9.2 Hz, 1H), 7.95-7.87 (m, 2H), 7.82 (d, J = 12.2 Hz, 1H), 7.74 (s, 1H), 7.66 (d, J = 5.2 Hz, 2H), 6.87 (t, J = 5.0 Hz, 1H), 4.72 (d, J = 5.8 Hz, 2H), 2.55 (s, 3H).	430.0
A124		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 2H), 8.61 (d, J = 5.2 Hz, 2H), 8.36 (s, 1H), 8.22 (d, J = 8.8 Hz, 1H), 8.01 (t, J = 7.6 Hz, 2H), 7.77 (s, 1H), 7.69 (d, J = 4.8 Hz, 1H), 7.63 (d, J = 11.6 Hz, 1H), 6.85 (t, J = 5.2 Hz, 1H), 5.31 (s, 1H), 4.88 (d, J = 5.8 Hz, 2H), 2.65 (s, 3H).	440.9
A-125		F	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (s, 1H), 8.51 (d, J = 10.3 Hz, 3H), 8.38 (s, 1H), 8.09 (d, J = 9.2 Hz, 2H), 7.69 (s, 3H), 7.44 (s, 1H), 7.26 (s, 1H), 5.28 (s, 1H), 4.83 (s, 2H), 3.88 (s, 3H), 2.62 (s, 3H).	453.0
A-126		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (d, J = 3.4 Hz, 1H), 8.91 (s, 1H), 8.62 (d, J = 5.2 Hz, 1H), 8.45 (m, 2H), 8.12 (s, 1H), 8.08 (d, J = 8.6 Hz, 1H), 7.99 (d, J = 5.2 Hz, 1H), 7.65 (m, 2H), 7.58 (d, J = 4.8 Hz, 1H), 7.28 (m, 1H), 5.33 (s, 1H), 4.84 (d, J = 6.0 Hz, 2H), 2.62 (s, 3H).	447.9
A-127		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.68 (s, 1H), 8.61 (s, 1H), 8.16 (s, 1H), 7.96 (s, 1H), 7.68 (s, 1H), 7.64 (s, 1H), 7.35 (s, 1H), 7.29 (s, 1H), 6.73 (s, 1H), 5.34 (s, 1H), 4.87 (d, J = 4.4 Hz, 2H), 2.66 (d, J = 10.6 Hz, 6H).	411.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

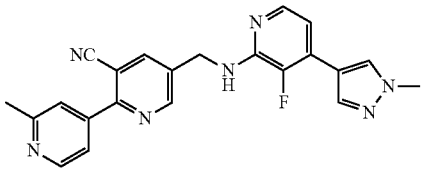
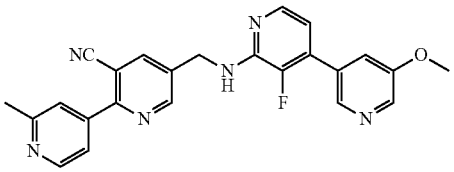
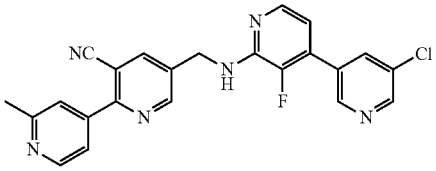
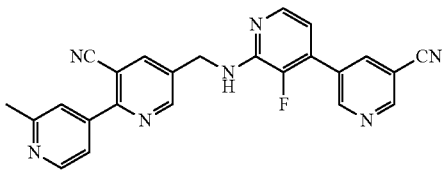
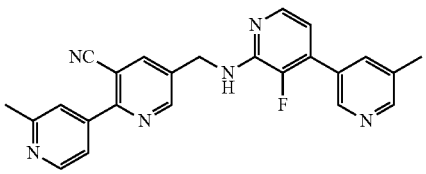
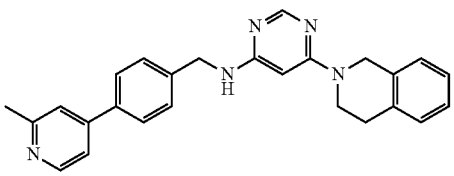
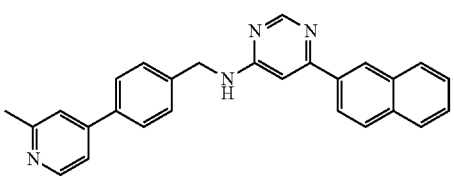
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): [M + 1]$^+$
A-128		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.67 (d, J = 5.2 Hz, 1H), 8.15 (s, 1H), 7.90 (s, 1H), 7.83 (d, J = 5.6 Hz, 2H), 7.67 (s, 1H), 7.63 (d, J = 4.8 Hz, 1H), 7.52 (s, 1H), 6.81 (t, J = 5.2 Hz, 1H), 5.23 (s, 1H), 4.84 (d, J = 6.0 Hz, 2H), 3.96 (d, J = 17.6 Hz, 3H), 2.66 (s, 3H).	
A-129		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.67 (d, J = 5.2 Hz, 1H), 8.44 (s, 1H), 8.38 (s, 1H), 8.16 (s, 1H), 7.96 (d, J = 5.2 Hz, 1H), 7.68 (s, 1H), 7.63 (d, J = 4.8 Hz, 1H), 7.40 (s, 1H), 6.74 (t, J = 5.0 Hz, 1H), 5.34 (s, 1H), 4.87 (d, J = 6 Hz, 2H), 3.93 (s, 3H), 2.67 (s, 3H).	427.0
A-130		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.72 (s, 1H), 8.68 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H), 8.15 (s, 1H), 7.98 (d, J = 5.0 Hz, 1H), 7.91 (s, 1H), 7.68 (s, 1H), 7.63 (d, J = 4.6 Hz, 1H), 6.72 (d, J = 4.8 Hz, 1H), 5.37 (s, 1H), 4.87 (d, J = 5.8 Hz, 2H), 2.67 (s, 3H).	
A-131		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.95 (s, 2H), 8.68 (d, J = 4.6 Hz, 1H), 8.17 (d, J = 14.4 Hz, 2H), 8.02 (d, J = 4.8 Hz, 1H), 7.69 (s, 1H), 7.64 (s, 1H), 6.72 (s, 1H), 5.41 (s, 1H), 4.88 (d, J = 5.8 Hz, 2H), 2.68 (s, 3H).	
A-132		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (s, 1H), 8.81-8.59 (m, 2H), 8.51 (s, 1H), 8.16 (s, 1H), 7.95 (d, J = 5.2 Hz, 1H), 7.69 (d, J = 10.2 Hz, 2H), 7.63 (d, J = 4.8 Hz, 1H), 6.73 (t, J = 5.2 Hz, 1H), 5.33 (s, 1H), 4.86 (d, J = 6.0 Hz, 2H), 2.67 (s, 3H), 2.43 (s, 3H).	411.0
A-133		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 1H), 8.22 (s, 1H), 7.61 (d, J = 7.2 Hz, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.36 (s, 1H), 7.30 (s, 1H), 7.17 (s, 4H), 5.44 (s, 1H), 5.20 (s, 1H), 4.64 (s, 2H), 4.56 (s, 2H), 3.77 (s, 2H), 2.91 (s, 2H), 2.61 (s, 3H).	408.0
A-134		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.54 (d, J = 5.2 Hz, 1H), 8.51 (s, 1H), 8.02 (d, J = 8.8 Hz, 1H), 7.93 (t, J = 8.0 Hz, 2H), 7.90-7.85 (m, 1H), 7.65 (s, 1H), 7.63 (s, 1H), 7.54 (t, J = 5.0 Hz, 1H), 7.51 (s, 2H), 7.49 (s, 1H), 7.37 (s, 1H), 7.31 (d, J = 5.2 Hz, 1H), 6.89 (s, 1H), 5.45 (s, 1H), 4.74 (d, J = 5.6 Hz, 2H), 2.62 (s, 3H).	403.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

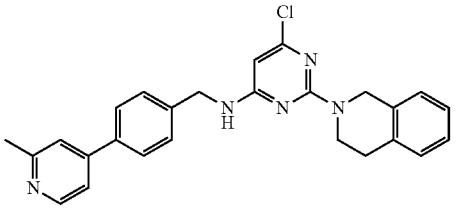
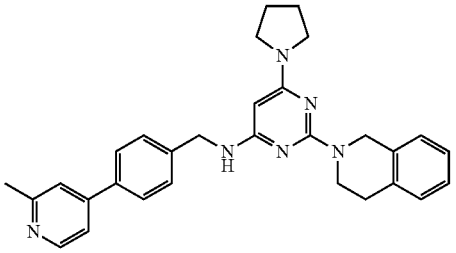
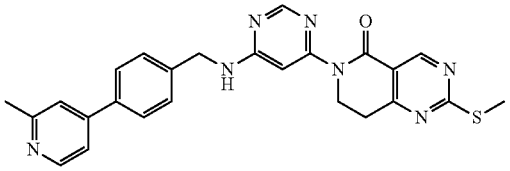
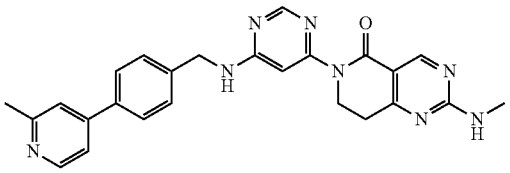
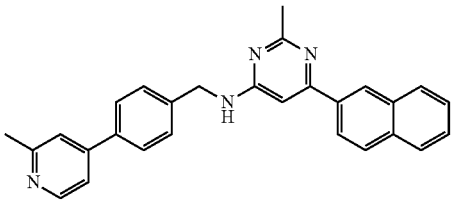
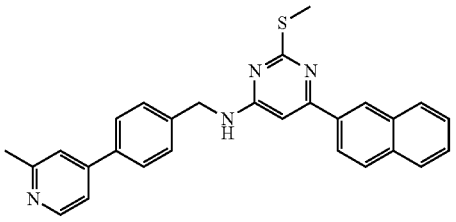
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-135		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.2 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.36 (s, 1H), 7.30 (d, J = 5.2 Hz, 1H), 7.16 (brs, 4H), 5.74 (s, 1H), 5.12 (brs, 1H), 4.85 (s, 2H), 4.61 (brs, 2H), 3.99 (t, J = 5.8 Hz, 2H), 2.88 (t, J = 5.4 Hz, 2H), 2.62 (s, 3H).	442.0
A-136		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.0 Hz, 2H), 7.36 (s, 1H), 7.30 (d, J = 5.2 Hz, 1H), 7.18-7.10 (m, 4H), 4.88 (s, 2H), 4.76 (s, 2H), 4.53 (d, J = 5.6 Hz, 2H), 4.01 (t, J = 5.6 Hz, 2H), 3.41 (s, 4H), 2.87 (t, J = 5.6 Hz, 2H), 2.62 (s, 3H), 1.92 (s, 4H).	477.1
A-137		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.54 (d, J = 5.2 Hz, 1H), 8.49 (s, 1H), 7.63 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 8.0 Hz, 2H), 7.39 (s, 1H), 7.38 (s, 1H), 7.32 (d, J = 4.8 Hz, 1H), 5.36 (br s, 1H), 4.68 (s, 2H), 4.44 (t, J = 6.0 Hz, 2H), 3.15 (t, J = 6.8 Hz, 2H), 2.64 (s, 6H).	470.0
A-138		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.98 (s, 0.4H), 8.84 (s, 0.6H), 8.60-8.55 (m, 1H), 8.46 (s, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.40-7.30 (m, 2H), 7.27 (s, 1H), 5.73-5.51 (m, 1H), 5.38 (br s, 1H), 4.65 (s, 2H), 4.37 (s, 2H), 3.09 (s, 3H), 3.09-2.88 (m, 2H), 2.62 (s, 3H).	453.0
A-139		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.47 (s, 1H), 8.00 (m, 1H), 7.89 (m, 3H), 7.63 (d, J = 8.4 Hz, 2H), 7.54-7.47 (m, 4H), 7.36 (s, 1H), 7.30 (d, J = 4.0 Hz, 1H), 6.67 (s, 1H), 5.49 (s, 1H), 4.70 (d, J = 6.0 Hz, 2H), 2.66 (s, 3H), 2.62 (s, 3H).	417.0
A-140		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.2 Hz, 1H), 8.50 (s, 1H), 8.05-8.03 (m, 1H), 7.96-7.82 (m, 3H), 7.62 (d, J = 8.4 Hz, 2H), 7.55-7.49 (m, 2H), 7.47 (d, J = 8.4 Hz, 2H), 7.36 (s, 1H), 7.30 (d, J = 4.0 Hz, 1H), 6.58 (s, 1H), 5.38 (s, 1H), 4.72 (d, J = 4.4 Hz, 2H), 2.63 (s, 3H), 2.62 (s, 3H).	449.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

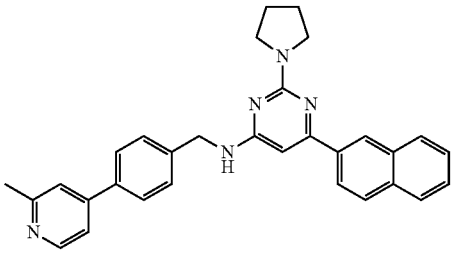
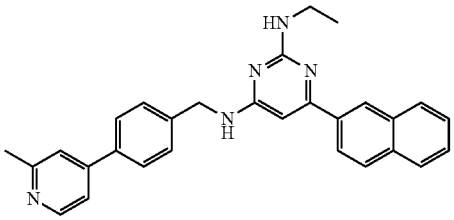
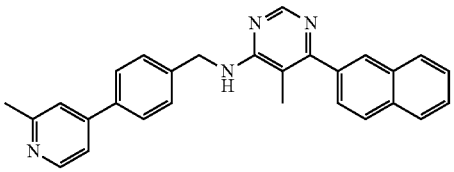
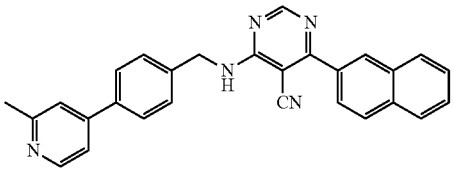
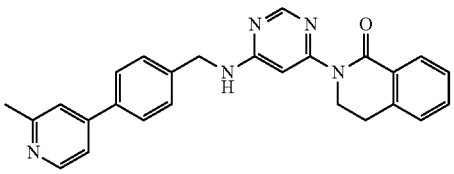
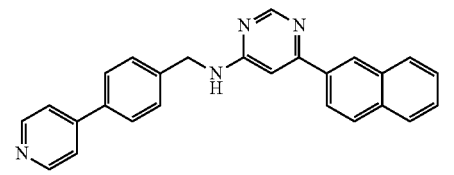
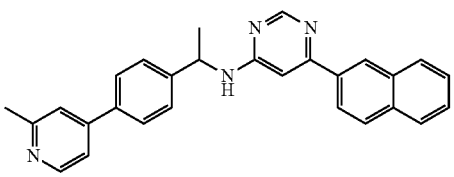
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-141		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.48 (s, 1H), 8.09 (d, J = 8.4 Hz, 1H), 7.94-7.81 (m, 3H), 7.61 (d, J = 8.0 Hz, 2H), 7.51-7.47 (m, 4H), 7.36 (s, 1H), 7.30 (d, J = 5.2 Hz, 1H), 6.27 (s, 1H), 5.08 (s, 1H), 4.71 (d, J = 6.0 Hz, 2H), 3.69 (s, 4H), 2.62 (s, 3H), 1.99 (t, J = 6.5 Hz, 4H).	472.0
A-142		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 4.8 Hz, 1H), 8.45 (s, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.95-7.82 (m, 3H), 7.62 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 7.6 Hz, 4H), 7.37 (s, 1H), 7.31 (d, J = 5.2 Hz, 1H), 6.29 (s, 1H), 5.10 (s, 1H), 4.95 (s, 1H), 4.70 (d, J = 5.2 Hz, 2H), 3.54 (s, 2H), 2.62 (s, 3H), 1.26 (t, J = 7.0 Hz, 3H).	446.1
A-143		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.55 (d, J = 5.2 Hz, 1H), 7.99 (s, 1H), 7.96-7.86 (m, 3H), 7.64 (d, J = 8.0 Hz, 3H), 7.52 (t, J = 6.8 Hz, 4H), 7.37 (s, 1H), 7.31 (d, J = 4.8 Hz, 1H), 5.10 (s, 1H), 4.87 (d, J = 5.2 Hz, 2H), 2.63 (s, 3H), 2.18 (s, 3H).	417.0
A-144		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.56 (d, J = 5.2 Hz, 1H), 8.54 (s, 1H), 8.06 (d, J = 8.8 Hz, 1H), 7.99 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 8.0 Hz, 2H), 7.62-7.55 (m, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.37 (s, 1H), 7.31 (d, J = 4.0 Hz, 1H), 6.14 (s, 1H), 4.90 (d, J = 5.6 Hz, 2H), 2.63 (s, 3H).	428.0
A-145		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.2 Hz, 1H), 8.48 (s, 1H), 8.14 (d, J = 7.6 Hz, 1H), 7.55-7.42 (m, 4H), 7.40 (d, J = 8.0 Hz, 1H), 7.36 (s, 1H), 7.31 (d, J = 9.2 Hz, 1H), 7.25 (s, 1H), 5.43 (br s, 1H), 4.66 (d, J = 5.6 Hz, 2H), 4.36 (d, J = 6.4 Hz, 2H), 3.07 (d, J = 6.4 Hz, 2H), 2.62 (s, 3H).	
A-146		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.65-8.58 (m, 3H), 8.57 (s, 1H), 8.20-7.95 (m, 5H), 7.79 (d, J = 8.0 Hz, 2H), 7.70 (d, J = 5.2 Hz, 2H), 7.57 (d, J = 9.2 Hz, 2H), 7.52 (d, J = 6.4 Hz, 1H), 7.19 (s, 1H), 4.69 (d, J = 6.0 Hz, 2H).	389.0
A-147		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.53 (d, J = 5.2 Hz, 1H), 8.42 (s, 1H), 7.95-7.80 (m, 4H), 7.64 (d, J = 8.4 Hz, 2H), 7.54-7.50 (m, 4H), 7.35 (s, 1H), 7.29 (d, J = 5.2 Hz, 2H), 6.73 (s, 1H), 5.39 (br s, 1H), 5.08 (m, 1H) 2.61 (s, 3H), 1.67 (d, J = 6.8 Hz, 3H).	417.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

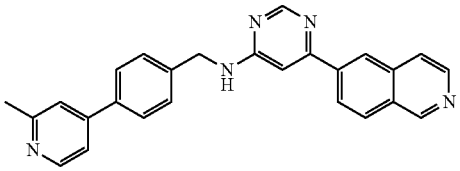
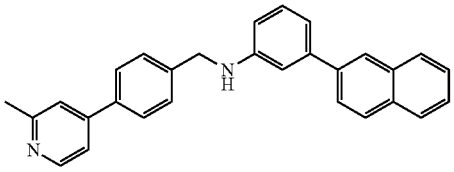
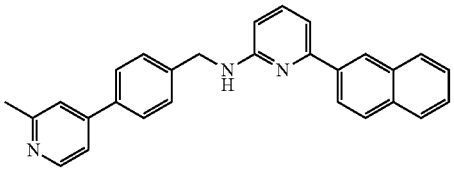
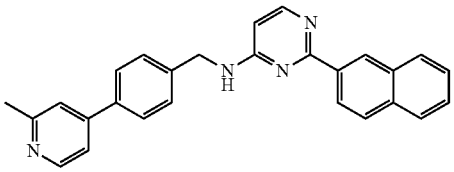
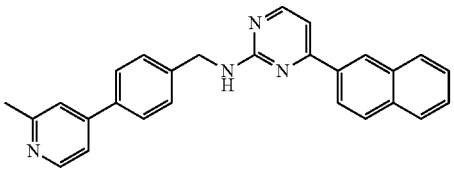
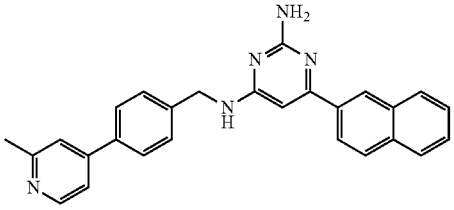
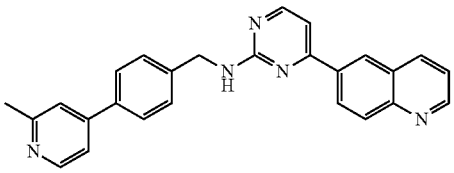
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-148		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.30 (s, 1H), 8.77 (s, 1H), 8.57 (d, J = 6.0 Hz, 1H), 8.54 (d, J = 6.0 Hz, 1H), 8.47 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 6.0 Hz, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.37 (s, 1H), 7.31 (d, J = 4.8 Hz, 1H), 6.90 (s, 1H), 5.30 (br s, 1H), 4.75 (s, 2H) 2.62 (s, 3H).	404.0
A-149		B	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 5.2 Hz, 1H), 7.99 (s, 1H), 7.91-7.83 (m, 3H), 7.71 (m, 1H), 7.64 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 8.4 Hz, 2H), 7.51-7.44 (m, 2H), 7.39 (s, 1H), 7.31 (m, 2H), 7.10 (d, J = 7.6 Hz, 1H), 7.00 (s, 1H), 6.68 (m, 1H), 4.50 (s, 2H), 4.30 (s, 1H), 2.65 (s, 3H).	401.1
A-150		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.2 Hz, 1H), 8.46 (s, 1H), 8.12 (d, J = 8.4 Hz, 1H), 7.90 (d, J = 8.4 Hz, 2H), 7.84 (s, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.55 (m, 3H), 7.51-7.45 (m, 2H), 7.38 (s, 1H), 7.33 (s, 1H), 7.24 (d, J = 8.0 Hz, 1H), 6.40 (d, J = 8.0 Hz, 1H), 4.72 (d, J = 5.6 Hz, 2H), 2.62 (s, 3H).	402.0
A-151		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.55 (s, 1H), 8.49 (d, J = 8.2 Hz, 1H), 8.37 (s, 1H), 7.97 (d, J = 6.4 Hz, 1H), 7.89 (dd, J = 16.2, 7.8 Hz, 2H), 7.63 (d, J = 7.2 Hz, 2H), 7.52 (d, J = 6.2 Hz, 4H), 7.37 (s, 1H), 7.31 (s, 1H), 6.31 (d, J = 5.2 Hz, 1H), 5.43 (s, 1H), 4.78 (s, 2H), 2.62 (s, 3H), 1.74 (s, 1H), 1.24 (s, 1H).	403.0
A-152		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (s, 2H), 8.41 (s, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.94 (s, 2H), 7.87 (s, 1H), 7.62 (d, J = 6.4 Hz, 2H), 7.55 (d, J = 4.2 Hz, 4H), 7.37 (s, 1H), 7.31 (s, 1H), 7.18 (s, 1H), 5.67 (s, 1H), 4.85 (s, 2H), 2.62 (s, 3H).	403.0
A-153		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.42 (s, 1H), 7.96 (d, J = 8.8 Hz, 1H), 7.93-7.82 (m, 3H), 7.61 (d, J = 8.4 Hz, 2H), 7.53-7.48 (m, 2H), 7.46 (d, J = 8.4 Hz, 2H), 7.35 (s, 1H), 7.29 (d, J = 5.2 Hz, 1H), 6.34 (s, 1H), 5.25 (s, 1H), 4.94 (s, 2H), 4.67 (d, J = 5.6 Hz, 2H), 2.61 (s, 3H).	418.0
A-154		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.52 (d, J = 8.8 Hz, 2H), 8.44 (d, J = 4.0 Hz, 1H), 8.36 (d, J = 8.8 Hz, 1H), 8.25 (d, J = 8.0 Hz, 1H), 8.19 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 7.6 Hz, 2H), 7.46 (dd, J = 7.6, 4.4 Hz, 1H), 7.36 (s, 1H), 7.30 (d, J = 4.4 Hz, 1H), 7.18 (d, J = 5.2 Hz, 1H), 5.65 (s, 1H), 4.84 (d, J = 5.2 Hz, 2H), 2.61 (s, 3H).	404.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

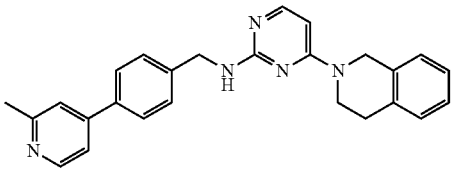
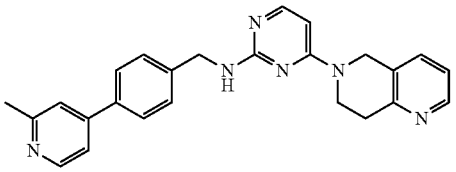
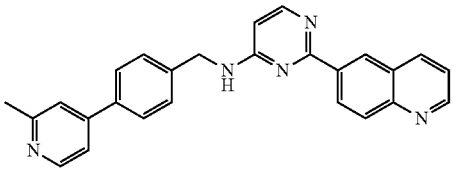
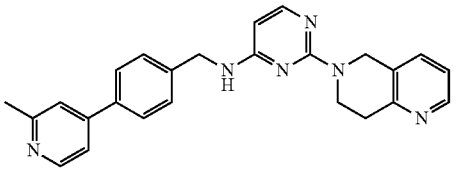
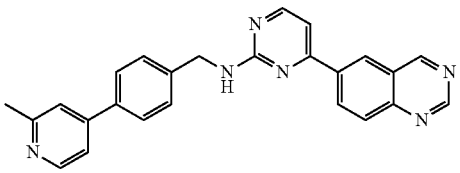
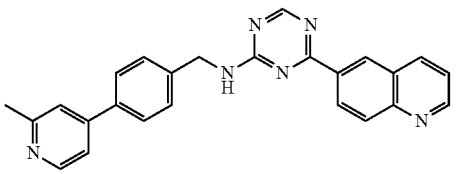
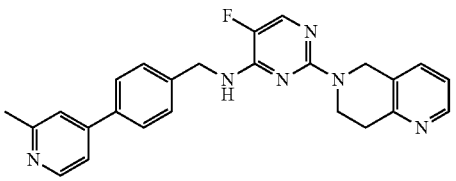
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-155		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, J = 5.2 Hz, 1H), 7.81 (d, J = 5.6 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.0 Hz, 2H), 7.35 (s, 1H), 7.30 (d, J = 4.8 Hz, 1H), 7.26 (s, 1H), 7.22-7.10 (m, 4H), 5.98 (d, J = 6.4 Hz, 1H), 4.69 (s, 2H), 4.68 (s, 2H), 3.80 (s, 2H), 2.91 (t, J = 5.6 Hz, 2H), 2.61 (s, 3H).	408.1
A156		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.44 (d, J = 4.4 Hz, 1H), 7.89 (d, J = 4.4 Hz, 1H), 7.59 (d, J = 7.6 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 7.2 Hz, 1H), 7.35 (s, 1H), 7.29 (d, J = 4.8 Hz, 1H), 7.16-7.10 (m, 1H), 6.02 (d, J = 6.0 Hz, 1H), 4.72 (s, 2H), 4.68 (d, J = 5.6 Hz, 2H), 3.92 (t, J = 5.6 Hz, 2H), 3.09 (t, J = 5.6 Hz, 2H), 2.61 (s, 3H).	409.0
A-157		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, J = 4.0 Hz, 1H), 8.89 (s, 1H), 8.74 (d, J = 8.8 Hz, 1H), 8.54 (d, J = 4.8 Hz, 1H), 8.37 (d, J = 5.6 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 7.64 (d, J = 7.6 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H), 7.43 (dd, J = 8.0, 4.4 Hz, 1H), 7.37 (s, 1H), 7.31 (d, J = 4.8 Hz, 1H), 6.34 (d, J = 5.6 Hz, 1H), 5.45 (s, 1H), 4.79 (s, 2H), 2.62 (s, 3H).	404.0
A-158		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 5.2 Hz, 1H), 8.41 (d, J = 4.0 Hz, 1H), 7.94 (d, J = 5.6 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.45 (d, J = 7.6 Hz, 3H), 7.36 (s, 1H), 7.30 (d, J = 5.2 Hz, 1H), 7.11 (dd, J = 7.2, 4.8 Hz, 1H), 5.76 (d, J = 6.0 Hz, 1H), 5.11 (s, 1H), 4.90 (s, 2H), 4.64 (d, J = 4.4 Hz, 2H), 4.13 (t, J = 6.0 Hz, 2H), 3.06 (t, J = 6.0 Hz, 2H), 2.62 (s, 3H).	409.0
A-159		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 9.37 (s, 1H), 8.61 (s, 1H), 8.58 (d, J = 8.8 Hz, 1H), 8.53 (d, J = 4.8 Hz, 1H), 8.48 (d, J = 5.2 Hz, 1H), 8.14 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 7.6 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.37 (s, 1H), 7.31 (d, J = 4.8 Hz, 1H), 7.18 (d, J = 4.8 Hz, 1H), 5.70 (s, 1H), 4.85 (d, J = 5.2 Hz, 2H), 2.62 (s, 3H).	405.0
A-160		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 2H), 8.79 (s, 1H), 8.74 (d, J = 8.6 Hz, 1H), 8.67 (s, 1H), 8.55 (s, 1H), 8.30 (d, J = 6.8 Hz, 1H), 8.19 (d, J = 8.6 Hz, 1H), 7.63 (d, J = 6.4 Hz, 2H), 7.51 (dd, J = 15.4, 8.5 Hz, 3H), 7.37 (s, 1H), 7.32 (s, 1H), 6.18 (s, 1H), 6.05 (s, 1H), 4.92 (s, 1H), 4.83 (s, 1H), 2.62 (s, 3H).	405.0
A-161		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 4.8 Hz, 1H), 8.41 (d, J = 4.0 Hz, 1H), 7.82 (d, J = 2.8 Hz, 1H), 7.62 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.0 Hz, 1H), 7.38 (s, 1H), 7.33 (d, J = 4.8 Hz, 1H), 7.11 (dd, J = 7.2, 4.4 Hz, 1H), 5.30 (s, 1H), 4.84 (s, 2H), 4.76 (d, J = 5.2 Hz, 2H), 4.08 (t, J = 5.6 Hz, 2H), 3.06 (t, J = 6.0 Hz, 2H), 2.64 (s, 3H).	427.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

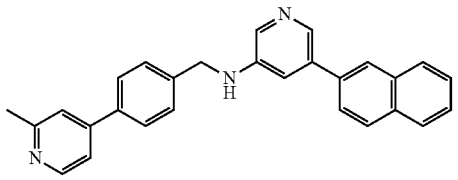
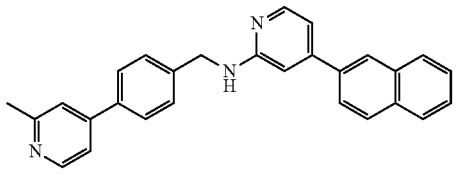
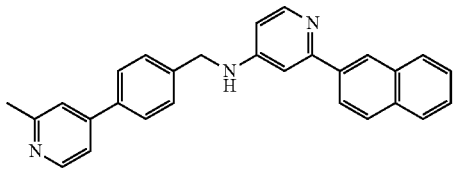
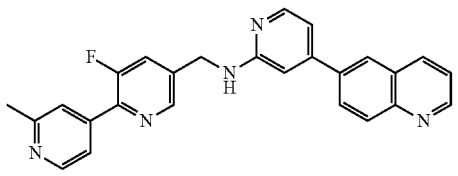
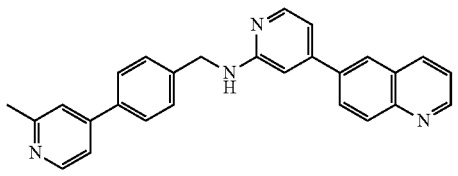
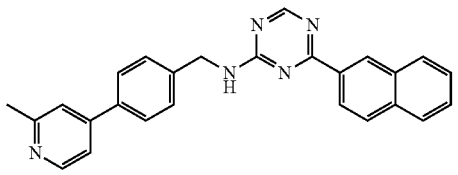
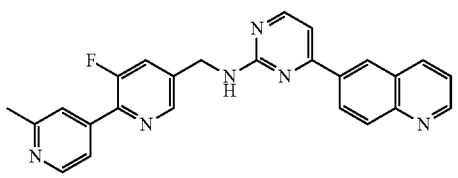
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-162		B	^{1}H NMR (400 MHz, DMSO) δ 8.46 (d, J = 5.2 Hz, 1H), 8.18 (d, J = 15.6 Hz, 2H), 8.07-7.89 (m, 5H), 7.77 (d, J = 8.0 Hz, 3H), 7.55 (m, 5H), 7.48 (d, J = 4.8 Hz, 1H), 7.30 (s, 1H), 6.74 (s, 1H), 4.50 (d, J = 5.6 Hz, 2H).	402.0
A-163		B	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, J = 4.8 Hz, 1H), 8.18 (d, J = 4.8 Hz, 1H), 8.02 (s, 1H), 7.96-7.82 (m, 3H), 7.68-7.56 (m, 4H), 7.52 (d, J = 8.0 Hz, 5H), 7.37 (s, 1H), 7.31 (d, J = 4.4 Hz, 1H), 6.75 (s, 1H), 4.68 (d, J = 5.2 Hz, 2H), 2.62 (s, 3H).	
A-164		B	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.2 Hz, 1H), 8.39 (s, 1H), 8.23 (d, J = 5.6 Hz, 1H), 7.97-7.78 (m, 4H), 7.63 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 5.6 Hz, 4H), 7.35 (s, 1H), 7.29 (d, J = 5.6 Hz, 1H), 7.09 (s, 1H), 6.53 (s, 1H), 4.54 (d, J = 5.2 Hz, 2H), 2.62 (s, 3H).	402.0
A-165		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.62 (s, 2H), 8.23 (t, J = 7.8 Hz, 2H), 8.16 (s, 1H), 8.03 (s, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 7.66 (d, J = 11.6 Hz, 1H), 7.50 (d, J = 4.2 Hz, 1H), 7.08 (s, 1H), 6.83 (s, 1H), 6.64 (s, 1H), 4.79 (s, 2H), 2.68 (s, 3H).	454.0
A-166		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (s, 1H), 8.55 (s, 1H), 8.21 (d, J = 8.4 Hz, 2H), 7.99 (s, 2H), 7.82 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 7.6 Hz, 2H), 7.55 (d, J = 7.8 Hz, 2H), 7.52-7.46 (m, 1H), 7.40 (d, J = 15.8 Hz, 2H), 7.09 (s, 1H), 6.89 (s, 1H), 4.72 (s, 2H), 2.68 (s, 3H).	
A-167		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (d, J = 10 Hz, 1H), 8.79 (s, 1H), 8.69 (s, 1H), 8.53 (s, 1H), 8.49 (d, J = 8.4 Hz, 1H), 8.44 (d, J = 8.8 Hz, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.91 (m, 2H), 7.64 (d, J = 7.6 Hz, 2H), 7.5 (m, 4H), 7.37 (s, 1H), 7.31 (d, J = 4.8 Hz, 1H), 5.91 (s, 1H), 4.93 (d, J = 5.6 Hz, 1H), 4.82 (d, J = 6 Hz, 1H), 2.62 (s, 3H).	404.0
A-168		A	^{1}H NMR (400 MHz, DMSO) δ 8.96 (d, J = 2.8 Hz, 1H), 8.75 (s, 1H), 8.68 (s, 1H), 8.56 (d, J = 5.2 Hz, 1H), 8.50-8.44 (m, 3H), 8.11 (d, J = 8.8 Hz, 1H), 8.07-8.01 (m, 1H), 7.88 (s, 1H), 7.74 (s, 1H), 7.66 (d, J = 4.4 Hz, 1H), 7.61 (dd, J = 8.4, 4.0 Hz, 1H), 7.40 (d, J = 5.2 Hz, 1H), 4.74 (s, 2H), 2.53 (s, 3H).	423.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

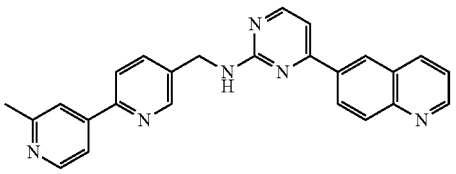
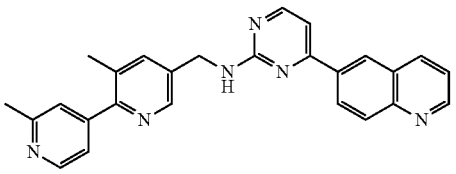
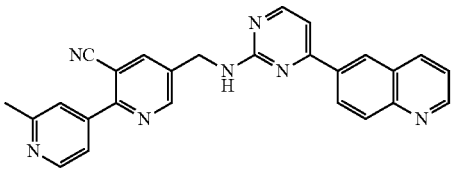
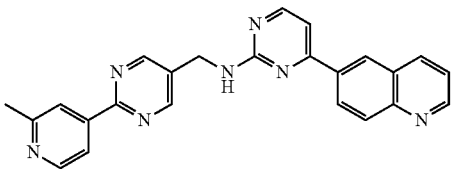
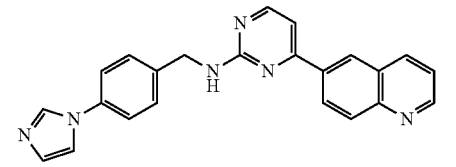
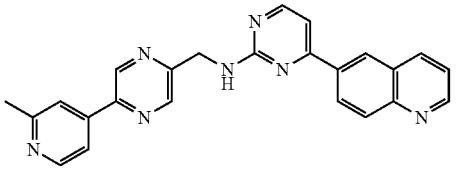
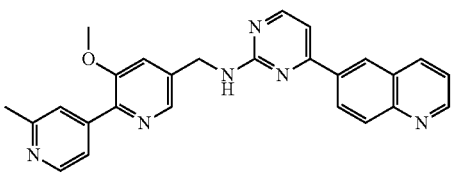
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-169		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (d, J = 4.0 Hz, 1H), 8.79 (s, 1H), 8.73 (s, 1H), 8.52 (d, J = 5.2 Hz, 1H), 8.50-8.43 (m, 3H), 8.11 (d, J = 8.8 Hz, 1H), 8.08-7.89 (m, 4H), 7.82 (d, J = 4.8 Hz, 1H), 7.60 (dd, J = 8.4, 4.4 Hz, 1H), 7.37 (d, J = 5.2 Hz, 1H), 4.70 (s, 2H), 2.53 (s, 3H).	405.0
A-170		A	^{1}H NMR (400 MHz, DMSO) δ 8.96 (d, J = 2.4 Hz, 1H), 8.76 (s, 1H), 8.59 (s, 1H), 8.52-8.43 (m, 4H), 8.12 (d, J = 8.8 Hz, 1H), 8.04-7.97 (m, 1H), 7.79 (s, 1H), 7.61 (dd, J = 8.4, 4.4 Hz, 1H), 7.42 (s, 1H), 7.39-7.32 (m, 2H), 4.66 (s, 2H), 2.51 (s, 3H), 2.32 (s, 3H).	419.0
A-171		A	^{1}H NMR (400 MHz, DMSO) δ 9.04 (s, 1H), 8.96 (d, J = 3.6 Hz, 1H), 8.76 (s, 1H), 8.62 (d, J = 4.8 Hz, 1H), 8.56-8.39 (m, 4H), 8.12 (d, J = 8.8 Hz, 1H), 8.08-8.02 (m, 1H), 7.68 (s, 1H), 7.65-7.59 (m, 2H), 7.41 (d, J = 4.8 Hz, 1H), 4.75 (s, 2H), 2.55 (s, 3H).	430.0
A-172		A	^{1}H NMR (400 MHz, DMSO) δ 9.03 (s, 2H), 8.96 (d, J = 2.8 Hz, 1H), 8.76 (s, 1H), 8.60 (d, J = 5.2 Hz, 1H), 8.51-8.44 (m, 3H), 8.12 (d, J = 8.0 Hz, 2H), 8.06-8.00 (m, 2H), 7.61 (dd, J = 8.4, 4.4 Hz, 1H), 7.40 (d, J = 5.2 Hz, 1H), 4.71 (s, 2H), 2.56 (s, 3H).	406.0
A-173		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 8.51 (s, 1H), 8.44 (s, 1H), 8.36 (d, J = 8.8 Hz, 1H), 8.26 (d, J = 7.6 Hz, 1H), 8.19 (d, J = 8.8 Hz, 1H), 7.85 (s, 1H), 7.55 (d, J = 7.6 Hz, 2H), 7.46 (s, 1H), 7.38 (d, J = 7.2 Hz, 2H), 7.27 (s, 1H), 7.22-7.18 (m, 2H), 5.67 (s, 1H), 4.83 (d, J = 4.4 Hz, 2H).	379.0
A-174		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (s, 1H), 8.97 (d, J = 2.8 Hz, 1H), 8.83 (s, 1H), 8.64 (d, J = 5.2 Hz, 1H), 8.50 (s, 1H), 8.45 (d, J = 4.8 Hz, 1H), 8.35 (dd, J = 8.8, 1.6 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 8.8 Hz, 1H), 7.79 (s, 1H), 7.70 (d, J = 4.8 Hz, 1H), 7.46 (dd, J = 8.0, 4.0 Hz, 1H), 7.21 (d, J = 5.2 Hz, 1H), 6.17 (t, J = 5.2 Hz, 1H), 5.00 (d, J = 5.6 Hz, 2H), 2.67 (s, 3H).	406.0
A-175		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 2.8 Hz, 1H), 8.55 (d, J = 4.4 Hz, 1H), 8.50 (s, 1H), 8.47-8.41 (m, 2H), 8.36 (d, J = 8.4 Hz, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 8.8 Hz, 1H), 7.82 (d, J = 10.8 Hz, 2H), 7.49-7.43 (m, 2H), 7.22 (d, J = 4.4 Hz, 1H), 5.73 (s, 1H), 4.86 (d, J = 4.8 Hz, 2H), 3.87 (s, 3H), 2.68 (s, 3H).	435.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

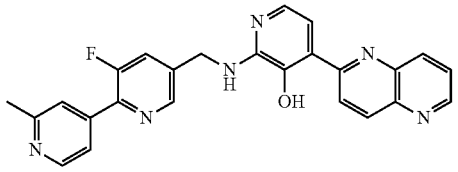
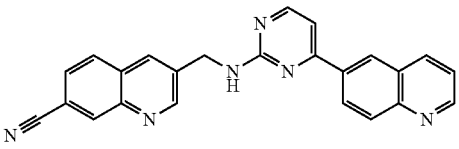
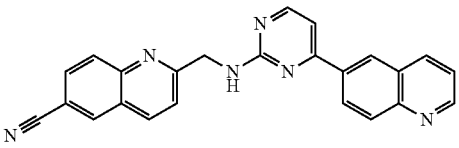
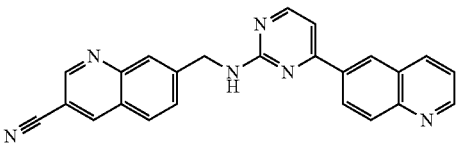
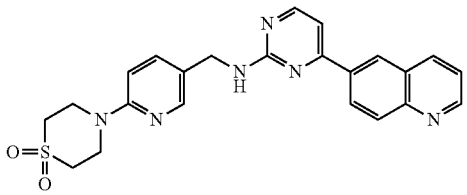
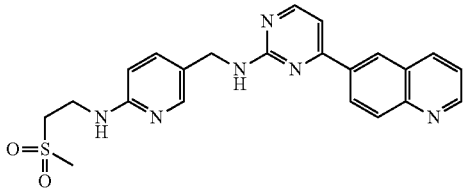
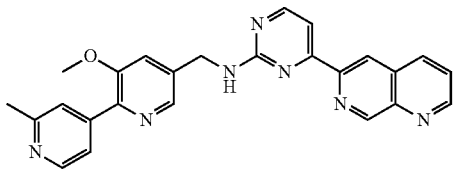
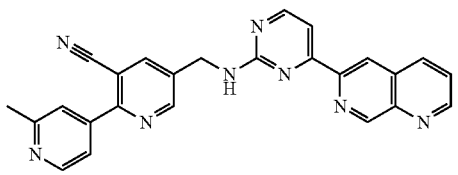
Compd NO.	Structure	Meth-od	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-176		G	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.04 (d, J = 3.2 Hz, 1H), 8.65-8.55 (m, 3H), 8.38 (d, J = 8.4 Hz, 1H), 8.30 (d, J = 9.2 Hz, 1H), 7.79 (d, J = 6.0 Hz, 2H), 7.74 (dd, J = 8.4, 4.0 Hz, 1H), 7.69 (d, J = 4.4 Hz, 1H), 7.62 (d, J = 11.6 Hz, 1H), 7.14 (d, J = 5.6 Hz, 1H), 5.77 (t, J = 5.2 Hz, 1H), 4.89 (d, J = 6.0 Hz, 2H), 2.65 (s, 3H).	
A-177		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.97 (d, J = 4.0 Hz, 1H), 8.48 (s, 1H), 8.45 (s, 1H), 8.44 (s, 1H) 8.32 (d, J = 9.2 Hz, 1H), 8.24 (d, J = 6.8 Hz, 2H), 8.18 (d, J = 8.8 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.68 (d, J = 8.4 Hz, 1H), 7.47 (m, 1H), 7.22 (d, J = 5.2 Hz, 1H), 5.85 (s, 1H), 5.02 (d, J = 6.4 Hz, 2H).	389.1
A-178		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 3.2 Hz, 1H), 8.52 (s, 1H), 8.48 (d, J = 5.2 Hz, 1H), 8.39 (d, J = 8.8 Hz, 1H), 8.18-8.25 (m, 5H), 7.89 (d, J = 8.8 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 7.47 (dd, J = 8.0, 4.0 Hz, 1H), 7.21 (d, J = 4.8 Hz, 1H), 6.67 (s, 1H), 5.10 (d, J = 4.0 Hz, 2H).	389.0
A-179		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.96 (d, J = 2.8 Hz, 1H), 8.52 (s, 1H), 8.48 (s, 1H), 8.44 (d, J = 5.2 Hz, 1H), 8.32 (d, J = 8.8 Hz, 1H), 8.24 (d, J = 8.0 Hz, 1H), 8.21 (s, 1H), 8.16 (d, J = 8.8 Hz, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.78 (d, J = 8.4 Hz, 1H), 7.47-7.44 (m, 1H), 7.20 (d, J = 4.8 Hz, 1H), 5.86 (s, 1H), 5.05 (d, J = 6.0 Hz, 2H).	389.1
A-180		A	^{1}H NMR (400 MHz, DMSO) δ 8.96 (d, J = 3.2 Hz, 1H), 8.76 (s, 1H), 8.50 (d, J = 7.6 Hz, 2H), 8.43 (d, J = 4.4 Hz, 1H), 8.23 (s, 1H), 8.13 (d, J = 8.8 Hz, 1H), 7.86-7.78 (m, 1H), 7.67 (s, 1H), 7.61 (dd, J = 8.0, 4.0 Hz, 1H), 7.34 (d, J = 5.2 Hz, 1H), 6.99 (d, J = 8.8 Hz, 1H), 4.51 (s, 2H), 4.01 (s, 4H), 3.05 (s, 4H).	447.0
A-181		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (d, J = 3.6 Hz, 1H), 8.52 (s, 1H), 8.43 (d, J = 5.2 Hz, 1H), 8.37 (d, J = 8.8 Hz, 1H), 8.28 (d, J = 8.0 Hz, 1H), 8.21-8.16 (m, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.47 (dd, J = 8.2, 4.2 Hz, 1H), 7.17 (d, J = 5.2 Hz, 1H), 6.46 (d, J = 8.8 Hz, 1H), 5.48 (s, 1H), 4.93 (s, 1H), 4.63 (d, J = 5.6 Hz, 2H), 3.97-3.91 (m, 2H), 3.38 (t, J = 5.8 Hz, 2H), 2.94 (s, 3H).	
A182		F	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 9.07 (s, 1H), 8.72 (s, 1H), 8.55 (d, J = 4.8 Hz, 2H), 8.44 (s, 1H), 8.28 (s, 1H), 7.83 (d, J = 3.6 Hz, 1H), 7.71 (s, 1H), 7.68-7.63 (m, 2H), 7.44 (s, 1H), 5.66 (s, 1H), 4.87 (d, J = 5.6 Hz, 2H), 3.86 (s, 3H), 2.62 (s, 3H).	436.0
A-183		F	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 9.07 (s, 1H), 8.67 (d, J = 8.4 Hz, 2H), 8.61 (d, J = 5.2 Hz, 1H), 8.54 (d, J = 5.2 Hz, 1H), 8.27 (d, J = 8.4 Hz, 1H), 7.85 (d, J = 5.2 Hz, 1H), 7.76 (s, 1H), 7.71-7.63 (m, 3H), 5.71 (s, 1H), 4.89 (d, J = 5.6 Hz, 2H), 2.64 (s, 3H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

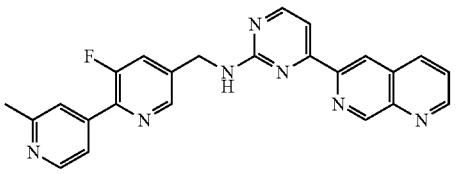
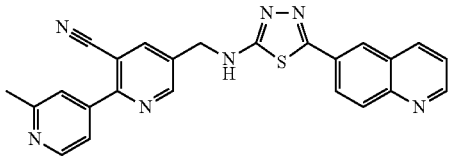
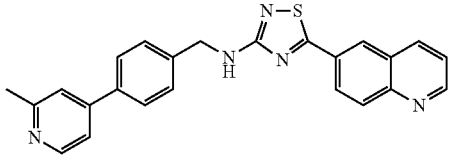
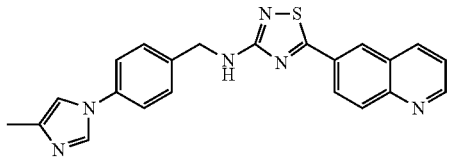
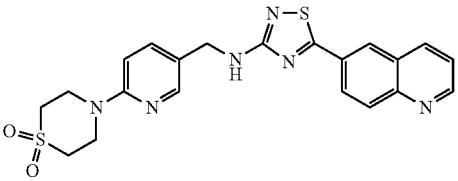
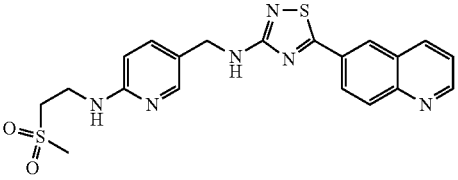
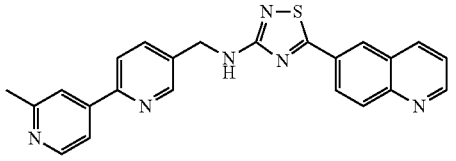
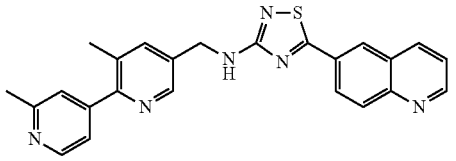
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A184		F	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.58 (s, 1H), 9.09 (d, J = 3.2 Hz, 1H), 9.01 (s, 1H), 8.69-8.64 (m, 2H), 8.54 (d, J = 4.8 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.22 (s, 1H), 7.88 (d, J = 4.8 Hz, 1H), 7.70-7.60 (m, 3H), 5.77 (m, 1H), 4.90 (d, J = 6.0 Hz, 2H), 2.86 (s, 3H).	
A185		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (s, 1H), 8.95 (d, J = 3.2 Hz, 1H), 8.68 (d, J = 5.2 Hz, 1H), 8.26 (s, 1H), 8.22-8.13 (m, 4H), 7.68 (s, 1H), 7.64 (d, J = 5.2 Hz, 1H), 7.46 (dd, J = 8.0, 4.4 Hz, 1H), 7.26 (s, 1H), 4.84 (s, 2H), 2.66 (s, 3H).	436.0
A-186		A	^{1}H NMR (400 MHz, DMSO) δ 9.00 (d, J = 2.8 Hz, 1H), 8.62 (s, 1H), 8.57 (d, J = 8.4 Hz, 1H), 8.47 (d, J = 5.2 Hz, 1H), 8.30-8.25 (m, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 7.76 (d, J = 8.0 Hz, 2H), 7.64 (dd, J = 8.4, 4.4 Hz, 1H), 7.57 (s, 1H), 7.52 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 4.8 Hz, 1H), 4.61 (d, J = 6.0 Hz, 2H), 2.51 (s, 3H).	410.0
A-187		A	^{1}H NMR (400 MHz, DMSO) δ 9.00 (d, J = 3.2 Hz, 1H), 8.61 (s, 1H), 8.56 (d, J = 8.0 Hz, 1H), 8.29-8.24 (m, 1H), 8.23-8.14 (m, 3H), 7.64 (dd, J = 8.0, 4.0 Hz, 1H), 7.58 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.8 Hz, 3H), 4.57 (d, J = 6.0 Hz, 2H), 2.19 (s, 3H).	
A-188		A	^{1}H NMR (400 MHz, DMSO) δ 9.00 (d, J = 2.8 Hz, 1H), 8.61 (s, 1H), 8.56 (d, J = 8.4 Hz, 1H), 8.23-8.07 (m, 4H), 7.68-7.61 (m, 2H), 7.00 (d, J = 8.8 Hz, 1H), 4.42 (d, J = 6.0 Hz, 2H), 4.03 (s, 4H), 3.06 (s, 4H).	
A-189		A	^{1}H NMR (400 MHz, DMSO) δ 9.00 (d, J = 3.2 Hz, 1H), 8.60 (s, 1H), 8.56 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 9.6 Hz, 1H), 8.15 (d, J = 8.8 Hz, 1H), 8.04 (s, 2H), 7.64 (dd, J = 8.4, 4.4 Hz, 1H), 7.48 (d, J = 8.0 Hz, 1H), 6.74 (s, 1H), 6.50 (d, J = 8.4 Hz, 1H), 4.35 (d, J = 6.0 Hz, 2H), 3.69-3.61 (m, 2H), 3.32-3.30 (m, 2H), 2.99 (s, 3H).	
A-190		A	^{1}H NMR (400 MHz, DMSO) δ 9.00 (d, J = 2.8 Hz, 1H), 8.76 (s, 1H), 8.62 (s, 1H), 8.59-8.51 (m, 2H), 8.34-8.29 (m, 1H), 8.22 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.92 (s, 1H), 7.82 (d, J = 5.2 Hz, 1H), 7.64 (dd, J = 8.0, 4.0 Hz, 1H), 4.63 (d, J = 6.0 Hz, 2H), 2.54 (s, 3H).	411.0
A-191		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (d, J = 2.8 Hz, 1H), 8.61 (s, 1H), 8.58 (d, J = 4.8 Hz, 1H), 8.40 (s, 1H), 8.26 (d, J = 8.0 Hz, 1H), 8.22-8.14 (m, 2H), 7.69 (s, 1H), 7.49 (dd, J = 8.0, 4.0 Hz, 1H), 7.33 (s, 1H), 7.24 (d, J = 5.6 Hz, 1H), 5.66 (s, 1H), 4.76 (d, J = 6.0 Hz, 2H), 2.62 (s, 3H), 2.37 (s, 3H).	425.0

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

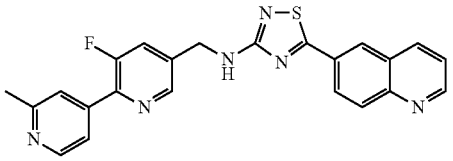
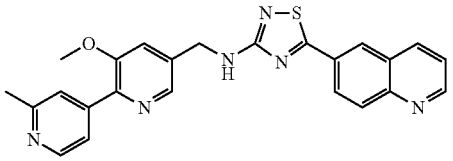
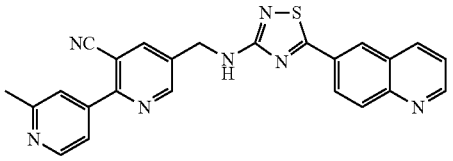
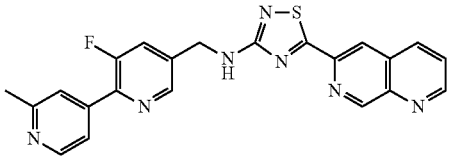
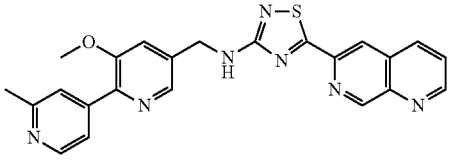
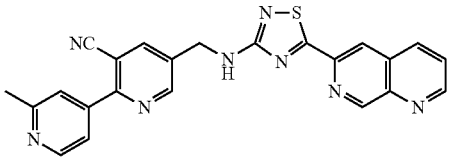
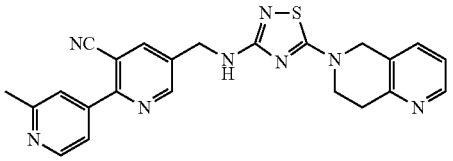
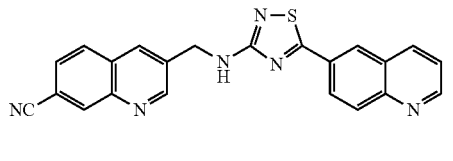
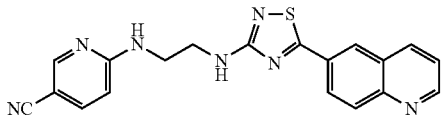
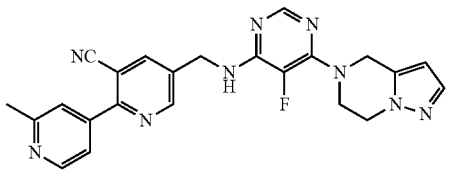
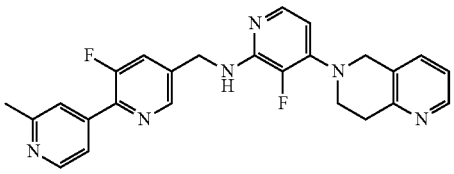
Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-192		A	^{1}H NMR (400 MHz, DMSO) δ 9.00 (d, J = 2.8 Hz, 1H), 8.64 (d, J = 9.2 Hz, 2H), 8.60-8.54 (m, 2H), 8.38-8.32 (m, 1H), 8.22 (d, J = 8.8 Hz, 1H), 8.16 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 12.0 Hz, 1H), 7.77 (s, 1H), 7.69 (d, J = 4.4 Hz, 1H), 7.64 (dd, J = 8.0, 4.0 Hz, 1H), 4.67 (d, J = 6.0 Hz, 2H), 2.55 (s, 3H).	429.0
A-193		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (d, J = 2.8 Hz, 1H), 8.55 (d, J = 4.8 Hz, 1H), 8.40 (s, 2H), 8.26 (d, J = 8.0 Hz, 1H), 8.22-8.14 (m, 2H), 7.73 (s, 1H), 7.69 (d, J = 4.4 Hz, 1H), 7.49 (dd, J = 8.0, 4.0 Hz, 1H), 7.45 (s, 1H), 5.70 (t, J = 5.6 Hz, 1H), 4.79 (d, J = 6.0 Hz, 2H), 3.90 (s, 3H), 2.63 (s, 3H).	440.9
A-194		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.00 (d, J = 3.2 Hz, 1H), 8.98 (s, 1H), 8.68 (d, J = 4.8 Hz, 1H), 8.39 (s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.21 (d, J = 7.2 Hz, 2H), 8.15 (d, J = 8.8 Hz, 1H), 7.69 (s, 1H), 7.64 (d, J = 4.8 Hz, 1H), 7.50 (dd, J = 8.0, 4.0 Hz, 1H), 5.83 (t, J = 5.6 Hz, 1H), 4.83 (d, J = 6.0 Hz, 2H), 2.67 (s, 3H).	435.9
A-195		A	^{1}H NMR (400 MHz, DMSO) δ 9.47 (s, 1H), 9.15 (d, J = 3.2 Hz, 1H), 8.71 (d, J = 8.4 Hz, 1H), 8.64 (d, J = 8.4 Hz, 2H), 8.57 (d, J = 5.2 Hz, 1H), 8.28-8.22 (m, 1H), 7.92-7.84 (m, 2H), 7.75 (s, 1H), 7.67 (d, J = 4.4 Hz, 1H), 4.68 (d, J = 6.0 Hz, 2H), 2.55 (s, 3H).	429.9
A-196		A	^{1}H NMR (400 MHz, DMSO) δ 9.47 (s, 1H), 9.15 (d, J = 3.2 Hz, 1H), 8.70 (d, J = 8.4 Hz, 1H), 8.64 (s, 1H), 8.48 (d, J = 4.8 Hz, 1H), 8.35 (s, 1H), 8.23-8.17 (m, 1H), 7.90 (dd, J = 8.4, 4.0 Hz, 1H), 7.73 (s, 1H), 7.68 (s, 1H), 7.67 (d, J = 6.0 Hz, 1H), 4.65 (d, J = 6.0 Hz, 2H), 3.89 (s, 3H), 2.51 (s, 3H).	441.9
A-197		A	^{1}H NMR (400 MHz, DMSO) δ 9.47 (s, 1H), 9.16 (d, J = 3.2 Hz, 1H), 9.01 (s, 1H), 8.71 (d, J = 8.4 Hz, 1H), 8.64 (s, 2H), 8.46 (s, 1H), 8.29-8.23 (m, 1H), 7.90 (dd, J = 8.4, 4.0 Hz, 1H), 7.69 (s, 1H), 7.64 (d, J = 4.8 Hz, 1H), 4.69 (d, J = 6.0 Hz, 2H), 2.57 (s, 3H).	437.0
A-198		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.67 (d, J = 4.8 Hz, 1H), 8.48 (d, J = 4.4 Hz, 1H), 8.15 (s, 1H), 7.67 (s, 1H), 7.62 (d, J = 4.8 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.20 (dd, J = 6.8, 4.8 Hz, 1H), 5.33 (t, J = 5.6 Hz, 1H), 4.68 (d, J = 6.4 Hz, 2H), 4.65 (s, 2H), 3.80 (t, J = 4.8 Hz, 2H), 3.19 (t, J = 6.0 Hz, 2H), 2.67 (s, 3H).	441.0
A-199		A	^{1}H NMR (400 MHz, DMSO) δ 9.12 (s, 1H), 9.00 (d, J = 3.2 Hz, 1H), 8.62 (s, 1H), 8.56 (d, J = 10.8 Hz, 2H), 8.45-8.39 (m, 2H), 8.21 (d, J = 8.0 Hz, 2H), 8.15 (d, J = 8.8 Hz, 1H), 7.90 (d, J = 8.4 Hz, 1H), 7.64 (dd, J = 8.0, 4.0 Hz, 1H), 4.79 (d, J = 5.6 Hz, 2H).	

TABLE 2-continued

Selected compounds (A-1 to A-202) of the present invention.

Compd NO.	Structure	Method	^{1}HNMR	ESI-MS (m/z): $[M + 1]^+$
A-200		A	^{1}H NMR (400 MHz, DMSO) δ 9.00 (d, J = 2.8 Hz, 1H), 8.59 (s, 1H), 8.56 (d, J = 8.0 Hz, 1H), 8.41 (s, 1H), 8.21-8.12 (m, 2H), 7.78-7.60 (m, 4H), 6.57 (d, J = 8.8 Hz, 1H), 3.57 (s, 2H), 3.52 (t, J = 5.2 Hz, 2H).	
A-201		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (s, 1H), 8.67 (d, J = 5.0 Hz, 1H), 8.10 (s, 1H), 8.02 (s, 1H), 7.67 (s, 1H), 7.62 (d, J = 4.8 Hz, 1H), 7.50 (s, 1H), 6.10 (s, 1H), 5.34 (s, 1H), 4.94 (s, 2H), 4.81 (d, J = 6.2 Hz, 2H), 4.32 (m, 2H), 4.18 (m, 2H), 2.67 (s, 3H).	
A-202		A	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 5.0 Hz, 1H), 8.54 (s, 1H), 8.45 (d, J = 3.2 Hz, 1H), 7.75 (s, 1H), 7.71 (d, J = 5.6 Hz, 1H), 7.67 (d, J = 4.6 Hz, 1H), 7.55 (d, J = 11.8 Hz, 1H), 7.43 (d, J = 7.6 Hz, 1H), 7.18 (m, 1H), 6.30 (m, 1H), 5.02 (s, 1H), 4.78 (d, J = 5.8 Hz, 2H), 4.48 (s, 2H), 3.71 (m, 2H), 3.15 (m, 2H), 2.63 (s, 3H).	445.0

Biological Activities:

[0301] The primary assay is based on Wnt pathway Super-top flash (STF) reporter gene assay:

[0302] HEK293 STF stable clones (HEK293 cells stably transfected with "Super-Top Flash" TCF-luciferase reporter plasmid) were kept in complete culture medium (DMEM with 4 mM L-Gln, 1.5 g/L sodium bicarbonate and 4.5 g/L glucose containing 6 μg/mL Blasticidin and 10% FBS). L Wnt3A cells (CRL-2647, ATCC) were kept in DMEM (Gibico) containing 10% FBS (Hyclone). HEK293 STF and L Wnt3A cells were harvested when 90% confluence and cell suspension was mixed with a fixed ratio of 1:1 (HEK293 STF:L Wnt3A). 100 μL/well of mixed cells suspension was added to the 96-well-plate with final cell concentration of 12,000 cells/well and then cultured for an additional 24 hours before adding compounds.

[0303] Compounds were diluted in DMSO in sequence and then diluted with DMEM medium. 20 μL medium containing compound was added to the cells according to the pre-setting dose. Cell plates were incubated at 37° C. for an additional 48 hours.

[0304] 50 μL luciferase solution (Bright-Glo, Promega) was added to each well during the 48 h incubation. The plates were incubated at room temperature for 5 min under gentle shaking. Luminescence signaling was measured with a plate reader (PHERAstar FS, BMG). The IC_{50} (potency) of compounds was calculated based on the inhibition of luminescence signaling.

[0305] The above mentioned compounds were tested in the primary assay described above and the data were summarized in Table 3. In particular, IC50 curves for compounds A-12, A-36, A-100, A-103, A-166, A-168, A-194, and A-198 are shown in FIGS. **1-8**, respectively.

TABLE 3

Results of selected compounds (A-1 to A-202) of the present invention when tested in the primary assay.

Compound number	IC_{50} (nM)	Compound number	IC_{50} (nM)	Compound number	IC_{50} (nM)
A-1	1.4	A-2	2.9	A-3	36
A-4	0.3	A-5	2.1	A-6	4.7
A-7	7.4	A-8	1.5	A-9	2.8
A-10	285	A-11	1.6	A-12	0.3
A-13	99	A-14	5.9	A-15	19
A-16	27	A-17	>1000	A-18	480
A-19	14	A-20	211	A-21	14
A-22	14	A-23	15	A-24	37
A-25	>1000	A-26	1.5	A-27	937
A-28	17	A-29	577	A-30	23
A-31	1	A-32	2	A-33	1.4
A-34	3	A-35	4	A-36	0.5
A-37	2.4	A-38	5	A-39	129
A-40	>1000	A-41	55	A-42	0.7
A-43	75	A-44	1	A-45	0.4
A-46	4.9	A-47	0.94	A-48	2.1
A-49	0.39	A-50	1.0	A-51	1.0
A-52	17	A-53	89	A-54	0.67
A-55	3000	A-56	1	A-57	0.39
A-58	34	A-59	230	A-60	0.81
A-61	1.3	A-62	6.2	A-63	2
A-64	16	A-65	0.44	A-66	58
A-67	10	A-68	16	A-69	73
A-70	147	A-71	0.29	A-72	0.64
A-73	1.3	A-74	1.6	A-75	0.52
A-76	1.3	A-77	1.6	A-78	777
A-79	416	A-80	768	A-81	625
A-82	338	A-83	3000	A-84	0.26
A-85	0.14	A-86	0.34	A-87	0.51
A-88	7.7	A-89	14	A-90	1.2
A-91	53	A-92	10	A-93	40
A-94	0.8	A-95	15	A-96	0.2
A-97	0.18	A-98	0.06	A-99	0.11
A-100	0.27	A-101	0.31	A-102	0.54

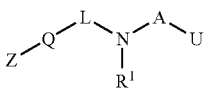
TABLE 3-continued

Results of selected compounds (A-1 to A-202) of the present invention when tested in the primary assay.

Compound number	IC_{50} (nM)	Compound number	IC_{50} (nM)	Compound number	IC_{50} (nM)
A-103	0.12	A-104	0.11	A-105	5.2
A-106	0.24	A-107	16	A-108	1
A-109	10	A-110	1	A-111	10
A-112	10	A-113	16	A-114	8
A-115	7	A-116	8	A-117	2
A-118	318	A-119	10	A-120	12
A-121	0.06	A-122	0.13	A-123	0.12
A-124	0.12	A-125	0.06	A-126	0.04
A-127	0.34	A-128	1.8	A-129	0.4
A-130	0.11	A-131	1.0	A-132	0.25
A-133	34	A-134	24	A-135	3000
A-136	4000	A-137	3000	A-138	712
A-139	3000	A-140	3000	A-141	3000
A-142	3000	A-143	2000	A-144	40
A-145	1131	A-146	68	A-147	40
A-148	10	A-149	603	A-150	250
A-151	2000	A-152	4.9	A-153	3000
A-154	1.2	A-155	229	A-156	12
A-157	3000	A-158	3000	A-159	17
A-160	6.7	A-161	3000	A-162	2000
A-162	3.2	A-164	3000	A-165	0.71
A-166	3.6	A-167	120	A-168	0.85
A-169	4.9	A-170	3.7	A-171	0.31
A-172	1.7	A-173	106	A-174	2.7
A-175	0.74	A-176	18	A-177	100
A-178	200	A-179	500	A-180	300
A-181	350	A-182	0.64	A-183	2.1
A-184	1	A-185	4.3	A-186	0.27
A-187	51	A-188	4.6	A-189	3000
A-190	0.4	A-191	0.38	A-192	0.1
A-193	0.07	A-194	0.09	A-195	0.84
A-196	0.78	A-197	0.31	A-198	0.42
A-199	0.17	A-200	25	A-201	0.8
A-202	0.5				

What is claimed is:

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt, solvate, stereoisomer or a tautomer thereof, wherein

A is A1, A2, A3 or A4;

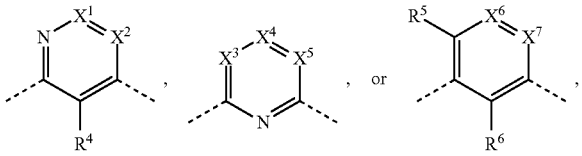
U is U1, U2, U3 or U4;

L is L, L2, or L3;

Q is Q1, Q2, Q3 or Q4;

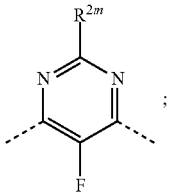
Z is Z1, Z2, Z3 or Z4;

A1 is



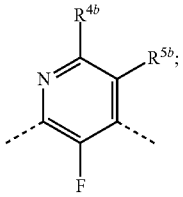
wherein X^1 to X^7 are independently selected from N and C—R^{13};

A2 is



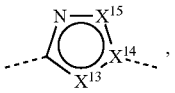
;

A3 is



;

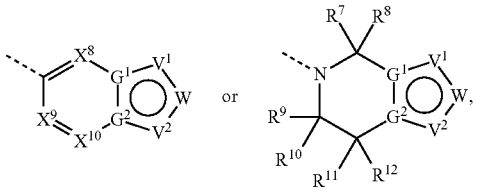
A4 is



,

wherein X^{13} and X^{15} are independently O, N, S or C—R^{4c}, and X^{14} is N or C;

U1 is



wherein X^8 to X^{10} are independently selected from N and C—R^{14};

G^1 and G^2 are independently selected from N and C;

V^1 and V^2 are independently selected from N, O, S and C—R^{15};

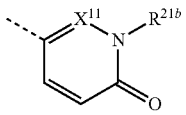
W is V^3, V^4—V^5 or V^4=V^5, wherein V^3 to V^5 are independently selected from N, O, S and C—R^{16}, wherein V^4 connects with V^1; and

V^5 connects with V^2;

U2 is C_6-C_{10} aryl, 5-12 membered heteroaryl, 11-13 membered heterocyclophenyl or 10-13 membered heterocycloheteroaryl, wherein heterocyclo and heteroaryl comprises 1 to 4 heteroatoms independently selected from N, O and S; and

C_6-C_{10} aryl, 5-12 membered heteroaryl, 11-13 membered heterocyclophenyl and 10-13 membered heterocycloheteroaryl are unsubstituted or substituted with 1 to 4 R^{6a} groups;

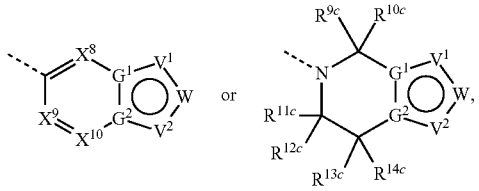
U3 is —OR^{14b}, —$NR^{14b}R^{15b}$, C_6-C_{12} aryl unsubstituted or substituted with 1-6 R^{13b} group, 5-14 membered heteroaryl unsubstituted or substituted with 1-6 R^{13b} group, 11-13 membered heterocyclophenyl unsubstituted or substituted with 1-6 R^{13b} group, 10-13 membered heterocycloheteroaryl unsubstituted or substituted with 1-6 R^{13b} group, C_2-C_8 alkenyl substituted with 5-6 membered aryl or heteroaryl, C_2-C_8 alkynyl substituted with 5-6 membered aryl or heteroaryl, or



unsubstituted or substituted with 1 to 2 R^{13b} groups, wherein heterocyclo and heteroaryl comprises 1 to 4 heteroatoms independently selected from N, O and S; and

X^{11} is N or C—R^{13b};

U4 is



wherein X^8 to X^{10} are independently selected from N and C—R^{15c};

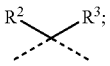
G^1 and G^2 are independently selected from N and C;

V^1 and V^2 are independently selected from N, O, S and C—R^{16c};

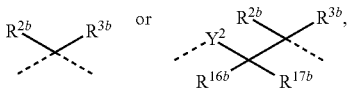
W is V^3, V^4—V^5 or V^4=V^5, wherein V^3 to V^5 are independently selected from N, O, S and C—R^{17c}, wherein V^4 connects with V^1; and

V^5 connects with V^2;

L1 is



L2 is



wherein Y^2 is blank, —O—, —S—, —N(R^{18b})— or —C(R^{18b})(R^{19b})—;

L3 is —C(R^{2c})(R^{3c})— or —$NHCH_2CH_2$—;

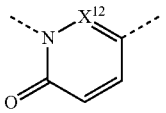
Q1 is C_6-C_{10} arylene or 5-12 membered heteroarylene, wherein 5-12 membered heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

C_6-C_{10} aryl and 5-12 membered heteroarylene are unsubstituted or substituted with 1 to 4 R^{17} groups;

Q2 is C_6-C_{10} arylene or 5-10 membered heteroarylene, wherein 5-10 membered heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

C_6-C_{10} arylene and 5-10 membered heteroarylene are unsubstituted or substituted with 1 to 4 R^{4a} groups;

Q3 is C_6-C_{12} arylene unsubstituted or substituted with 1-6 R^{6b} group, 5-14 membered heteroarylene unsubstituted or substituted with 1-6 R^{6b} group, C_3-C_6 cycloalkylene unsubstituted or substituted with 1-6 R^{6b} group, C_3-C_6 heterocylene unsubstituted or substituted with 1-6 R^{6b} group, or



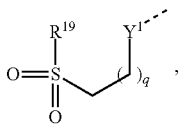
unsubstituted or substituted with 1 to 2 R^{6b} groups, wherein heterocyclene and heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

X^{12} is N or C—R^{6b};

Q4 is C_6-C_{10} arylene or 5-12 membered heteroarylene, wherein 5-12 membered heteroarylene comprises 1 to 4 heteroatoms independently selected from N, O and S; and

C_6-C_{10} arylene and 5-12 membered heteroarylene are unsubstituted or substituted with 1 to 4 R^{5c} groups;

Z1 is —CN, C_6 aryl, 5-6 membered heteroaryl, or



wherein 5-6 membered heteroaryl comprises 1 to 3 heteroatoms independently selected from N, O and S;

C_6 aryl and 5-6 membered heteroaryl are unsubstituted or substituted with 1 to 3 R^{18} groups;

Y^1 is O or NR^{20}; and

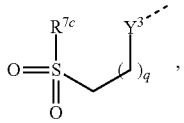
q is 0, 1, 2, or 3;

Z2 is H, —CN, halide, —OH, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkylsulfonyl, C_1-C_8 acyl, aminoacyl, C_1-C_8 acylamino, C_1-C_8 alkylcarbamoylamino, C_1-C_8 alkoxycarbamoyl, C_1-C_8 alkylsulfonamido, C_1-C_8 alkylaminosulphonyl, C_1-C_8 alkoxy, C_2-C_8 alkoxyacyl, phenyl, 5-6 membered heteroaryl, or 5-7 membered heterocyclo, wherein 5-6 membered heteroaryl and 5-7 membered heterocyclo comprise one or more hetero atoms independently selected from N, O and S; and

phenyl, 5-6 membered heteroaryl and 5-7 membered heterocycle are unsubstituted or substituted with 1 to 3 R^{5a} groups;

Z3 is H, —CN, halide, —OH, C_1-C_8 alkyl unsubstituted or substituted with 1 to 3 R^{12b} groups, C_3-C_8 cycloalkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkylsulfonyl, C_1-C_8 acyl, aminoacyl, C_1-C_8 acylamino, C_1-C_8 alkylcarbamoylamino, C_1-C_8 alkoxycarbamoyl, C_1-C_8 alkylsulfonamido, C_1-C_8 alkylaminosulphonyl, C_1-C_8 alkoxy, C_2-C_8 alkoxyacyl, —$N(R^{7b})(R^{8b})$ unsubstituted or substituted with 1 to 3 R^{12b} groups, phenyl unsubstituted or substituted with 1 to 3 R^{9b} groups, 5-6 membered heteroaryl unsubstituted or substituted with 1 to 3 R^{10b} groups, or 5-7 membered heterocyclo unsubstituted or substituted with 1 to 3 R^{11b} groups, wherein 5-6 membered heteroaryl and 5-7 membered heterocyclo comprises 1-3 hetero atoms independently selected from N, O and S;

Z4 is —CN, C_6 aryl, 5-6 membered heteroaryl, or



wherein 5-6 membered heteroaryl comprises 1 to 3 heteroatoms independently selected from N, O and S;

C_6 aryl and 5-6 membered heteroaryl are unsubstituted or substituted with 1 to 3 R^{6c} groups;

Y^3 is O or NR^{8c}; and

q is 0, 1, 2, or 3;

R^1 to R^3 are independently selected from H and C_1-C_6 alkyl, wherein C_1-C_6 alkyl is unsubstituted or substituted with 1 to 3 halide, —CN, —OH, C_1-C_3 alkyl, C_3-C_5 cycloalkyl, or C_1-C_3 alkoxy groups;

R^4 is H, halide, —CN, —OH, —NO_2, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, or C_1-C_6 alkoxy, wherein C_1-C_6 alkyl, C_3-C_8 cycloalkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide;

R^5 and R^6 are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl and C_1-C_6 alkoxy, wherein C_1-C_6 alkyl, C_3-C_6 cycloalkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide;

R^7 and R^8 are independently selected from H and C_1-C_6 alkyl, or R^7 and R^8 together are oxo (═O);

R^9 to R^{12} are independently selected from H, C_1-C_6 alkyl;

R^{13} is H, halide, —CN, —OH, amino, —NO_2, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_1-C_6 alkylthio or 1-pyrrolidino, wherein amino, C_1-C_6 alkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide, C_1-C_3 alkyl or C_3-C_6 cycloalkyl groups;

R^{14} to R^{17} are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy and C_1-C_6 alkylthio, wherein amino, C_1-C_6 alkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide, C_1-C_3 alkyl or C_3-C_6 cycloalkyl groups;

R^{18} is H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl or C_1-C_6 alkoxy, wherein amino, C_1-C_6 alkyl and C_1-C_6 alkoxy are unsubstituted or substituted with 1 to 3 halide, C_1-C_3 alkyl or C_3-C_6 cycloalkyl groups;

R^{19} and R^{20} are independently selected from H and C_1-C_3 alkyl, or R^{19} and R^{20} together, with adjacent atoms they attached to, form a cyclic structure;

R^{4a}, R^{5a} and R^{6a} are independently selected from halide, —CN, and —OH, or R^{4a}, R^{5a} and R^{6a} are independently selected from C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_1-C_8 alkoxy, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_1-C_8 alkylsulfonyl, C_1-C_8 acyl, aminoacyl, C_1-C_8 acylamino, C_1-C_8 alkylcarbamoylamino, C_1-C_8 alkoxycarbamoyl, C_1-C_8 alkylsulfonamido, C_1-C_8 alkylaminosulphonyl, C_2-C_8 alkoxyacyl, and 3-8 membered heterocycle, all of which are unsubstituted or substituted with 1-3 halide, —OH, —CN, C_1-C_3 alkyl, C_1-C_3 alkoxyl or C_3-C_8 cycloalkyl groups, wherein 3-8 membered heterocycle comprises one or more hetero atoms from N, O or S;

R^{2m} is H, deuterium, tritium, halide, —OH, —CN, C_1-C_8 alkyl, C_3-C_8 cycloalkyl or C_1-C_5 alkoxy;

R^{2b} and R^{3b} are independently selected from H, C_1-C_6 alkyl unsubstituted or substituted with 1-3 groups selected from halide, —CN, —OH, C_1-C_6 alkyl, C_3-C_5 cycloalkyl and C_1-C_3 alkoxy;

R^{4b} and R^{5b} are independently selected from H, halide, —CN, amino, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, C_1-C_8 alkoxy, and C_1-C_3 alkylamino;

R^{6b} is H, halide, —CN or —OH, or R^{6b} is selected from amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, and C_1-C_3 alkylamino, all of which are unsubstituted or substituted with 1-3 halide, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl groups;

R^{7b} and R^{8b} are independently selected from H, C_1-C_8 alkyl and C_3-C_8 cycloalkyl, the latter two of which are unsubstituted or substituted with 1-3 R^{12b}, or R^7 and R^8 together, with adjacent atoms they attached to, form a cyclic structure;

R^{9b} and R^{10b} are independently selected from H, halide, —CN and —OH, or R^{9b} and R^{10b} are independently selected from amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and C_1-C_6 alkoxy, all of which are unsubstituted or substituted with 1-3 halide, C_1-C_3 alkyl, or C_3-C_6 cycloalkyl groups;

R^{11b} is H, halide, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with halide, C_3-C_6 cycloalkyl, oxo, or C_1-C_6 alkoxy;

R^{12b} is H, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with halide, C_3-C_6 cycloalkyl, oxo, or C_1-C_6 alkoxy;

R^{13b} is H, halide, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, C_2-C_6 alkylcarbamoylamino, C_2-C_6 alkoxycarbamoyl, C_1-C_3 alkylsulphonyl, —$N(R^{16b})S(O)_2$—C_1-C_3 alkyl, or —$N(R^{16b})C(O)$—C_1-C_3 alkyl;

R^{14b} and R^{15b} are independently selected from H, C_3-C_6 cycloalkyl unsubstituted or substituted with 1 to 3 R^{20b} groups, C_1-C_6 alkyl unsubstituted or substituted with 1 to 3 R^{20b} groups, 5-6 membered aryl unsubstituted or substituted with 1 to 3 R^{20b} groups, 5-6 membered heteroaryl unsubstituted or substituted with 1 to 3 R^{20b} groups, and 5-6 membered

heterocyclo unsubstituted or substituted with 1 to 3 R^{20b} groups, wherein 5-6 membered heteroaryl and 5-7 membered heterocyclo comprise 1 to 3 hetero atoms independently selected from N, O and S, or R^{14b} and R^{15b} together, with adjacent atoms they attached to, form a cyclic structure;

R^{16b} to R^{19b} are independently selected from H and C_1-C_6 alkyl unsubstituted or substituted with halide;

R^{20b} is H, —CN, —OH, amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_1-C_6 alkoxy, 5-6 membered aryl, or 5-6 membered heteroaryl, wherein 5-6 membered heteroaryl comprises 1 to 3 hetero atoms independently selected from N, O and S;

R^{21b} is H or C_1-C_6 alkyl;

R^{2c} and R^{3c} are independently selected from H and C_1-C_6 alkyl unsubstituted or substituted with 1-3 halide;

R^{4c} is H, halide, C_1-C_3 alkyl, C_3-C_5 cycloalkyl, or C_1-C_3 alkoxy;

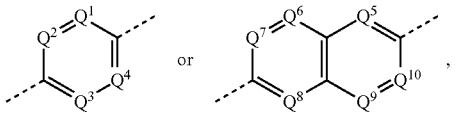
R^{5c} and R^{6c} are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with 1-3 halide, C_3-C_5 cycloalkyl, and C_1-C_6 alkoxy;

R^{7c} and R^{8c} are independently selected from H and C_1-C_6 alkyl, or R^{7c} and R^{8c} together, with adjacent atoms they attached to, form a cyclic structure;

R^{9c} to R^{14c} are independently selected from H, C_1-C_6 alkyl and —CF_3;

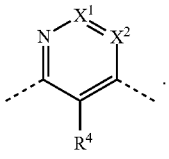
R^{15c} to R^{17c} are independently selected from H, halide, —CN, —OH, amino, C_1-C_6 alkyl unsubstituted or substituted with 1-3 halide, C_3-C_5 cycloalkyl, and C_1-C_6 alkoxy.

2. The compound of claim **1**, wherein Q is

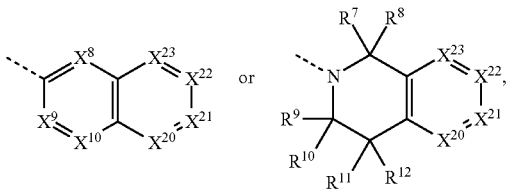


wherein Q^1 to Q^{10} are independently N or C—R^{17}.

3. The compound of claim **1**, wherein A is

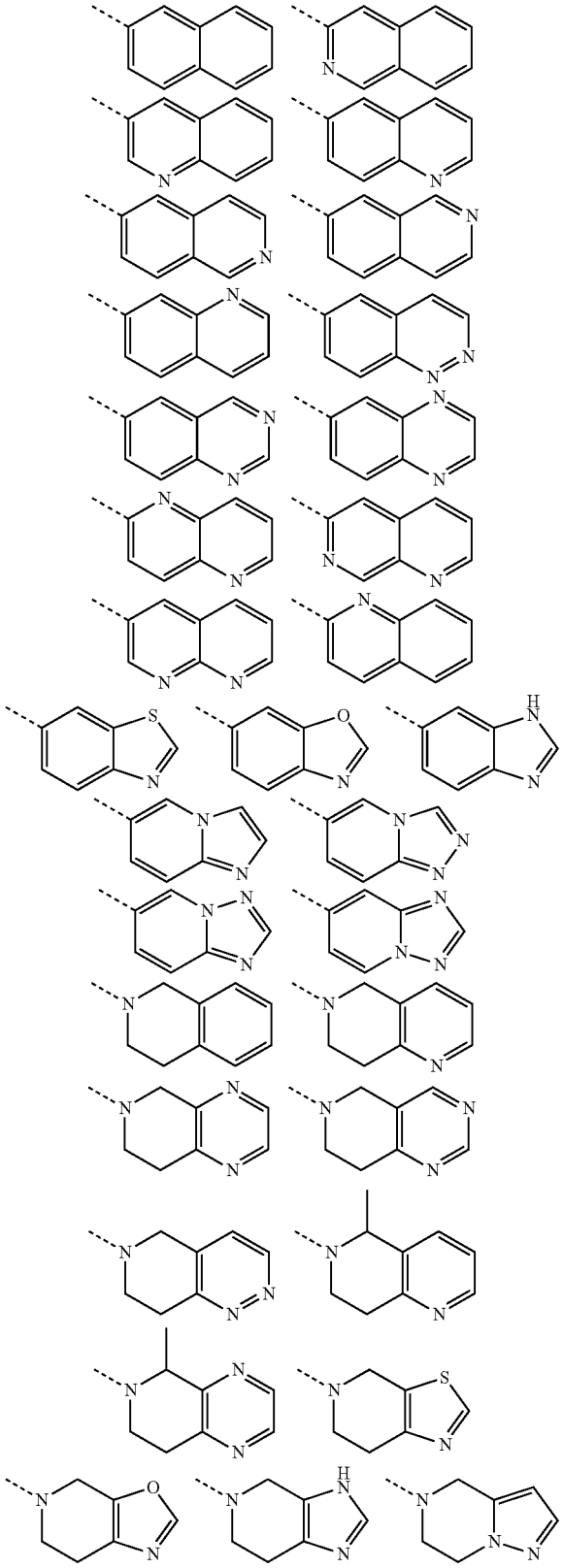


4. The compound of claim **1**, wherein U is

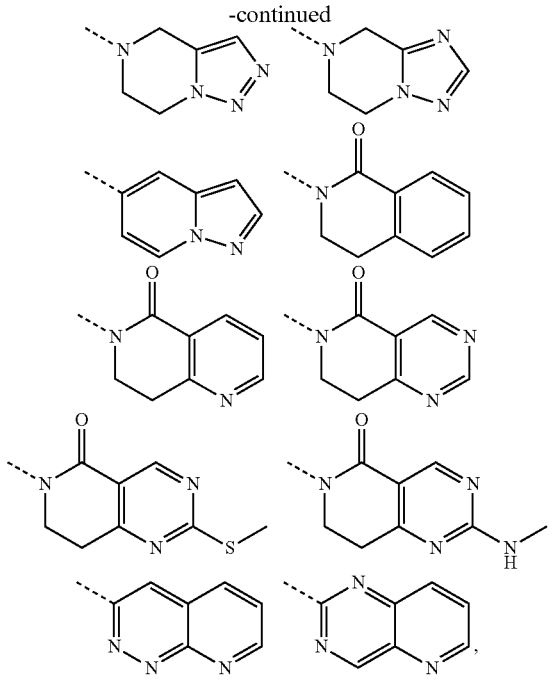


wherein X^{20} to X^{23} are independently N or C—R^{15}.

5. The compound of claim **1**, wherein U is selected from:

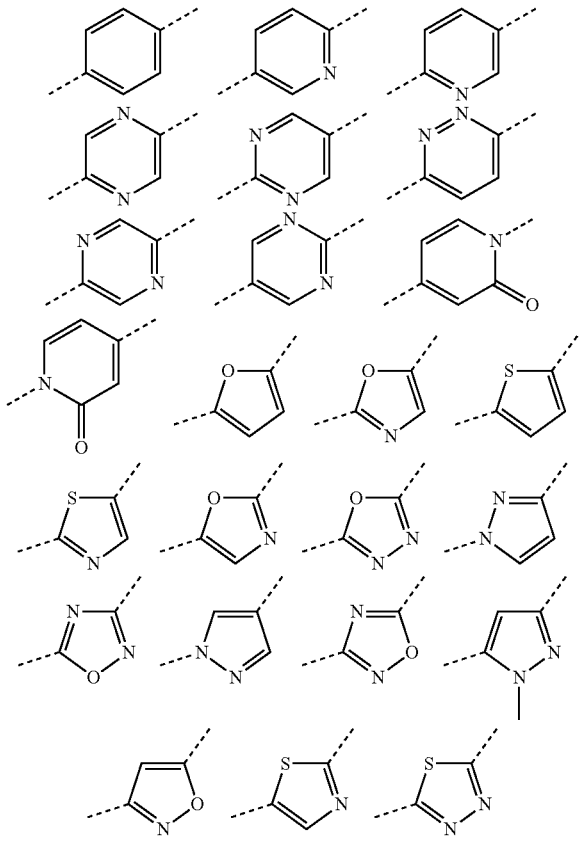


-continued

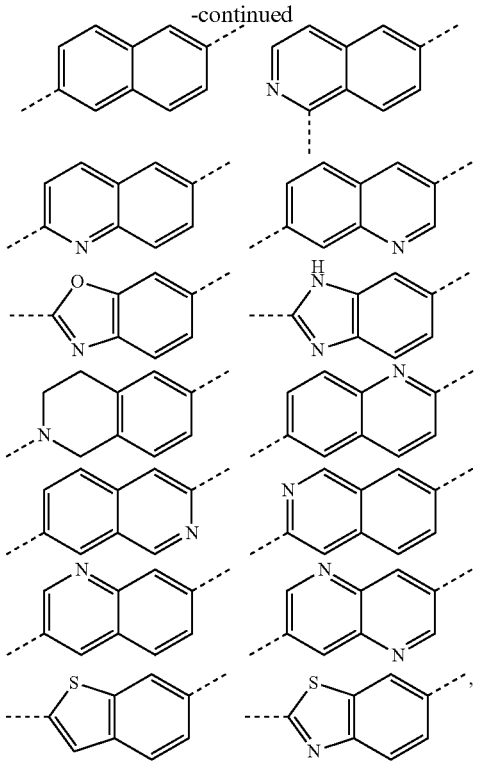


unsubstituted or substituted with 1 to 3 R^{15} groups.

6. The compound of claim **1**, wherein Q is selected from:

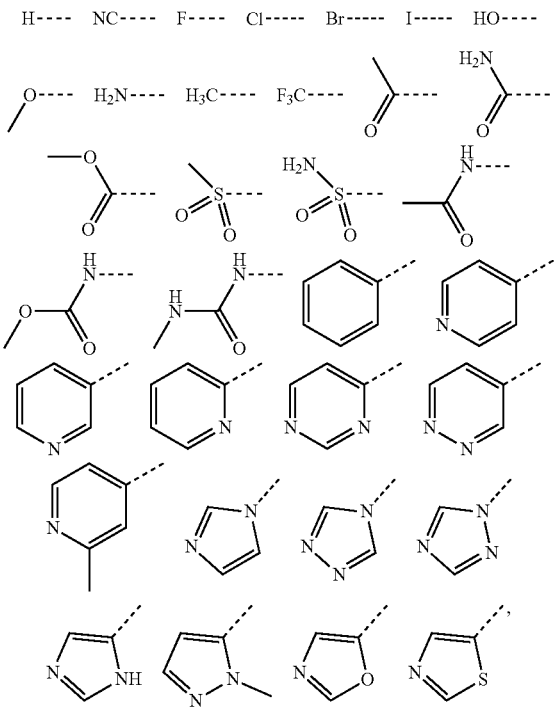


-continued



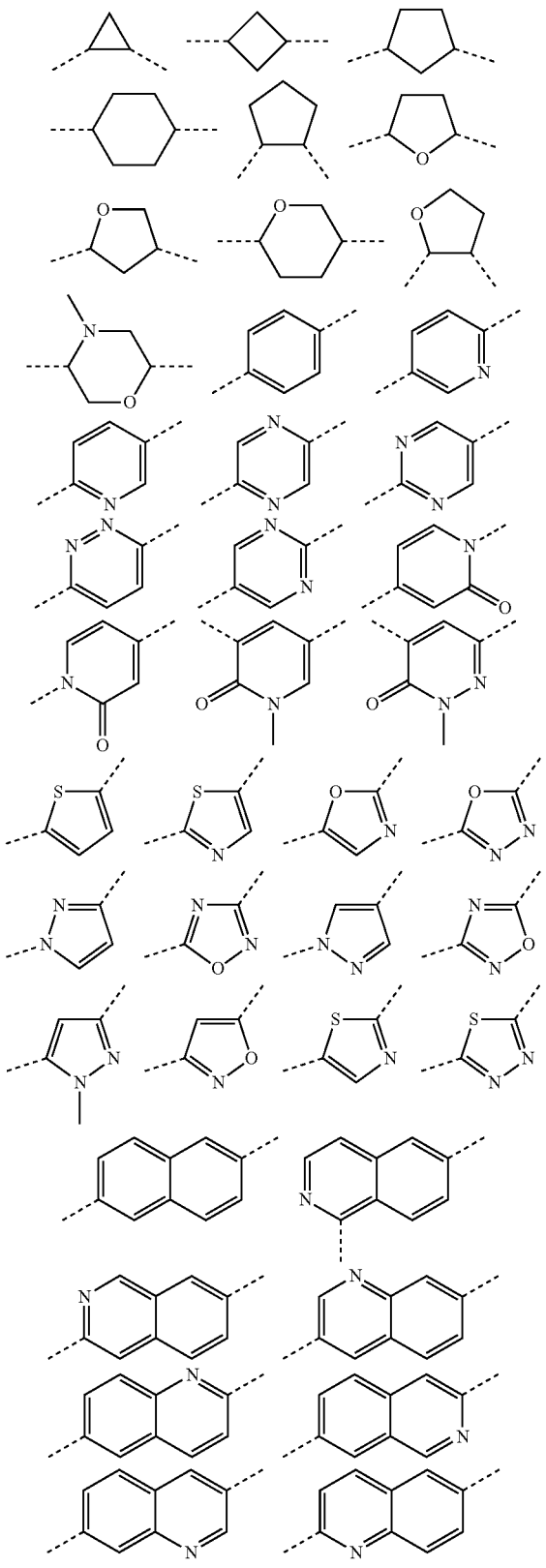
unsubstituted or substituted with 1 to 3 R^{4a} groups.

7. The compound of claim **1**, wherein Z is selected from:

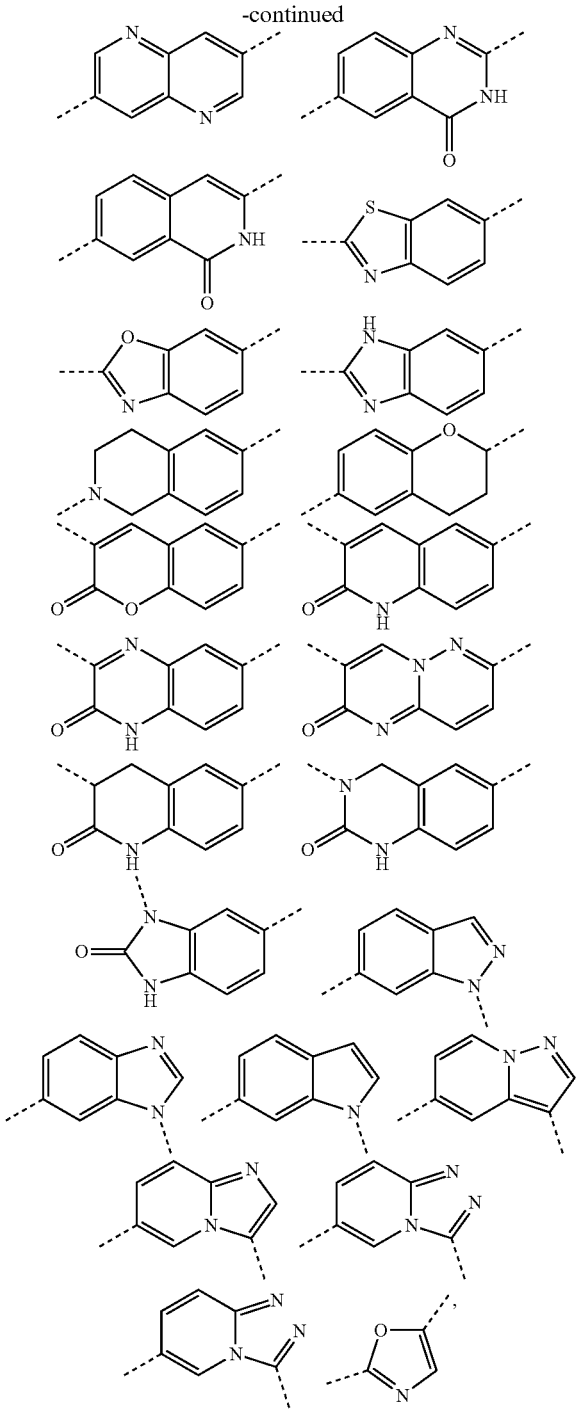


unsubstituted or substituted with 1 to 3 R^{5a} groups.

8. The compound of claim **1**, wherein Q is selected from:

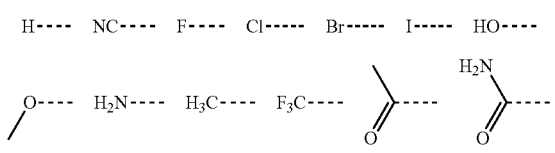


-continued

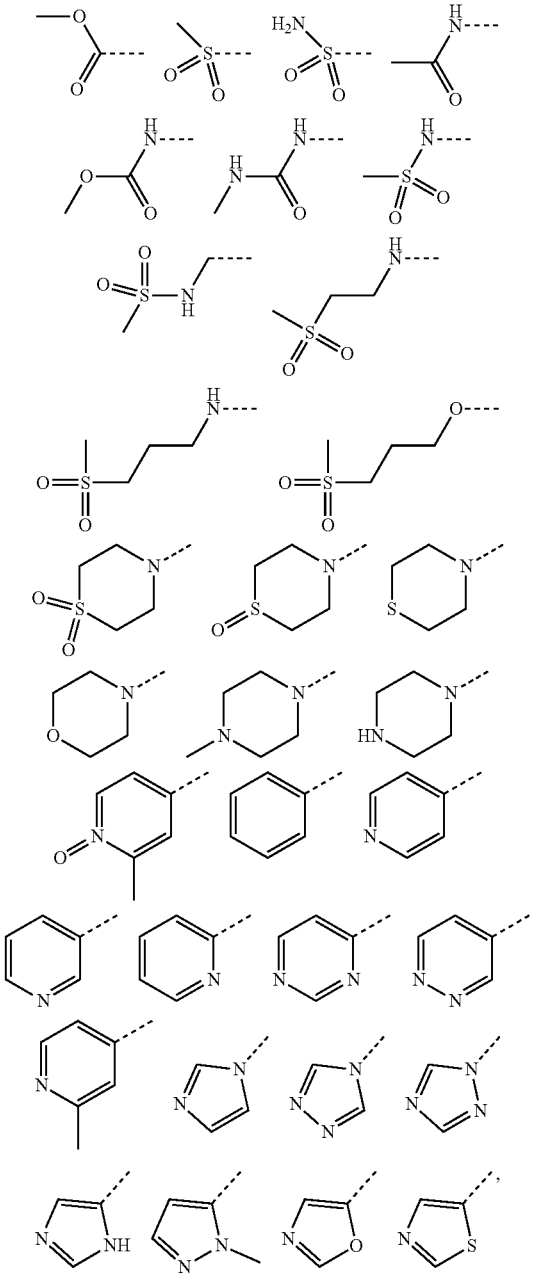


unsubstituted or substituted with 1 to 6 R^{6b} groups.

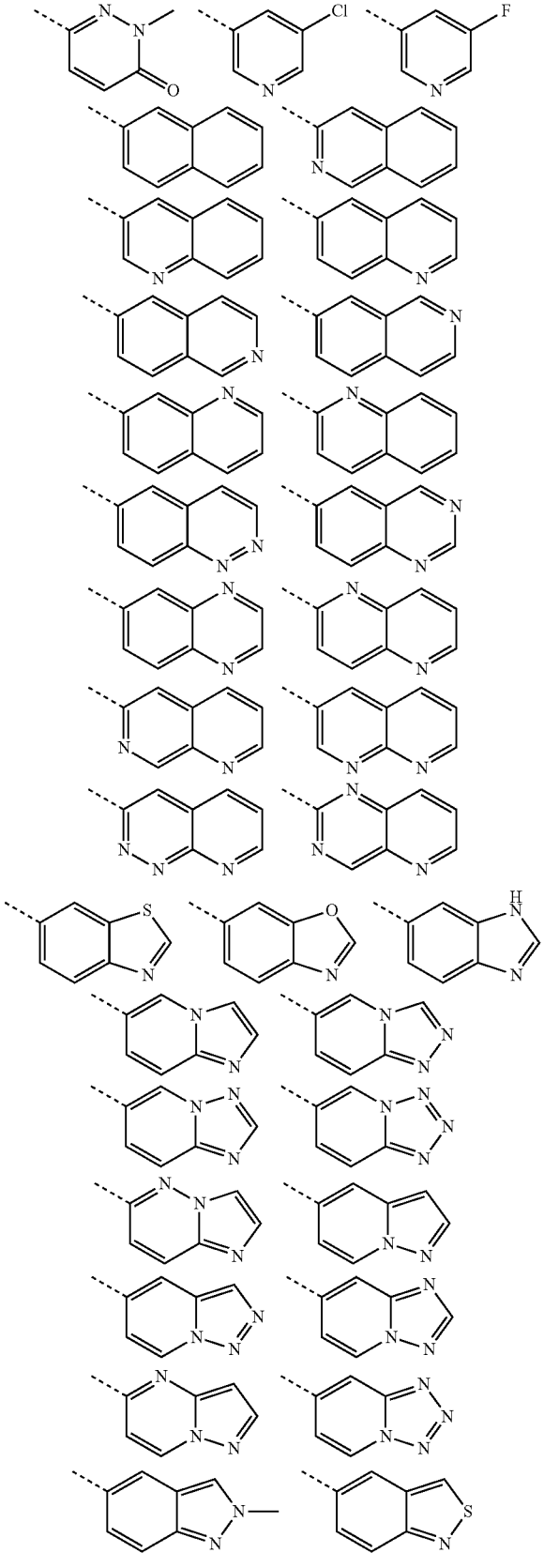
9. The compound of claim **1**, wherein Z is selected from:



-continued

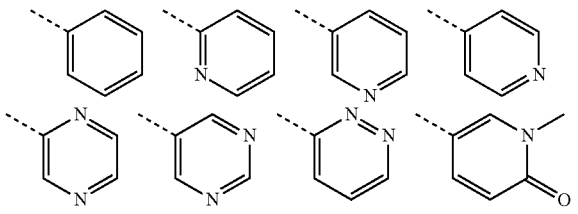


-continued

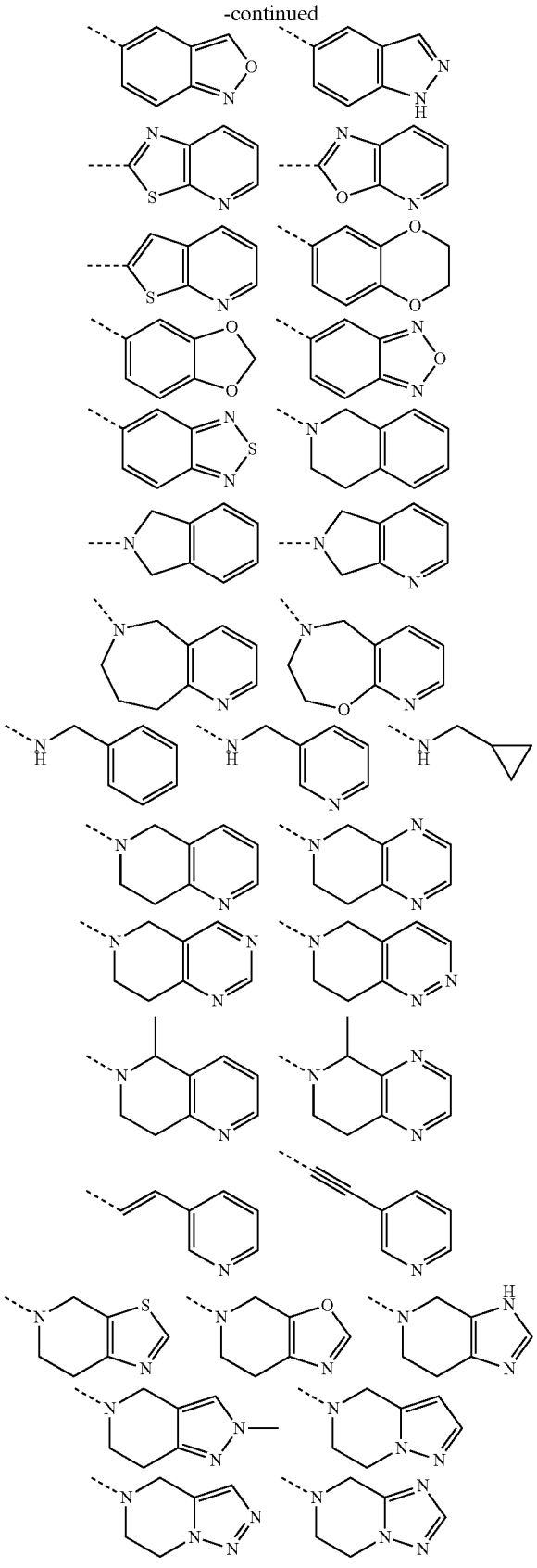


unsubstituted or substituted with 1-2 R^{10b} groups.

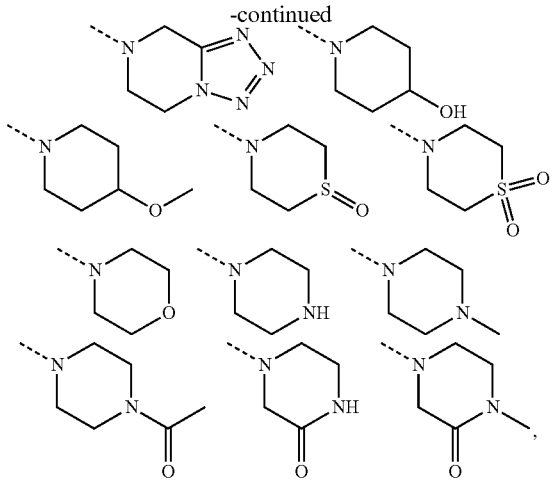
10. The compound of claim **1**, wherein U is selected from:



-continued

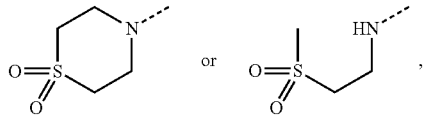


-continued

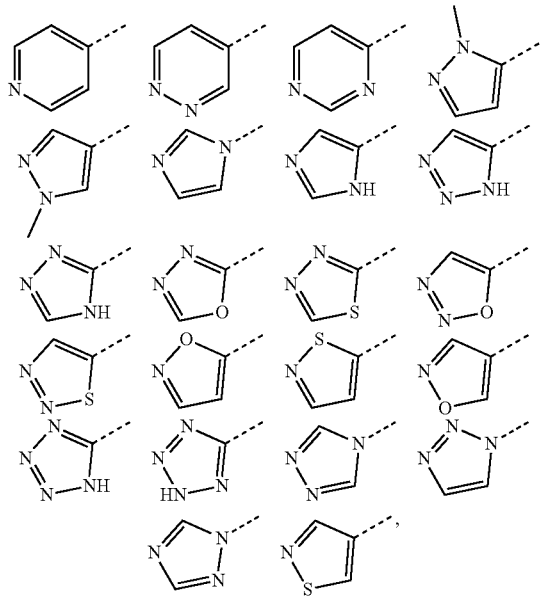


unsubstituted or substituted with 1-6 R^{13c} groups.

11. The compound of claim **1**, wherein Z is

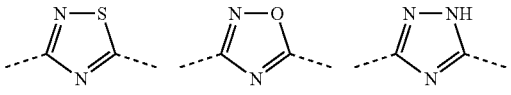


or Z is selected from:

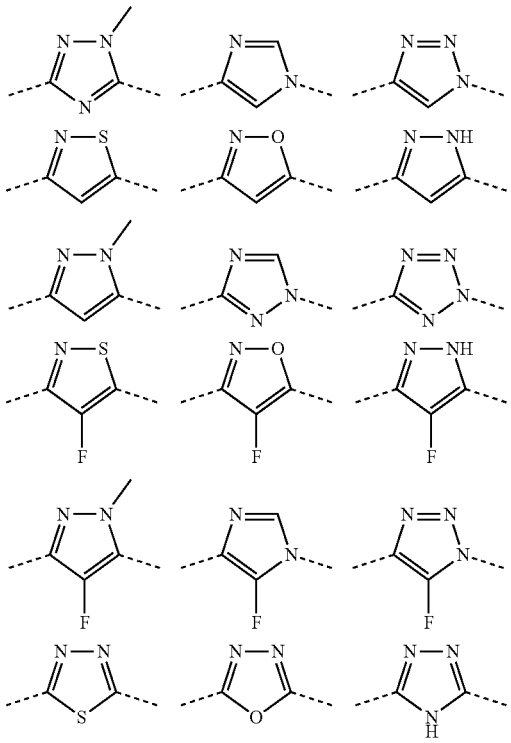


unsubstituted or substituted with 1-3 R^{6c} groups.

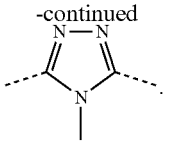
12. The compound of claim **1**, wherein A is selected from:



-continued



-continued



13. The compound of claim **1**, wherein the compound is selected from Table 1.

14. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim **1** and a pharmaceutically acceptable carrier.

15. A method for treating a Wnt-mediated disorder in a mammal suffering therefrom, comprising administering to the mammal a therapeutically effective amount of at least one compound of claim **1**, or a pharmaceutical composition thereof, and optionally in combination with a second therapeutic agent.

16. The method of claim **15**, wherein the disorder is a cell proliferative disorder selected from the group consisting of systemic sclerosis, skin fibrosis, idiopathic pulmonary fibrosis, renal fibrosis, liver fibrosis, drug-induced fibrosis, radiation-induced fibrosis, colorectal cancer, breast cancer, head and neck squamous cell carcinoma, esophageal squamous cell carcinoma, non-small cell lung cancer, gastric cancer, pancreatic cancer, leukemia, lymphoma, neuroblastoma, retinoblastoma, sarcoma, osteosarcoma, chondosarcoma, Ewing's sarcoma, rhabdomysarcoma, brain tumor, Wilms' tumor, basal cell carcinoma, melanoma, head and neck cancer, cervical cancer and prostate cancer.

* * * * *