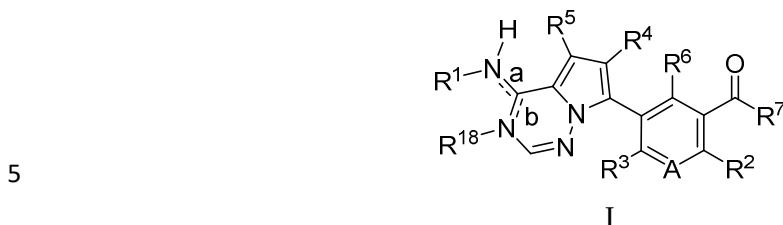


CLAIMS

1. A compound of formula I, or a salt thereof,



wherein:

A is N or CR;

10

R is hydrogen, halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy, amino, C₁₋₃ alkylamino, or C₁₋₃ dialkylamino;

15 R¹ is hydrogen, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ deuterioalkyl, C₁₋₃ alkoxy-C₁₋₃ alkyl, or C₂₋₃ hydroxyalkyl, C(O)-C₁₋₃ alkyl, C(O)-C₁₋₃ haloalkyl;

R² is hydrogen, halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy, amino, C₁₋₃ alkylamino, or C₁₋₃ dialkylamino;

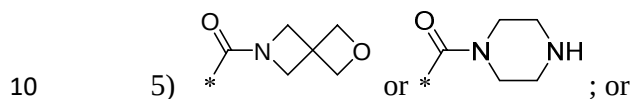
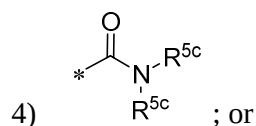
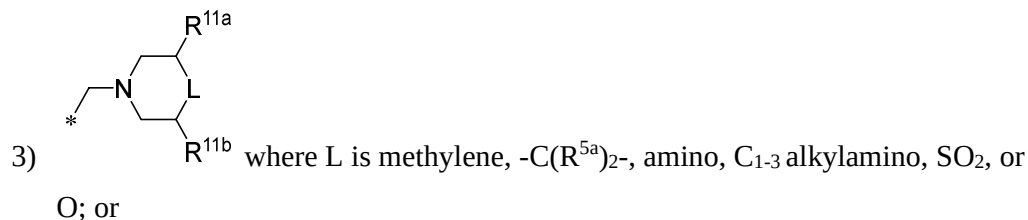
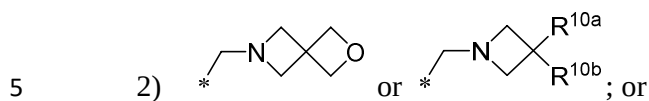
20 R³ is hydrogen, halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy, amino, C₁₋₃ alkylamino, or C₁₋₃ dialkylamino;

25 R⁴ is hydrogen, halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy, C₁₋₃ alkoxy, amino, C₁₋₃ alkylamino, or C₁₋₃ dialkylamino, tetrazolyl, C₁₋₃ alkyl-tetrazolyl;

R⁵ is

- 30 1) hydrogen, halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ haloalkoxy, C₁₋₃ hydroxyalkyl, C₁₋₃ alkoxyalkyl, aminoalkyl, C₁₋₃ alkylaminoalkyl, C₁₋₃ dialkylaminoalkyl, amino, C₁₋₃ alkylamino, C₁₋₃

dialkylamino, (C₁₋₃ alkylCONH)-C₁₋₃alkyl, (C₁₋₃ alkoxyCONH)-C₁₋₃alkyl, or (C₁₋₃ alkylSO₂NH)-C₁₋₃alkyl, -(CH₂)_n-NH-OCH₃, C₃₋₆ cycloalkyl, methyl-phenyl-SO₂-O-; or



6) -(CH₂)_r- phenyl, -(CH₂)_r- 4 to 10 membered heterocycle or 4 to 10 membered heteroaryl, wherein the heterocycle and heteroaryl contain 1, 2, 3, or 4 heteroatoms selected from N, O, and S, and wherein any of the phenyl, heterocycle, or heteroaryl may be substituted with 0-3 of halo, C₁₋₃ alkyl, or amino; or

15

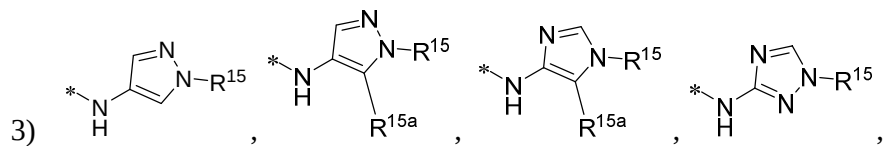
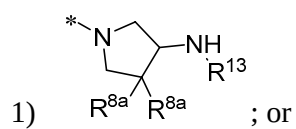
R^{5a} is independently, hydrogen, halo, C₁₋₃ haloalkyl;

20 R^{5c} is independently selected from hydrogen, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ cyanoalkyl-, C₁₋₃ hydroxyalkyl, C₁₋₃ (imidazolyl)alkyl, and C₁₋₃ (C₁₋₃ alkylCO)alkyl;

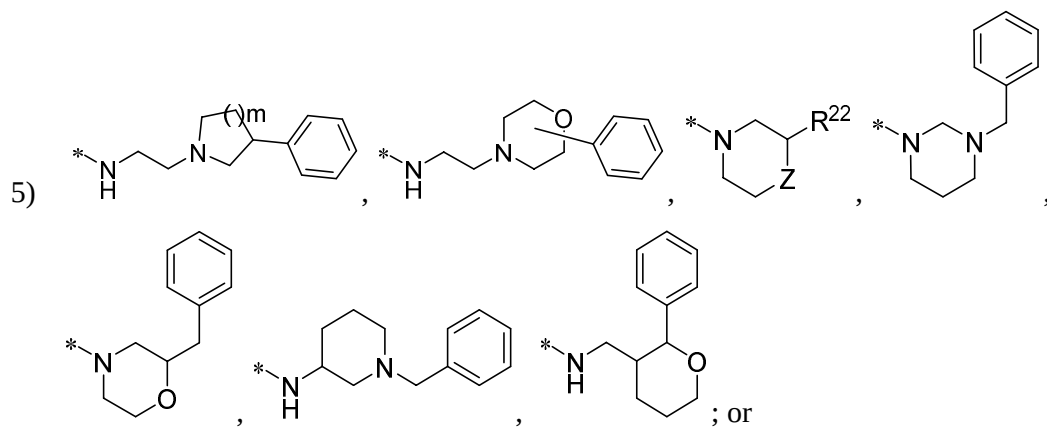
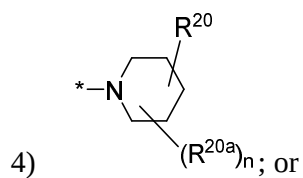
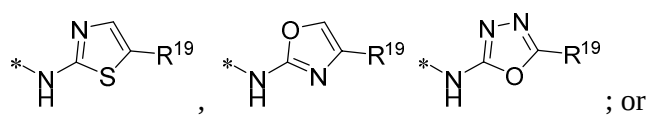
R⁶ is hydrogen, halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy, amino, C₁₋₃ alkylamino, or C₁₋₃ dialkylamino;

25

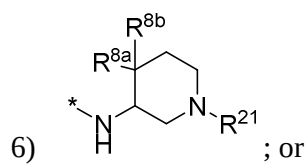
R⁷ is

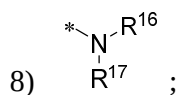
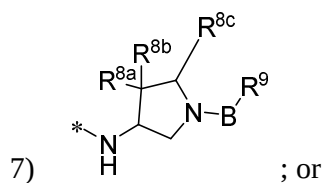


5



10





B is absent, CO, C(O)O, C(O)NR^{12a}, SO₂, or CR^{12a}R^{12b};

5

Z is O, NH, CH₂, or CF₂;

R^{8a} and R^{8b} are each independently selected from hydrogen, halo, C₁₋₃ alkyl, and C₁₋₃ haloalkyl;

10

R^{8c} is hydrogen, or CH₂-O-CH₃, or CH₂-O-CH₂-phenyl;

R⁹ is

1) phenyl, naphthalenyl, pyridyl, pyrimidyl, pyridazinyl, pyrazinyl
 15 quinolinyl, benzisoxazolyl, or benzthiazolyl, and each of which are
 optionally substituted with 1-3 groups selected from halo, cyano, C₁₋₃
 alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ phenylalkyl, C₁₋₃
 (phenyl)hydroxyalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy,
 and C₁₋₃ alkylSO₂; or

20

2) thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, imidazolyl, thiadiazolyl,
 oxadiazolyl, triazolyl, or tetrazolyl, and each of which are optionally
 substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃
 deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ phenylalkyl, C₁₋₃ (phenyl)hydroxyalkyl,
 25 C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy, and C₁₋₃ alkylSO₂⁻
 cyclopropyl; or

25

3) dihydro-1H-indenyl, tetrahydro-5H-benzo[7]annulene,
 tetrahydronaphthalene, and 6,7-dihydro-5H-cyclopenta[b]pyridine, any of

which are substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ phenylalkyl, C₁₋₃ (phenyl)hydroxyalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, C₁₋₃ haloalkoxy, and C₁₋₃ alkylSO₂; or

5

4) C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₁₋₆ deuterioalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxyalkyl, C₃₋₆ cycloalkyl, or C₁₋₆ halocycloalkyl, each of which are optionally substituted with 1-3 groups selected from halo, NH₂, -NC(O)O-C₁₋₆ alkyl, -C(O)-C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, and C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, phenyl, thiazolyl, pyrdinyl, wherein the phenyl, pyridinyl, and thiazolyl are optionally substituted with 0-2 of halo, nitro, or C₁₋₆haloalkyl; or

10

5) C₀₋₂ (C₃₋₇ cycloalkyl)alkyl, cyclohexenyl, oxetanyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, dioxanyl, pyridinonyl, or tetrahydrothiophenyl dioxide, each of which are optionally substituted with 1-4 groups selected from halo, hydroxy, C₁₋₃ alkyl, and C₁₋₃ haloalkyl, C₁₋₃ alkoxy, hydroxyl C₁₋₃ haloalkyl, C₃₋₆ cycloalkyl, C(O)O-C₁₋₆ alkyl, and amino;

15

6) tetrahydropyranyl optionally substituted with 1-4 groups selected from halo, hydroxy, C₁₋₃ alkyl, C₁₋₃ haloalkyl; C₁₋₂ (C₁₋₃ alkoxy)alkyl, C₁₋₄ alkoxy, and phenyl;

20

7) C₁₋₄ alkylamino, C₁₋₄ dialkylamino, azetidiny, pyrrolidinyl, or piperidinyl;

25

or B and R⁹, together with the atom to which they are attached, join to form a C₃₋₆ cycloalkyl optionally substituted with 1-2 groups selected from halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₂₋₃ hydroxyalkyl, C₂₋₄ (hydroxyl)haloalkyl, C₃₋₆ hydroxycycloalkyl, and C₁₋₃ alkoxycarbonyl;

30

R^{10a} and R^{10b} are independently selected from hydrogen, halo, cyano, hydroxy, amino, C₁₋₃ alkylamino, C₁₋₃ dialkylamino, acetylamino, (amino)carbonyl, (C₁₋₃ alkylamino)carbonyl, and (C₁₋₃ dialkylamino)carbonyl;

R^{11a} and R^{11b} are independently selected from hydrogen and C₁₋₆ alkyl;

5 R^{12a} and R^{12b} are independently selected from hydrogen, deuterium, methyl, amino, or OH, or R^{12a} and R^{12b}, along with the atom to which they are attached, join together to form C₃₋₆ cycloalkyl;

10 R¹³ is C₁₋₃ (phenyl)alkyl- or phenylcarbonyl-, and where the phenyl is optionally substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, and C₁₋₃ haloalkoxy;

R¹⁴ is phenyl, C₁₋₃ (phenyl)alkyl-, or phenylcarbonyl, and where the phenyl is optionally substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, and C₁₋₃ haloalkoxy;

15

R¹⁵ is C₁₋₆ alkyl, C₁₋₃ haloalkyl, hydroxy-C₁₋₆ haloalkyl, C₁₋₃ (C₃₋₆ cycloalkyl)alkyl, phenyl-C₁₋₃ alkyl, phenyl-C₁₋₃ haloalkyl-, or phenylcarbonyl, where the phenyl is optionally substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuterioalkoxy, and C₁₋₃ haloalkoxy;

20

R^{15a} is hydrogen, halo, or C₁₋₃ alkyl;

R¹⁶ is hydrogen, alkyl, or deuterioalkyl;

25 R¹⁷ is

1) C₁₋₆(phenyl)alkyl, where the alkyl is optionally substituted with 1-3 groups selected from hydroxy, =O, alkoxy, and haloalkyl, or haloalkoxy, and where the phenyl is optionally substituted with 1-3 groups selected from halo, cyano, hydroxy, NH₂, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ haloalkoxy, C₁₋₃ hydroxyalkyl, C₁₋₃ alkoxyalkyl, C₃₋₆ cycloalkyl, C₁₋₃ alkoxy, C₁₋₃ (C₁₋₃ alkoxy)deuterioalkoxy, C₁₋₃ haloalkoxy, and phenoxy;

30

- 2) C₀₋₆ (cyclopropyl)alkyl, where the alkyl is optionally substituted with 1-3 groups selected from hydroxy, alkoxy, and haloalkyl, and where the phenyl is optionally substituted with 1-3 groups selected from halo, cyano, hydroxy, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ hydroxyalkyl, C₁₋₃ alkoxyalkyl, C₃₋₆ cycloalkyl, C₁₋₃ alkoxy, C₁₋₃ (C₁₋₃ alkoxy)deuteroalkoxy, C₁₋₃ haloalkoxy, =N-O-CH₂-cyclopropyl, (-OCH₂C(CH₃)₂CH₂O-), phenoxy, and phenyl which is substituted with 0-3 of F, Cl, or Br;
- 3) C₁₋₃ (phenoxy)alkyl, C₁₋₃ (phenylamino)alkyl or C₁₋₃ ((phenyl)(alkyl)amino)alkyl where the phenoxy or phenyl is optionally substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ hydroxyalkyl, C₁₋₃ alkoxyalkyl, C₁₋₃ alkoxy, C₁₋₃ deuteroalkoxy, and C₁₋₃ haloalkoxy;
- 4) C₁₋₂ (phenylcyclopropyl)alkyl where the phenyl is optionally substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deuteroalkoxy, and C₁₋₃ haloalkoxy;
- 5) C₁₋₃ (pyridyl)alkyl, C₁₋₃ (pyrimidyl) alkyl, or C₁₋₃ (pyrazinyl)alkyl where the pyridyl, pyrimidyl, and pyridazyl are optionally substituted with 1-2 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deuterioalkyl, C₁₋₃ haloalkyl, C₁₋₃ hydroxyalkyl, C₁₋₃ alkoxy, C₃₋₆ cycloalkyl C₁₋₃ alkoxy-, C₁₋₃ deuteroalkoxy, and C₁₋₃ haloalkoxy;
- 6) C₃₋₇ cycloalkyl, wherein the cycloalkyl is substituted with 0-3 of halo, OH, =N-O-CH₂-cyclopropyl, (-OCH₂C(CH₃)₂CH₂O-), phenyl which is substituted with 0-3 of F, Cl, Br;

7) C₁₋₃ (C₁₋₄ alkoxy)alkyl;

R¹⁹ is -CH₂-phenyl, or -C(O)-NR^{19a}R^{19b};

R^{19a} is hydrogen or C₁₋₃ alkyl;

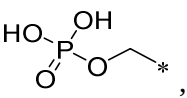
R^{19b} is hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl-C₀₋₃ alkyl-, phenyl-C₀₋₃ alkyl-, phenyl, wherein each are independently substituted with 0-3 of halo, C₁₋₃ alkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ haloalkoxy, or phenyl-C₁₋₃ haloalkyl-;

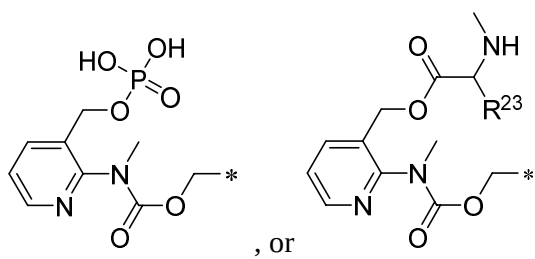
- 5 R²⁰ is H, -CH₂-phenyl, -CH(OH)-phenyl, -C(CH₃)(OH)-phenyl, phenyl, wherein each of the phenyls are independently substituted with 0-1 F;

R^{20a} is independently methyl, or OH;

- 10 R²¹ is phenyl, CO-phenyl, CO-C₃₋₆ cycloalkyl, any of which are substituted with 0-4 of F, CO-C₁₋₆ alkyl, OH, and with 0-6 F;

R²² is C₀₋₁ (phenoxy)alkyl, C₀₋₁ (phenylthio)alkyl, or C₀₋₁ phenylalkyl, and where the phenyl is optionally substituted with 1-3 groups selected from halo, cyano, C₁₋₃ alkyl, C₁₋₃ deutoalkyl, C₁₋₃ haloalkyl, C₁₋₃ alkoxy, C₁₋₃ deutoalkoxy, and C₁₋₃ haloalkoxy;

and either R¹ or R¹⁸ are C₁₋₃ hydroxyalkyl, C₁₋₃ (C₁₋₃ alkoxy)alkyl, ,



or where R²³ is C₁₋₃ alkyl, C₁₋₃ hydroxyalkyl,

or (C₁₋₃ alkoxy)alkyl;

20

a is single or double bond; and

b is single or double bond;

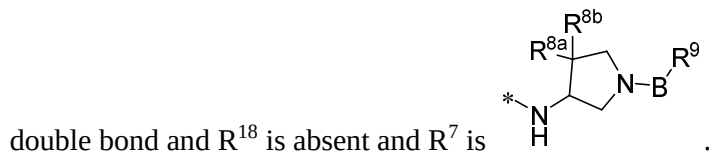
provided that when a is a single bond, b is a double bond and R¹⁸ is absent and when a is a double bond, b is a single bond and R¹ is absent;

- 25 n is 0, 1, or 2;

m is 1 or 2; and

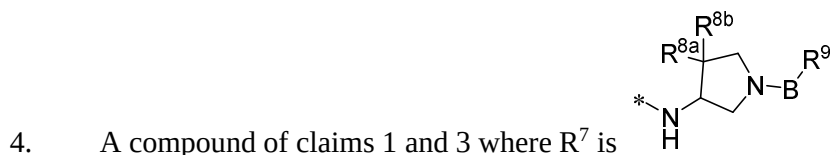
r is 1 or 2.

2. A compound of claim 1 where A is N; R¹ is hydrogen; R² is C₁₋₃ alkoxy; R³ is hydrogen; R⁴ is hydrogen; R⁵ is C₁₋₃ haloalkoxy; R⁶ is hydrogen; a is a single bond, b is a

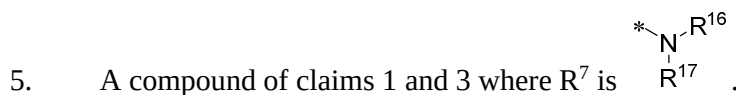


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3. A compound of claim 1 where A is N; R¹ is hydrogen; R² is C₁₋₃ alkoxy; R³ is hydrogen; R⁴ is hydrogen; R⁵ is C₁₋₃ haloalkoxy; R⁶ is hydrogen; a is a single bond, b is a double bond and R¹⁸ is absent.



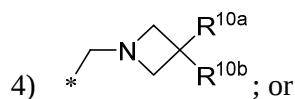
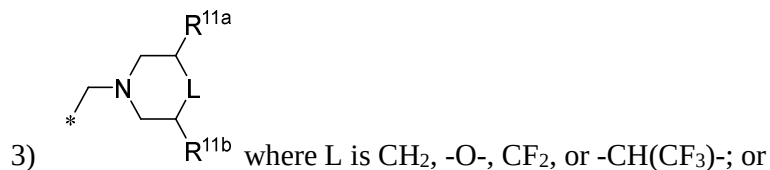
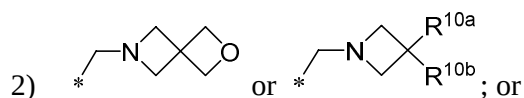
10



6. A compound of claims 1 and 3, wherein R⁵ is

1) H or CF₃; or

15



20

5) -(CH₂)_r phenyl, -(CH₂)_r pyrrolidinyl, -(CH₂)_r piperidinyl, -(CH₂)_r azetidinyl, -(CH₂)_r azaspiroheptanyl, -(CH₂)_r benzimidazolyl, -(CH₂)_r

azabicyclooctane, $-(CH_2)_r$ - azaspirooctane, $-(CH_2)_r$ - tetrazolyl, $-(CH_2)_r$ - tetrahydroquinoliny, $-(CH_2)_r$ -pyrazolyl, $-(CH_2)_r$ -imidazolyl, or $-(CH_2)_r$ -triazolyl, any of which may be substituted with 0-3 of halo, C_{1-3} alkyl, or amino.

5 7. A compound of claims 1, 3 or 6, or salt thereof, wherein

R^1 is H;

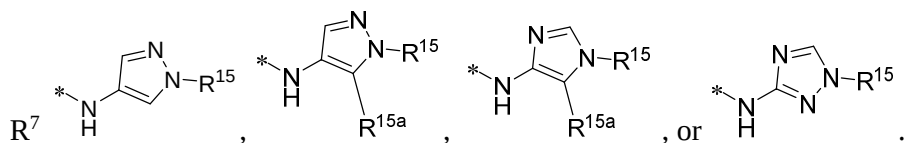
R^2 is H, F, CH_3 , or OCH_3 ;

R^3 is H or F; and

R^4 is H.

10

8. A compound of claims 1, 3, 6 or 7, or salt thereof, wherein



9. A compound of claims 1 – 4, or salt thereof, wherein

15 R^{8a} is halo;

R^{8b} is hydrogen;

B is absent, CO, $C(O)O$, $C(O)NR^{12a}$, SO_2 , or $CR^{12a}R^{12b}$.

R^9 is

- 1) phenyl, naphthalenyl, pyridyl, pyrimidyl, pyridazinyl, pyrazinyl quinoliny, benzisoxazolyl, or benzthiazolyl, and each of which are optionally substituted with 1-3 groups selected from halo, cyano, C_{1-3} alkyl, C_{1-3} deuterioalkyl, C_{1-3} haloalkyl, C_{1-3} phenylalkyl, C_{1-3} (phenyl)hydroxyalkyl, C_{1-3} alkoxy, C_{1-3} deuterioalkoxy, C_{1-3} haloalkoxy, and C_{1-3} alkyl SO_2 ; or
- 2) thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, imidazolyl, thiadiazolyl, oxadiazolyl, triazolyl, or tetrazolyl, and each of which are optionally substituted with 1-3 groups selected from halo, cyano, C_{1-3} alkyl, C_{1-3} deuterioalkyl, C_{1-3} haloalkyl, C_{1-3} phenylalkyl, C_{1-3} (phenyl)hydroxyalkyl, C_{1-3} alkoxy, C_{1-3} deuterioalkoxy, C_{1-3} haloalkoxy, and C_{1-3} alkyl SO_2 -cyclopropyl; or

30

3) C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkynyl, C₁₋₆ deuterioalkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxyalkyl, C₃₋₆ cycloalkyl, or C₁₋₆ halocycloalkyl, each of which are optionally substituted with 1-3 groups selected from halo, NH₂, -NC(O)O-C₁₋₆ alkyl, -C(O)-C₁₋₆ alkyl, hydroxyl, C₁₋₆ alkoxy, and C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, phenyl, thiazolyl, pyridinyl, wherein the phenyl, pyridinyl, and thiazolyl are optionally substituted with 0-2 of halo, nitro, or C₁₋₆haloalkyl; or

4) C₀₋₂ (C₃₋₇ cycloalkyl)alkyl, cyclohexenyl, oxetanyl, tetrahydrofuranyl, pyrrolidinyl, piperidinyl, dioxanyl, pyridinonyl, or tetrahydrothiophenyl dioxide, each of which are optionally substituted with 1-4 groups selected from halo, hydroxy, C₁₋₃ alkyl, and C₁₋₃ haloalkyl, C₁₋₃ alkoxy, hydroxyl C₁₋₃ haloalkyl, C₃₋₆ cycloalkyl, C(O)O-C₁₋₆ alkyl, and amino;

5) tetrahydropyranyl optionally substituted with 1-4 groups selected from halo, hydroxy, C₁₋₃ alkyl, C₁₋₃ haloalkyl; C₁₋₂ (C₁₋₃ alkoxy)alkyl, C₁₋₄ alkoxy, and phenyl.

10. A compound of claim 9, or salt thereof, wherein

B is CO, C(O)O, or SO₂; and

R⁹ is

1) phenyl, or pyridyl, each of which are optionally substituted with 1-3 from halo; or

2) C₂₋₆ alkyl, C₂₋₆ deuterioalkyl, C₂₋₆ haloalkyl, C₂₋₆ alkoxyalkyl, C₃₋₆ cycloalkyl, or C₁₋₆ halocycloalkyl, each of which are optionally substituted with 1-3 groups selected from halo, hydroxyl, and C₁₋₆ haloalkyl; or

3) C₁₋₂ (C₃₋₆ cycloalkyl)alkyl, of which is optionally substituted with 1-4 groups selected from halo, hydroxy, C₁₋₃ alkyl, and C₁₋₃ haloalkyl.

11. A compound of claim 1, or salt thereof, wherein the compound is selected from the examples.

12. A pharmaceutical composition comprising a compound of claims 1-11, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

5 13. Use of one or more of the compound of claims 1-11 in the manufacture of a medicament for~~A method of~~ inhibiting casein kinase RIPK1 activity in a patient, wherein comprising administering to the patient in need thereof, a therapeutically effective amount of the one or more of thea compound of claims 1-11is to be administered to the patent in need thereof.

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14. Use of the compound of claims 1 to 11 in the manufacture of a medicament~~A method~~ for treating a condition selected from inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, rheumatoid arthritis (RA), NASH, and heart failure, wherein comprising the administration of a therapeutically effective amount of athe
15 compound is to be administered of claims 1to 11 to a patient in need thereof~~wherein the condition is selected from inflammatory bowel disease, ulcerative colitis, Crohn's disease, psoriasis, rheumatoid arthritis (RA), NASH, and heart failure.~~

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15. The compound of claims 1 to 11 for use in therapy.