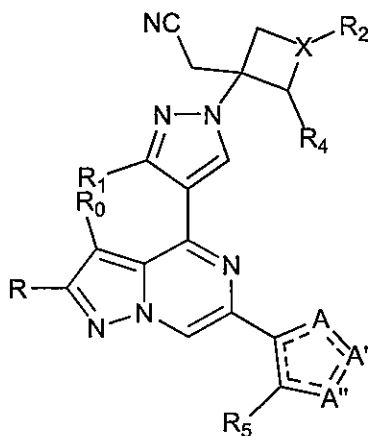


CLAIMS

What is claimed is:

1. A compound having the structure (I):



(I)

or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

A, A' and A'' are independently O, C=O, C-R' or N-R'', where R' and R'' may independently be H, amino, -NR₇COR₆, COR₆, -CONR₇R₈, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-, and R'' may be present or absent, and is present where the rules of valency permit, and where not more than one of A, A' and A'' is O or C=O;

R₀ and R are independently H, Br, Cl, F, or C₁-C₆ alkyl;

R₁ is H, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-;

R₂ is selected from the group consisting of H, C₁-C₆ alkyl-, C₁-C₆ alkoxy-, hydroxy(C₁-C₆ alkyl)-, phenyl(C₁-C₆ alkyl)-, formyl, heteroaryl, heterocyclic, -COR₆, -OCOR₆, -COOR₆, -NR₇COR₆, CONR₇R₈, and -(CH₂)_n-W, where W is cyano, hydroxy, C₃-C₈ cycloalkyl, -SO₂NR₇R₈, and -SO₂-R₉, where R₉ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl, heteroaryl, or heterocyclic; wherein each of said alkyl, cycloalkyl, heterocyclic, or heteroaryl may be unsubstituted or substituted by halo, cyano, hydroxy, or C₁-C₆ alkyl;

X is C-R₃ or N, where R₃ may be H or C₁-C₆ alkyl;

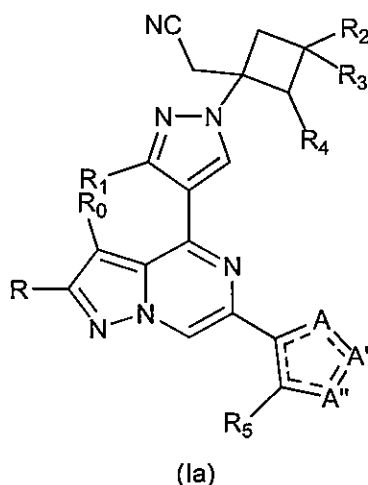
R₄ and R₅ are independently H, amino, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-;

R₆, R₇ and R₈ are each independently H, C₁-C₆ alkyl, C₁-C₄ alkoxy(C₁-C₆ alkyl) or C₃-C₈ cycloalkyl, said C₁-C₆ alkyl is optionally substituted by halo, CN or hydroxy; or, R₇ and R₈ together with the atom

bonded thereto form a 5- or 6-membered ring, said ring being optionally substituted by halo, hydroxy, CN, or C₁-C₆ alkyl;

and, *n* is 0, 1, 2 or 3.

2. The compound of claim 1 having the structure (Ia):



or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

A, A' and A'' are independently O, C=O, C-R' or N-R'', where R' and R'' may independently be H, amino, -NR₇COR₆, COR₆, -CONR₇R₈, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl), and R'' may be present or absent, and is present where the rules of valency permit, and where not more than one of A, A' and A'' is O or C=O;

R₀ and R are independently H, Br, Cl, F, or C₁-C₆ alkyl;

R₁ is H, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl);

R₂ is selected from the group consisting of H, C₁-C₆ alkyl-, C₁-C₆ alkoxy-, hydroxy(C₁-C₆ alkyl)-, phenyl(C₁-C₆ alkyl)-, formyl, heteroaryl, heterocyclic, -COR₆, -OCOR₆, -COOR₆, -NR₇COR₆, -CONR₇R₈, and -(CH₂)_n-W, where W is cyano, hydroxy, C₃-C₈ cycloalkyl, -SO₂NR₇R₈, and -SO₂-R₉, where R₉ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl, heteroaryl, or heterocyclic; wherein each of said alkyl, cycloalkyl, heterocyclic, or heteroaryl may be unsubstituted or substituted by halo, cyano, hydroxy, or C₁-C₆ alkyl;

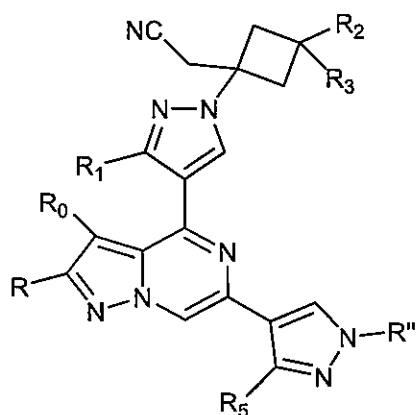
R₃ may be H or C₁-C₆ alkyl;

R₄ and R₅ are independently H, amino, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-;

R₆, R₇ and R₈ are each independently H, C₁-C₆ alkyl, C₁-C₄ alkoxy(C₁-C₆ alkyl)-, or C₃-C₈ cycloalkyl, said C₁-C₆ alkyl is optionally substituted by halo, CN or hydroxy; or, R₇ and R₈ together with the atom bonded thereto form a 5- or 6-membered ring, said ring being optionally substituted by halo, hydroxy, CN, or C₁-C₆ alkyl;

and, *n* is 0, 1, 2 or 3.

3. The compound of claim 1 having the structure (Ib):



(Ib)

or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

R'' is H, -COR₆, -CONR₇R₈, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-;

R₀ and R are independently H, Br, Cl, F, or C₁-C₆ alkyl;

R₁ is H, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl);

R₂ is selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ alkoxy, hydroxy(C₁-C₆ alkyl), phenyl(C₁-C₆ alkyl), formyl, heteroaryl, heterocyclic, -COR₆, -OCOR₆, -COOR₆, -NR₇COR₆, -CONR₇R₈, and -(CH₂)_n-W, where W is cyano, hydroxy, C₃-C₈ cycloalkyl, -SO₂NR₇R₈, and -SO₂-R₉, where R₉ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl, heteroaryl, or heterocyclic; wherein each of said alkyl, cycloalkyl, heterocyclic, or heteroaryl may be unsubstituted or substituted by halo, cyano, hydroxy, or C₁-C₆ alkyl;

R₃ may be H or C₁-C₆ alkyl;

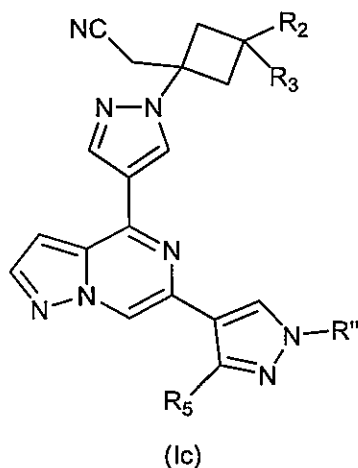
R₅ is independently H, amino, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl);

R₆, R₇ and R₈ are each independently H, C₁-C₆ alkyl, C₁-C₄ alkoxy(C₁-C₆ alkyl), or C₃-C₈ cycloalkyl, said C₁-C₆ alkyl is optionally substituted by halo, CN or hydroxy; or, R₇ and R₈ together with the atom bonded thereto form a 5- or 6-membered ring, said ring being optionally substituted by halo, hydroxy, CN, or C₁-C₆ alkyl;

and, *n* is 0, 1, 2 or 3.

4. The compound of claim 3 wherein R'' is C₁-C₆ alkyl and R₅ is H.

5. The compound of claim 1 having the structure (Ic):



or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

R'' is H, -COR₆, -CONR₇R₈, C₁-C₆ alkyl-, or hydroxy(C₁-C₆ alkyl)-;

R₂ is selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ alkoxy-, hydroxy(C₁-C₆ alkyl)-, phenyl(C₁-C₆ alkyl)-, formyl, heteroaryl, heterocyclic, -COR₆, -OCOR₆, -COOR₆, -NR₇COR₆, -CONR₇R₈, and -(CH₂)_n-W, where W is cyano, hydroxy, C₃-C₈ cycloalkyl, -SO₂NR₇R₈, and -SO₂-R₉, where R₉ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl, heteroaryl, or heterocyclic; wherein each of said alkyl, cycloalkyl, heterocyclic, or heteroaryl may be unsubstituted or substituted by halo, cyano, hydroxy, or C₁-C₆ alkyl;

R₃ is H, C₁-C₆ alkyl, amino, cyano, or C₁-C₆ alkoxy-;

R₅ is H, amino, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-;

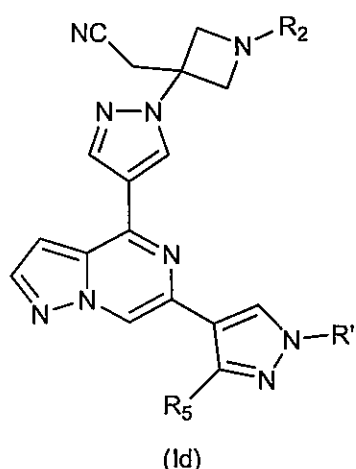
R₆, R₇ and R₈ are each are each independently H, C₁-C₆ alkyl, C₁-C₄ alkoxy(C₁-C₆ alkyl)-, or C₃-C₈ cycloalkyl, said C₁-C₆ alkyl is optionally substituted by halo, CN or hydroxy; or, R₇ and R₈ together

with the atom bonded thereto form a 5- or 6-membered ring, said ring being optionally substituted by halo, hydroxy, CN, or C₁-C₆ alkyl;

and, *n* is 0, 1, 2 or 3.

6. The compound of claim 5 wherein R'' is C₁-C₆ alkyl and R₅ is H.

7. The compound of claim 1 having the structure (Id):



or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

R'' is H, -COR₆, -CONR₇R₈, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-;

R₂ is selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ alkoxy-, hydroxy(C₁-C₆ alkyl)-, phenyl(C₁-C₆ alkyl)-, formyl, heteroaryl, heterocyclic, -COR₆, -OCOR₆, -COOR₆, -CONR₇R₈, and -(CH₂)_n-W, where W is cyano, hydroxy, C₃-C₈ cycloalkyl-, -SO₂NR₇R₈, and -SO₂-R₉, where R₉ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl, heteroaryl, or heterocyclic; wherein each of said alkyl, cycloalkyl, heterocyclic, or heteroaryl may be unsubstituted or substituted by halo, cyano, hydroxy, or C₁-C₆ alkyl;

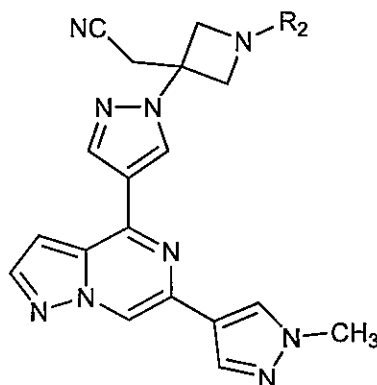
R₅ is H, amino, C₁-C₆ alkyl-, or hydroxy(C₁-C₆ alkyl)-;

R₆, R₇ and R₈ are each are each independently H, C₁-C₆ alkyl, C₁-C₄ alkoxy(C₁-C₆ alkyl), or C₃-C₈ cycloalkyl, said C₁-C₆ alkyl is optionally substituted by halo, CN or hydroxy; or, R₇ and R₈ together with the atom bonded thereto form a 5- or 6-membered ring, said ring being optionally substituted by halo, hydroxy, CN, or C₁-C₆ alkyl;

and, *n* is 0, 1, 2 or 3.

8. The compound of claim 7 wherein R¹¹ is C₁-C₆ alkyl and R₅ is H.

9. The compound of claim 1 having the structure (Ie):



(Ie)

or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

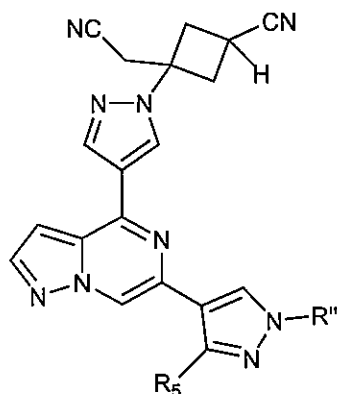
R₂ is selected from the group consisting of H, C₁-C₆ alkyl, C₁-C₆ alkoxy-, hydroxy(C₁-C₆ alkyl)-, phenyl(C₁-C₆ alkyl)-, formyl, heteroaryl, heterocyclic -COR⁶, -OCOR⁶, -COOR⁶, -CONR⁷R⁸, and -(CH₂)_n-W, where W is cyano, hydroxy, C₃-C₈ cycloalkyl, -SO₂NR⁷R⁸, and -SO₂-R⁹, where R⁹ is C₁-C₆ alkyl, C₃-C₈ cycloalkyl, heteroaryl, or heterocyclic; wherein each of said alkyl, cycloalkyl, heterocyclic, or heteroaryl may be unsubstituted or substituted by halo, cyano, hydroxy, or C₁-C₆ alkyl;

R₆, R₇ and R₈ are each are each independently H, C₁-C₆ alkyl, C₁-C₄ alkoxy(C₁-C₆ alkyl), or C₃-C₈ cycloalkyl, said C₁-C₆ alkyl is optionally substituted by halo, CN or hydroxy; or, R₇ and R₈ together with the atom bonded thereto form a 5- or 6-membered ring, said ring being optionally substituted by halo, hydroxy, CN, or C₁-C₆ alkyl;

and, *n* is 0, 1, 2 or 3.

10. The compound of claim 9 wherein R₂ is -(CH₂)_n-W, where W is cyano and *n* is 1, 2 or 3.

11. The compound of claim 1 having the structure (If):



(If)

or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

R'' is H, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-; and,

R₅ is H, amino, C₁-C₆ alkyl, or hydroxy(C₁-C₆ alkyl)-.

12. The compound of claim 11 wherein R'' is C₁-C₆ alkyl and R₅ is H.

13. The compound of claim 1 selected from the group consisting of:

(1r,3r)-3-(4-(6-(3-amino-1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)-3-(cyanomethyl)cyclobutane-1-carbonitrile;

2,2'-(3-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)azetidine-1,3-diyl)diacetonitrile;

2-((1s,3r)-1-(4-(6-(5-(hydroxymethyl)-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)-3-methoxycyclobutyl)acetonitrile;

5-(4-(1-((1s,3r)-1-(cyanomethyl)-3-methoxycyclobutyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazole-3-carboxamide;

(1s,3s)-3-(cyanomethyl)-3-(4-(6-(5-(hydroxymethyl)isoxazol-3-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile;

(1r,3r)-3-(cyanomethyl)-3-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile;

(1s,3s)-3-(cyanomethyl)-3-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile;

(1r,3r)-3-(cyanomethyl)-3-(4-(3-methyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile;

2-((1r,3s)-1-(4-(6-(3-amino-1H-pyrazol-5-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)-3-methoxycyclobutyl)acetonitrile;

2-(1-ethyl-3-(4-(6-(5-(hydroxymethyl)-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)azetidin-3-yl)acetonitrile;

(1r,3r)-3-(Cyanomethyl)-3-(4-(6-(1-methyl-3-oxo-2,3-dihydro-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile (trans isomer);

(1r,3r)-3-(cyanomethyl)-3-(4-(6-(1-(hydroxymethyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile; and,

or, a pharmaceutically acceptable salt thereof.

14. The compound of claim 1 wherein the compound is (1r,3r)-3-(4-(6-(3-amino-1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)-3-(cyanomethyl)cyclobutane-1-carbonitrile, or a pharmaceutically acceptable salt thereof.

15. The compound of claim 1 wherein the compound is 2,2'-(3-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)azetidine-1,3-diyl)diacetonitrile, or a pharmaceutically acceptable salt thereof.

16. The compound of claim 1 wherein the compound is 2-((1s,3r)-1-(4-(6-(5-(hydroxymethyl)-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)-3-methoxycyclobutyl)acetonitrile, or a pharmaceutically acceptable salt thereof.

17. The compound of claim 1 wherein the compound is 5-(4-(1-((1s,3r)-1-(cyanomethyl)-3-methoxycyclobutyl)-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-6-yl)-1H-pyrazole-3-carboxamide, or a pharmaceutically acceptable salt thereof.

18. The compound of claim 1 wherein the compound is (1s,3s)-3-(cyanomethyl)-3-(4-(6-(5-(hydroxymethyl)isoxazol-3-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile, or, a pharmaceutically acceptable salt thereof.

19. The compound of claim 1 wherein the compound is (1r,3r)-3-(cyanomethyl)-3-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile, or a pharmaceutically acceptable salt thereof.

20. The compound of claim 1 wherein the compound is (1s,3s)-3-(cyanomethyl)-3-(4-(6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile, or a pharmaceutically acceptable salt thereof.

21. The compound of claim 1 wherein the compound is (1r,3r)-3-(cyanomethyl)-3-(4-(3-methyl-6-(1-methyl-1H-pyrazol-4-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)cyclobutane-1-carbonitrile, or a pharmaceutically acceptable salt thereof.

22. The compound of claim 1 wherein the compound is 2-((1r,3s)-1-(4-(6-(3-amino-1H-pyrazol-5-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)-3-methoxycyclobutyl)acetonitrile, or a pharmaceutically acceptable salt thereof.

23. The compound of claim 1 wherein the compound is 2-(1-ethyl-3-(4-(6-(5-(hydroxymethyl)-1H-pyrazol-3-yl)pyrazolo[1,5-a]pyrazin-4-yl)-1H-pyrazol-1-yl)azetidin-3-yl)acetonitrile, or, a pharmaceutically acceptable salt thereof.

24. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or salt, and a pharmaceutically acceptable excipient.