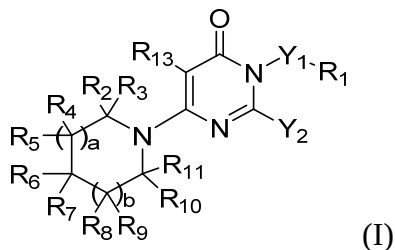


CLAIMS

1. A compound represented by Formula I



or a salt, ester, or prodrug thereof, wherein:

subscript a is 0 or 1;

subscript b is 0 or 1;

Y₁ is a direct bond or CR₁₇R₁₈;

Y₂ is selected from the group consisting of C₁₋₄alkyl, amino, C₁₋₄alkylC(O)O-,

C₁₋₄alkylamino and C₁₋₄aminoalkyl;

R₁ is selected from the group consisting of C₆₋₁₀aryl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, and a 5-10 membered heteroaryl group having 1 to 4 heteroatoms or groups as ring vertices independently selected from N, C(O), O, and S; said aryl or heteroaryl of R₁ is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄haloalkyl, C₁₋₄aminoalkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, NR₁₅C(O)R₁₄, NR₁₅C(O)OR₁₄, NR₁₄C(O)NR₁₅R₁₆, NR₁₅S(O)R₁₄, NR₁₅S(O)₂R₁₄, C(O)NR₁₅R₁₆, S(O)NR₁₅R₁₆, S(O)₂NR₁₅R₁₆, C(O)R₁₄, C(O)OR₁₄, OR₁₄, SR₁₄, S(O)R₁₄, and S(O)₂R₁₄;

R₂, R₃, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen, C₁₋₄alkyl, and C₃₋₈cycloalkyl;

R₄, R₅, R₈, and R₉ are each independently selected from the group consisting of hydrogen, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, amino, hydroxy, C₃₋₈cycloalkyl, halo, and C₁₋₄alkylamino;

R₆ is selected from the group consisting of amino, C₁₋₄aminoalkyl, and C₁₋₄alkylamino;

R₇ is selected from the group consisting of hydrogen, amido, cyano, halo, and hydroxy, or is selected from the group consisting of C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₃₋₆cycloalkyl, phenyl, and 5- or 6- membered heteroaryl, any of which is optionally substituted with one to five groups independently selected from the group consisting of amino, halo, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkylamino, and C₁₋₄aminoalkyl;

or R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-membered saturated or unsaturated ring, having 0 to 3 heteroatoms or groups as ring vertices independently selected from N, C(O), O, and S(O)_m;

subscript m is 0, 1, or 2;

said saturated or unsaturated ring formed by R₆ and R₇ is unsubstituted or substituted with 1 to 3 groups independently selected from the group consisting of amino, halo, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkylamino and C₁₋₄aminoalkyl;

any two groups of R₂, R₃, R₄, R₅, R₇, R₈, R₉, R₁₀ and R₁₁ can form a 5 to 6 membered ring, having 0 to 2 heteroatoms as ring vertices selected from N, O and S;

any two groups of R₂, R₄, R₆, R₈ and R₁₀ can form a direct bond, or a 1 or 2 atom carbon bridge;

R₁₃ is selected from the group consisting of hydrogen, halo, cyano, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆ dihydroxyalkyl, -NH-NHR₁₉, -NHR₁₉, -OR₁₉, -NHC(O)R₁₉, -NHC(O)NHR₁₉, -NHS(O)₂NHR₁₉, -NHS(O)₂R₁₉, -C(O)OR₁₉, -C(O)NR₁₉R₂₀, -C(O)NH(CH₂)_qOH, -C(O)NH(CH₂)_qR₂₁, -C(O)R₂₁, -NH₂, -OH, -S(O)₂NR₁₉R₂₀, C₃₋₈cycloalkyl, aryl, heterocyclyl having 1-5 heteroatoms as ring vertices selected from N, O, S and P, heteroaryl having 1-5 heteroatoms as ring vertices selected from N, O, S and P; wherein the subscript q is an integer of from 0 to 6; and wherein aryl, heteroaryl, heterocyclyl and cycloalkyl are substituted with 0 to 3 groups independently selected from the group consisting of C₁₋₄alkyl, -OH, -NH₂, -OR₂₁, halo, cyano, and oxo;

R₁₄, R₁₅ and R₁₆ are each independently selected from the group consisting of hydrogen, C₁₋₄alkyl, C₃₋₈cycloalkyl, C₆₋₁₀aryl and 5-10 membered heteroaryl, each of which is

optionally substituted by one or more groups independently selected from the group consisting of amido, amino, halo, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkylamino and C₁₋₄aminoalkyl;
R₁₇ and R₁₈ are each independently selected from the group consisting of hydrogen, C₁₋₄alkyl, and CF₃;
R₁₉ and R₂₀ are each independently selected from the group consisting of hydrogen, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₂₋₆alkenyl, C₂₋₆alkynyl and C₃₋₆cycloalkyl; and
each R₂₁ is independently selected from the group consisting of hydrogen, -OH, C₁₋₆ alkyl, C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₂₋₆alkenyl, C₂₋₆alkynyl and C₃₋₆cycloalkyl.

2. The compound of claim **1**, wherein:
subscript a is 0 or 1;
subscript b is 0 or 1;
Y₁ is a direct bond or CR₁₇R₁₈;
Y₂ is selected from the group consisting of C₁₋₄alkyl, amino, C₁₋₄alkylC(O)O-, C₁₋₄alkylamino and C₁₋₄aminoalkyl;
R₁ is selected from the group consisting of C₆₋₁₀aryl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, and a 5-10 membered heteroaryl group having 1 to 4 heteroatoms or groups as ring vertices independently selected from N, C(O), O, and S; said aryl or heteroaryl of R₁ is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄haloalkyl, C₁₋₄aminoalkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, NR₁₅C(O)R₁₄, NR₁₅C(O)OR₁₄, NR₁₄C(O)NR₁₅R₁₆, NR₁₅S(O)R₁₄, NR₁₅S(O)₂R₁₄, C(O)NR₁₅R₁₆, S(O)NR₁₅R₁₆, S(O)₂NR₁₅R₁₆, C(O)R₁₄, C(O)OR₁₄, OR₁₄, SR₁₄, S(O)R₁₄, and S(O)₂R₁₄;
R₂, R₃, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen, C₁₋₄alkyl, and C₃₋₈cycloalkyl;

18 R₄, R₅, R₈, and R₉ are each independently selected from the group consisting of hydrogen,
 19 cyano, C₁₋₄alkyl, C₁₋₄alkoxy, amino, hydroxy, C₃₋₈cycloalkyl, halo, and
 20 C₁₋₄alkylamino;
 21 R₆ is selected from the group consisting of amino, C₁₋₄aminoalkyl, and C₁₋₄alkylamino;
 22 R₇ is selected from the group consisting of hydrogen, halo, and hydroxy, or is selected from
 23 the group consisting of amido, C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₃₋₆cycloalkyl, phenyl,
 24 and 5- or 6- membered heteroaryl, any of which is optionally substituted with one to
 25 five groups independently selected from the group consisting of amino, halo,
 26 hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkylamino,
 27 and C₁₋₄aminoalkyl;
 28 or R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-
 29 membered saturated or unsaturated ring, having 0 to 3 heteroatoms or groups as ring
 30 vertices independently selected from N, C(O), O, and S(O)_m;
 31 subscript m is 0, 1, or 2;
 32 said saturated ring formed by R₆ and R₇ is unsubstituted or substituted with 1 to 3 groups
 33 independently selected from the group consisting of amino, halo, hydroxy, cyano,
 34 C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkylamino and
 35 C₁₋₄aminoalkyl;
 36 any two groups of R₂, R₃, R₄, R₅, R₇, R₈, R₉, R₁₀ and R₁₁ can form a 5 to 6 membered ring,
 37 having 0 to 2 heteroatoms as ring vertices selected from N, O and S;
 38 any two groups of R₂, R₄, R₆, R₈ and R₁₀ can form a direct bond, or a 1 or 2 atom carbon
 39 bridge;
 40 R₁₃ is selected from the group consisting of hydrogen, halo, cyano, C₁₋₆ alkyl,
 41 C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆dihydroxyalkyl, -NH-NHR₁₉, -NHR₁₉, -OR₁₉,
 42 -NHC(O)R₁₉, -NHC(O)NHR₁₉, -NHS(O)₂NHR₁₉, -NHS(O)₂R₁₉, -C(O)OR₁₉,
 43 -C(O)NR₁₉R₂₀, -C(O)NH(CH₂)_qOH, -C(O)NH(CH₂)_qR₂₁, -C(O)R₂₁, -NH₂, -OH,
 44 -S(O)₂NR₁₉R₂₀, C₃₋₈cycloalkyl, aryl, heterocyclyl having 1-5 heteroatoms as ring
 45 vertices selected from N, O, S and P, heteroaryl having 1-5 heteroatoms as ring
 46 vertices selected from N, O, S and P; wherein the subscript q is an integer of from 0
 47 to 6; and wherein aryl, heteroaryl, heterocyclyl and cycloalkyl are substituted with 0

48 to 3 groups independently selected from the group consisting of C₁₋₄alkyl, -OH,
 49 -NH₂, -OR₂₁, halo, cyano, and oxo;
 50 R₁₄, R₁₅ and R₁₆ are each independently selected from the group consisting of hydrogen,
 51 C₁₋₄alkyl, C₃₋₈cycloalkyl, C₆₋₁₀aryl and 5-10 membered heteroaryl, each of which is
 52 optionally substituted by one or more groups independently selected from the group
 53 consisting of halo, hydroxy, cyano, and C₁₋₄alkyl;
 54 R₁₇ and R₁₈ are each independently selected from the group consisting of hydrogen,
 55 C₁₋₄alkyl, and CF₃;
 56 R₁₉ and R₂₀ are each independently selected from the group consisting of hydrogen,
 57 C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₂₋₆alkenyl, C₂₋₆alkynyl and
 58 C₃₋₆cycloalkyl; and
 59 each R₂₁ is independently selected from the group consisting of hydrogen, -OH, C₁₋₆ alkyl,
 60 C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₂₋₆alkenyl, C₂₋₆alkynyl and C₃₋₆cycloalkyl.

1 **3.** The compound of claim 1, wherein subscripts a and b are each 1.

1 **4.** The compound of claim 1, wherein Y₁ is a direct bond.

1 **5.** The compound of claim 1, wherein Y₂ is C₁₋₄alkyl.

1 **6.** The compound of claim 5, wherein Y₂ is methyl.

1 **7.** The compound of claim 1, wherein
 2 R₁₃ is selected from the group consisting of hydrogen, halo, C₁₋₆alkyl, C₁₋₆haloalkyl,
 3 C₁₋₆hydroxyalkyl, C₁₋₆dihydroxyalkyl, C₃₋₈cycloalkyl, a 3- or 6-membered
 4 heterocyclyl having 1-3 heteroatoms as ring vertices selected from N, O and S;
 5 wherein heterocyclyl and cycloalkyl are substituted with 0 to 3 groups independently
 6 selected from the group consisting of C₁₋₄alkyl, -OH, -NH₂, -OR₂₁, halo, cyano and
 7 oxo.

1 **8.** The compound of claim 7, wherein R₁₃ is selected from the group
 2 consisting of hydrogen, halo, C₁₋₆alkyl, and C₁₋₆haloalkyl.

1 **9.** The compound of claim **8**, wherein R₁₃ is hydrogen, Cl, Br, methyl, or
2 CF₃.

1 **10.** The compound of claim **1**, wherein
2 R₁ is selected from the group consisting of C₆₋₁₀aryl and a 5- to 9- membered heteroaryl
3 group having 1 to 4 heteroatoms groups as ring vertices independently selected from
4 N, C(O), O, and S; and is optionally substituted with 1 to 5 R₁₂ groups independently
5 selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino,
6 di(C₁₋₄alkyl)amino, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄haloalkyl,
7 C₁₋₄aminoalkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, NR₁₅C(O)R₁₄, NR₁₅C(O)OR₁₄,
8 NR₁₄C(O)NR₁₅R₁₆, NR₁₅S(O)R₁₄, NR₁₅S(O)₂R₁₄, C(O)NR₁₅R₁₆, S(O)NR₁₅R₁₆,
9 S(O)₂NR₁₅R₁₆, C(O)R₁₄, C(O)OR₁₄, OR₁₄, SR₁₄, S(O)R₁₄, and S(O)₂R₁₄.

1 **11.** The compound of claim **10**, wherein
2 R₁ is phenyl or a 5- to 6-member heteroaryl group having 1 to 4 heteroatoms as ring vertices
3 independently selected from N, O, and S; and is optionally substituted with 1, 2 or 3
4 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino,
5 C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl,
6 C₁₋₄aminoalkyl, and OR₁₄.

1 **12.** The compound of claim **1**, wherein R₂, R₃, R₄, R₅, R₈, R₉, R₁₀ and R₁₁ are
2 hydrogen.

1 **13.** The compound of claim **1**, wherein:
2 R₆ is selected from the group consisting of amino, C₁₋₄aminoalkyl, and C₁₋₄alkylamino; and
3 R₇ is selected from the group consisting of hydrogen, amido, cyano, halo, and hydroxy, or is
4 selected from the group consisting of C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₃₋₆cycloalkyl,
5 phenyl, and 5- or 6- membered heteroaryl, any of which is optionally substituted with
6 one or two groups selected from the group consisting of amino, halo, hydroxy, cyano,
7 trifluoromethyl, trifluoromethoxy, C₁₋₄alkyl, and C₁₋₄alkoxy.

1 **14.** The compound of claim **13**, wherein
2 R₆ is amino or aminomethyl; and
3 R₇ is selected from the group consisting of hydroxy, C₁₋₄alkyl, and C₁₋₄hydroxyalkyl.

1 **15.** The compound of claim **1**, wherein
2 R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-
3 membered saturated or unsaturated ring having 1 to 3 heteroatoms or groups as ring
4 vertices independently selected from N, C(O), O, and S(O)_m, and that is optionally
5 substituted with one or two groups independently selected from the group consisting
6 of amino, halo, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄alkylamino and C₁₋₄aminoalkyl.

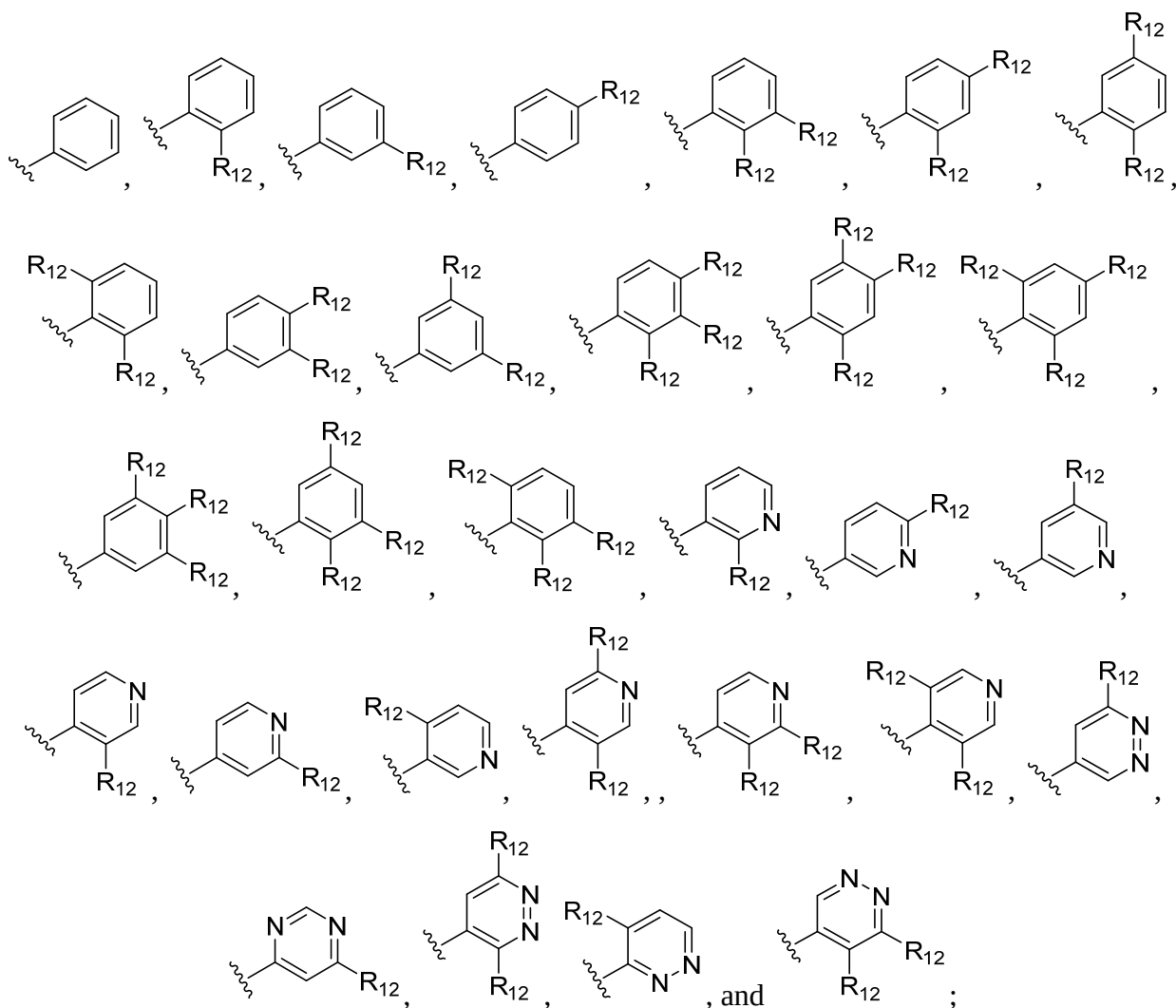
1 **16.** The compound of claim **15**, wherein
2 R₆ and R₇ together with the carbon atom to which they are both attached form a 4- to 6-
3 membered saturated ring having 1 to 3 heteroatoms as ring vertices independently
4 selected from N and O, and that is optionally substituted with one or two groups
5 independently selected from the group consisting of amino, halo, hydroxy, C₁₋₄alkyl,
6 C₁₋₄alkoxy, C₁₋₄alkylamino and C₁₋₄aminoalkyl.

1 **17.** The compound of claim **1**, wherein
2 R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-
3 membered cycloalkyl ring that is optionally substituted with one or two groups
4 independently selected from the group consisting of amino, halo, hydroxy, C₁₋₄alkyl,
5 C₁₋₄alkoxy, C₁₋₄alkylamino and C₁₋₄aminoalkyl.

1 **18.** The compound of claim **1**, wherein
2 R₁ is selected from the group consisting of phenyl, pyridyl, pyrimidinyl, pyrazinyl,
3 pyridazinyl, and 1,2,4-triazinyl; and is optionally substituted with 1, 2, or 3 R₁₂
4 independently selected from the group consisting of halo, hydroxy, amino,
5 C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl,
6 C₁₋₄aminoalkyl, and OR₁₄.

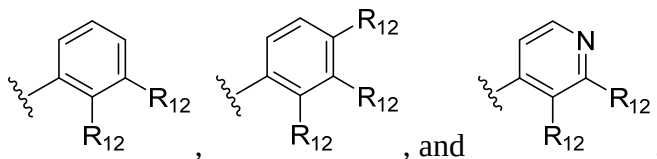
19. The compound of claim **18**, wherein R₁ is phenyl or pyridyl, each of which is substituted with 1 to 3 R₁₂.

20. The compound of claim **1**, wherein R₁ is selected from the group consisting of:



each R₁₂ is independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄aminoalkyl, and OR₁₄.

21. The compound of claim **20**, wherein R₁ is selected from the group consisting of:

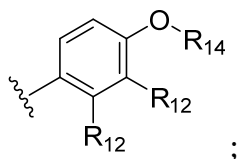


22. The compound of claim 1, wherein R₁₄ is selected from the group consisting of C₆₋₁₀aryl and a 5-10 membered heteroaryl, each of which is optionally substituted by one or more groups independently selected from the group consisting of halo, hydroxy, cyano, and C₁₋₄alkyl.

23. The compound of claim 22, wherein R₁₄ is phenyl or a 5-6 membered heteroaryl having 1 to 4 heteroatoms as ring vertices independently selected from N, O, and S, each of which is optionally substituted by one or two groups independently selected from the group consisting of halo, hydroxy, cyano, and C₁₋₄alkyl.

24. The compound of claim 1, wherein R₁₄ is selected from the group consisting of C₆₋₁₀aryl and a 5-10 membered heteroaryl, each of which is optionally substituted by one or more groups independently selected from the group consisting of C₁₋₄alkylamido, amino, halo, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄haloalkoxy, C₁₋₄alkylamino and C₁₋₄aminoalkyl.

25. The compound of claim 1, wherein R₁ is



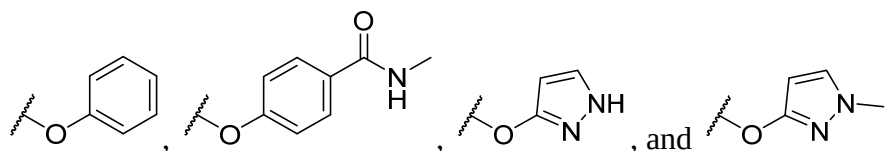
each R₁₂ is independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, di(C₁₋₄alkyl)amino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, and C₁₋₄aminoalkyl; and

R₁₄ is phenyl or a 5-6 membered heteroaryl having

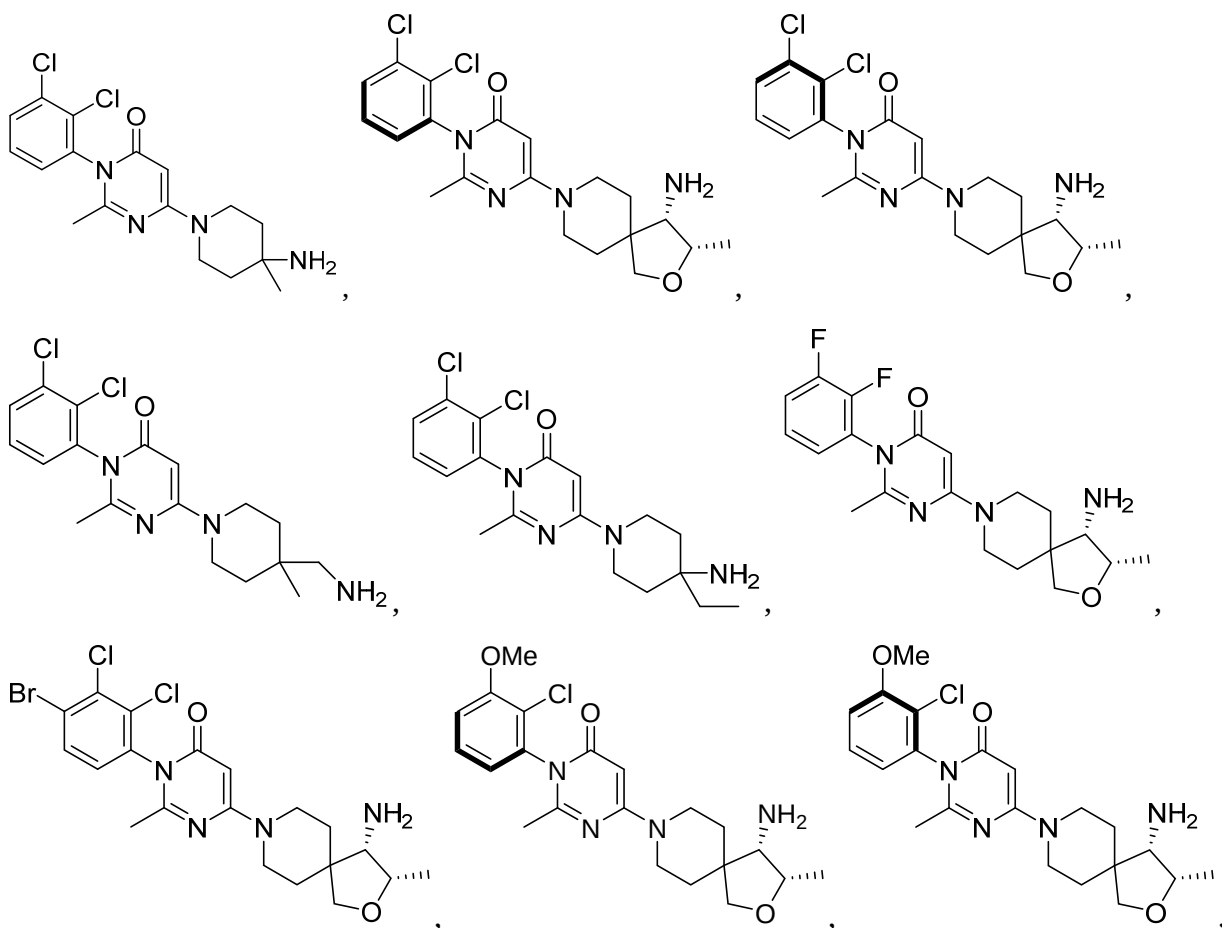
1 to 4 heteroatoms as ring vertices independently selected from N, O, and S, each of

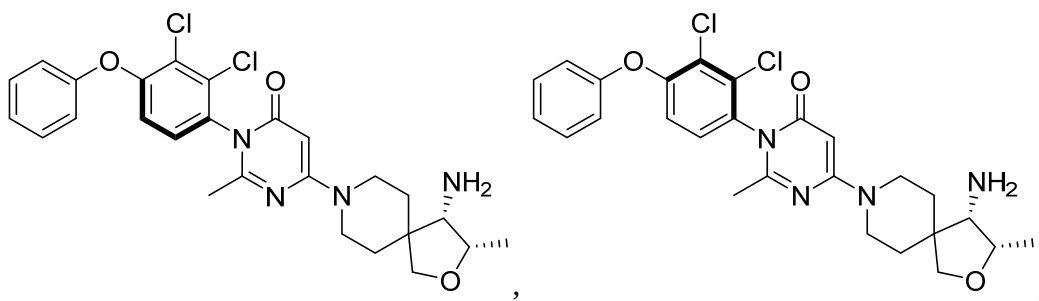
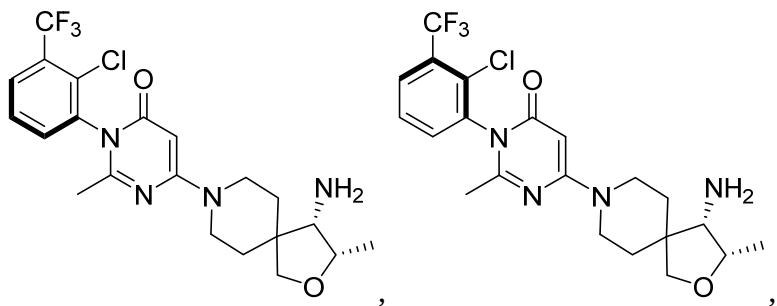
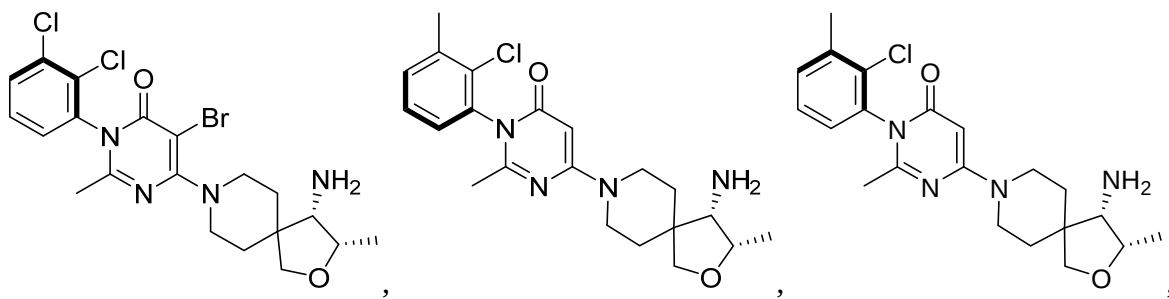
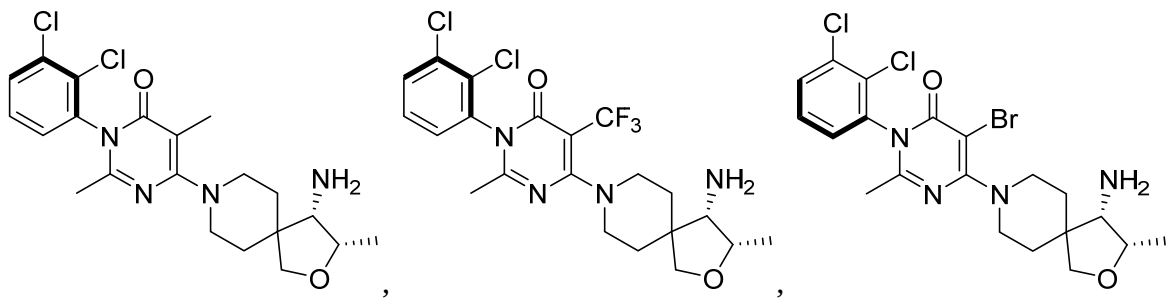
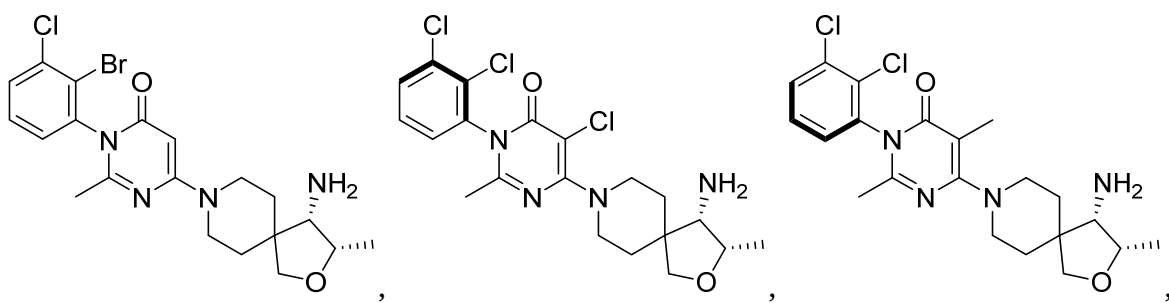
which is optionally substituted by one or two groups independently selected from the group consisting of C₁₋₄alkylamido, halo, hydroxy, cyano, and C₁₋₄alkyl.

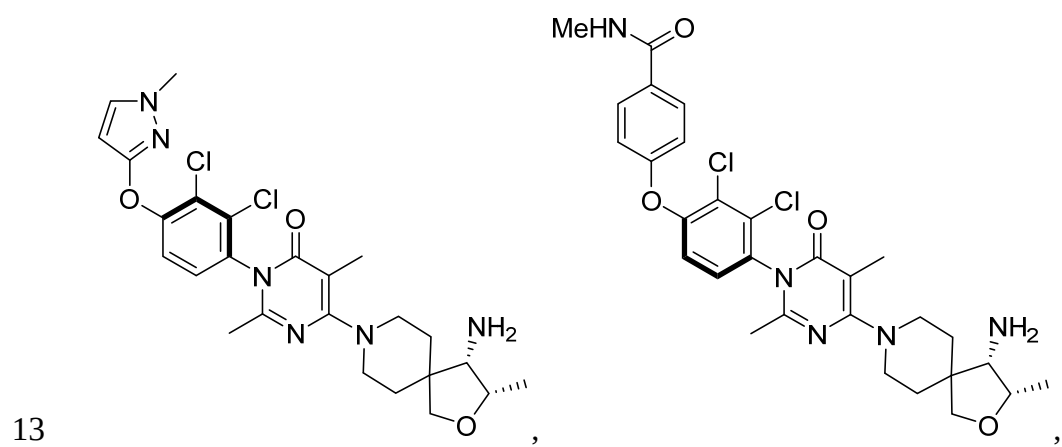
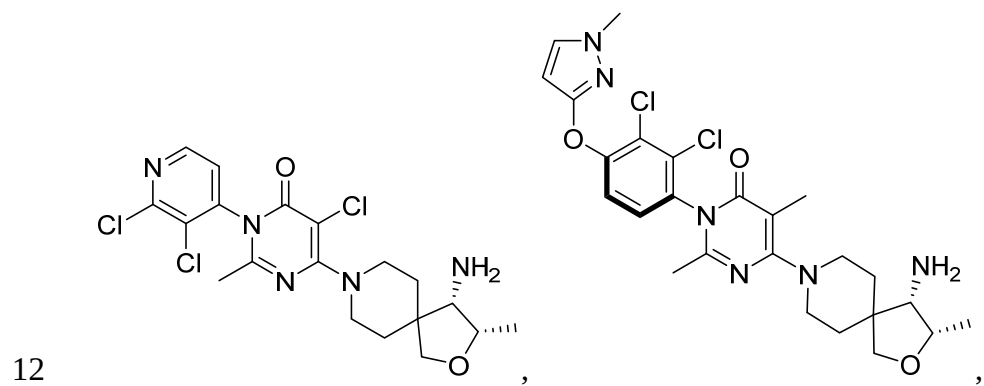
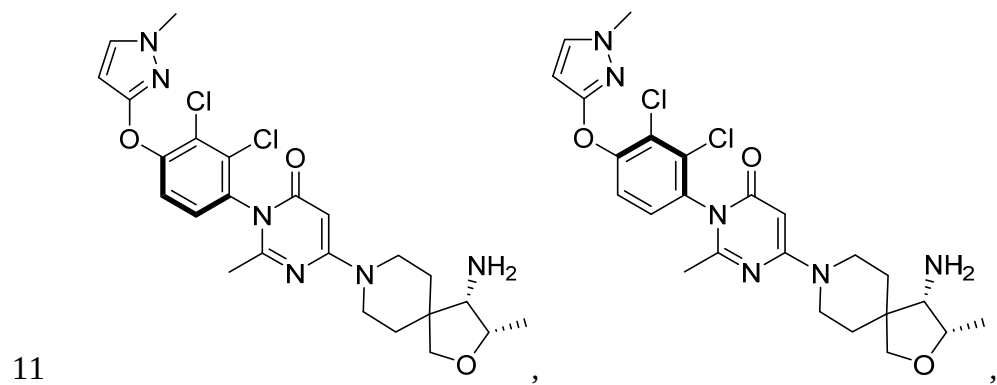
26. The compound of claim 1, wherein each R₁₂ is independently selected from the group consisting of F, Cl, Br, CH₃, OCH₃, CF₃,

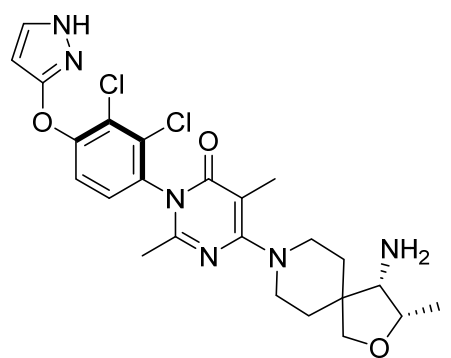
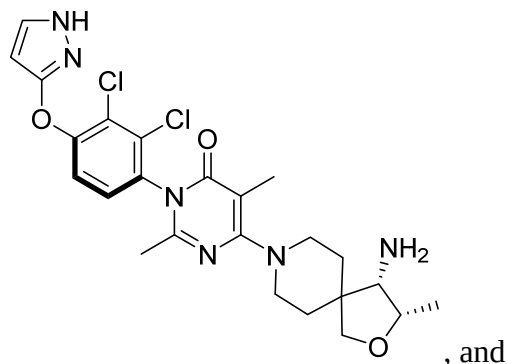
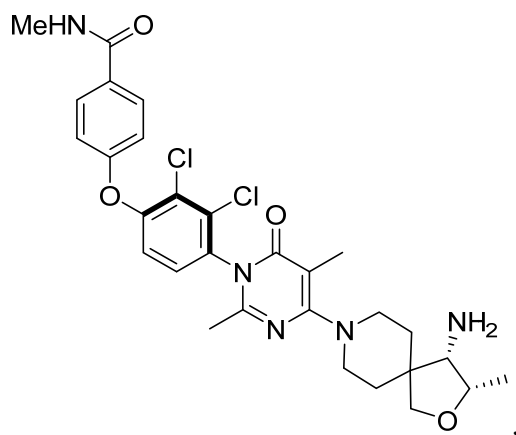


27. The compound of claim 1, having a structure selected from the group consisting of:









1 28. A compound of claim 1, for use as a medicament.

1 29. A compound of claim 1, for use in the treatment of a disease driven by one
2 or more PTPN11 mutations.

1 30. A compound of claim 1, for use in the treatment of cancer.

1 31. The compound of claim 30, wherein the cancer is selected from the group
2 consisting of leukemia, melanoma, breast cancer, and colon cancer.

1 32. A compound of claim 1, for use in the manufacture of a medicament for
2 the prevention or treatment of a disease or condition ameliorated by the inhibition of PTPN11.

1 33. A pharmaceutical composition comprising a compound of claim 1,
2 together with a pharmaceutically acceptable carrier.

1 **34.** A method of inhibition of PTPN11 comprising contacting PTPN11 with a
2 compound of claim **1**.

1 **35.** Use of a compound of claim **1** in the manufacture of a medicament for the
2 treatment of a PTPN11-mediated disease.

1 **36.** The use of claim **35**, wherein the disease is cancer.

1 **37.** The use of claim **36**, wherein the cancer is selected from the group
2 consisting of breast cancer, colon cancer, leukemia, and melanoma.

1 **38.** Use of a compound of claim **1** in the manufacture of a medicament for
2 the treatment of a PTPN11-mediated disease, wherein the medicament further comprises
3 another therapeutic agent.

1 **39.** The use of claim **38**, wherein the disease is cancer.

1 **40.** The use of claim **39**, wherein the cancer is selected from the group
2 consisting of breast cancer, colon cancer, leukemia, and melanoma.