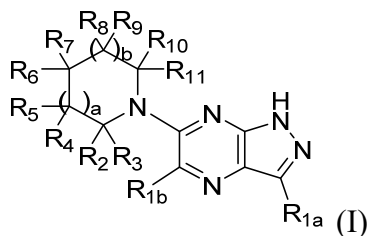


CLAIMS

1. A compound of structural Formula I



or a salt or tautomer thereof, wherein:

a is 0 or 1;

b is 0 or 1;

R_{1a} is selected from the group consisting of halo, C₆₋₁₀aryl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, and a 5-9 membered heteroaryl group containing 1 to 4 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S; said aryl or heteroaryl of R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, C₁₋₄dialkylamino, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄hydroxyalkyl, C₁₋₄dihydroxyalkyl, hydroxyC₁₋₄alkoxy, dihydroxyC₁₋₄alkoxy, C₁₋₄haloalkyl, C₁₋₄aminoalkyl, C₃₋₈cycloalkyl, C₃₋₈cycloalkenyl, NR₁₅C(O)R₁₃, NR₁₅C(O)OR₁₃, NR₁₃C(O)NR₁₅R₁₆, NR₁₅S(O)R₁₃, NR₁₅S(O)₂R₁₃, C(O)NR₁₅R₁₆, S(O)NR₁₅R₁₆, S(O)₂NR₁₅R₁₆, C(O)R₁₃, C(O)OR₁₃, OR₁₃, SR₁₃, S(O)R₁₃, and S(O)₂R₁₃;

R_{1b} is selected from the group consisting of halogen, cyano, C₁₋₆alkyl, C₁₋₆haloalkyl, CH₂OH and C₁₋₆hydroxyalkyl, C₁₋₆dihydroxyalkyl, CF₂OH, CHFOH, NH-NHR₁₉, NH-OR₁₉, -O-NR₁₉R₂₀, NHR₁₉, OR₁₉, NHC(O)R₁₉, NHC(O)NHR₁₉, NHS(O)₂NHR₁₉, NHS(O)₂R₁₉, C(O)OR₁₉, C(O)NR₁₉R₂₀, C(O)NH(CH₂)_nOH, C(O)NH(CH₂)_nR₂₁, C(O)R₂₁, NH₂, OH, S(O)₂NR₁₉R₂₀, C₃₋₈cycloalkyl, aryl, heterocyclyl having 1-5 heteroatom ring vertices selected from the group consisting of N, O, S and P; heteroaryl having 1-5 heteroatom ring vertices selected from the group consisting of N, O, S and P; wherein the subscript n is an integer of from 0 to 6; and wherein aryl, heteroaryl, heterocyclyl and cycloalkyl are substituted with 0 to 3 members

independently selected from the group consisting of C₁₋₄alkyl, OH, NH₂, OR₂₄, halogen, cyano and oxo;

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

R₄, R₅, R₈, and R₉ are each independently selected from the group consisting of hydrogen, cyano, and 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, cyano, amido, halo, and hydroxy, or is selected from the group consisting of C₁₋₄alkyl, and C₁₋₄hydroxyalkyl, C₃₋₆cycloalkyl, phenyl, and 5- or 6- membered heteroaryl, any of which is optionally substituted with one or more R₁₇ groups;

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 that can contain 1 to 3 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S(O)_m, and that is optionally substituted with one R₁₇ group, and that is optionally substituted with one or more R₁₈ groups;

m is 0, 1, or 2;

any two groups of R₂, R₃, R₄, R₅, R₇, R₈, R₉, R₁₀ and R₁₁ can form a 5- to 6- membered ring, optionally containing a N, O or S heteroatom;

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

R₁₃, R₁₅, and R₁₆ are independently selected from the group consisting of hydrogen, C₁₋₄alkyl, C₃₋₈cycloalkyl, and 3- to 6- membered heterocyclyl, wherein said alkyl, cycloalkyl and 3- to 6- membered heterocyclyl is optionally substituted by one or more substituents selected from the group consisting of hydroxy, cyano and halo;

R₁₇ is selected from the group consisting of amino, halo, hydroxy, cyano, trifluoromethyl, trifluoromethoxy, C₁₋₄alkyl, and C₁₋₄alkoxy;

each R₁₈ is independently selected from the group consisting of halo, hydroxy, and cyano;

each R₁₉ and R₂₀ is independently selected from the group consisting of H, C₁₋₆alkyl, C₁₋₆haloalkyl, C₁₋₆hydroxyalkyl, C₂₋₆alkenyl, C₂₋₆alkynyl and C₃₋₆cycloalkyl; and

each R_{21} is independently selected from the group consisting of H, OH, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} hydroxyalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl and C_{3-6} cycloalkyl.

2. The compound as recited in claim 1, wherein

R_{1b} is selected from the group consisting of halogen, cyano, C_{1-6} alkyl, C_{1-6} haloalkyl, and CH_2OH

~~C_{1-6} hydroxyalkyl, C_{1-6} dihydroxyalkyl, CF_2OH , $CHFOH$, C_3-C_8 cycloalkyl, 5- or 6-membered heterocyclyl having 1-3 heteroatom ring vertices selected from the group consisting of N, O and S, 5- or 6-membered heteroaryl having 1-4 heteroatom ring vertices selected from the group consisting of N, O, and S; wherein heteroaryl, heterocyclyl and cycloalkyl are substituted with 0 to 3 members independently selected from the group consisting of C_{1-4} alkyl, OH, NH_2 , OR_{21} , halogen, cyano and oxo.~~

3. The compound as recited in claim 1, wherein

R_{1a} is C_{6-10} aryl or a 5- to 9- membered heteroaryl group containing 1 to 4 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S; said aryl or heteroaryl of R_{1a} is optionally substituted with 1 to 5 R_{12} groups independently

~~selected from the group consisting of halo, hydroxy, amino, and C_{1-4} alkylamino, C_{1-4} dialkylamino, cyano, C_{1-4} alkyl, C_{1-4} alkoxy, C_{1-4} hydroxyalkyl, C_{1-4} haloalkyl, C_{1-4} aminoalkyl, C_{3-8} cycloalkyl, C_{3-8} cycloalkenyl, $NR_{15}C(O)R_{13}$, $NR_{15}C(O)OR_{13}$, $NR_{13}C(O)NR_{15}R_{16}$, $NR_{15}S(O)R_{13}$, $NR_{15}S(O)_2R_{13}$, $C(O)NR_{15}R_{16}$, $S(O)NR_{15}R_{16}$, $S(O)_2NR_{15}R_{16}$, $C(O)R_{13}$, $C(O)OR_{13}$, SR_{13} , $S(O)R_{13}$, and $S(O)_2R_{13}$; and~~

~~R_{13} , R_{15} , and R_{16} are independently selected from the group consisting of hydrogen, C_{1-4} alkyl, and C_{3-8} cycloalkyl, wherein said alkyl or cycloalkyl is optionally substituted by one or more substituents selected from the group consisting of hydroxy, cyano and halo.~~

4. The compound as recited in claim 3, wherein

R_{1a} is C_{6-10} aryl or a 5- to 9- membered heteroaryl group containing 1 to 4 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S;

said aryl or heteroaryl of R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, and C₁₋₄alkylamino, C₁₋₄dialkylamino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, and C₁₋₄aminoalkyl.

~~5.~~ The compound as recited in claim 1, wherein:

R_{1a} is C₆₋₁₀aryl or a 5- to 9-membered heteroaryl group containing 1 to 4 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S; said aryl or heteroaryl of R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, C₁₋₄dialkylamino, C₁₋₄alkyl, C₁₋₄alkoxy, C₁₋₄haloalkyl, and C₁₋₄aminoalkyl; and R₄, R₅, R₈, and R₉ are independently selected from the group consisting of hydrogen, C₁₋₄alkyl, C₁₋₄alkoxy, amino, hydroxy, C₃₋₆cycloalkyl, and C₁₋₄alkylamino.

~~65.~~ The compound as recited in claim ~~51~~, wherein R₂, R₃, R₄, R₅, R₈, R₉, R₁₀ and R₁₁ are each hydrogen.

~~76.~~ The compound as recited in any one of claims ~~1 to 6~~, wherein:

R₆ is selected from the group consisting of amino, C₁₋₄aminoalkyl, and C₁₋₄alkylamino; and R₇ is selected from the group consisting of hydrogen, cyano, amido, halo, and hydroxy, and 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 or more R₁₇ groups.

~~8.~~ The compound as recited in any one of claims ~~1 to 6~~, wherein R₆ and R₇ together with the carbon atom to which they are both attached forms a 3- to 7-membered saturated or unsaturated ring that can contain 1 to 3 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S(O)_m, and that is optionally substituted with one R₁₇ group, and that is optionally substituted with one or more R₁₈ groups.

~~9.~~ The compound as recited in any one of claims ~~1 to 6~~, wherein R₆ and R₇ together with the carbon atom to which they are both attached forms a 3- to 7-membered cycloalkyl ring that is optionally substituted with one R₁₇ group, and that is optionally substituted with one or more R₁₈ groups.

~~10.~~—The compound as recited in any one of claims ~~1 to 6~~, wherein R₆ and R₇ together with the carbon atom to which they are both attached form a ~~3 to 6~~-membered heterocycloalkyl ring that is optionally substituted with one R₁₇-group, and that is optionally substituted with one or more R₁₈-groups.

~~11.~~—The compound as recited in any one of claims ~~1 to 6~~, wherein R₆ and R₇ together with the carbon atom to which they are both attached form a ~~3 to 6~~-membered heterocycloalkyl ring that is optionally substituted with one R₁₇-group.

~~12.~~—The compound as recited in any one of claims ~~1 to 6~~, wherein each R₁₇ is independently selected from the group consisting of amino, halo, hydroxy, and cyano.

~~13.~~—The compound as recited in any one of claims ~~1 to 6~~, wherein each R₁₈ is independently selected from the group consisting of halo, hydroxy, cyano, and C₁₋₄alkyl.

~~14.~~—The compound as recited in any one of claims ~~1 to 6~~, wherein each R₁₇ is amino; and each R₁₈ is methyl.

~~157.~~ The compound as recited in any one of claims ~~1 to 6~~, wherein R₆ is C₁₋₄aminoalkyl; and

R₇ is selected from the group consisting of hydroxy, C₁₋₄alkyl, and C₁₋₄hydroxyalkyl, C₃₋₆cycloalkyl, phenyl, and ~~5 or 6~~-membered heteroaryl, any of which is optionally substituted with one or more R₁₇-groups.

~~168.~~ The compound as recited in any one of claims ~~1 to 6~~, wherein R₆ is aminomethyl; and

R₇ is selected from the group consisting of hydroxy, and C₁₋₄alkyl, C₁₋₄hydroxyalkyl, C₃₋₆cycloalkyl, phenyl, and ~~5 or 6~~-membered heteroaryl.

~~179.~~ The compound as recited in any one of claims ~~1 to 6~~, wherein R₆ is amino; and

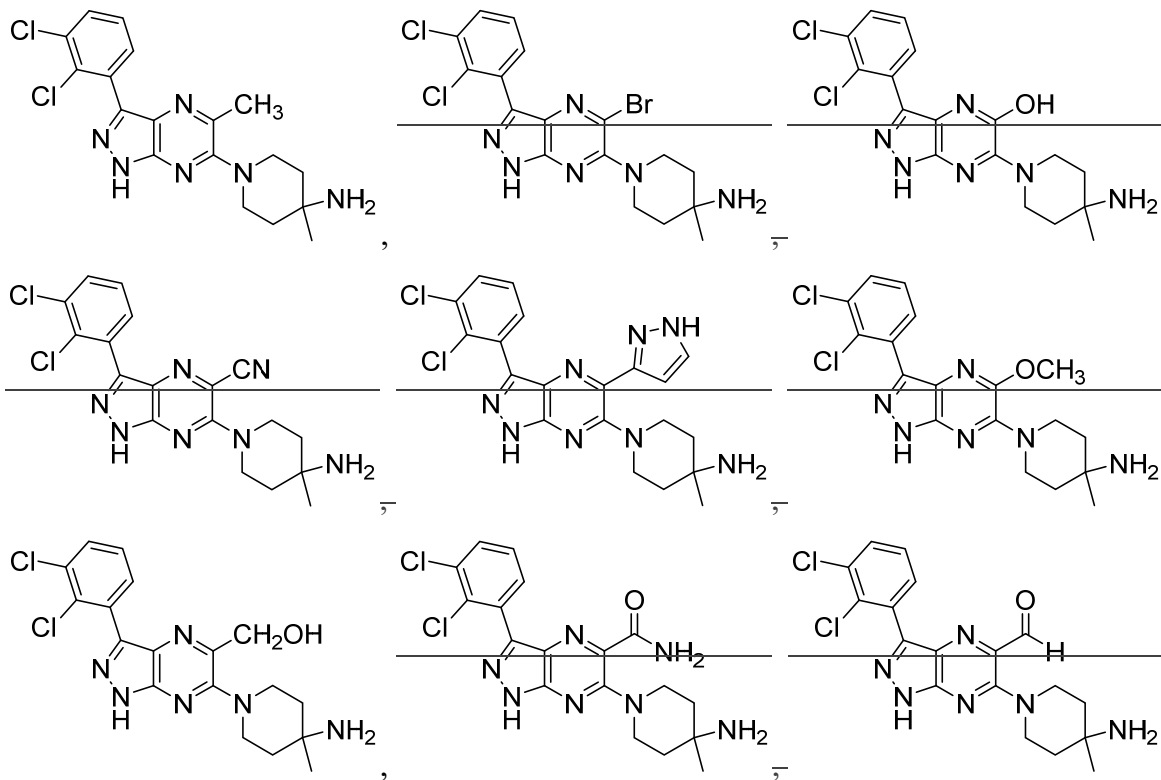
members independently selected from the group consisting of C₁₋₄ alkyl, OH, NH₂, C₁₋₄ alkoxy, halogen, cyano and oxo.

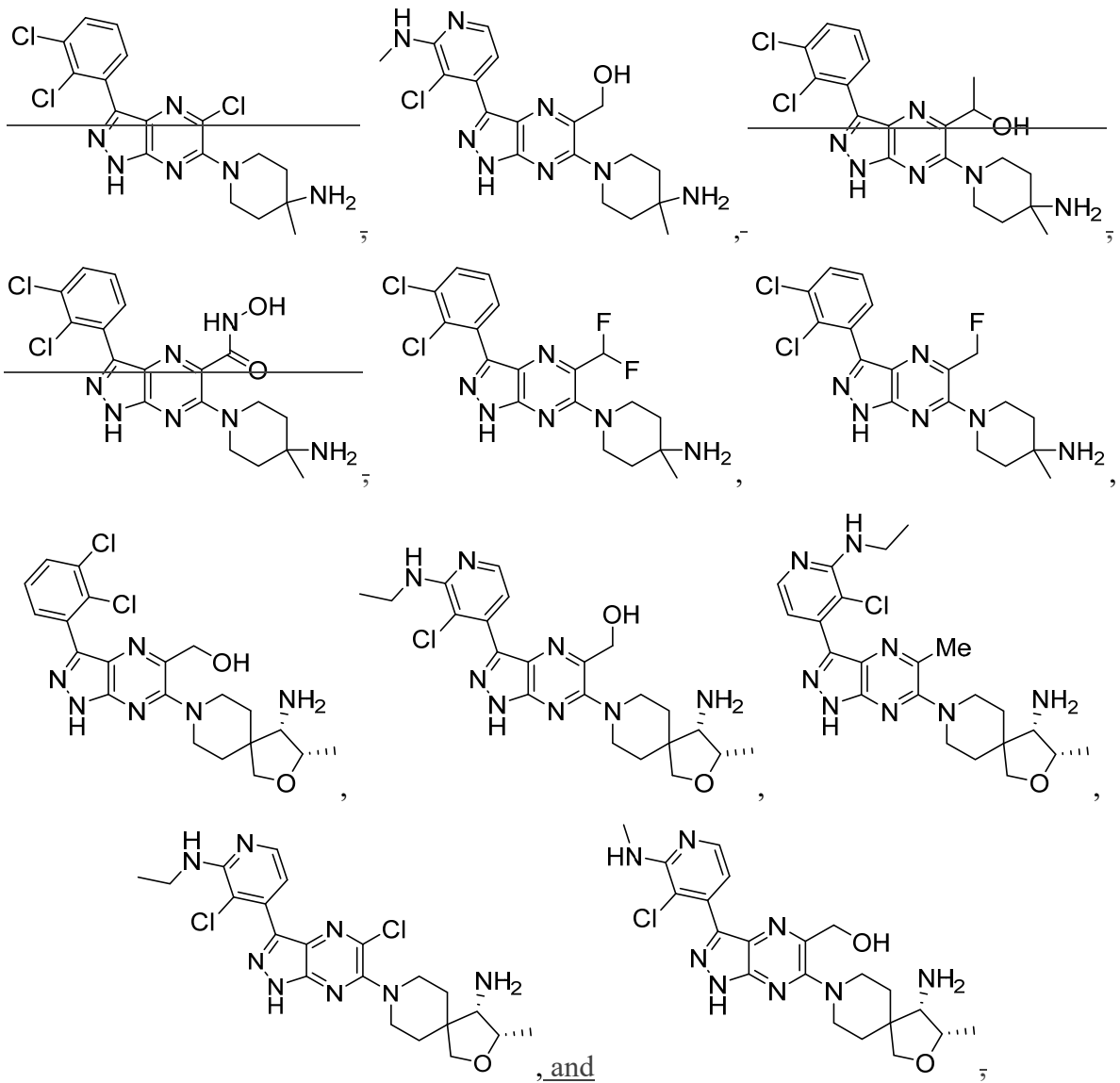
~~28.~~ The compound as recited in any one of claims ~~1 to 26~~, wherein R_{1b} is chloro.

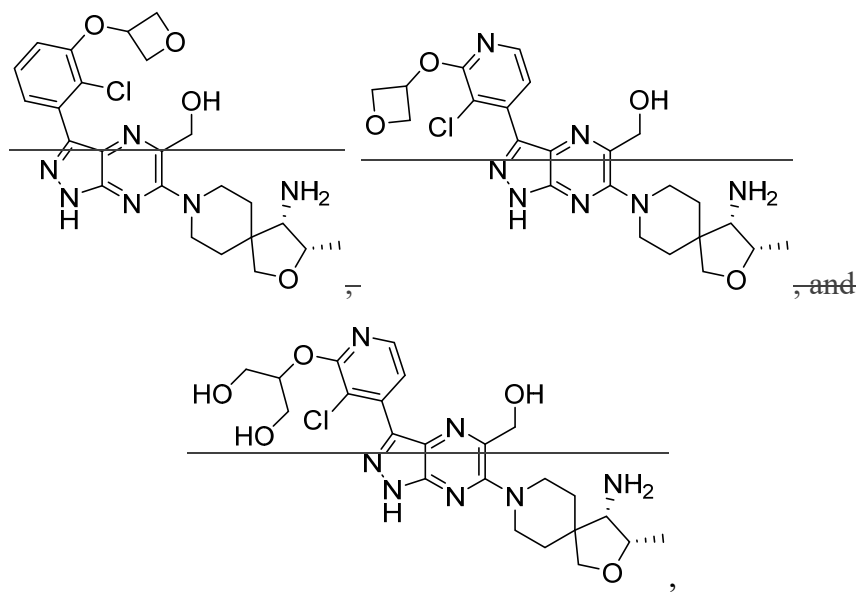
~~29~~17. The compound as recited in any one of claims ~~1 to 26~~, wherein R_{1b} is -CH₂OH.

~~30~~18. The compound as recited in any one of claims ~~1 to 26~~, wherein R_{1b} is methyl.

~~31~~19. The A compound as recited in claim 1, which has a structure selected from the group consisting of:







or a salt or tautomer thereof.

~~32. A compound as recited in claim 1, for use as a medicament.~~

~~33. A compound as recited in claim 1, for use in the treatment of a disease driven by one or more PTPN11 mutations.~~

~~34. A compound as recited in claim 1, for use in the treatment of cancer.~~

~~35. The compound as recited in claim 34, wherein the cancer is selected from the group consisting of leukemia, melanoma, breast cancer, and colon cancer.~~

~~36. A compound as recited in claim 1, for use in the manufacture of a medicament for the prevention or treatment of a disease or condition ameliorated by the inhibition of PTPN11.~~

~~37. A pharmaceutical composition comprising a compound as recited in claim 1, together with a pharmaceutically acceptable carrier.~~

~~38. A method of inhibition of PTPN11 comprising contacting PTPN11 with a compound as recited in claim 1.~~

~~39. — Use of a compound as recited in claim 1 in the manufacture of a medicament for the treatment of a PTPN11-mediated disease.~~

~~40. — The use as recited in claim 39, wherein the disease is cancer.~~

~~41. — The use as recited in claim 40, wherein the cancer is selected from the group consisting of breast cancer, colon cancer, leukemia, and melanoma.~~

~~42. — Use of a compound as recited in claim 1 in the manufacture of a medicament for the treatment of a PTPN11-mediated disease, wherein the medicament further comprises another therapeutic agent.~~

~~43. — The use as recited in claim 42, wherein the disease is cancer.~~

~~44. — The use as recited in claim 43, wherein the cancer is selected from the group consisting of breast cancer, colon cancer, leukemia, and melanoma.~~

20. The compound as recited in claim 1, wherein:

a is 1;

b is 1;

R_{1a} is selected from the group consisting of C₆₋₁₀aryl, and a 5-9 membered heteroaryl group containing 1 to 4 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S; said aryl or heteroaryl of R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, and C₁₋₄alkylamino;

R_{1b} is selected from the group consisting of C₁₋₆ alkyl, and C₁₋₆ haloalkyl;

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

R₄, R₅, R₈, and R₉ are independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;

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

R₇ is selected from the group consisting of C₁₋₄alkyl, and C₁₋₄hydroxyalkyl.

21. The compound as recited in claim 20, wherein:

a is 1;

b is 1;

R_{1a} is selected from the group consisting of phenyl, pyridyl, piperazinyl, pyrimidinyl, pyrazolyl, and pyridazinyl; said R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, and C₁₋₄alkylamino;

R_{1b} is selected from the group consisting of C₁₋₆ alkyl, and C₁₋₆ haloalkyl;

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

R₄, R₅, R₈, and R₉ are each independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;

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

R₇ is selected from the group consisting of C₁₋₄alkyl, and C₁₋₄hydroxyalkyl.

22. The compound as recited in claim 21, wherein:

a is 1;

b is 1;

R_{1a} is selected from the group consisting of phenyl, and pyridyl; said R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, and C₁₋₄alkylamino;

R_{1b} is C₁₋₆ haloalkyl;

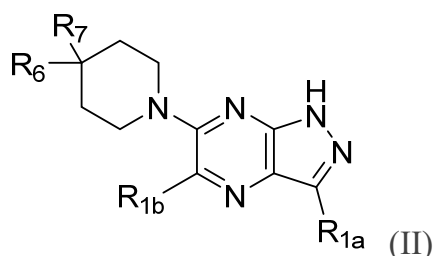
R₂, R₃, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;

R₄, R₅, R₈, and R₉ are each independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;

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

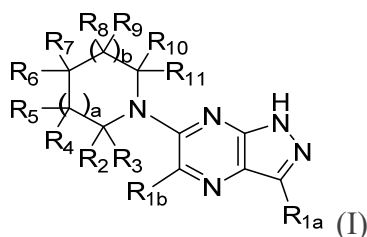
R₇ is selected from the group consisting of C₁₋₄alkyl, and C₁₋₄hydroxyalkyl.

23. The compound as recited in claim 20, wherein the compound has structural Formula II:



wherein R_{1a}, R_{1b}, R₆ and R₇ are as defined in claim 20.

24. A compound of structural Formula I



or a salt or tautomer thereof, wherein:

a is 1;

b is 1;

R_{1a} is selected from the group consisting of C₆₋₁₀aryl, and a 5-9 membered heteroaryl group containing 1 to 4 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S; said aryl or heteroaryl of R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino and C₁₋₄dialkylamino;

R_{1b} is selected from the group consisting of halogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆hydroxyalkyl, C₁₋₆dihydroxyalkyl, -CF₂OH, and -CHFOH;

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

R₄, R₅, R₈, and R₉ are independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;

R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-membered saturated or unsaturated ring that can contain 1 to 3 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S, and that is

optionally substituted with one R₁₇ group, and that is optionally substituted with one or more R₁₈ groups; and
each R₁₇ and R₁₈ is independently selected from the group consisting of amino, hydroxy, C₁₋₄alkyl, and C₁₋₄alkoxy.

25. The compound as recited in claim 24, wherein:
a is 1;
b is 1;
R_{1a} is selected from the group consisting of C₆₋₁₀aryl, and a 5-9 membered heteroaryl group containing 1 to 4 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S; said aryl or heteroaryl of R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, amino, C₁₋₄alkylamino, and C₁₋₄dialkylamino;
R_{1b} is selected from the group consisting of halogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ dihydroxyalkyl;
R₂, R₃, R₁₀, and R₁₁ are each independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;
R₄, R₅, R₈, and R₉ are independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;
R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-membered saturated or unsaturated ring that can contain 1 to 3 heteroatoms or groups independently selected from the group consisting of N, C(O), O, and S, and that is optionally substituted with one R₁₇ group, and that is optionally substituted with one or more R₁₈ groups; and
each R₁₇ and R₁₈ is independently selected from the group consisting of amino, hydroxy, and C₁₋₄alkyl.

26. The compound as recited in claim 25, wherein:
a is 1;
b is 1;

R_{1a} is selected from the group consisting of phenyl, pyridyl, piperazinyl, pyrimidinyl, pyrazolyl, and pyridazinyl; said R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, and C₁₋₄dialkylamino;

R_{1b} is selected from the group consisting of halogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ dihydroxyalkyl;

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

R₄, R₅, R₈, and R₉ are independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;

R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-membered saturated or unsaturated ring that can contain 1 to 3 heteroatoms or groups independently selected from the group consisting of N, C(O), and O, and that is optionally substituted with one R₁₇ group, and that is optionally substituted with one or more R₁₈ groups; and

each R₁₇ and R₁₈ is independently selected from the group consisting of amino, hydroxy, and C₁₋₄alkyl.

27. The compound as recited in claim 26, wherein:

a is 1;

b is 1;

R_{1a} is selected from the group consisting of phenyl, and pyridyl; said R_{1a} is optionally substituted with 1 to 5 R₁₂ groups independently selected from the group consisting of halo, hydroxy, amino, C₁₋₄alkylamino, and C₁₋₄dialkylamino;

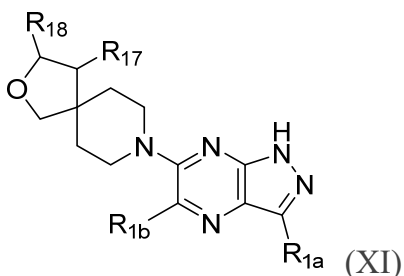
R_{1b} is selected from the group consisting of halogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ hydroxyalkyl, and C₁₋₆ dihydroxyalkyl;

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

R₄, R₅, R₈, and R₉ are independently selected from the group consisting of hydrogen, and C₁₋₄alkyl;

R₆ and R₇ together with the carbon atom to which they are both attached form a 3- to 7-membered saturated or unsaturated ring that can contain 1 to 3 heteroatoms or groups independently selected from the group consisting of N, C(O), and O, and that is optionally substituted with one R₁₇ group, and that is optionally substituted with one or more R₁₈ groups; and
each R₁₇ and R₁₈ is independently selected from the group consisting of amino, hydroxy, and C₁₋₄alkyl.

28. The compound as recited in claim 24, wherein the compound has structural Formula XI:



wherein R_{1a}, R_{1b}, R₁₇ and R₁₈ are as defined in claim 24.