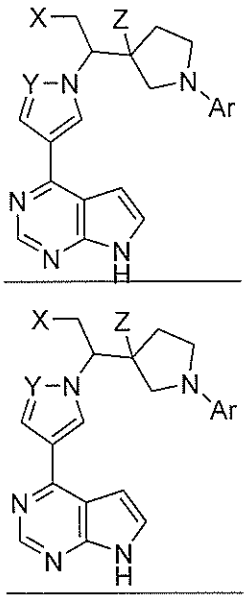
WHAT IS CLAIMED IS:

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt or N-oxide thereof; wherein:

X is cyano or halogen;

Y is CH or N;

Z is hydrogen, C_{1-4} alkyl, C_{1-4} fluorinated alkyl, or fluoro;

Ar is C_{6-14} aryl, C_{1-14} heteroaryl, C_{7-14} fused cycloalkylaryl, C_{6-14} fused heterocycloalkylaryl, C_{2-14} fused cycloalkylheteroaryl, or C_{2-14} fused heterocycloalkylheteroaryl, each of which is optionally substituted by 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-14} cycloalkyl, C_{3-14} cycloalkyl-C_{1-4}-alkyl, C_{2-14} heterocycloalkyl, C_{2-14} heterocycloalkyl-C_{1-4}-alkyl, C_{6-14} aryl, C_{6-14} aryl-C_{1-4}-alkyl, C_{1-13} heteroaryl, C_{1-13} heteroaryl-C_{1-4}-alkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, $-OC(=O)R^b$, $-OC(=O)NR^eR^f$, $-NR^eR^f$, $-NR^cC(=O)R^d$, $-NR^cC(=O)OR^d$, ~~$-NR^eC(=O)NR^d$~~, $-NR^cS(=O)_2R^d$, and $-NR^bS(=O)_2NR^eR^f$; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{1a} groups; and wherein said C_{3-14} cycloalkyl, C_{3-14} cycloalkyl-C_{1-4}-alkyl, C_{2-14} heterocycloalkyl, C_{2-14} heterocycloalkyl-C_{1-4}-alkyl, C_{6-14} aryl, C_{6-14} aryl-C_{1-4}-alkyl, C_{1-13} heteroaryl, and C_{1-13} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{2a} groups;

each R^{1a} is independently selected from halogen, cyano, nitro, hydroxyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4} alkylcarbonyl, carboxy, C_{1-4} alkoxycarbonyl, C_{1-4}-alkylcarbonylamino, di-C_{1-4}-

alkylcarbonylamino, C_{1-4}-alkoxycarbonylamino, C_{1-4}-alkoxycarbonyl-(C_{1-4} alkyl)amino, carbamyl, C_{1-4} alkylcarbamyl, and di-C_{1-4}-alkylcarbamyl;

each R^{2a} is independently selected from halogen, cyano, nitro, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, di-C_{1-4}-alkylamino, C_{1-4} alkylcarbonyl, carboxy, C_{1-4} alkoxycarbonyl, C_{1-4}-alkylcarbonylamino, di-C_{1-4}-alkylcarbonylamino, C_{1-4}-alkoxycarbonylamino, C_{1-4}-alkoxycarbonyl-(C_{1-4} alkyl)amino, carbamyl, C_{1-4} alkylcarbamyl, and di-C_{1-4}-alkylcarbamyl;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^x groups; and wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^y groups;

or any R^c and R^d, together with the moiety to which they are attached, can form a 3-, 4-, 5-, 6-, or 7-membered heterocycloalkyl ring, wherein said heterocycloalkyl ring is optionally substituted with 1, 2, 3, or 4 groups independently selected from hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

or any R^e and R^f, together with the nitrogen atom to which they are attached, can form a 3-, 4-, 5-, 6- or 7-membered heterocycloalkyl ring or heteroaryl ring, wherein said heterocycloalkyl or heteroaryl ring is optionally substituted with 1, 2, 3, or 4 groups independently selected from hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

each R^x is independently selected from hydroxyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino; and

each R^y is independently selected from hydroxyl, halogen, cyano, nitro, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

provided that the valency of each atom in the optionally substituted moieties is not exceeded.

2. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein (a) Y is N; or (b) Y is CH.

~~3.~~ A compound according to ~~claim~~any one of claims 1 to 2, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~Y is CH.~~

~~4. A compound according to any one of claims 1 to 3, or (a pharmaceutically acceptable salt or N-oxide thereof, wherein)~~ X is cyano~~.~~

~~5.~~3. ~~A compound according to any one of claims 1 to 3, or a pharmaceutically acceptable salt or N-oxide thereof, wherein;~~ (b)X is chloro or fluoro~~.~~; or (c) X is fluoro.

~~6.~~4. A compound according to any one of claims 1 to 3, or a pharmaceutically acceptable salt or N-oxide thereof, wherein ~~X~~(a) Z is hydrogen; or (b) Z is fluoro.

~~7.~~5. A compound according to any one of claims 1 to ~~6~~4, or a pharmaceutically acceptable salt or N-oxide thereof,wherein ~~Z is hydrogen.~~

~~8. A compound according to any one of claims 1 to 6, or a pharmaceutically acceptable salt or N-oxide thereof, wherein Z is fluoro.~~

~~9. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (a) Ar is selected from phenyl, C_{1-6} monocyclic heteroaryl, C_{1-9} bicyclic hetereoaryl, bicyclic C_{7-14} fused cycloalkylaryl, bicyclic C_{6-14} fused heterocycloalkylaryl, bicyclic C_{2-14} fused cycloalkylheteroaryl, and bicyclic C_{2-14} fused heterocycloalkylheteroaryl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~10. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (b) Ar is selected from phenyl, C_{1-6} monocyclic heteroaryl, C_{1-9} bicyclic hetereoaryl, and bicyclic C_{2-14} fused heterocycloalkylheteroaryl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~11. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (c) Ar is phenyl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~12. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (d) Ar is C_{1-6} monocyclic heteroaryl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~13. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (e) Ar is C_{1-9} bicyclic hetereoaryl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~14. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (f) Ar is bicyclic C_{2-14} fused heterocycloalkylheteroaryl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~15. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (g) Ar is bicyclic C_{2-14} fused cycloalkylheteroaryl, which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~16. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (h) Ar is selected from phenyl, a thiazole ring, a pyridine ring, a pyridimine ring, a pyrazine ring, a benzo[d]oxazole ring, an oxazolo[4,5-c]pyridine ring, an oxazolo[5,4-b]pyridine ring, an oxazolo[5,4-d]pyrimidine ring, a 7H-pyrrolo[2,3-d]pyrimidine ring, a 2,3-dihydrothieno[2,3-b]pyridine ring, a S-oxo-2,3-dihydrothieno[2,3-b]pyridine ring, a S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridine ring, a quinazoline ring, a quinoline ring, and a quinoxaline ring; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~;

~~17. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (i) Ar is selected from phenyl, a thiazole ring, a pyridine ring, a pyridimine ring, a pyrazine ring, a benzo[d]oxazole ring, an oxazolo[4,5-c]pyridine ring, an oxazolo[5,4-b]pyridine ring, an oxazolo[5,4-d]pyrimidine ring, a 7H-pyrrolo[2,3-d]pyrimidine ring, a 2,3-dihydrothieno[2,3-b]pyridine ring, a S-oxo-2,3-dihydrothieno[2,3-b]pyridine ring, a S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridine ring, a quinazoline ring, a quinoline ring, a pyrrolo[2,3-b]pyridine ring, an

oxazolo[4,5-b]pyridine ring, a 3-oxo-3,4-dihydropyrazine ring, and a quinoxaline ring; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups.;

~~18. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (j) Ar is selected from phenyl, a thiazole ring, a pyridine ring, a pyridimine ring, a pyrazine ring, a benzo[d]oxazole ring, an oxazolo[4,5-c]pyridine ring, an oxazolo[5,4-b]pyridine ring, an oxazolo[5,4-d]pyrimidine ring, a 7H-pyrrolo[2,3-d]pyrimidine ring, a 2,3-dihydrothieno[2,3-b]pyridine ring, a S-oxo-2,3-dihydrothieno[2,3-b]pyridine ring, a S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridine ring, a quinazoline ring, a quinoline ring, a pyrrolo[2,3-b]pyridine ring, an oxazolo[4,5-b]pyridine ring, a 3-oxo-3,4-dihydropyrazine ring, a quinoxaline ring, a oxazolo[5,4-d]pyrimidinering, a thieno[3,2-b]pyridinering, a thieno[2,3-c]pyridinering, a thiophenering, a thiazolo[5,4-d]pyrimidinering, a thieno[2,3-b]pyridinering, a 2,3-dihydrofuro[2,3-b]pyridinering, a 6,7-dihydro-5H-cyclopenta[b]pyridinering, a furo[3,2-c]pyridinering, a 2,3-dihydrothieno[3,2-c]pyridinering, a S-oxo-2,3-dihydrothieno[3,2-c]pyridinering, a S,S-dioxo-2,3-dihydrothieno[3,2-c]pyridinering, a thieno[3,2-c]pyridinering, and a 1H-pyrrolo[3,2-c]pyridinering; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups.;

~~19. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (k) Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups.;

~~20. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (l) Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, pyrrolo[2,3-b]pyridin-6-yl,

oxazolo[4,5-b]pyridin-2-yl, 3-oxo-3,4-dihydropyrazin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups~~.~~; or

~~21. A compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (m) Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3- yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, pyrrolo[2,3-b]pyridin-6-yl, oxazolo[4,5-b]pyridin-2-yl, 3-oxo-3,4-dihydropyrazin-2-yl, quinoxalin-2-yl, thiazol-4-yl, thiazol-5-yl, pyrimidin-5-yl, oxazolo[5,4-d]pyrimidin-2-yl, thieno[3,2-b]pyridin-5-yl, thieno[2,3-c]pyridin-5-yl, thiophen-2-yl, thiophen-3-yl, thiazolo[5,4-d]pyrimidin-5-yl, thieno[2,3-b]pyridin-6-yl, 2,3-dihydrofuro[2,3-b]pyridin-6-yl, 6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl, furo[3,2-c]pyridin-6-yl, 2,3-dihydrothieno[3,2-c]pyridin-6-yl, S-oxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, thieno[3,2-c]pyridin-6-yl, and 1H-pyrrolo[3,2-c]pyridin-6-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups.

6. A compound according to any one of claims 1 to ~~21~~5, or a pharmaceutically acceptable salt or N-oxide thereof, wherein

~~22.~~ (a) each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, C_{1-6} heteroaryl-C_{1-4}-alkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, $-NR^cC(=O)R^d$, and $-NR^cC(=O)OR^d$; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{1a} groups; wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, and C_{1-6} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{2a} groups~~.~~;

~~23. A compound according to any one of claims 1 to 21, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (b) each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$,

-S(=O)R^b, -S(=O)$_2R^b$, -S(=O)NR^eR^f, -NR^eR^f, -C(=O)R^b, -C(=O)OR^b, -C(=O)NR^eR^f, and -NR^cC(=O)R^d~~.~~;

~~24. A compound according to any one of claims 1 to 21, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (c) each R^1 is independently selected from C_{1-6} alkyl, C_{1-6} haloalkyl, -OR^a, -SR^a, -S(=O)R^b, -S(=O)$_2R^b$, and -NR^eR^f~~.~~; or

~~25. A compound according to any one of claims 1 to 21, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (d) each R^1 is independently selected from fluoro, bromo, chloro, cyano, hydroxyl, methyl, trifluoromethyl, methoxy, isopropylamino, dimethylamino, methylthio, methylsulfinyl, and methylsulfonyl.

7. A compound according to any one of claims 1 to 6, or a pharmaceutically acceptable salt or N-oxide thereof, wherein ~~A compound according to any one of claims 1 to 24, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~

~~26.~~ (a) each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl~~.~~;

~~27. A compound according to any one of claims 1 to 24, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (b) each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, C_{2-7} heterocycloalkyl, phenyl, and C_{1-7} heteroaryl~~.~~;

~~28. A compound according to any one of claims 1 to 24, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (c) each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl~~.~~; or

~~29. A compound according to any one of claims 1 to 24, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (d) each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H and C_{1-6} alkyl.

~~30.~~ 8. A compound according to any one of claims 1 to ~~29~~7, or a pharmaceutically acceptable salt or N-oxide thereof, wherein each R^{1a} is independently selected from fluoro,

chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino; and

each R^{2a} is independently selected from fluoro, chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkynyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino.

34-9. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:

(a) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, C_{1-6} monocyclic heteroaryl, C_{1-9} bicyclic hetereoaryl, bicyclic C_{7-14} fused cycloalkylaryl, bicyclic C_{6-14} fused heterocycloalkylaryl, bicyclic C_{2-14} fused cycloalkylheteroaryl, and bicyclic C_{2-14} fused heterocycloalkylheteroaryl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, C_{1-6} heteroaryl-C_{1-4}-alkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, $-NR^cC(=O)R^d$, and $-NR^cC(=O)OR^d$; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{1a} groups; wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, and C_{1-6} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{2a} groups;

each R^{1a} is independently selected from fluoro, chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

each R^{2a} is independently selected from fluoro, chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkynyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^x groups; and

wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^y groups;

each R^x is independently selected from hydroxyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino; and

each R^y is independently selected from hydroxyl, halogen, cyano, nitro, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino.

~~32. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

~~(b)~~ X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, C_{1-6} monocyclic heteroaryl, C_{1-9} bicyclic hetereoaryl, bicyclic C_{7-14} fused cycloalkylaryl, bicyclic C_{6-14} fused heterocycloalkylaryl, bicyclic C_{2-14} fused cycloalkylheteroaryl, bicyclic C_{2-14} fused cycloalkylheteroaryl, and bicyclic C_{2-14} fused heterocycloalkylheteroaryl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, C_{1-6} heteroaryl-C_{1-4}-alkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, $-NR^cC(=O)R^d$, and $-NR^cC(=O)OR^d$; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{1a} groups; wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, and C_{1-6} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{2a} groups;

each R^{1a} is independently selected from fluoro, chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

each R^{2a} is independently selected from fluoro, chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkynyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^x groups; and wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^y groups;

each R^x is independently selected from hydroxyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino; and

each R^y is independently selected from hydroxyl, halogen, cyano, nitro, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino.

~~33. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(c) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, C_{1-6} monocyclic heteroaryl, C_{1-9} bicyclic hetereoaryl, and bicyclic C_{2-14} fused heterocycloalkylheteroaryl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, C_{1-6} heteroaryl-C_{1-4}-alkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, $-NR^cC(=O)R^d$, and $-NR^cC(=O)OR^d$; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{1a} groups; wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-6} heterocycloalkyl, C_{2-6} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-6} heteroaryl, and C_{1-6} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^{2a} groups;

each R^{1a} is independently selected from fluoro, chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

each R^{2a} is independently selected from fluoro, chloro, bromo, cyano, nitro, hydroxyl, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{2-4} alkynyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, C_{1-4} alkylthio, C_{1-4} alkylsulfinyl, C_{1-4} alkylsulfonyl, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl; wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, and C_{2-6} alkynyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^x groups; and wherein said C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl are each optionally substituted by 1, 2, 3, or 4 independently selected R^y groups;

each R^x is independently selected from hydroxyl, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino; and

each R^y is independently selected from hydroxyl, halogen, cyano, nitro, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, C_{1-4} haloalkoxy, amino, C_{1-4} alkylamino, and di-C_{1-4}-alkylamino.

~~34. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(d) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, C_{1-6} monocyclic heteroaryl, C_{1-9} bicyclic hetereoaryl, bicyclic C_{2-14} fused cycloalkylheteroaryl, and bicyclic C_{2-14} fused heterocycloalkylheteroaryl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, and $-NR^cC(=O)R^d$;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl.

~~35. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(e) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, C_{1-6} monocyclic heteroaryl, C_{1-9} bicyclic hetereoaryl, and bicyclic C_{2-14} fused heterocycloalkylheteroaryl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, and $-NR^cC(=O)R^d$;

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl-C_{1-4}-alkyl, C_{2-7} heterocycloalkyl, C_{2-7} heterocycloalkyl-C_{1-4}-alkyl, phenyl, phenyl-C_{1-4}-alkyl, C_{1-7} heteroaryl, and C_{1-7} heteroaryl-C_{1-4}-alkyl~~.~~;

~~36. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(f) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, a thiazole ring, a pyridine ring, a pyridimine ring, a pyrazine ring, a benzo[d]oxazole ring, an oxazolo[4,5-c]pyridine ring, an oxazolo[5,4-b]pyridine ring, an oxazolo[5,4-d]pyrimidine ring, a 7H-pyrrolo[2,3-d]pyrimidine ring, a 2,3-dihydrothieno[2,3-b]pyridine ring, a S-oxo-2,3-dihydrothieno[2,3-b]pyridine ring, a S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridine ring, a quinazoline ring, a quinoline ring, and a quinoxaline ring; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, and $-NR^cC(=O)R^d$; and

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, C_{2-7} heterocycloalkyl, phenyl, and C_{1-7} heteroaryl~~.~~;

~~37. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(g) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, a thiazole ring, a pyridine ring, a pyridimine ring, a pyrazine ring, a benzo[d]oxazole ring, an oxazolo[4,5-c]pyridine ring, an oxazolo[5,4-b]pyridine ring, an oxazolo[5,4-d]pyrimidine ring, a 7H-pyrrolo[2,3-d]pyrimidine ring, a 2,3-dihydrothieno[2,3-b]pyridine ring, a S-oxo-2,3-dihydrothieno[2,3-b]pyridine ring, a S,S-dioxo-2,3-

dihydrothieno[2,3-b]pyridine ring, a quinazoline ring, a quinoline ring, a pyrrolo[2,3-b]pyridine ring, an oxazolo[4,5-b]pyridine ring, a 3-oxo-3,4-dihydropyrazine ring, and a quinoxaline ring; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, and $-NR^cC(=O)R^d$; and

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, C_{2-7} heterocycloalkyl, phenyl, and C_{1-7} heteroaryl~~,~~;

~~38. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(h) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, a thiazole ring, a pyridine ring, a pyridimine ring, a pyrazine ring, a benzo[d]oxazole ring, an oxazolo[4,5-c]pyridine ring, an oxazolo[5,4-b]pyridine ring, an oxazolo[5,4-d]pyrimidine ring, a 7H-pyrrolo[2,3-d]pyrimidine ring, a 2,3-dihydrothieno[2,3-b]pyridine ring, a S-oxo-2,3-dihydrothieno[2,3-b]pyridine ring, a S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridine ring, a quinazoline ring, a quinoline ring, a pyrrolo[2,3-b]pyridine ring, an oxazolo[4,5-b]pyridine ring, a 3-oxo-3,4-dihydropyrazine ring, a quinoxaline ring, a oxazolo[5,4-d]pyrimidinering, a thieno[3,2-b]pyridinering, a thieno[2,3-c]pyridinering, a thiophenering, a thiazolo[5,4-d]pyrimidinering, a thieno[2,3-b]pyridinering, a 2,3-dihydrofuro[2,3-b]pyridinering, a 6,7-dihydro-5H-cyclopenta[b]pyridinering, a furo[3,2-c]pyridinering, a 2,3-dihydrothieno[3,2-c]pyridinering, a S-oxo-2,3-dihydrothieno[3,2-c]pyridinering, a S,S-dioxo-2,3-dihydrothieno[3,2-c]pyridinering, a thieno[3,2-c]pyridinering, and a 1H-pyrrolo[3,2-c]pyridinering; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, $-S(=O)NR^eR^f$, $-NR^eR^f$, $-C(=O)R^b$, $-C(=O)OR^b$, $-C(=O)NR^eR^f$, and $-NR^cC(=O)R^d$; and

each R^a, R^b, R^c, R^d, R^e, and R^f is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-7} cycloalkyl, C_{2-7} heterocycloalkyl, phenyl, and C_{1-7} heteroaryl~~,~~;

~~39. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(i) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, and $-NR^eR^f$; and

each R^a, R^b, R^e, and R^f is independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl~~.~~;

~~40. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(j) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, and $-NR^eR^f$; and

each R^a, R^b, R^e, and R^f is independently selected from H and C_{1-6} alkyl~~.~~;

~~41. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(k) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, pyrrolo[2,3-b]pyridin-6-yl, oxazolo[4,5-b]pyridin-2-yl, 3-oxo-3,4-dihydropyrazin-2-yl, quinolin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, and $-NR^eR^f$; and

each R^a, R^b, R^e, and R^f is independently selected from H and C_{1-6} alkyl~~.~~;

~~42. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(l) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, and $-NR^eR^f$; and

each R^a, R^b, R^e, and R^f is independently selected from H and methyl~~.~~;

~~43. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(m) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, pyrrolo[2,3-b]pyridin-6-yl, oxazolo[4,5-b]pyridin-2-yl, 3-oxo-3,4-dihydropyrazin-2-yl, quinolin-2-yl, quinoxalin-2-yl, thiazol-4-yl, thiazol-5-yl, pyrimidin-5-yl, oxazolo[5,4-d]pyrimidin-2-yl, thieno[3,2-b]pyridin-5-yl, thieno[2,3-c]pyridin-5-yl, thiophen-2-yl, thiophen-3-yl, thiazolo[5,4-d]pyrimidin-5-yl, thieno[2,3-b]pyridin-6-yl, 2,3-dihydrofuro[2,3-b]pyridin-6-yl, 6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl, furo[3,2-c]pyridin-6-yl, 2,3-dihydrothieno[3,2-c]pyridin-6-yl, S-oxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, thieno[3,2-c]pyridin-6-yl, and 1H-pyrrolo[3,2-c]pyridin-6-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, cyano, nitro, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, and $-NR^eR^f$; and

each R^a, R^b, R^e, and R^f is independently selected from H, C_{1-6} alkyl, and C_{1-6} haloalkyl~~.~~;

~~44. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(n) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, pyrrolo[2,3-b]pyridin-6-yl, oxazolo[4,5-b]pyridin-2-yl, 3-oxo-3,4-dihydropyrazin-2-yl, quinolin-2-yl, quinoxalin-2-yl, thiazol-4-yl, thiazol-5-yl, pyrimidin-5-yl, oxazolo[5,4-d]pyrimidin-2-yl, thieno[3,2-b]pyridin-5-yl, thieno[2,3-c]pyridin-5-yl, thiophen-2-yl, thiophen-3-yl, thiazolo[5,4-d]pyrimidin-5-yl, thieno[2,3-b]pyridin-6-yl, 2,3-dihydrofuro[2,3-b]pyridin-6-yl, 6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl, furo[3,2-c]pyridin-6-yl, 2,3-dihydrothieno[3,2-c]pyridin-6-yl, S-oxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, thieno[3,2-c]pyridin-6-yl, and 1H-pyrrolo[3,2-c]pyridin-6-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from halogen, C_{1-6} alkyl, C_{1-6} haloalkyl, $-OR^a$, $-SR^a$, $-S(=O)R^b$, $-S(=O)_2R^b$, and $-NR^eR^f$; and

each R^a, R^b, R^e, and R^f is independently selected from H and C_{1-6} alkyl~~.~~;

~~45. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(o) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from fluoro, bromo, chloro, cyano, hydroxyl, methyl, trifluoromethyl, methoxy, isopropylamino, dimethylamino, methylthio, methylsulfinyl, and methylsulfonyl~~.~~;

~~46. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(p) X is cyano or fluoro;

Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, pyrrolo[2,3-b]pyridin-6-yl, oxazolo[4,5-b]pyridin-2-yl, 3-oxo-3,4-dihydropyrazin-2-yl, and quinoxalin-2-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from fluoro, bromo, chloro, cyano, hydroxyl, methyl, trifluoromethyl, methoxy, isopropylamino, dimethylamino, methylthio, methylsulfinyl, and methylsulfonyl~~.~~; or

~~47. A compound according to claim 1, or a pharmaceutically acceptable salt or N-oxide thereof, wherein:~~

(q) X is cyano or fluoro;

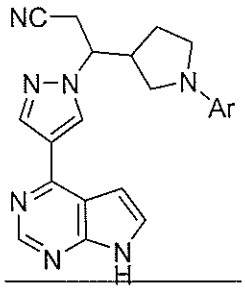
Y is CH or N;

Z is hydrogen or fluoro;

Ar is selected from phenyl, thiazol-2-yl, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridimin-2-yl, pyrimidin-4-yl, pyrazin-2-yl, benzo[d]oxazol-2-yl, oxazolo[4,5-c]pyridin-2-yl, oxazolo[5,4-b]pyridin-2-yl, oxazolo[5,4-d]pyrimidin-2-yl, 7H-pyrrolo[2,3-d]pyrimidin-2-yl, 2,3-dihydrothieno[2,3-b]pyridin-6-yl, S-oxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[2,3-b]pyridin-6-yl, quinazolin-2-yl, quinolin-2-yl, pyrrolo[2,3-b]pyridin-6-yl, oxazolo[4,5-b]pyridin-2-yl, 3-oxo-3,4-dihydropyrazin-2-yl, quinoxalin-2-yl, thiazol-4-yl, thiazol-5-yl, pyrimidin-5-yl, oxazolo[5,4-d]pyrimidin-2-yl, thieno[3,2-b]pyridin-5-yl, thieno[2,3-c]pyridin-5-yl, thiophen-2-yl, thiophen-3-yl, thiazolo[5,4-d]pyrimidin-5-yl, thieno[2,3-b]pyridin-6-yl, 2,3-dihydrofuro[2,3-b]pyridin-6-yl, 6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl, furo[3,2-c]pyridin-6-yl, 2,3-dihydrothieno[3,2-c]pyridin-6-yl, S-oxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, S,S-dioxo-2,3-dihydrothieno[3,2-c]pyridin-6-yl, thieno[3,2-c]pyridin-6-yl, and 1H-pyrrolo[3,2-c]pyridin-6-yl; each of which is optionally substituted with 1, 2, 3, 4, 5, or 6 independently selected R^1 groups;

each R^1 is independently selected from fluoro, bromo, chloro, cyano, hydroxyl, methyl, trifluoromethyl, methoxy, isopropylamino, dimethylamino, methylthio, methylsulfinyl, and methylsulfonyl.

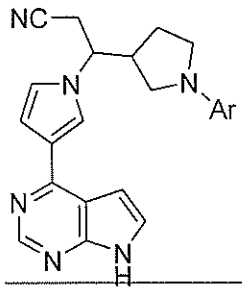
~~48.~~ 10. A compound according to any one of claims 1 and 5-9-~~47~~, having ~~formula Ia~~:



~~Ia~~

~~or (a pharmaceutically acceptable salt or N-oxide thereof.~~

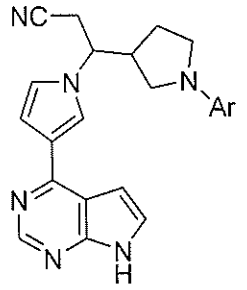
~~49. A compound according to any one of claims 1 and 9-47, having~~) formula ~~Ib~~Ia:



Ia

or a pharmaceutically acceptable salt or N-oxide thereof;

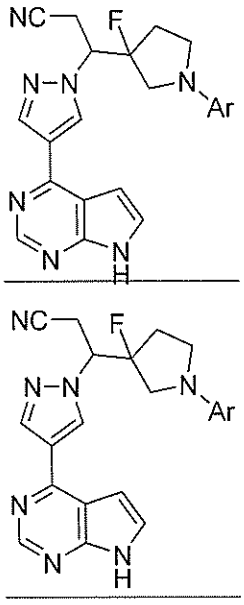
(b) formula Ib:



Ib

or a pharmaceutically acceptable salt or N-oxide thereof~~.~~;

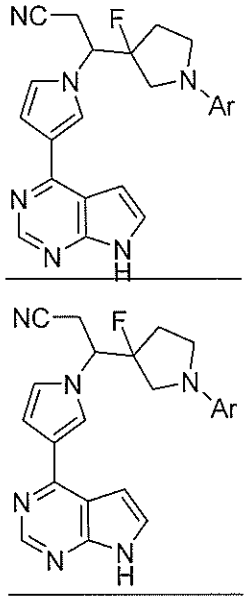
~~50. A compound according to any one of claims 1 and 9-47, having~~ (c) formula Ic:



Ic

or a pharmaceutically acceptable salt or N-oxide thereof.;

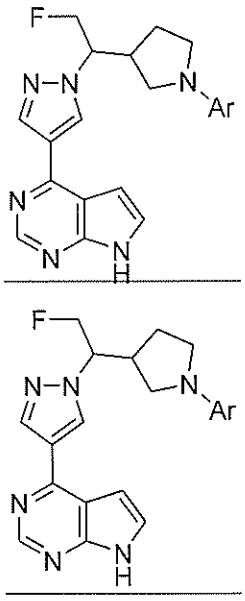
~~51. A compound according to any one of claims 1 and 9-47, having~~ (d) formula Id:



Id

or a pharmaceutically acceptable salt or N-oxide thereof.;

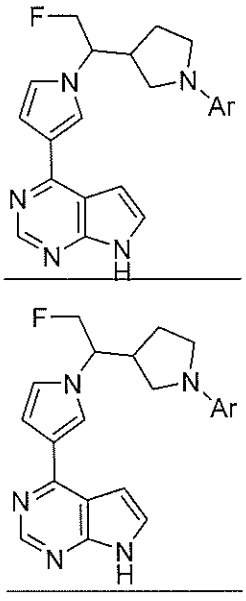
~~52. A compound according to any one of claims 1 and 9-47, having~~ (e) formula Ie:



Ie

or a pharmaceutically acceptable salt or N-oxide thereof~~.~~; or

~~53. A compound according to any one of claims 1 and 9-47, having~~ (f) formula If:



If

or a pharmaceutically acceptable salt or N-oxide thereof.

11. A compound according to any one of claims 1 to ~~53~~10, or a pharmaceutically acceptable salt or N-oxide thereof, wherein

~~54.~~ (a) said Ar is optionally substituted with 1, 2, 3, or 4 independently selected R^1 groups~~.~~;

~~55. A compound according to any one of claims 1 to 53, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (b) said Ar is optionally substituted with 1, 2, or 3 independently selected R^1 groups~~.~~; or

~~56. A compound according to any one of claims 1 to 53, or a pharmaceutically acceptable salt or N-oxide thereof, wherein~~ (c) said Ar is optionally substituted with 1 or 2 independently selected R^1 groups.

12. A compound according to claim 1, wherein

~~57.~~ (a) said compound is selected from:

3-[1-(6-chloropyrazin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(6-chloropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(2-chloropyrimidin-4-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(4-chloropyrimidin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(4-bromo-1,3-thiazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[4-(dimethylamino)pyrimidin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[4-(isopropylamino)pyrimidin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(5-chloro-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(1-[1,3]oxazolo[4,5-c]pyridin-2-ylpyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(1-[1,3]oxazolo[4,5-b]pyridin-2-ylpyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(1-[1,3]oxazolo[5,4-b]pyridin-2-ylpyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(6-methyl[1,3]oxazolo[5,4-b]pyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-

pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(6-fluoro[1,3]oxazolo[5,4-b]pyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-3-[1-(7H-pyrrolo[2,3-d]pyrimidin-2-yl)pyrrolidin-3-yl]propanenitrile;

3-[1-(7-methyl-7H-pyrrolo[2,3-d]pyrimidin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(1-[1,3]oxazolo[5,4-d]pyrimidin-2-ylpyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(5-fluoro-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(4-fluoro-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(7-fluoro-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(5,7-difluoro-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[2-(methylthio)pyrimidin-4-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[2-(methylsulfinyl)pyrimidin-4-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[2-(methylsulfonyl)pyrimidin-4-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[6-(methylsulfonyl)pyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[2-(methylsulfonyl)pyridin-4-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(1-oxido-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(1,1-dioxido-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(3-fluoro-1-[1,3]oxazolo[5,4-b]pyridin-2-ylpyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(1-[1,3]oxazolo[5,4-b]pyridin-2-ylpyrrolidin-3-yl)-3-[3-(7H-pyrrolo[2,3-

d]pyrimidin-4-yl)-1H-pyrrol-1-yl]propanenitrile;

3-[1-(1,1-dioxido-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]propanenitrile;

3-[1-(1-oxido-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]propanenitrile;

3-[1-(6-chloro-4-methyl-3-oxo-3,4-dihydropyrazin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(4-methyl-3-oxo-3,4-dihydropyrazin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-chloro-2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)isonicotinonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)pyridine-3,4-dicarbonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-(methylthio)benzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-(methylsulfonyl)benzonitrile;

3-[1-(8-chloroquinolin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(3-hydroxyquinoxalin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(8-chloroquinazolin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(6-chloro-1-oxidopyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(8-fluoroquinazolin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(5-bromo-1,3-thiazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

2-chloro-6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)benzonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)phthalonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-(trifluoromethyl)nicotinonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-

yl]ethyl}pyrrolidin-1-yl)pyrazine-2-carbonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)benzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-methylbenzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol- 1-yl]ethyl}pyrrolidin-1-yl)-6-fluorobenzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol- 1-yl]ethyl}pyrrolidin-1-yl)-6-methoxybenzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol- 1-yl]ethyl}pyrrolidin-1-yl)-6-(trifluoromethyl)benzonitrile;

2-bromo-6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)- 1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)benzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-3-fluorobenzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)isophthalonitrile;

6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-2,3-difluorobenzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-3,5,6-trifluorobenzonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)nicotinonitrile;

3-chloro-5-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)isonicotinonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-2,5,6-trifluoroisonicotinonitrile;

3-{1-[3-fluoro-4-(trifluoromethyl)pyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-3-[1-(3,5,6-trifluoropyridin-2-yl)pyrrolidin-3-yl]propanenitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)pyridine-2-carbonitrile;

2-chloro-6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)nicotinonitrile;

2-(3-{2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin- 4-yl)-1H-pyrazol-1-

yl]ethyl}pyrrolidin-1-yl)[1,3]oxazolo[5, 4-b]pyridine;

2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-fluoroethyl)pyrrolidin-1-yl)oxazolo[5,4-b]pyridine; and

3-[1-(1H-pyrrolo[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile,

or a pharmaceutically acceptable salt or N-oxide thereof~~.~~; or

~~58. A compound according to claim 1, wherein~~ (b) said compound is selected from:

5-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)thieno[2,3-c]pyridine-4-carbonitrile;

5-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)thieno[3,2-b]pyridine-6-carbonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-hydroxythiophene-3-carbonitrile;

4-bromo-2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)thiophene-3-carbonitrile;

4-chloro-2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)thiophene-3-carbonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)thiophene-3,4-dicarbonitrile;

2-(3-{(1R)-2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)thiophene-3,4-dicarbonitrile;

2-(3-{2-cyano-1-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]ethyl}pyrrolidin-1-yl)thiophene-3,4-dicarbonitrile;

4-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-1,3-thiazole-5-carbonitrile;

5-(3-{2-fluoro-1-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]ethyl}pyrrolidin-1-yl)-1,3-thiazole-4-carbonitrile;

4-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

4-(1-{2-fluoro-1-[1-(5-fluoro-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]ethyl}-1H-pyrazol-4-yl)-7H-pyrrolo[2,3-d]pyrimidine;

4-(1-{2-fluoro-1-[1-(5-fluoro-1,1-dioxido-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]ethyl}-1H-pyrazol-4-yl)-7H-pyrrolo[2,3-d]pyrimidine;

3-[1-(5-fluoro-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[4-(7H-

pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(6-bromo-3-fluoropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(5,6-difluoropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[6-chloro-3-fluoro-5-(hydroxymethyl)pyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-(1-(5-amino-6-chloro-3-fluoropyridin-2-yl)pyrrolidin-3-yl)propanenitrile;

N-(2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-6-chloro-5-fluoropyridin-3-yl)formamide;

3-{1-[6-(ethylsulfonyl)-3-fluoropyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(6-chloro-3-fluoropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-5-fluoro-4-(methoxymethyl)nicotinonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-(methoxymethyl)nicotinonitrile;

4-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-6-methoxypyrimidine-5-carbonitrile;

3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-(1-(6-(ethylsulfonyl)-3-fluoropyridin-2-yl)pyrrolidin-3-yl)propanenitrile;

2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-4-methylnicotinonitrile;

3-{1-[3,5-difluoro-4-(methoxymethyl)pyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-3-[1-[1,3]thiazolo[5,4-d]pyrimidin-5-ylpyrrolidin-3-yl]propanenitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-(difluoromethyl)nicotinonitrile;

3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-(1-(5-fluoro-2-methoxypyrimidin-4-yl)pyrrolidin-3-yl)propanenitrile;

3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-(1-(3-amino-6-chloropyridin-2-yl)pyrrolidin-3-yl)propanenitrile;

4-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-

1-yl)pyridazine-3-carbonitrile;

6-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-5-fluoronicotinonitrile;

2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-5-fluoronicotinonitrile;

2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-5-methylnicotinonitrile;

4-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-6-(difluoromethyl)pyrimidine-5-carbonitrile;

2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-6-(difluoromethyl)benzonitrile;

2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-6-(methoxymethyl)benzonitrile;

4-(3-(1-(3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)pyridazine-3-carbonitrile;

2-(3-(1-(3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)nicotinonitrile;

3-(3-(1-(3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)pyrazine-2-carbonitrile;

4-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-fluoroethyl)pyrrolidin-1-yl)pyridazine-3-carbonitrile;

3-(3-{2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)pyridine-2-carbonitrile;

2-(3-{2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)nicotinonitrile;

4-(1-{1-[1-(1,1-dioxido-2,3-dihydrothieno[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-2-fluoroethyl}-1H-pyrazol-4-yl)-7H-pyrrolo[2,3-d]pyrimidine;

2-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-fluoroethyl)pyrrolidin-1-yl)pyridine-3,4-dicarbonitrile;

3-(3-{2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)phthalonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-iodonicotinonitrile;

2-chloro-4-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)nicotinonitrile;

4-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-

yl]ethyl}pyrrolidin-1-yl)pyridine-2,3-dicarbonitrile;

3-[1-(2,6-dichloropyridin-3-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

5-(3-{2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-1,3-thiazole-4-carbonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-(methylthio)nicotinonitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-(methylsulfonyl)nicotinonitrile;

3-{1-[3,5-difluoro-6-(methylthio)pyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[3,5-difluoro-6-(methylsulfonyl)pyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(1-{3,5-difluoro-6-[(2,2,2-trifluoroethyl)-sulfonyl]pyridin-2-yl}pyrrolidin-3-yl)-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

4-[1-(1-{1-[3,5-difluoro-6-(methylsulfonyl)pyridin-2-yl]pyrrolidin-3-yl}-2-fluoroethyl)-1H-pyrazol-4-yl]-7H-pyrrolo-[2,3-d]pyrimidine;

3-{1-[3-fluoro-6-(methylsulfonyl)pyridin-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[2,5-difluoro-6-(methylsulfonyl)pyridin-3-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-4-(1-fluoroethyl)nicotinonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-(difluoromethyl)pyrazine-2-carbonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-(2,2-difluoroethyl)pyrazine-2-carbonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-(hydroxymethyl)pyrazine-2-carbonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-(methoxymethyl)pyrazine-2-carbonitrile;

6-bromo-3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)pyrazine-2-carbonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-ethynylpyrazine-2-carbonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-

yl]ethyl}pyrrolidin-1-yl)-6-ethylpyrazine-2-carbonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-methylpyrazine-2-carbonitrile;

3-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-6-methylpyrazine-2-carbonitrile;

3-fluoro-5-(3-{2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)pyridine-2-carbonitrile;

3-{1-[2-(ethylsulfonyl)pyridin-4-yl]pyrrolidin-3-yl}-3-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]propanenitrile;

5-(3-{2-cyano-1-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]ethyl}pyrrolidin-1-yl)-1,3-thiazole-4-carbonitrile;

3-[1-(2-mercaptopyrimidin-4-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

N-[4-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)pyrimidin-2-yl]-N,N-dimethylsulfonamide;

4-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-N-methylpyridine-2-carboxamide;

4-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-N,N-dimethylpyridine-2-carboxamide;

4-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-N-phenylpyridine-2-carboxamide;

3-[1-(2,3-dihydrofuro[2,3-b]pyridin-6-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]-3-(1-thieno[2,3-b]pyridin-6-ylpyrrolidin-3-yl)propanenitrile;

3-[1-(7,7-difluoro-6,7-dihydro-5H-cyclopenta[b]pyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(7-fluoro-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]propanenitrile;

3-[1-(7-bromo-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

2-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-1,3-benzoxazole-7-carbonitrile;

3-[1-(7-hydroxy-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-[1-(7-methoxy-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-

d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-(1-(7-ethoxybenzo[d]oxazol-2-yl)pyrrolidin-3-yl)propanenitrile;

3-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-3-(1-(7-(difluoromethoxy)benzo[d]oxazol-2-yl)pyrrolidin-3-yl)propanenitrile;

3-[1-(4-hydroxy-1,3-benzoxazol-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

3-{1-[7-(hydroxymethyl)-1,3-benzoxazol-2-yl]pyrrolidin-3-yl}-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile;

6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)furo[3,2-c]pyridine-7-carbonitrile;

6-(3-{2-cyano-1-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]ethyl}pyrrolidin-1-yl)furo[3,2-c]pyridine-7-carbonitrile;

6-(3-{2-cyano-1-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]ethyl}pyrrolidin-1-yl)-2,3-dihydrothieno[3,2-c]pyridine-7-carbonitrile 1,1-dioxide;

6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-2,3-dihydrothieno[3,2-c]pyridine-7-carbonitrile 1,1-dioxide;

6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-2,3-dihydrothieno[3,2-c]pyridine-7-carbonitrile;

6-(3-{2-cyano-1-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]ethyl}pyrrolidin-1-yl)-2,3-dihydrothieno[3,2-c]pyridine-7-carbonitrile;

6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)thieno[3,2-c]pyridine-7-carbonitrile;

6-(3-{2-cyano-1-[3-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrrol-1-yl]ethyl}pyrrolidin-1-yl)thieno[3,2-c]pyridine-7-carbonitrile;

6-(3-{2-cyano-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-1H-pyrrolo[3,2-c]pyridine-7-carbonitrile; and

6-((3S)-3-{2-fluoro-1-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]ethyl}pyrrolidin-1-yl)-2,3-dihydrothieno[3,2-c]pyridine-7-carbonitrile 1,1-dioxide,

or a pharmaceutically acceptable salt or N-oxide thereof.

59-13. The compound according to claim 1, wherein the compound is 6-(3-(1-(4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl)-2-cyanoethyl)pyrrolidin-1-yl)-2-chloro-5-fluoronicotinonitrile, or a pharmaceutically acceptable salt or N-oxide thereof.

~~60.~~14. A salt selected from a trifluoroacetic acid salt and a phosphoric acid salt of the compound according to any one of claims ~~57-59~~12-13.

15. A compound according to claim 1, wherein the compound is 3-[1-(6-chloropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt or N-oxide thereof.

16. A compound according to claim 1, wherein the compound is (R)-3-[1-(6-chloropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt or N-oxide thereof.

17. A compound according to claim 1, wherein the compound is (S)-3-[1-(6-chloropyridin-2-yl)pyrrolidin-3-yl]-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-1H-pyrazol-1-yl]propanenitrile, or a pharmaceutically acceptable salt or N-oxide thereof.

~~61.~~18. A pharmaceutical composition, comprising a compound according to any one of claims 1 to ~~60~~17, or a pharmaceutically acceptable salt or N-oxide thereof, and a pharmaceutically acceptable carrier.

~~62.~~19. A method of modulating an activity of JAK1 *ex vivo* comprising contacting JAK1 with a compound according to any one of claims 1 to ~~60~~17, or a pharmaceutically acceptable salt or N-oxide thereof.

~~63.~~20. A method according to claim ~~62~~19, wherein said compound, or pharmaceutically acceptable salt or N-oxide thereof, is selective for JAK1 over JAK2.

~~64.~~21. ~~A method of~~ A compound of any one of claims 1 to 17, or a pharmaceutically acceptable salt or N-oxide thereof for use in treating an autoimmune disease, a cancer, a myeloproliferative disorder, an inflammatory disease, or organ transplant rejection ~~in a patient in need thereof, comprising administering to said patient a therapeutically effective amount of a compound of any one of claims 1 to 60, or a pharmaceutically acceptable salt or N-oxide thereof~~.

~~65.~~22. A ~~method~~compound, salt or N-oxide for use according to claim ~~64~~21, wherein said autoimmune disease is a skin disorder, multiple sclerosis, rheumatoid arthritis, psoriatic arthritis, juvenile arthritis, type I diabetes, lupus, inflammatory bowel disease, Crohn's

disease, myasthenia gravis, immunoglobulin nephropathies, myocarditis, or autoimmune thyroid disorder.

66. 23. A methodcompound, salt or N-oxide for use according to claim 6421, wherein said autoimmune disease is rheumatoid arthritis.

67. A method according to claim 64, wherein said autoimmune diseases is a skin disorder.

68. A method according to claim 67, wherein and said skin disorder is atopic dermatitis, psoriasis, skin sensitization, skin irritation, skin rash, contact dermatitis or allergic contact sensitization.

24. A methodcompound, salt or N-oxide for use according to claim 6421, wherein said cancer is

69. (a) a solid tumor.;

70. A method according to claim 64, wherein said cancer is (b) prostate cancer, renal cancer, hepatic cancer, breast cancer, lung cancer, thyroid cancer, Kaposi's sarcoma, Castleman's disease or pancreatic cancer.; or

71. A method according to claim 64, wherein said cancer is (c) lymphoma, leukemia, or multiple myeloma.

72. 25. A methodcompound, salt or N-oxide for use according to claim 6421, wherein said myeloproliferative disorder (MPD) is polycythemia vera (PV), essential thrombocythemia (ET), myeloid metaplasia with myelofibrosis (MMM), primary myelofibrosis (PMF), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), hypereosinophilic syndrome (HES), idiopathic myelofibrosis (IMF), or systemic mast cell disease (SMCD).

26. A method A compound, salt or N-oxide for use according to claim 6421, wherein said myeloproliferative disorder is

73. (a) myelofibrosis.; or

74. A method according to claim 64, wherein said myeloproliferative disorder is (b) primary myelofibrosis (PMF).

~~75.~~27. A compound according to any one of claims 1 to ~~60~~17, or a pharmaceutically acceptable salt or N-oxide thereof, for use in a method of modulating a JAK1.

~~76. A compound according to any one of claims 1 to 60, or a pharmaceutically acceptable salt or N-oxide thereof, for use in a method of treating an autoimmune disease, a cancer, a myeloproliferative disorder, an inflammatory disease, or organ transplant rejection.~~

~~77.~~28. Use of a compound according to any one of claims 1 to ~~60~~17, or a pharmaceutically acceptable salt or N-oxide thereof, for the preparation of a medicament for use in ~~a method of modulating a JAK1.~~

~~78. Use of a compound according to any one of claims 1 to 60, or a pharmaceutically acceptable salt or N-oxide thereof, for preparation of a medicament for use in a method of~~(a) a method of modulating a JAK1; or

(b) treating an autoimmune disease, a cancer, a myeloproliferative disorder, an inflammatory disease, or organ transplant rejection.