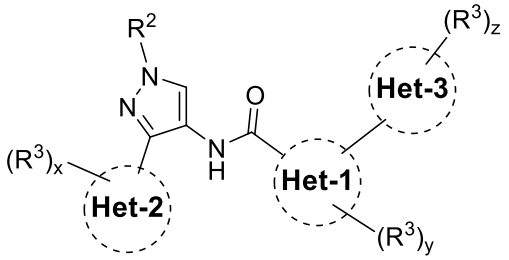
Claims

1. A compound having a formula



or salt thereof, wherein:

R^2 is H, substituted or unsubstituted aliphatic, substituted or unsubstituted heteroaliphatic, substituted or unsubstituted heterocycloaliphatic, substituted or unsubstituted aryl, amide, substituted or unsubstituted heterocyclyl or substituted or unsubstituted araliphatic;

each R^3 independently is H, substituted or unsubstituted aliphatic, halogen, substituted or unsubstituted heteroaliphatic, substituted or unsubstituted -O-aliphatic, substituted or unsubstituted heterocyclyl, substituted or unsubstituted aryl, substituted or unsubstituted araliphatic, substituted or unsubstituted –O-heterocyclyl, hydroxyl, nitro, cyano, carboxyl, carboxyl ester, acyl, amide, amino, sulfonyl, sulfonamide, sulfanyl, sulfinyl, haloalkyl, alkylphosphate, or alkylphosphonate, wherein R^3 is not pyridinyl;

x is from 1 to 6;

y is from 1 to 6;

z is from 1 to 6;

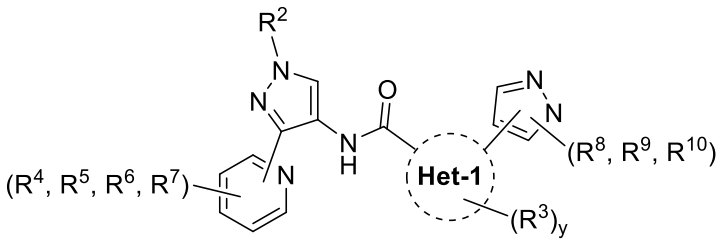
Het-1 is furyl, thiazolyl or oxazolyl;

Het-2 is 5- or 6- membered heteroaryl; and

Het-3 is pyrazolyl.

2. The compound of claim 1, wherein Het-2 is pyridinyl, pyrimidinyl, pyrazinyl, oxadiazolyl, or thiazolyl.

3. The compound of claim 1 or claim 2, wherein the compound has a formula



wherein:

R^4, R^5, R^6 and R^7 are each independently H, substituted or unsubstituted aliphatic, halogen,

haloalkyl, substituted or unsubstituted heteroaliphatic, alkoxy, substituted or unsubstituted heterocyclyl, or substituted or unsubstituted –O-heterocyclyl;

R^8 and R^9 are each independently H , halogen, haloalkyl, or substituted or unsubstituted alkyl; and

R^{10} is H, substituted or unsubstituted aliphatic, substituted or unsubstituted -O-aliphatic, substituted or unsubstituted heteroaliphatic, carboxyl ester, substituted or unsubstituted aryl, acyl, substituted or unsubstituted araliphatic, substituted or unsubstituted heterocyclyl, sulfonyl, amino, NO_2, CN, OH, haloalkyl, alkyl phosphate or alkylphosphonate.

4. The compound of claim 3, wherein:

R^2 is R^a, R^b, R^a substituted with 1, 2 or 3 R^b, R^a substituted with R^b and R^c, R^a substituted with R^c, $–(CR^aR^a)_n$-R^a, -$(CH_2)_n$-R^a, -$(CR^aR^a)_n$-R^b or -$(CH_2)_n$-R^b;

each of R^4, R^5, R^6, and R^7 independently is R^a, R^b, R^a substituted with R^c, -OR^a, -O-$(CR^aR^a)_p$-R^b;

R^{10} is R^a, R^b, R^a substituted with $–OP(O)(R^f)_2$, R^a substituted with 1, 2 or 3 R^b, R^a substituted with R^c, R^a substituted with $–P(O)(R^f)_2$, aralkyl, -$(CR^aR^a)_n$-R^a, -$(CH_2)_n$-R^a or -$C(O)C(R^a)_2NR^aR^b$

n is 1, 2 or 3;

p is 1, 2, or 3;

R^a is independently for each occurrence H, D, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkenyl or C_{3-6}heteroalicyclyl;

R^b is independently for each occurrence -OH, -CF_3, -OR^c, -NR^dR^d, -C(O)OH, -$C(O)R^c$, -$C(O)OR^c$, -$C(O)NR^dR^d$ or halogen;

R^c is independently for each occurrence C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}heteroalicyclyl, aralkyl, C_{1-6}alkyl substituted with 1, 2 or 3 R^e, C_{3-6}cycloalkyl substituted with 1, 2 or 3 R^e, or C_{3-6}heteroalicyclyl substituted with 1, 2 or 3 R^e;

R^d is independently for each occurrence H, C_{1-6}alkyl, C_{1-6}alkyl substituted with 1, 2 or 3 R^e, C_{3-6}cycloalkyl, C_{3-6}cycloalkyl optionally substituted with 1, 2 or 3 R^e, or two R^d groups together with the nitrogen bound thereto form a C_{3-6}heteroalicyclyl moiety optionally substituted with C_{1-6}alkyl;

R^e is independently for each occurrence halogen, C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}heteroalicyclyl, C_{1-6}alkyl-OH, -OR^a, -$OC(O)R^a$ or -O-aralkyl;

R^f is independently for each occurrence -OR^a, -O^-M^+ or $–O^-[M^{2+}]_{0.5}$;

each M^+ independently is an alkali metal ion or an ammonium ion; and

M^{2+} is an alkaline metal earth ion.

5. The compound of any one of claims 3-4, wherein:

R^5 is H, F, CF_3, methoxy, morpholin-4-yl, 1-methylpiperidin-4-yl, -O-$CH_2C(CH_3)_2OH$, or –O-(oxetan-3-yl);

each of R^4, R^6 and R^7 independently is H, F or CF_3; or

a combination thereof.

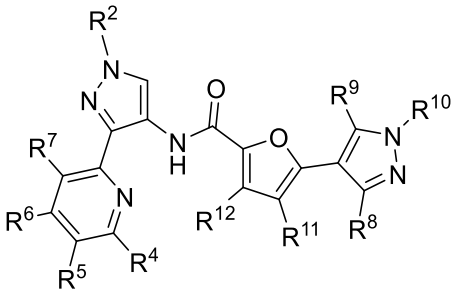
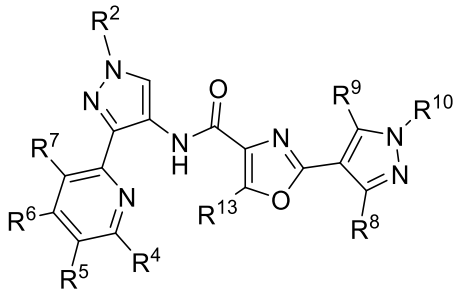
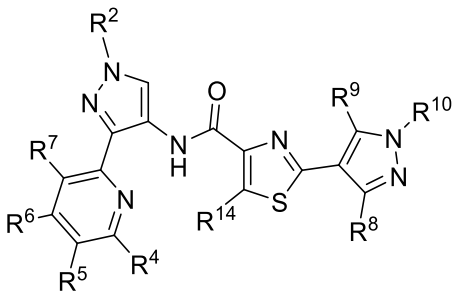
6. The compound of claim 5, wherein:

R^3 is H;

R^2 is H, substituted or unsubstituted alkyl, haloalkyl, substituted or unsubstituted cycloaliphatic, substituted or unsubstituted heteroaliphatic, or substituted or unsubstituted heterocycloaliphatic;

R^{10} is H, substituted or unsubstituted alkyl, carboxyl ester, acyl, alkyl phosphate, alkyl phosphonate or substituted or unsubstituted aralkyl.

7. The compound of any one of claims 3-6, wherein the compound has a formula selected from


,

, or

; and

each of R^{11}, R^{12}, R^{13}, and R^{14} independently is H or substituted or unsubstituted alkyl.

8. The compound of any one of claims 1-7, wherein R^2 comprises cyclobutyl, azetidinyl, morpholinyl, 4-methylpiperazinyl, oxetanyl, tetrahydrofuranyl, tetrahydropyranyl, or a combination thereof.

9. The compound any one of claims 1-8, wherein R^2 is H, methyl, difluoromethyl, trifluoroethyl, isopropyl, tetrahydropyranyl, tetrahydrofuranyl, oxetanyl, N-*tert*-butyloxycarbonyl azetidin-3-yl, 3-methyoxy cyclobutyl, 3-benzyloxycyclobutyl, 3-ethyloxy cyclobutyl, 3-isopropyl cyclobutyl, 3-hydroxy cyclobutyl, 4-ethoxy cyclohexyl, 4-hydroxy cyclohexyl, 4-((2,2-difluoroethyl)amino)cyclohexyl, 3-ethyloxy cyclopentyl, or 3-hydroxy cyclopentyl.

10. The compound of claim 1, or a salt thereof, wherein the compound is selected from:

II-1: N-(1-(2-hydroxy-2-methylpropyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-2: 1-(isobutyryloxy)ethyl 4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazole-1-carboxylate;

II-3: *tert*-butyl (R)-(3-methyl-1-(4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)-1-oxobutan-2-yl)carbamate;

II-4: 2-(1-((5-methyl-2-oxo-1,3-dioxol-4-yl)methyl)-1H-pyrazol-4-yl)-N-(1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-5: 1-methylcyclopropyl 4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazole-1-carboxylate;

II-6: 1-((4-methoxybenzyl)oxy)-2-methylpropan-2-yl 4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazole-1-carboxylate;

II-7: diethyl ((4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl)phosphonate;

II-8: sodium ((4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl)phosphonate;

II-9: ((4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl)phosphonic acid;

II-10: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-11: N-(1-((1,3-cis)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-12: N-(1-((1,3-trans)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-13: N-(1-((1,3-cis)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-14: N-(1-((1,3-cis)-3-hydroxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-15: N-(1-((1s,3s)-3-(dimethylamino)cyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-16: (4-(4-((1-((1,3-cis)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate bis-sodium salt;

II-17: (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl dihydrogen phosphate;

II-18: *N*-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(1*H*-pyrazol-4-yl)thiazole-4-

carboxamide, formic acid salt;

II-19: N-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(5-(trifluoromethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide, formic acid salt;

II-20: N-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(5-(trifluoromethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-21: *N*-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(3-methyl-1*H*-pyrazol-4-yl)thiazole-4-carboxamide, formic acid salt;

II-22: *N*-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(3-methyl-1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-23: 2-(3,5-dimethyl-1*H*-pyrazol-4-yl)-*N*-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)thiazole-4-carboxamide, formic acid salt;

II-24: 2-(3,5-dimethyl-1*H*-pyrazol-4-yl)-*N*-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-25: N-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-26: *N*-(1-methyl-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-27: 2-(3-methyl-1*H*-pyrazol-4-yl)-*N*-(1-methyl-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-28: *N*-(1-(2-methoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-29: *N*-(1-(2-methoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(3-methyl-1*H*-pyrazol-4-yl)thiazole-4-carboxamide, formic acid salt;

II-30: *N*-(1-(2-methoxyethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(3-methyl-1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-31: N-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-32: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-33: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-34: *N*-(1-(oxetan-3-yl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-35: (4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl dihydrogen phosphate;

II-36: Sodium (4-(4-((1-methyl-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1*H*-pyrazol-1-yl)methyl phosphate;

II-37: *N*-(1-(2-(2-methoxyethoxy)ethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(1*H*-pyrazol-4-

yl)thiazole-4-carboxamide;

II-38: potassium (4-(4-((1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate;

II-39: N-(1-(2-(2-methoxyethoxy)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-40: N-(1-(2-(2-methoxyethoxy)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-41: 2-(3-methyl-1*H*-pyrazol-4-yl)-*N*-(1-(oxetan-3-yl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)thiazole-4-carboxamide, formic acid salt;

II-42: 2-(3-methyl-1*H*-pyrazol-4-yl)-*N*-(1-(oxetan-3-yl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-43: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-44: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-45: 2-(3-methyl-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-46: 2-(3-methyl-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-47: N-(1-((3-(hydroxymethyl)oxetan-3-yl)methyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-48: N-(1-((3-(hydroxymethyl)oxetan-3-yl)methyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-49: *N*-(1-(2-(diethylamino)ethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(1*H*-pyrazol-4-yl)thiazole-4-carboxamide, formic acid salt;

II-50: *N*-(1-(2-(diethylamino)ethyl)-3-(pyridin-2-yl)-1*H*-pyrazol-4-yl)-2-(1*H*-pyrazol-4-yl)thiazole-4-carboxamide;

II-51: 2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-(1-(3-methoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-52: N-(1-(2-fluoroethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-53: 2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-54: *tert*-Butyl-3-[4-{2-(1H-pyrazole-4-yl)thiazole-2-carboxamido}-3-(pyridine-2-yl)-1H-pyrazol-1-yl]azetidine-1-carboxylate, free base;

II-55: N-{1-(Azetidin-3-yl)-3-(pyridine-2-yl)-1H-pyrazol-4-yl}-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide, TFA salt;

II-56: N-{1-(Azetidin-3-yl)-3-(pyridine-2-yl)-1H-pyrazol-4-yl}-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-57: N-{1-(3-Methoxycyclobutyl)-3-(pyridine-2-yl)-1H-pyrazol-4-yl}-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide, free base, Cis isomer;

II-58: N-(3-(5-methoxypyridin-2-yl)-1-methyl-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-59: N-(1-isopropyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-60: N-(1-(2-morpholinoethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-61: N-(1-(2-(4-methylpiperazin-1-yl)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-65: N-(3-(3-fluoropyridin-2-yl)-1-((1s,3s)-3-hydroxycyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-66: 2-(1H-pyrazol-3-yl)-N-(3-(pyridin-2-yl)-1-(2-(2,2,2-trifluoroethoxy)ethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-71: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(5-fluoro-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-72: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(5-fluoro-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-73: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(5-fluoro-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-74: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(1,3,4-oxadiazol-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-75: N-(3-(1,3,4-oxadiazol-2-yl)-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-76: N-(1-((1s,3s)-3-isopropoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-77: potassium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate;

II-78: calcium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate;

II-79: N-(1-((1r,3r)-3-hydroxy-3-methylcyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-80: ammonium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate;

II-81: 5-amino-5-carboxypentan-1-aminium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-

2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate;

II-82: 1-(4-amino-4-carboxybutyl)guanidinium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate;

II-83: (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl dihydrogen phosphate;

II-84: 1,3-dihydroxy-2-(hydroxymethyl)propan-2-aminium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl hydrogen phosphate;

II-85: triethylammonium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl hydrogen phosphate;

II-86: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(5-(trifluoromethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-87: N-(1-(3-hydroxy-3-methylcyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-88: N-(1-(difluoromethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-89: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(3-(trifluoromethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-90: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(6-(trifluoromethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-91: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-(trifluoromethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-92: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-93: 2-(3,5-dimethyl-1H-pyrazol-4-yl)-N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-94: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-95: N-(1-(difluoromethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-(trifluoromethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-96: N-(1-(difluoromethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-97: N-(1-(difluoromethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-98: 2-(1-(difluoromethyl)-1H-pyrazol-4-yl)-N-(1-(difluoromethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-99: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(6-(trifluoromethyl)pyridin-2-yl)-1H-pyrazol-4-yl)-

2-(3-methyl-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-100: 2-(3-methyl-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-101: N-(1-((1s,3s)-3-hydroxycyclobutyl)-3-(pyrazin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-102: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyrimidin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-103: 2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(3,3,3-trifluoro-2-hydroxypropyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-104: 2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(3,3,3-trifluoro-2-hydroxypropyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-105: N-(1-(dimethylcarbamoyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-106: N-(1-(dimethylcarbamoyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-107: 2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(3,3,3-trifluoro-2-hydroxy-2-(trifluoromethyl)propyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-108: 2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-(3,3,3-trifluoro-2-hydroxy-2-(trifluoromethyl)propyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-109: N-(1-(2-ethoxyethyl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-110: N-(1-(2-ethoxyethyl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-111: 2-(1H-pyrazol-4-yl)-N-(1-(tetrahydro-2H-pyran-4-yl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-112: 2-(1H-pyrazol-4-yl)-N-(1-(tetrahydro-2H-pyran-4-yl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-113: N-(1-(2-(2-methoxyethoxy)ethyl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-114: N-(1-(2-(2-methoxyethoxy)ethyl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-115: 2-(1H-pyrazol-4-yl)-N-(1-(tetrahydrofuran-3-yl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-116: 2-(1H-pyrazol-4-yl)-N-(1-(tetrahydrofuran-3-yl)-3-(thiazol-2-yl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-117: N-(1-(2-(diethylamino)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-118: N-(1-(2-(2-fluoroethoxy)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-119: N-(1-(2-(2-fluoroethoxy)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-120: N-(1-benzyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-121: N-(1-cyclobutyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-122: N-(1-(2-(2,2-difluoroethoxy)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-123: N-(1-(((1r,3r)-3-hydroxycyclobutyl)methyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-124: N-(1-(((1r,3r)-3-hydroxycyclobutyl)methyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-125: N-(1-(dimethylcarbamoyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-126: N-(1-(dimethylcarbamoyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-127: N-(1-((1s,3s)-3-(ethoxy-d5)cyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-128: N-(1-(diethylcarbamoyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-129: N-(1-(morpholine-4-carbonyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-130: N-(1-((1s,3s)-3-(2-fluoroethoxy)cyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-131: N-(1-(morpholine-4-carbonyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-132: N-(1-(3-fluorocyclobut-2-en-1-yl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-133: N-(1-(3-fluorocyclobut-2-en-1-yl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-134: N-(1-(3,3-difluorocyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-135: N-(1-(3,3-difluorocyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-140: N-(3-(3-fluoropyridin-2-yl)-1-(1,4-dioxaspiro[4.5]decan-8-yl)-1H-pyrazol-4-yl)-2-(1H-

pyrazol-4-yl)thiazole-4-carboxamide;

II-141: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-((1r,3r)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-142: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-((1r,3r)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-143: N-(1-((1r,4r)-4-hydroxycyclohexyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-144: N-(1-((1r,4r)-4-hydroxycyclohexyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-145: N-(1-((1r,4r)-4-ethoxycyclohexyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-146: N-(1-((1r,4r)-4-ethoxycyclohexyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-147: N-(1-((1S,3R)-3-ethoxycyclopentyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-148: N-(1-((1S,3R)-3-ethoxycyclopentyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-149: N-(1-((1S,3R)-3-hydroxycyclopentyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-150: N-(1-((1S,3R)-3-hydroxycyclopentyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-151: N-(1-((1S,3S)-3-hydroxycyclopentyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-152: N-(1-((1S,3S)-3-hydroxycyclopentyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-153: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(5-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-154: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(5-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-155: N-(1-((1S,3R)-3-ethoxy-2-fluorocyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-156: N-(1-((1S,3R)-3-ethoxy-2-fluorocyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-157: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(3-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-158: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(4-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-159: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(4-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-160: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(6-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-161: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-((1s,3s)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-162: 2-(1H-pyrazol-4-yl)-N-(3-(pyridin-2-yl)-1-((1s,3s)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-163: (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(3-fluoropyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl dihydrogen phosphate;¥

II-164: sodium (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(3-fluoropyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl phosphate;

II-165: N-(3-(3-fluoropyridin-2-yl)-1-((1s,3s)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-166: N-(3-(3-fluoropyridin-2-yl)-1-((1s,3s)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-167: N-(3-(3-fluoropyridin-2-yl)-1-((1r,3r)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-168: N-(3-(3-fluoropyridin-2-yl)-1-((1r,3r)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-169: N-(1-((1r,4r)-4-ethoxycyclohexyl)-3-(3-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-170: N-(3-(6-fluoropyridin-2-yl)-1-((1s,3s)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide formate;

II-171: N-(3-(6-fluoropyridin-2-yl)-1-((1s,3s)-3-(2,2,2-trifluoroethoxy)cyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-172: N-(3-(6-fluoropyridin-2-yl)-1-((1s,3s)-3-hydroxycyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-173: (4-(4-((1-((1s,3s)-3-ethoxycyclobutyl)-3-(6-fluoropyridin-2-yl)-1H-pyrazol-4-yl)carbamoyl)thiazol-2-yl)-1H-pyrazol-1-yl)methyl dihydrogen phosphate;

II-174: N-(3-(3,6-difluoropyridin-2-yl)-1-((1s,3s)-3-ethoxycyclobutyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-175: N-(1-((1s,4s)-4-ethoxycyclohexyl)-3-(3-fluoropyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-176: N-(3-(3,6-difluoropyridin-2-yl)-1-((1r,4r)-4-ethoxycyclohexyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-177: N-(3-(3,6-difluoropyridin-2-yl)-1-((1s,4s)-4-ethoxycyclohexyl)-1H-pyrazol-4-yl)-2-

(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-178: N-(1-((1r,4r)-4-ethoxycyclohexyl)-3-(1,3,4-oxadiazol-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-179: N-(1-((1r,4r)-4-((2,2-difluoroethyl)amino)cyclohexyl)-3-(pyrimidin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

II-180: N-(3-(3,5-difluoropyridin-2-yl)-1-((1r,4r)-4-ethoxycyclohexyl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)thiazole-4-carboxamide;

III-1: 2-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-N-(1-methyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)oxazole-4-carboxamide;

III-2: 2-(1*H*-pyrazol-4-yl)-*N*-(3-(pyridin-2-yl)-1-(tetrahydro-2*H*-pyran-4-yl)-1*H*-pyrazol-4-yl)oxazole-4-carboxamide;

III-3: N-(1-(2-ethoxyethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)oxazole-4-carboxamide;

III-4: N-(1-((1s,3s)-3-ethoxycyclobutyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)oxazole-4-carboxamide;

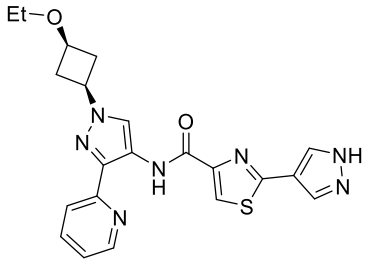
III-5: N-(1-cyclobutyl-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)oxazole-4-carboxamide;

III-6: N-(1-(2-(2-methoxyethoxy)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)oxazole-4-carboxamide;

2-(1H-pyrazol-3-yl)-N-(3-(pyridin-2-yl)-1-(2-(2,2,2-trifluoroethoxy)ethyl)-1H-pyrazol-4-yl)oxazole-4-carboxamide; or

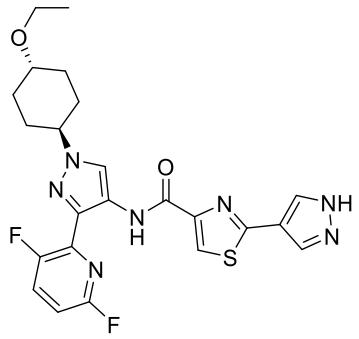
III-8: N-(1-(2-(2,2-difluoroethoxy)ethyl)-3-(pyridin-2-yl)-1H-pyrazol-4-yl)-2-(1H-pyrazol-4-yl)oxazole-4-carboxamide.

11. The compound of claim 1, having a structure



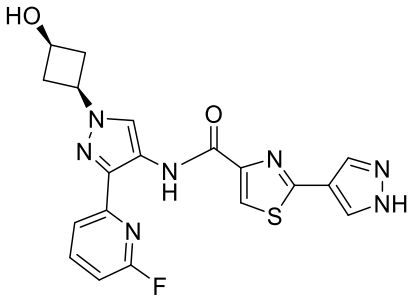
or a pharmaceutically acceptable salt thereof.

12. The compound of claim 1, having a structure



or a pharmaceutically acceptable salt thereof.

13. The compound of claim 1, having a structure



or a pharmaceutically acceptable salt thereof.

14. A composition, comprising a compound of any one of claims 1-13, and a pharmaceutically acceptable excipient.

15. A composition for use in treating a disease or condition in a subject, comprising a compound of any one of claims 1-13.

16. The composition for use according to claim 15, for use in treating a disease or condition for which an IRAK inhibitor is indicated.

17. The composition for use of claim 16, wherein the disease is an auto-immune disease, inflammatory disorder, cardiovascular disease, neurodegenerative disorder, allergic disorder, multi-organ failure, kidney disease, platelet aggregation, cancer, transplantation, sperm motility, erythrocyte deficiency, graft rejection, lung injury, respiratory disease, ischemic condition, bacterial infection, viral infection, immune regulatory disorder or a combination thereof.

18. Use of a compound according to any one of claims 1-13, or a composition according to claim 18, in the manufacture of a medicament for treating a disease or condition for which an IRAK

inhibitor is indicated.

19. A method, comprising contacting the IRAK protein with a compound of any one of claims 1-13 or a composition of claim 14 *in vitro*.

20. Use of a composition according to any one of claims 1-13 in the manufacturing of a medicament for a proliferative disease.

21. The use according to claim 20, wherein the proliferative disease is selected from benign or malignant tumors, solid tumor, carcinoma of the brain, kidney, liver, adrenal gland, bladder, breast, stomach, gastric tumors, ovaries, colon, rectum, prostate, pancreas, lung, vagina, cervix, testis, genitourinary tract, esophagus, larynx, skin, bone or thyroid, sarcoma, glioblastomas, neuroblastomas, multiple myeloma, gastrointestinal cancer, colon carcinoma, colorectal adenoma, a tumor of the neck and head, an epidermal hyperproliferation, psoriasis, prostate hyperplasia, a neoplasia, a neoplasia of epithelial character, adenoma, adenocarcinoma, keratoacanthoma, epidermoid carcinoma, large cell carcinoma, non-small-cell lung carcinoma, lymphomas, Hodgkins and Non-Hodgkins, a mammary carcinoma, follicular carcinoma, undifferentiated carcinoma, papillary carcinoma, seminoma, melanoma, IL-1 driven disorders, a MyD88 driven disorder, ABC diffuse large B-cell lymphoma (DLBCL), Waldenström's macroglobulinemia, Hodgkin's lymphoma, primary cutaneous T-cell lymphoma, chronic lymphocytic leukemia, smoldering or indolent multiple myeloma.

22. The use according to claim 20, wherein the proliferative disease is a hematological malignancy.

23. The use according to claim 22, wherein the hematological malignancy is selected from leukemia, acute myeloid leukemia (AML), DLBCL, ABC DLBCL, chronic lymphocytic leukemia (CLL), chronic lymphocytic lymphoma, primary effusion lymphoma, Burkitt lymphoma/leukemia, acute lymphocytic leukemia, B-cell prolymphocytic leukemia, lymphoplasmacytic lymphoma, myelodysplastic syndromes (MDS), myelofibrosis, polycythemia vera, Kaposi’s sarcoma, Waldenström's macroglobulinemia (WM), splenic marginal zone lymphoma, multiple myeloma, plasmacytoma, or intravascular large B-cell lymphoma.

24. The use according to claim 22, wherein the hematological malignancy is a myelodysplastic syndrome.

25. The use according to claim 20, wherein the proliferative disease is a hyperproliferative skin disease.

26. The use according to claim 25, wherein the hyperproliferative skin disease is selected from psoriasis, atopic dermatitis, contact dermatitis, eczematous dermatitis, seborrhoeic dermatitis, lichen planus, pemphigus, bullous pemphigoid, epidermolysis bullosa, urticaria, angioedemas, vasculitis, erythema, cutaneous eosinophilia, lupus erythematosus, acne, or alopecia areata.

27. The use according to claim 25, wherein the psoriasis is pustular psoriasis.