PYRAZOLE AMINOPYRIMIDINE DERIVATIVES AS LRRK2 MODULATORS

FIELD OF THE INVENTION

This invention pertains to compounds that modulate the function of LRRK2 and are useful for treatment of LRRK2-mediated diseases and conditions such as Parkinson's disease.

BACKGROUND OF THE INVENTION

Neurodegenerative diseases such as Parkinson's disease, Lewy body dementia and Huntington's disease affect millions of individuals. Parkinson's disease is a chronic, progressive motor system disorder that afflicts approximately one out of every 1000 people, with hereditary Parkinson's disease accounting for 5-10% of all of patients. Parkinson's disease is caused by progressive loss of mid-brain dopamine neurons, leaving patients with impaired ability to direct and control their movements. The primary Parkinson's disease symptoms are trembling, rigidity, slowness of movement, and impaired balance. Many Parkinson's disease patients also experience other symptoms such as emotional changes, memory loss, speech problems, and sleeping disorders.

The gene encoding the leucine-rich repeat kinase 2 protein (LRRK2) has been identified in association with hereditary Parkinson's disease (Paisan-Ruiz et al., *Neuron*, Vol. 44(4), 2004, pp 595-600; Zimprich et al., *Neuron*, Vol. 44(4), 2004, 601-607). *In-vitro* studies show that Parkinson's disease -associated mutation leads to increased LRRK2 kinase activity and decreased rate of GTP hydrolysis compared to wild-type (Guo et al., *Experimental Cell Research,* Vol. 313(16), 2007, pp. 3658-3670. Anti-LRRK2 antibodies have been used to label brainstem Lewy bodies associated with Parkinson's disease and cortical antibodies associated with Lewis bodydementia suggesting that LRRK2 may play an important role in Lewie body formation and pathogenesis associated with these diseases (Zhou et al., *Molecular Degeneration*, 2006, 1:17 doi:10.1186/1750-1326-1-17). LRRK2 has also been identified as a gene potentially associated with increased susceptibility to Crohn's disease and susceptibility to leprosy (Zhang et al., *New England J. Med.* Vol. 361 (2009) pp.2609-2618.

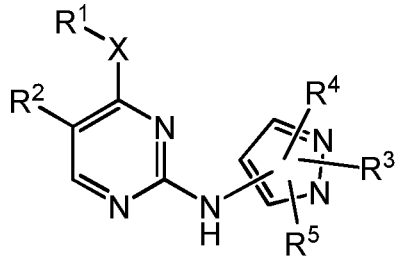
LRRK2 has also been associated with the transition of mild cognitive impairment to Alzheimer's disease (WO2007/149789); L-Dopa induced dyskinesia (Hurley et al., *Eur. J. Neurosci.,* Vol. 26, 2007, pp. 171-177; CNS disorders associated with neuronal progenitor differentiation (Milosevic et al., *Neurodegen.*, Vol. 4, 2009, p. 25); cancers such as kidney, breast, prostate, blood and lung cancers and acute myelogenous leukemia (WO2011/038572); papillary renal and thyroid carcinomas (Looyenga et al., www.pnas.org/cgi/doi/10.1073/pnas.1012500108); multiple myeloma (Chapman et al., *Nature* Vol. 471, 2011, pp. 467-472); amyotrophic lateral sclerosis (Shtilbans et al., *Amyotrophic*

Lateral Sclerosis "Early Online 2011, pp. 1-7); rheumatoid arthritis (Nakamura et al., *DNA Res.* Vol. 13(4), 2006, pp. 169-183); and ankylosing spondylytis (Danoy et al., *PLoS Genetics*, Vol. 6(12), 2010, e1001195, pp. 1-5).

Accordingly, compounds and compositions effective at modulating LRRK2 activity may provide a treatment for neurodegenerative diseases such as Parkinson's disease and Lewie body dementia, for CNS disorders such as Alzheimer's disease and L-Dopa induced dyskinesia, for cancers such as kidney, breast, prostate, blood, papillary and lung cancers, acute myelogenous leukemia and multiple myeloma, and for inflammatory diseases such as leprosy, Crohn's disease, amyotrophic lateral sclerosis, rheumatoid arthritis, and ankylosing spondylytis. Particularly, there is a need for compounds with LRRK2 affinity that are selective for LRRK2 over other kinases, such as JAK2, which can provide effective drugs for treatment of neurodegenerative disorders such as PD.

SUMMARY OF THE INVENTION

The invention provides compounds of the formula I:



I

or pharmaceutically acceptable salts thereof,

wherein:

X is: $-NR^a-$; or -O- wherein R^a is hydrogen or C_{1-6}alkyl;

R^1 is: C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with C_{1-6}alkyl; heterocyclyl optionally substituted one or more times with R^7; or heterocyclyl-C_{1-6}alkyl optionally substituted one or more times with R^7;

or X and R^1 together form C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6;

or R^1 and R^a together with the atoms to which they are attached may form a three- to six-membered heterocyclic ring optionally substituted one or more times with R^7;

R^2 is: C_{1-6}alkyl; halo; C_{1-6}alkoxy; cyano; C_{2-6}alkynyl; C_{2-6}alkenyl; halo-C_{1-6}alkyl; halo-C_{1-6}alkoxy; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6;

-OR^b wherein R^b is C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted one or more times with R^6, or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl optionally substituted one or more times with R^7;

R^3 is: hydrogen; C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano-C_{1-6}alkyl; C_{1-6}alkylsulfonyl; C_{1-6}alkylsulfonylC_{1-6}alkyl; amino-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-sulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; heterocyclyl optionally substituted one or more times with R^7; heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7; aryl optionally substituted one or more times with R^8; aryl-C_{1-6}alkyl wherein the aryl portion is optionally substituted one or more times with R^8; heteroaryl optionally substituted one or more times with R^8; heteroaryl-C_{1-6}alkyl wherein the heteroaryl portion is optionally substituted one or more times with R^8;or -Y-C(O)-R^d;

Y is C_{2-6}alkylene or a bond;

R^d is C_{1-6}alkyl, C_{1-6}alkoxy, amino, C_{1-6}alkyl-amino, di-C_{1-6}alkyl-amino, halo-C_{1-6}alkyl-amino, di-halo-C_{1-6}alkyl-amino, halo-C_{1-6}alkyl, hydroxy-C_{1-6}alkyl, hydroxy, C_{1-6}alkoxy-C_{1-6}alkyl, cyano-C_{1-6}alkyl, C_{1-6}alkylsulfonylC_{1-6}alkyl, amino-C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted one or more times with R^6, C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6,–heterocyclyl optionally substituted one or more times with R^7, or heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7;

R^4 is: hydrogen; C_{1-6}alkyl; halo; cyano; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; C_{1-6}alkoxy; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; or -Y-C(O)-R^d;

R^5 is: hydrogen; or C_{1-6}alkyl;

each R^6 is independently: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy; oxo; cyano; halo; or Y-C(O)-R^d;

each R^7 is independently: C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; oxo; C_{1-6}alkoxy; C_{1-6}alkylsulfonyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; -Y-C(O)-R^d; heterocyclyl; heterocyclyl-C_{1-6}alkyl; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl; or C_{3-6}cycloalkylsulfonyl; and

each R^8 is independently: oxo; C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; C_{1-6}alkyl-sulfonyl; C_{1-6}alkoxy; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; hetoeryclyl; heterocyclyl-C_{1-6}alkyl; -Y-C(O)-R^d; C_{3-6}cycloalkyl, C_{3-6}cycloalkyl-C_{1-6}alkyl, or C_{3-6}cycloalkyl-sulfonyl.

The invention also provides pharmaceutical compositions comprising the compounds, methods of using the compounds, and methods of preparing the compounds.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

Unless otherwise stated, the following terms used in this Application, including the specification and claims, have the definitions given below. It must be noted that, as used in the specification and the appended claims, the singular forms "a", "an," and "the" include plural referents unless the context clearly dictates otherwise.

"Alkyl" means the monovalent linear or branched saturated hydrocarbon moiety, consisting solely of carbon and hydrogen atoms, having from one to twelve carbon atoms. "Lower alkyl" refers to an alkyl group of one to six carbon atoms, i.e. C_1-C_6alkyl. Examples of alkyl groups include, but are not limited to, methyl, ethyl, propyl, isopropyl, isobutyl, sec-butyl, tert-butyl, pentyl, n-hexyl, octyl, dodecyl, and the like.

"Alkenyl" means a linear monovalent hydrocarbon radical of two to six carbon atoms or a branched monovalent hydrocarbon radical of three to six carbon atoms, containing at least one double bond, *e.g.*, ethenyl, propenyl, and the like.

"Alkynyl" means a linear monovalent hydrocarbon radical of two to six carbon atoms or a branched monovalent hydrocarbon radical of three to six carbon atoms, containing at least one triple bond, *e.g.*, ethynyl, propynyl, and the like.

"Alkylene" means a linear saturated divalent hydrocarbon radical of one to six carbon atoms or a branched saturated divalent hydrocarbon radical of three to six carbon atoms, e.g., methylene, ethylene, 2,2-dimethylethylene, propylene, 2-methylpropylene, butylene, pentylene, and the like.

"Alkoxy" and "alkyloxy", which may be used interchangeably, mean a moiety of the formula –OR, wherein R is an alkyl moiety as defined herein. Examples of alkoxy moieties include, but are not limited to, methoxy, ethoxy, isopropoxy, and the like.

"Alkoxyalkyl" means a moiety of the formula R^a–O–R^b–, where R^a is alkyl and R^b is alkylene as defined herein. Exemplary alkoxyalkyl groups include, by way of example, 2-methoxyethyl, 3-methoxypropyl, 1-methyl-2-methoxyethyl, 1-(2-methoxyethyl)-3-methoxypropyl, and 1-(2-methoxyethyl)-3-methoxypropyl.

"Alkoxyalkoxy' means a group of the formula -O-R-R' wherein R is alkylene and R' is alkoxy as defined herein.

"Alkylcarbonyl" means a moiety of the formula –C(O)–R, wherein R is alkyl as defined herein.

"Alkoxycarbonyl" means a group of the formula -C(O)-R wherein R is alkoxy as defined herein.

"Alkylcarbonylalkyl" means a group of the formula -R-C(O)-R wherein R is alkylene and R' is alkyl as defined herein.

"Alkoxycarbonylalkyl" means a group of the formula -R-C(O)-R wherein R is alkylene and R' is alkoxy as defined herein.

"Alkoxycarbonylalkoxy"means a group of the formula -O-R-C(O)-R' wherein R is alkylene and R' is alkoxy as defined herein.

"Hydroxycarbonylalkoxy" means a group of the formula -O-R-C(O)-OH wherein R is alkylene as defined herein.

"Alkylaminocarbonylalkoxy" means a group of the formula -O-R-C(O)-NHR' wherein R is alkylene and R' is alkyl as defined herein.

"Dialkylaminocarbonylalkoxy" means a group of the formula -O-R-C(O)-NR'R" wherein R is alkylene and R' and R" are alkyl as defined herein.

"Alkylaminoalkoxy" means a group of the formula -O-R-NHR' wherein R is alkylene and R' is alkyl as defined herein.

"Dialkylaminoalkoxy" means a group of the formula -O-R-NR'R' wherein R is alkylene and R' and R" are alkyl as defined herein.

"Alkylsulfonyl" means a moiety of the formula $-SO_2-R$, wherein R is alkyl as defined herein.

"Alkylsulfonylalkyl means a moiety of the formula -R'-SO_2-R" where where R' is alkylene and R" is alkyl as defined herein.

"Alkylsulfonylalkoxy" means a group of the formula -O-R-SO_2-R' wherein R is alkylene and R' is alkyl as defined herein.

"Amino means a moiety of the formula -NRR' wherein R and R' each independently is hyrdogen or alkyl as defined herein. "Amino thus includes "alkylamino (where one of R and R' is alkyl and the other is hydrogen) and "dialkylamino (where R and R' are both alkyl.

"Aminocarbonyl" means a group of the formula -C(O)-R wherein R is amino as defined herein.

"Alkoxyamino" means a moiety of the formula -NR-OR' wherein R is hydrogen or alkyl and R' is alkyl as defined herein.

"Alkylsulfanyl" means a moiety of the formula -SR wherein R is alkyl as defined herein.

"Aminoalkyl" means a group -R-R' wherein R' is amino and R is alkylene as defined herein. "Aminoalkyl" includes aminomethyl, aminoethyl, 1-aminopropyl, 2-aminopropyl, and the like. The amino moiety of "aminoalkyl" may be substituted once or twice

with alkyl to provide "alkylaminoalkyl" and "dialkylaminoalkyl" respectively. "Alkylaminoalkyl" includes methylaminomethyl, methylaminoethyl, methylaminopropyl, ethylaminoethyl and the like. "Dialkylaminoalkyl" includes dimethylaminomethyl, dimethylaminoethyl, dimethylaminopropyl, N-methyl-N-ethylaminoethyl, and the like.

"Aminoalkoxy" means a group -OR-R' wherein R' is amino and R is alkylene as defined herein.

"Alkylsulfonylamido" means a moiety of the formula -NR'SO_2-R wherein R is alkyl and R' is hydrogen or alkyl.

"Aminocarbonyloxyalkyl" or "carbamylalkyl" means a group of the formula -R-O-C(O)-NR'R" wherein R is alkylene and R', R" each independently is hydrogen or alkyl as defined herein.

"Alkynylalkoxy" means a group of the formula -O-R-R' wherein R is alkylene and R' is alkynyl as defined herein.

“Aryl” means a monovalent cyclic aromatic hydrocarbon moiety consisting of a mono-, bi- or tricyclic aromatic ring. The aryl group can be optionally substituted as defined herein. Examples of aryl moieties include, but are not limited to, phenyl, naphthyl, phenanthryl, fluorenyl, indenyl, pentalenyl, azulenyl, oxydiphenyl, biphenyl, methylenediphenyl, aminodiphenyl, diphenylsulfidyl, diphenylsulfonyl, diphenylisopropylidenyl, benzodioxanyl, benzofuranyl, benzodioxylyl, benzopyranyl, benzoxazinyl, benzoxazinonyl, benzopiperadinyl, benzopiperazinyl, benzopyrrolidinyl, benzomorpholinyl, methylenedioxyphenyl, ethylenedioxyphenyl, and the like, including partially hydrogenated derivatives thereof, each being optionally substituted.

"Arylalkyl" and "Aralkyl", which may be used interchangeably, mean a radical-R^aR^b where R^a is an alkylene group and R^b is an aryl group as defined herein; *e.g.*, phenylalkyls such as benzyl, phenylethyl, 3-(3-chlorophenyl)-2-methylpentyl, and the like are examples of arylalkyl.

"Arylsulfonyl means a group of the formula -SO_2-R wherein R is aryl as defined herein.

"Aryloxy" means a group of the formula -O-R wherein R is aryl as defined herein.

"Aralkyloxy" means a group of the formula -O-R-R" wherein R is alkylene and R' is aryl as defined herein.

“Carboxy” or “hydroxycarbonyl”, which may be used interchangeably, means a group of the formula -C(O)-OH.

"Cyanoalkyl" ” means a moiety of the formula –R’–R”, where R’ is alkylene as defined herein and R” is cyano or nitrile.

"Cycloalkyl" means a monovalent saturated carbocyclic moiety consisting of mono- or bicyclic rings. Particular cycloalkyl are unsubstituted or substituted with alkyl. Cycloalkyl can optionally be substituted with one or more substituents, wherein each substituent is independently hydroxy, alkyl, alkoxy, halo, haloalkyl, amino, monoalkylamino, or dialkylamino, unless otherwise specifically indicated. Examples of cycloalkyl moieties include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and the like, including partially unsaturated (cycloalkenyl) derivatives thereof.

"Cycloalkylalkyl" means a moiety of the formula –R'–R", where R' is alkylene and R" is cycloalkyl as defined herein.

"Cycloalkylalkoxy" means a group of the formula -O-R-R' wherein R is alkylene and R' is cycloalkyl as defined herein.

"Heteroalkyl" means an alkyl radical as defined herein wherein one, two or three hydrogen atoms have been replaced with a substituent independently selected from the group consisting of $-OR^a$, $-NR^bR^c$, and $-S(O)_nR^d$ (where n is an integer from 0 to 2), with the understanding that the point of attachment of the heteroalkyl radical is through a carbon atom, wherein R^a is hydrogen, acyl, alkyl, cycloalkyl, or cycloalkylalkyl; R^b and R^c are independently of each other hydrogen, acyl, alkyl, cycloalkyl, or cycloalkylalkyl; and when n is 0, R^d is hydrogen, alkyl, cycloalkyl, or cycloalkylalkyl, and when n is 1 or 2, R^d is alkyl, cycloalkyl, cycloalkylalkyl, amino, acylamino, monoalkylamino, or dialkylamino. Representative examples include, but are not limited to, 2-hydroxyethyl, 3-hydroxypropyl, 2-hydroxy-1-hydroxymethylethyl, 2,3-dihydroxypropyl, 1-hydroxymethylethyl, 3-hydroxybutyl, 2,3-dihydroxybutyl, 2-hydroxy-1-methylpropyl, 2-aminoethyl, 3-aminopropyl, 2-methylsulfonylethyl, aminosulfonylmethyl, aminosulfonylethyl, aminosulfonylpropyl, methylaminosulfonylmethyl, methylaminosulfonylethyl, methylaminosulfonylpropyl, and the like.

"Heteroaryl" means a monocyclic or bicyclic radical of 5 to 12 ring atoms having at least one aromatic ring containing one, two, or three ring heteroatoms selected from N, O, or S, the remaining ring atoms being C, with the understanding that the attachment point of the heteroaryl radical will be on an aromatic ring. The heteroaryl ring may be optionally substituted as defined herein. Examples of heteroaryl moieties include, but are not limited to, optionally substituted imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, pyrazinyl, thienyl, benzothienyl, thiophenyl, furanyl, pyranyl, pyridyl, pyrrolyl, pyrazolyl, pyrimidyl, quinolinyl, isoquinolinyl, benzofuryl, benzothiophenyl, benzothiopyranyl, benzimidazolyl, benzooxazolyl, benzooxadiazolyl, benzothiazolyl, benzothiadiazolyl, benzopyranyl, indolyl, isoindolyl, triazolyl, triazinyl, quinoxalinyl, purinyl, quinazolinyl, quinolizinyl, naphthyridinyl, pteridinyl, carbazolyl, azepinyl, diazepinyl, acridinyl and the like, including partially hydrogenated derivatives thereof, each optionally substituted.

Heteroarylalkyl" or "heteroaralkyl" means a group of the formula -R-R' wherein R is alkylene and R' is heteroaryl as defined herein.

"Heteroarylsulfonyl means a group of the formula $-SO_2$-R wherein R is heteroaryl as defined herein.

"Heteroaryloxy" means a group of the formula -O-R wherein R is heteroaryl as defined herein.

"Heteroaralkyloxy" means a group of the formula -O-R-R" wherein R is alkylene and R' is heteroaryl as defined herein.

The terms “halo”, “halogen” and "halide", which may be used interchangeably, refer to a substituent fluoro, chloro, bromo, or iodo.

“Haloalkyl” means alkyl as defined herein in which one or more hydrogen has been replaced with same or different halogen. Exemplary haloalkyls include $–CH_2Cl$, $–CH_2CF_3$, $–CH_2CCl_3$, perfluoroalkyl (e.g., $–CF_3$), and the like.

“Haloalkoxy” means a moiety of the formula –OR, wherein R is a haloalkyl moiety as defined herein. An exemplary haloalkoxy is difluoromethoxy.

“Heterocycloamino” means a saturated ring wherein at least one ring atom is N, NH or N-alkyl and the remaining ring atoms form an alkylene group.

“Heterocyclyl” means a monovalent saturated moiety, consisting of one to three rings, incorporating one, two, or three or four heteroatoms (chosen from nitrogen, oxygen or sulfur). The heterocyclyl ring may be optionally substituted as defined herein. Examples of heterocyclyl moieties include, but are not limited to, optionally substituted piperidinyl, piperazinyl, homopiperazinyl, azepinyl, pyrrolidinyl, pyrazolidinyl, imidazolinyl, imidazolidinyl, pyridinyl, pyridazinyl, pyrimidinyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiazolidinyl, isothiazolidinyl, quinuclidinyl, quinolinyl, isoquinolinyl, benzimidazolyl, thiadiazolylidinyl, benzothiazolidinyl, benzoazolylidinyl, dihydrofuryl, tetrahydrofuryl, dihydropyranyl, tetrahydropyranyl, thiamorpholinyl, thiamorpholinylsulfoxide, thiamorpholinylsulfone, dihydroquinolinyl, dihydrisoquinolinyl, tetrahydroquinolinyl, tetrahydrisoquinolinyl, and the like.

"Heterocyclylalkyl" means a moiety of the formula -R-R' wherein R is alkylene and R' is heterocyclyl as defined herein.

"Heterocyclyloxy" means a moiety of the formula -OR wherein R is heterocyclyl as defined herein.

"Heterocyclylalkoxy" means a moiety of the formula -OR-R' wherein R is alkylene and R' is heterocyclyl as defined herein.

"Hydroxyalkoxy" means a moiety of the formula -OR wherein R is hydroxyalkyl as defined herein.

"Hydroxyalkylamino" means a moiety of the formula -NR-R' wherein R is hydrogen or alkyl and R' is hydroxyalkyl as defined herein.

"Hydroxyalkylaminoalkyl" means a moiety of the formula -R-NR'-R" wherein R is alkylene, R' is hydrogen or alkyl, and R" is hydroxyalkyl as defined herein.

"Hydroxycarbonylalkyl" or "carboxyalkyl" means a group of the formula -R-(CO)-OH where R is alkylene as defined herein.

"Hydroxycarbonylalkoxy" means a group of the formula -O-R-C(O)-OH wherein R is alkylene as defined herein.

"Hydroxyalkyloxycarbonylalkyl" or "hydroxyalkoxycarbonylalkyl" means a group of the formula -R-C(O)-O-R-OH wherein each R is alkylene and may be the same or different.

"Hydroxyalkyl" means an alkyl moiety as defined herein, substituted with one or more, for example, one, two or three hydroxy groups, provided that the same carbon atom does not carry more than one hydroxy group. Representative examples include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 1-(hydroxymethyl)-2-methylpropyl, 2-hydroxybutyl, 3-hydroxybutyl, 4-hydroxybutyl, 2,3-dihydroxypropyl, 2-hydroxy-1-hydroxymethylethyl, 2,3-dihydroxybutyl, 3,4-dihydroxybutyl and 2-(hydroxymethyl)-3-hydroxypropyl

"Hydroxycycloalkyl" means a cycloalkyl moiety as defined herein wherein one, two or three hydrogen atoms in the cycloalkyl radical have been replaced with a hydroxy substituent. Representative examples include, but are not limited to, 2-, 3-, or 4-hydroxycyclohexyl, and the like.

"Alkoxy hydroxyalkyl" and "hydroxy alkoxyalkyl", which may be used interchangeably, means an alkyl as defined herein that is substituted at least once with hydroxy and at least once with alkoxy. "Alkoxy hydroxyalkyl" and "hydroxy alkoxyalkyl" thus encompass, for example, 2-hydroxy-3-methoxy-propan-1-yl and the like.

"Urea"or "ureido" means a group of the formula -NR'-C(O)-NR"R'" wherein R', R" and R'" each independently is hydrogen or alkyl.

"Carbamate" means a group of the formula -O-C(O)-NR'R" wherein R' and R" each independently is hydrogen or alkyl.

"Carboxy" means a group of the formula -O-C(O)-OH.

"Sulfonamido" means a group of the formula -SO_2-NR'R" wherein R', R" and R'" each independently is hydrogen or alkyl.

"Optionally substituted", when used in association with "aryl", phenyl", "heteroaryl" "cycloalkyl" or "heterocyclyl", means an aryl, phenyl, heteroaryl, cycloalkyl or heterocyclyl which is optionally substituted independently with one to four substituents, for

example one or two substituents selected from alkyl, cycloalkyl, cycloalkylalkyl, heteroalkyl, hydroxyalkyl, halo, nitro, cyano, hydroxy, alkoxy, amino, acylamino, mono-alkylamino, di-alkylamino, haloalkyl, haloalkoxy, heteroalkyl, -COR, $-SO_2R$ (where R is hydrogen, alkyl, phenyl or phenylalkyl), $-(CR'R'')_n-COOR$ (where n is an integer from 0 to 5, R' and R" are independently hydrogen or alkyl, and R is hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, phenyl or phenylalkyl), or $-(CR'R'')_n-CONR^aR^b$ (where n is an integer from 0 to 5, R' and R" are independently hydrogen or alkyl, and R^a and R^b are, independently of each other, hydrogen, alkyl, cycloalkyl, cycloalkylalkyl, phenyl or phenylalkyl). Certain particular optional substituents for "aryl", phenyl", "heteroaryl" "cycloalkyl" or "heterocyclyl" include alkyl, halo, haloalkyl, alkoxy, cyano, amino and alkylsulfonyl. In one embodiment substituents are methyl, fluoro, chloro, trifluoromethyl, methoxy, amino and methanesulfonyl.

"Leaving group" means the group with the meaning conventionally associated with it in synthetic organic chemistry, i.e., an atom or group displaceable under substitution reaction conditions. Examples of leaving groups include, but are not limited to, halogen, alkane- or arylenesulfonyloxy, such as methanesulfonyloxy, ethanesulfonyloxy, thiomethyl, benzenesulfonyloxy, tosyloxy, and thienyloxy, dihalophosphinoyloxy, optionally substituted benzyloxy, isopropyloxy, acyloxy, and the like.

"Modulator" means a molecule that interacts with a target. The interactions include, but are not limited to, agonist, antagonist, and the like, as defined herein.

"Optional" or "optionally" means that the subsequently described event or circumstance may but need not occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not.

"Disease" and "Disease state" means any disease, condition, symptom, disorder or indication.

"Inert organic solvent" or "inert solvent" means the solvent is inert under the conditions of the reaction being described in conjunction therewith, including for example, benzene, toluene, acetonitrile, tetrahydrofuran, N,N-dimethylformamide, chloroform, methylene chloride or dichloromethane, dichloroethane, diethyl ether, ethyl acetate, acetone, methyl ethyl ketone, methanol, ethanol, propanol, isopropanol, *tert*-butanol, dioxane, pyridine, and the like. Unless specified to the contrary, the solvents used in the reactions of the present invention are inert solvents.

"Pharmaceutically acceptable" means that which is useful in preparing a pharmaceutical composition that is generally safe, non-toxic, and neither biologically nor otherwise undesirable and includes that which is acceptable for veterinary as well as human pharmaceutical use.

"Pharmaceutically acceptable salts" of a compound means salts that are pharmaceutically acceptable, as defined herein, and that possess the desired pharmacological activity of the parent

compound. It refers to salts that are suitable for use in contact with the tissues of humans and animals. Examples of suitable salts with inorganic and organic acids are, but are not limited to acetic acid, citric acid, formic acid, fumaric acid, hydrochloric acid, lactic acid, maleic acid, malic acid, methane-sulfonic acid, nitric acid, phosphoric acid, p-toluenesulphonic acid, succinic acid, sulfuric acid, sulphuric acid, tartaric acid, trifluoroacetic acid and the like. The terms "pharmaceutically acceptable carrier" and "pharmaceutically acceptable auxiliary substance" refer to carriers and auxiliary substances such as diluents or excipients that are compatible with the other ingredients of the formulation. Compounds of formula I can form pharmaceutically acceptable salts. The term "pharmaceutically acceptable salts" refers to those salts which retain the biological effectiveness and properties of the free bases or free acids, which are not biologically or otherwise undesirable. In particular, the pharmaceutically acceptable salts of the compounds of formula I are the acid addition salts with physiologically compatible mineral acids, such as hydrochloric acid, sulfuric acid, sulfurous acid or phosphoric acid; or with organic acids, such as methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, formic acid, acetic acid, propionic acid, glycolic acid, pyruvic acid, oxylic acid, lactic acid, trifluoroacetic acid, citric acid, fumaric acid, maleic acid, malonic acid, tartaric acid, benzoic acid, cinnamic acid, mandelic acid, succinic acid or salicylic acid. In addition, pharmaceutically acceptable salts can be prepared from addition of an inorganic base or an organic base to the free acid. Salts derived from an inorganic base include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium salts and the like. Salts derived from organic bases include, but are not limited to salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, lysine, arginine, *N*-ethylpiperidine, piperidine, polymine resins and the like. The compound of formula I can also be present in the form of zwitterions. Particular pharmaceutically acceptable salts of compounds of formula I are the acid addition salts such as the hydrochloride salts, the formate salts or trifluoroacetate salts. Specific are the formate salts (salts of formic acid).

The corresponding pharmaceutically acceptable salts with acids can be obtained by standard methods known to the person skilled in the art, e.g. by dissolving the compound of formula I in a suitable solvent such as e.g. dioxan or THF and adding an appropriate amount of the corresponding acid. The products can usually be isolated by filtration or by chromatography. The conversion of a compound of formula **I** into a pharmaceutically acceptable salt with a base can be carried out by treatment of such a compound with such a base. One possible method to form such a salt is e.g. by addition of 1/n equivalents of a basic salt such as e.g. $M(OH)_n$, wherein M = metal or ammonium cation and n = number of hydroxide anions, to a solution of the compound in a suitable solvent (e.g. ethanol, ethanol-water mixture, tetrahydrofuran-water mixture) and to remove the solvent by evaporation or lyophilisation. Particular salts are hydrochloride, formate and trifluoroacetate.

Insofar as their preparation is not described in the examples, the compounds of formula I as well as all intermediate products can be prepared according to analogous methods or according to the methods set forth herein. Starting materials are commercially available, known in the art or can be prepared by methods known in the art or in analogy thereto.

It will be appreciated that the compounds of general formula I in this invention can be derivatised at functional groups to provide derivatives which are capable of conversion back to the parent compound *in vivo*.

The term "half maximal inhibitory concentration" (IC_{50}) denotes the concentration of a particular compound required for obtaining 50% inhibition of a biological process in vitro. IC_{50} values can be converted logarithmically to pIC_{50} values (-log IC_{50}), in which higher values indicate exponentially greater potency. The IC_{50} value is not an absolute value but depends on experimental conditions e.g. concentrations employed. The IC_{50} value can be converted to an absolute inhibition constant (Ki) using the Cheng-Prusoff equation (Biochem. Pharmacol. (1973) 22:3099). The term "inhibition constant" (Ki) denotes the absolute binding affinity of a particular inhibitor to a receptor. It is measured using competition binding assays and is equal to the concentration where the particular inhibitor would occupy 50% of the receptors if no competing ligand (e.g. a radioligand) was present. Ki values can be converted logarithmically to pKi values (-log Ki), in which higher values indicate exponentially greater potency.

The term "as defined herein" and "as described herein" when referring to a variable incorporates by reference the broad definition of the variable as well as preferred, more preferred and most preferred definitions, if any.

It should be understood that all references to pharmaceutically acceptable salts include solvent addition forms (solvates) or crystal forms (polymorphs) as defined herein, of the same acid addition salt.

"Protective group" or "protecting group" means the group which selectively blocks one reactive site in a multifunctional compound such that a chemical reaction can be carried out selectively at another unprotected reactive site in the meaning conventionally associated with it in synthetic chemistry. Certain processes of this invention rely upon the protective groups to block reactive nitrogen and/or oxygen atoms present in the reactants. For example, the terms "amino-protecting group" and "nitrogen protecting group" are used interchangeably herein and refer to those organic groups intended to protect the nitrogen atom against undesirable reactions during synthetic procedures. Exemplary nitrogen protecting groups include, but are not limited to, trifluoroacetyl, acetamido, benzyl (Bn), benzyloxycarbonyl (carbobenzyloxy, CBZ), p-methoxybenzyloxycarbonyl, p-nitrobenzyloxycarbonyl, *tert*-butoxycarbonyl (BOC), and the like. The artisan in the art will know how to chose a group for the ease of removal and for the ability to withstand the following reactions.

"Solvates" means solvent additions forms that contain either stoichiometric or non stoichiometric amounts of solvent. Some compounds have a tendency to trap a fixed molar ratio of solvent molecules in the crystalline solid state, thus forming a solvate. If the solvent is water the solvate formed is a hydrate, when the solvent is alcohol, the solvate formed is an alcoholate. Hydrates are formed by the combination of one or more molecules of water with one of the substances in which the water retains its molecular state as H_2O, such combination being able to form one or more hydrate.

"Parkinson's disease" means a degenerative disorder of the central nervous system that impairs motor skills, speech, and/or cognitive function. Symptoms of Parkinson's disease may include, for example, muscle rigidity, tremor, slowing of physical movement (bradykinesia) and loss of physical movement (akinesia).

"Lewie (Lewy) body disease" also called "Lewie body dementia", diffuse Lewie body disease", cortical Lewie body disease", means a neurogenerative disorder characterized anatomically by the presence of Lewie bodies in the brain.

"Subject" means mammals and non-mammals. Mammals means any member of the mammalia class including, but not limited to, humans; non-human primates such as chimpanzees and other apes and monkey species; farm animals such as cattle, horses, sheep, goats, and swine; domestic animals such as rabbits, dogs, and cats; laboratory animals including rodents, such as rats, mice, and guinea pigs; and the like. Examples of non-mammals include, but are not limited to, birds, and the like. The term "subject" does not denote a particular age or sex.

"Therapeutically effective amount" means an amount of a compound that, when administered to a subject for treating a disease state, is sufficient to effect such treatment for the disease state. The "therapeutically effective amount" will vary depending on the compound, disease state being treated, the severity or the disease treated, the age and relative health of the subject, the route and form of administration, the judgment of the attending medical or veterinary practitioner, and other factors.

The terms "those defined above" and "those defined herein" when referring to a variable incorporates by reference the broad definition of the variable as well as particular definitions, if any.

"Treating" or "treatment" of a disease state includes, inter alia, inhibiting the disease state, *i.e.*, arresting the development of the disease state or its clinical symptoms, and/or relieving the disease state, *i.e.*, causing temporary or permanent regression of the disease state or its clinical symptoms.

The terms "treating", "contacting" and "reacting" when referring to a chemical reaction means adding or mixing two or more reagents under appropriate conditions to produce the indicated and/or the desired product. It should be appreciated that the reaction which

produces the indicated and/or the desired product may not necessarily result directly from the combination of two reagents which were initially added, i.e., there may be one or more intermediates which are produced in the mixture

which ultimately leads to the formation of the indicated and/or the desired product.

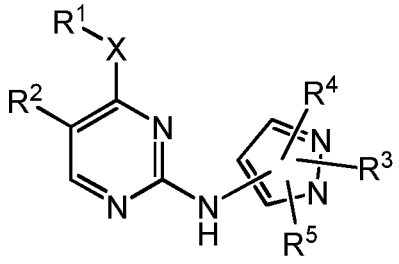
Nomenclature and Structures

In general, the nomenclature used in this Application is based on AUTONOM™ v.4.0, a Beilstein Institute computerized system for the generation of IUPAC systematic nomenclature. Chemical structures shown herein were prepared using ISIS® version 2.2. Any open valency appearing on a carbon, oxygen sulfur or nitrogen atom in the structures herein indicates the presence of a hydrogen atom unless indicated otherwise. Where a nitrogen-containing heteroaryl ring is shown with an open valency on a nitrogen atom, and variables such as R^a, R^b or R^c are shown on the heteroaryl ring, such variables may be bound or joined to the open valency nitrogen. Where one or more chiral centers exist in a structure but no specific stereochemistry is shown for the chiral centers, both enantiomers associated with each such chiral center are encompassed by the structure. Where a structure shown herein may exist in multiple tautomeric forms, all such tautomers are encompassed by the structure. The atoms represented in the structures herein are intended to encompass all naturally occurring isotopes of such atoms. Thus, for example, the hydrogen atoms represented herein are meant to include deuterium and tritium, and the carbon atoms are meant to include C^{13} and C^{14} isotopes.

All patents and publications identified herein are incorporated herein by reference in their entirety.

Compounds of the Invention

The invention provides compounds of the formula I:



I

or pharmaceutically acceptable salts thereof,

wherein:

X is: $-NR^a-$; or -O- wherein R^a is hydrogen or C_{1-6}alkyl;

R^1 is: C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is

optionally substituted one or more times with C_{1-6}alkyl; heterocyclyl optionally substituted one or more times with R^7; or heterocyclyl-C_{1-6}alkyl optionally substituted one or more times with R^7;

or X and R^1 together form C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6;

or R^1 and R^a together with the atoms to which they are attached may form a three- to six-membered heterocyclic ring optionally substituted one or more times with R^7;

R^2 is: C_{1-6}alkyl; halo; C_{1-6}alkoxy; cyano; C_{2-6}alkynyl; C_{2-6}alkenyl; halo-C_{1-6}alkyl; halo-C_{1-6}alkoxy; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; -OR^b wherein R^b is C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted one or more times with R^6, or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl optionally substituted one or more times with R^7;

R^3 is: hydrogen; C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano-C_{1-6}alkyl; C_{1-6}alkylsulfonyl; C_{1-6}alkylsulfonylC_{1-6}alkyl; amino-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-sulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; heterocyclyl optionally substituted one or more times with R^7; heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7; aryl optionally substituted one or more times with R^8; aryl-C_{1-6}alkyl wherein the aryl portion is optionally substituted one or more times with R^8; heteroaryl optionally substituted one or more times with R^8; heteroaryl-C_{1-6}alkyl wherein the heteroaryl portion is optionally substituted one or more times with R^8;or -Y-C(O)-R^d;

Y is C_{2-6}alkylene or a bond;

R^d is C_{1-6}alkyl, C_{1-6}alkoxy, amino, C_{1-6}alkyl-amino, di-C_{1-6}alkyl-amino, halo-C_{1-6}alkyl-amino, di-halo-C_{1-6}alkyl-amino, halo-C_{1-6}alkyl, hydroxy-C_{1-6}alkyl, hydroxy, C_{1-6}alkoxy-C_{1-6}alkyl, cyano-C_{1-6}alkyl, C_{1-6}alkylsulfonylC_{1-6}alkyl, amino-C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted one or more times with R^6, C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; heterocyclyl optionally substituted one or more times with R^7, or heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7;

R^4 is: hydrogen; C_{1-6}alkyl; halo; cyano; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; C_{1-6}alkoxy; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; or -Y-C(O)-R^d;

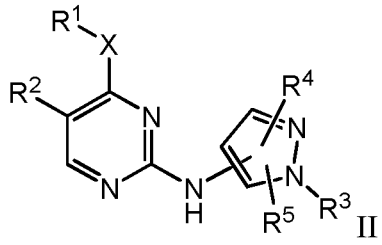
R^5 is: hydrogen; or C_{1-6}alkyl;

each R^6 is independently: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy; oxo; cyano; halo; or Y-C(O)-R^d;

each R^7 is independently: C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; oxo; C_{1-6}alkoxy; C_{1-6}alkylsulfonyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; -Y-C(O)-R^d; heterocyclyl; heterocyclyl-C_{1-6}alkyl; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl; or C_{3-6}cycloalkylsulfonyl; and

each R^8 is independently: oxo; C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; C_{1-6}alkyl-sulfonyl; C_{1-6}alkoxy; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; hetoeryclyl; heterocyclyl-C_{1-6}alkyl; -Y-C(O)-R^d; C_{3-6}cycloalkyl, C_{3-6}cycloalkyl-C_{1-6}alkyl, or C_{3-6}cycloalkyl-sulfonyl.

In certain embodiments the invention provides compounds of the formula II:



II

or pharmaceutically acceptable salts thereof,

wherein:

X is: -NR^a-; or -O- wherein R^a is hydrogen or C_{1-6}alkyl;

R^1 is: C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; heterocyclyl; or heterocyclyl-C_{1-6}alkyl;

or X and R^1 together form C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl;

or R^1 and R^a together with the atoms to which they are attached may form a three- to six-membered heterocyclic ring.

R^2 is: C_{1-6}alkyl; halo; C_{1-6}alkoxy; cyano; C_{2-6}alkynyl; C_{2-6}alkenyl; halo-C_{1-6}alkyl; halo-C_{1-6}alkoxy; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; -OR^b wherein R^b is C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl, or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl;

R^3 is: hydrogen; C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano-C_{1-6}alkyl; C_{1-6}alkylsulfonyl; C_{1-6}alkylsulfonylalkyl; amino-C_{1-6}alkyl;

C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; heterocyclyl; heterocyclyl-C_{1-6}alkyl; aryl; heteroaryl; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl;

R^4 is: hydrogen; C_{1-6}alkyl; halo; cyano; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl; and

R^5 is: hydrogen; or C_{1-6}alkyl.

In certain embodiments of formula I or formula II, X is -NR^a-or -O-.

In certain embodiments of formula I or formula II, X is -NR^a.

In certain embodiments of formula I or formula II, X is -O-.

In certain embodiments of formula I or formula II, X is -NH-or -O-.

In certain embodiments of formula I or formula II, X is -NH-.

In certain embodiments of formula I or formula II, X is -O-.

In certain embodiments of formula I or formula II, R^a is hydrogen.

In certain embodiments of formula I or formula II, R^a is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is: C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; heterocyclyl; or heterocyclyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; C_{3-6}cycloalkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is: C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; tetrahydrofuranyl; tetrahydrofuranyl-C_{1-6}alkyl; oxetanyl; or oxetan-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; or C_{1-6}alkylsulfonyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is C_{1-6}alkyl or halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is C_{1-6}alkoxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is amino-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is C_{1-6}alkylsulfonyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is heterocyclyl or heterocyclyl-C_{1-6}alkyl.

In embodiments of formula I or formula II wherein R^1 is heterocyclyl or heterocyclyl-C_{1-6}alkyl, such heterocyclyl may be piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, pyrrolidinyl, tetrahydrofuranyl or oxetanyl, each optionally substituted as defined herein.

In embodiments of formula I or formula II wherein R^1 is heterocyclyl or heterocyclyl-C_{1-6}alkyl, such heterocyclyl may be tetrahydropyranyl, piperidinyl, tetrahydrofuranyl or oxetanyl, each optionally substituted as defined herein..

In certain embodiments of formula I or formula II, R^1 is tetrahydrofuranyl.

In certain embodiments of formula I or formula II, R^1 is tetrahydropyranyl.

In certain embodiments of formula I or formula II, R^1 is tetrahydrofuranyl-C_{1-6}alkyl or oxetanyl.

In certain embodiments of formula I or formula II, R^1 is tetrahydrofuranyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is oxetanyl.

In certain embodiments of formula I or formula II, R^1 is or oxetan-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^1 is: methyl; ethyl; n-propyl; isopropyl; isobutyl; 3,3-dimethylpropyl; cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; cyclopropylmethyl; cyclobutylmethyl; cyclopentylmethyl; cyclopropylethyl; methoxyethyl; oxetanyl; tetrahydropyranyl; 2,2-difluoroethyl; or tetrahydrofuranylmethyl.

In certain embodiments of formula I or formula II, R^1 is: methyl; ethyl; n-propyl; isopropyl; isobutyl; 3,3-dimethylpropyl; cyclopentyl; cyclohexyl; cyclopropylmethyl; cyclobutylmethyl; cyclopentylmethyl; cyclopropylethyl; methoxyethyl; oxetanyl; tetrahydropyranyl; 2,2-difluoroethyl ; or tetrahydrofuranylmethyl.

In certain embodiments of formula I or formula II, R^1 is: methyl; ethyl; n-propyl; isopropyl; isobutyl; 3,3-dimethylpropyl; cyclopentyl; cyclohexyl; cyclopentylmethyl; methoxyethyl; oxetanyl; tetrahydropyranyl; or tetrahydrofuranylmethyl.

In certain embodiments of formula I or formula II, R^1 is 2,2-difluoroethyl.

In certain embodiments of formula I or formula II, R^1 is: methyl; ethyl; n-propyl; isopropyl; or isobutyl.

In certain embodiments of formula I or formula II, R^1 is methyl or ethyl.

In certain embodiments of formula I or formula II, R^1 is methyl.

In certain embodiments of formula I or formula II, R^1 is ethyl.

In certain embodiments of formula I or formula II, R^1 is: cyclopropyl; cyclobutyl; cyclopentyl; cyclohexyl; cyclopropylmethyl; cyclobutylmethyl; cyclopentylmethyl; or cyclopropylethyl.

In certain embodiments of formula I or formula II, R^1 is: cyclopentyl; cyclohexyl; or cyclopentylmethyl.

In certain embodiments of formula I or formula II, R^1 is: cyclopropyl.

In certain embodiments of formula I or formula II, R^1 and R^a together with the atoms to which they are attached may form a three- to six-membered heterocyclic ring.

In certain embodiments of formula I or formula II, R^1 and R^a together with the atoms to which they are attached may form a three-membered heterocyclic ring.

In certain embodiments of formula I or formula II, R^1 and R^a together with the atoms to which they are attached may form a four-membered heterocyclic ring.

In certain embodiments of formula I or formula II, R^1 and R^a together with the atoms to which they are attached may form a five-membered heterocyclic ring.

In certain embodiments of formula I or formula II, R^1 and R^a together with the atoms to which they are attached may form a six-membered heterocyclic ring.

In certain embodiments of formula I or formula II, X and R^1 together form C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, X and R^1 together form C_{1-6}alkyl.

In certain embodiments of formula I or formula II, X and R^1 together form C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, X and R^1 together form C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is: C_{1-6}alkyl; halo; C_{1-6}alkoxy; cyano; C_{2-6}alkynyl; C_{2-6}alkenyl; halo-C_{1-6}alkyl; halo-C_{1-6}alkoxy; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; -OR^b wherein R^b is C_{1-6}alkyl, C_{3-6}cycloalkyl optionally

substituted with C_{1-6}alkyl, or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; or -C(O)-R^c.

In certain embodiments of formula I or formula II, R^2 is: halo; C_{1-6}alkoxy; halo-C_{1-6}alkyl; halo-C_{1-6}alkoxy; C_{3-6}cycloalkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; tetrahydrofuranyl; tetrahydrofuranyl-C_{1-6}alkyl; oxetanyl; or oxetan-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is: halo; C_{1-6}alkoxy; halo-C_{1-6}alkyl; cyano; C_{2-6}alkynyl; C_{2-6}alkenyl; C_{3-6}cycloalkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is: halo; C_{1-6}alkoxy; halo-C_{1-6}alkyl; cyano; C_{3-6}cycloalkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is: halo; C_{1-6}alkoxy; halo-C_{1-6}alkyl; C_{3-6}cycloalkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is: halo; halo-C_{1-6}alkyl or cyano.

In certain embodiments of formula I or formula II, R^2 is: fluoro; bromo; chloro; iodo; trifluoromethyl; or cyano.

In certain embodiments of formula I or formula II, R^2 is: chloro; trifluoromethyl; or cyano.

In certain embodiments of formula I or formula II, R^2 is: halo; or halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is halo.

In certain embodiments of formula I or formula II, R^2 is C_{1-6}alkoxy.

In certain embodiments of formula I or formula II, R^2 is halo-C_{1-6}alkoxy.

In certain embodiments of formula I or formula II, R^2 is halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is C_{3-6}cycloalkyl.

In certain embodiments of formula I or formula II, R^2 is C_{3-6}cycloalkyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is tetrahydrofuranyl.

In certain embodiments of formula I or formula II, R^2 is tetrahydrofuranyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is oxetanyl.

In certain embodiments of formula I or formula II, R^2 is oxetan-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^2 is fluoro, chloro or bromo.

In certain embodiments of formula I or formula II, R^2 is chloro.

In certain embodiments of formula I or formula II, R^2 is fluoro.

In certain embodiments of formula I or formula II, R^2 is bromo.

In certain embodiments of formula I or formula II, R^2 is iodo.

In certain embodiments of formula I or formula II, R^2 is trifluoromethyl.

In certain embodiments of formula I or formula II, R^2 is methoxy.

In certain embodiments of formula I or formula II, R^2 is cyano.

In certain embodiments of formula I or formula II, R^2 is C_{2-6}alkynyl.

In certain embodiments of formula I or formula II, R^2 is C_{2-6}alkenyl.

In certain embodiments of formula I or formula II, R^2 is $-OR^b$ wherein R^b is C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl, or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I, R^2 is $-C(O)-R^c$ wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^3 is: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano-C_{1-6}alkyl; C_{1-6}alkylsulfonyl; C_{1-6}alkylsulfonylC_{1-6}alkyl; amino-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; heterocyclyl optionally substituted one or more times with R^7; heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7; aryl optionally substituted one or more times with R^8; heteroaryl optionally substituted one or more times with R^8; or $-Y-C(O)-R^d$.

In certain embodiments of formula I or formula II, R^3 is: hydrogen; C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano-C_{1-6}alkyl; C_{1-6}alkylsulfonyl; C_{1-6}alkylsulfonylalkyl; amino-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; heterocyclyl; heterocyclyl-C_{1-6}alkyl; aryl; heteroaryl; or $-C(O)-R^c$.

In certain embodiments of formula I or formula II, R^3 is: C_{1-6}alkyl; halo-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; heterocyclyl; heterocyclyl-C_{1-6}alkyl; or $-C(O)-R^b$ wherein R^b is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^3 is: C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; heterocyclyl; heterocyclyl-C_{1-6}alkyl; or $-C(O)-R^c$ wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^3 is: C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; heterocyclyl optionally substituted one or more times with R^7; heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7; or -C(O)-R^d.

In certain embodiments of formula I or formula II, R^3 is: C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; heterocyclyl; heterocyclyl-C_{1-6}alkyl; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^3 is: C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; heterocyclyl; or heterocyclyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is: C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; or C_{1-6}alkoxy-C_{1-6}alkyl.

In embodiments of formula I or formula II wherein R^3 is heterocyclyl or heterocyclyl-C_{1-6}alkyl, such heterocyclyl may be piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, pyrrolidinyl, tetrahydrofuranyl or oxetanyl.

In embodiments of formula I or formula II wherein R^3 is heterocyclyl or heterocyclyl-C_{1-6}alkyl, such heterocyclyl may be piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, pyrrolidinyl, azetidinyl, tetrahydrofuranyl or oxetanyl, each optionally substituted one or more times, or one or two times, with R^7 as defined herein.

In embodiments of formula I or formula II wherein R^3 is heterocyclyl or heterocyclyl-C_{1-6}alkyl, such heterocyclyl may be piperidinyl, morpholinyl, tetrahydropyranyl, tetrahydrofuranyl or oxetanyl.

In embodiments of formula I or formula II wherein R^3 is heterocyclyl or heterocyclyl-C_{1-6}alkyl, such heterocyclyl may be piperidinyl, pyrrolidinyl, azetidinyl, morpholinyl, tetrahydropyranyl, tetrahydrofuranyl or oxetanyl, each optionally substituted one or more times, or one or two times, with R^7 as defined herein.

In certain embodiments of formula I or formula II, R^3 is: methyl; ethyl; n-propyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; 2-(morpholin-4-yl)-ethyl; 2-hydroxy-2-methyl-propan-1-yl; tetrahydropyran-4-yl; or morpholin-4-yl-carbonyl.

In certain embodiments of formula I, R^3 is: methyl; ethyl; n-propyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; 2-(morpholin-4-yl)-ethyl; 2-hydroxy-2-methyl-propan-1-yl; or tetrahydropyran-4-yl.

In certain embodiments of formula I or formula II, R^3 is hydrogen.

In certain embodiments of formula I or formula II, R^3 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is C_{2-6}alkenyl.

In certain embodiments of formula I or formula II, R^3 is C_{2-6}alkynyl.

In certain embodiments of formula I or formula II, R^3 is hydroxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is C_{1-6}alkoxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is C_{3-6}cycloalkyl optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^3 is C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^3 isC_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is heterocyclyl optionally substituted one or more times with R^7.

In certain embodiments of formula I or formula II, R^3 is heterocyclyl.

In certain embodiments of formula I or formula II, R^3 is heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7.

In certain embodiments of formula I or formula II, R^3 is heterocyclyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is -C(O)-R^c.

In certain embodiments of formula I or formula II, R^3 is cyano-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is C_{1-6}alkylsulfonyl.

In certain embodiments of formula I or formula II, R^3 is C_{1-6}alkylsulfonyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is amino-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^3 is aryl optionally substituted one or more times with R^8.

In certain embodiments of formula I or formula II, R^3 is aryl.

In certain embodiments of formula I or formula II, R^3 is phenyl optionally substituted one or more times, or one or two times, with R^8.

In certain embodiments of formula I or formula II, R^3 is heteroaryl optionally substituted one or more times, or one or two times, with R^8.

In certain embodiments of formula I or formula II, R^3 is heteroaryl.

In certain embodiments of formula I or formula II, R^3 is C_{3-6}cycloalkyl-sulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^3 is: hydrogen; methyl; ethyl; propyl; isopropyl; butyl; cyclopropyl; cyclopropylmethyl; cyclobutyl; methanesulfonyl; ethylsulfonyl; cyclopropylsulfonyl; sec-butylsulfonyl; morpholin-4-yl-ethyl; oxetan-3-yl; 2-methoxyethyl; 2-hydroxy-2-methyl-propyl; 3-hydroxy-2-methyl-propan-2-yl; 2-methoxy-propyl; tetrahydro-2H-pyran-4-yl; tetrahydrofuran-3-yl; 2,6-dimethyltetrahydro-2H-pyran-4-yl; tetrahydro-2H-pyran-3-yl); phenyl; 4-(methylsulfonyl)phenyl); 4-cyano-phenyl; 4-fluoro-phenyl; 4-chloro-phenyl; 3,5-difluorophenyl; 4-(dimethylamino-carbonyl)-phenyl); 4-(cyclopropylsulfonyl)phenyl; 2,2,2-trifluoroethyl; 2-fluoroethyl; difluoromethyl; 2-dimethyl-1,3-dioxan-5-yl; 1-methyl-cyclopropyl-carbonyl; 3-methylpyridin-4-yl; 2-methylpyridin-4-yl; pyridin-2-yl; pyrimidin-2-yl; pyrimidin-5-yl; pyridin-2-ylmethyl; 1-(pyridin-2-yl)ethyl; cyclopropylsulfonyl; 1-cyano-1-methyl-ethyl (also called 2-cyano-propan-2-yl); 2-cyano-ethyl; 1-cyano-ethyl; 2-cyano-2-methyl-propyl; 1-(2,2,2-trifluoroethyl)piperidin-4-yl; 1-(methylsulfonyl)azetidin-3-yl; (3-methyloxetan-3-yl)methyl; (1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl; 1-(oxetan-3-yl)piperidin-4-yl; 1-acetyl-piperidin-4-yl; 1-(cyclopropyl-carbonyl)-piperidin-4-yl; 1-methyl-piperidin-4-yl; 1-methyl-2-oxo-piperidin-5-yl; 2-oxo-piperidin-5-yl; 1-(isopropyl-carbonyl)-piperidin-4-yl; 1-(oxetan-3-yl)azetidin-3-yl; 1-(cyclopropyl-carbonyl)-piperidin-4-yl; 2-methoxycyclopentyl; 3-methoxycyclopentyl; 1-methoxy-2-methylpropan-2-yl; tetrahydro-2H-1,1-dioxo-thiopyran-4-yl; 3-fluoro-1-(oxetan-3-yl)piperidin-4-yl; 1-methoxypropan-2-yl; 1-(2,2,2-trifluoroethyl)azetidin-3-yl); 1-(oxetan-3-yl)pyrrolidin-3-yl; 1-isopropylazetidin-3-yl; 3-fluoro-1-methylpiperidin-4-yl; 1-ethyl-3-fluoropiperidin-4-yl; 1-methylpyrrolidin-3-yl; 2-methoxyethyl)piperidin-4-yl); 1-methyl-1-(methylamino-carbonyl)-ethyl; 2-methyl-2-morpholino-propyl; 4,4-difluorocyclohexyl; morpholin-4-yl-carbonyl; dimethylamino-carbonyl-methyl; methylamino-carbonyl-methyl; 1-methyl-1-(dimethylamino-carbonyl)-ethyl; pyrrolidin-1-yl-carbonyl; 1-cyano-cyclopropyl; 1-(pyrrolidin-1-yl-carbonyl)-ethyl; 1-(dimethylamino-carbonyl)-ethyl; 1-(methoxy-carbonyl)-ethyl; 1-(tert-butylamino-carbonyl)-1-methyl-ethyl; 1-(2,2,2-trifluoroethyllamino-carbonyl)-1-methyl-ethyl; 1-(ethylamino-carbonyl)-1-methyl-ethyl; 1-(cyclopropylmethylamino-carbonyl)-1-methyl-ethyl; 1-(ethylamino-carbonyl)-cyclobutyl; 1-(isopropylamino-carbonyl)-1-methyl-ethyl; 1-cyano-cyclobutyl; 2-methoxy-1-methyl-ethyl; 1-methyl-1-(methoxy-carbonyl)-ethyl; 2-methoxy-2-methyl-propan-1-yl; 1-(oxetan-3-yl)-pyrrolidin-3-yl; isopropylsulfonyl; butane-2-sulfonyl; 1-(2-fluoroethyl)-piperidin-4-yl; 3-fluoro-1-methyl-piperidin-4-yl; 1-ethyl-3-fluoro-piperidin-4-yl; pyridin-3-ylmethyl; 6-methyl-pyridin-2-ylmethyl; 2-(morpholin-1-yl)-1,1,dimethyl-ethyl; pyrimdin-2-yl-methyl; 3-fluoro-1-(oxetan-3-yl)-piperidin-4-yl; 1-(oxetan-3-yl)-piperidin-3-yl; 1-([1,3]Dioxolan-2-ylmethyl)-piperidin-4-yl; pyridazin-3-ylmethyl; piperidin-3-yl; pyrazin-2-ylmethyl; 2-hydroxy-3-methyl-butan-1-yl; 1-([1,3]Dioxolan-2-ylmethyl)-pyrrolidin-3-yl; pyrimidin-4-ylmethyl; 1-methyl-1H-pyrazol-3-ylmethyl; 1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl; 1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl; 3-fluoro-piperidin-4-yl; 2-hydroxy-cyclopentyl; dimethyl-[1,3]dioxan-5-yl, 2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl; 2-(4-

methyl-4H-1,2,4-triazol-3-yl)propan-2-yl; 2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-5-yl; 2-(4H-1,2,4-triazol-3-yl)propan-2-yl; or 1-methyl-1H-pyrazole-4-yl.

In certain embodiments of formula I or formula II, R^3 is: methyl; ethyl; propyl; isopropyl; butyl; cyclopropyl; cyclopropylmethyl; cyclobutyl; methanesulfonyl; ethylsulfonyl; cyclopropylsulfonyl; sec-butylsulfonyl; morpholin-4-yl-ethyl; oxetan-3-yl; 2-methoxyethyl; 2-hydroxy-2-methyl-propyl; 3-hydroxy-2-methyl-propan-2-yl; 2-methoxy-propyl; tetrahydro-2H-pyran-4-yl; tetrahydrofuran-3-yl; 2,6-dimethyltetrahydro-2H-pyran-4-yl; tetrahydro-2H-pyran-3-yl); phenyl; 4-(methylsulfonyl)phenyl); 4-cyano-phenyl; 4-fluoro-phenyl; 4-chloro-phenyl; 3,5-difluorophenyl; 4-(dimethylamino-carbonyl)-phenyl); 4-(cyclopropylsulfonyl)phenyl; 2,2,2-trifluoroethyl; 2-fluoroethyl; difluoromethyl; 2-dimethyl-1,3-dioxan-5-yl; 1-methyl-cyclopropyl-carbonyl; 3-methylpyridin-4-yl; 2-methylpyridin-4-yl; pyridin-2-yl; pyrimidin-2-yl; pyrimidin-5-yl; pyridin-2-ylmethyl; 1-(pyridin-2-yl)ethyl; cyclopropylsulfonyl; 1-cyano-1-methyl-ethyl (also called 2-cyano-propan-2-yl); 2-cyano-ethyl; 1-cyano-ethyl; 2-cyano-2-methyl-propyl; 1-(2,2,2-trifluoroethyl)piperidin-4-yl; 1-(methylsulfonyl)azetidin-3-yl; (3-methyloxetan-3-yl)methyl; (1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl; 1-(oxetan-3-yl)piperidin-4-yl; 1-acetyl-piperidin-4-yl; 1-(cyclopropyl-carbonyl)-piperidin-4-yl; 1-methyl-piperidin-4-yl; 1-methyl-2-oxo-piperidin-5-yl; 2-oxo-piperidin-5-yl; 1-(isopropyl-carbonyl)-piperidin-4-yl; 1-(oxetan-3-yl)azetidin-3-yl; 1-(cyclopropyl-carbonyl)-piperidin-4-yl; 2-methoxycyclopentyl; 3-methoxycyclopentyl; 1-methoxy-2-methylpropan-2-yl; tetrahydro-2H-1,1-dioxo-thiopyran-4-yl; 3-fluoro-1-(oxetan-3-yl)piperidin-4-yl; 1-methoxypropan-2-yl; 1-(2,2,2-trifluoroethyl)azetidin-3-yl); 1-(oxetan-3-yl)pyrrolidin-3-yl; 1-isopropylazetidin-3-yl; 3-fluoro-1-methylpiperidin-4-yl; 1-ethyl-3-fluoropiperidin-4-yl; 1-methylpyrrolidin-3-yl; 2-methoxyethyl)piperidin-4-yl); 1-methyl-1-(methylamino-carbonyl)-ethyl; 2-methyl-2-morpholino-propyl; 4,4-difluorocyclohexyl; morpholin-4-yl-carbonyl; dimethylamino-carbonyl-methyl; methylamino-carbonyl-methyl; 1-methyl-1-(dimethylamino-carbonyl)-ethyl; pyrrolidin-1-yl-carbonyl; 1-cyano-cyclopropyl; 1-(pyrrolidin-1-yl-carbonyl)-ethyl; 1-(dimethylamino-carbonyl)-ethyl; 1-(methoxy-carbonyl)-ethyl; 1-(tert-butylamino-carbonyl)-1-methyl-ethyl; 1-(2,2,2-trifluoroethyllamino-carbonyl)-1-methyl-ethyl; 1-(ethylamino-carbonyl)-1-methyl-ethyl; 1-(cyclopropylmethylamino-carbonyl)-1-methyl-ethyl; 1-(ethylamino-carbonyl)-cyclobutyl; 1-(isopropylamino-carbonyl)-1-methyl-ethyl; 1-cyano-cyclobutyl; 2-methoxy-1-methyl-ethyl; 1-methyl-1-(methoxy-carbonyl)-ethyl; 2-methoxy-2-methyl-propan-1-yl; 1-(oxetan-3-yl)-pyrrolidin-3-yl; isopropylsulfonyl; butane-2-sulfonyl; 1-(2-fluoroethyl)-piperidin-4-yl; 3-fluoro-1-methyl-piperidin-4-yl; 1-ethyl-3-fluoro-piperidin-4-yl; pyridin-3-ylmethyl; 6-methyl-pyridin-2-ylmethyl; 2-(morpholin-1-yl)-1,1,dimethyl-ethyl; pyrimdin-2-yl-methyl; 3-fluoro-1-(oxetan-3-yl)-piperidin-4-yl; 1-(oxetan-3-yl)-piperidin-3-yl; 1-([1,3]Dioxolan-2-ylmethyl)-piperidin-4-yl; pyridazin-3-ylmethyl; piperidin-3-yl; pyrazin-2-ylmethyl; 2-hydroxy-3-methyl-butan-1-yl; 1-([1,3]Dioxolan-2-ylmethyl)-pyrrolidin-3-yl; pyrimidin-4-ylmethyl; 1-methyl-1H-pyrazol-3-ylmethyl; 1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl; 1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl; 3-fluoro-piperidin-4-yl; 2-hydroxy-

cyclopentyl; dimethyl-[1,3]dioxan-5-yl; 2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl; 2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl; 2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-5-yl; 2-(4H-1,2,4-triazol-3-yl)propan-2-yl; or 1-methyl-1H-pyrazole-4-yl.

In certain embodiments of formula I or formula II, R^3 is: hydrogen; methyl; ethyl; n-propyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; 2-hydroxy-2-methyl-propan-1-yl; tetrahydropyran-4-yl; or morpholin-4-yl-carbonyl.

In certain embodiments of formula I or formula II, R^3 is: methyl; ethyl; n-propyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; 2-hydroxy-2-methyl-propan-1-yl; or tetrahydropyran-4-yl.

In certain embodiments of formula I or formula II, R^3 is: methyl; ethyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; or 2-hydroxy-2-methyl-propan-1-yl.

In certain embodiments of formula I or formula II, R^3 is: methyl; ethyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; or 2-hydroxy-2-methyl-propan-1-yl.

In certain embodiments of formula I or formula II, R^3 is: methyl; ethyl; or isopropyl.

In certain embodiments of formula I or formula II, R^3 is hydrogen.

In certain embodiments of formula I or formula II, R^3 is methyl.

In certain embodiments of formula I or formula II, R^3 is ethyl.

In certain embodiments of formula I or formula II, R^3 is n-propyl.

In certain embodiments of formula I or formula II, R^3 is isopropyl.

In certain embodiments of formula I or formula II, R^3 is 2-methoxy-ethyl.

In certain embodiments of formula I or formula II, R^3 is oxetan-3-yl.

In certain embodiments of formula I or formula II, R^3 is 2-hydroxy-2-methyl-propan-1-yl.

In certain embodiments of formula I or formula II, R^3 is tetrahydropyran-4-yl.

In certain embodiments of formula I or formula II, R^3 is morpholin-4-yl-carbonyl.

In certain embodiments of formula I or formula II, R^3 is butyl.

In certain embodiments of formula I or formula II, R^3 is cyclopropyl.

In certain embodiments of formula I or formula II, R^3 is cyclopropylmethyl.

In certain embodiments of formula I or formula II, R^3 is cyclobutyl.

In certain embodiments of formula I or formula II, R^3 is methanesulfonyl.

In certain embodiments of formula I or formula II, R^3 is ethylsulfonyl.

In certain embodiments of formula I or formula II, R^3 is cyclopropylsulfonyl.

In certain embodiments of formula I or formula II, R^3 is sec-butylsulfonyl.

In certain embodiments of formula I or formula II, R^3 is morpholin-4-yl-ethyl.

In certain embodiments of formula I or formula II, R^3 is 2-hydroxy-2-methyl-propyl.

In certain embodiments of formula I or formula II, R^3 is 3-hydroxy-2-methyl-propan-2-yl.

In certain embodiments of formula I or formula II, R^3 is 2-methoxy-propyl.

In certain embodiments of formula I or formula II, R^3 is tetrahydro-2H-pyran-4-yl.

In certain embodiments of formula I or formula II, R^3 is tetrahydrofuran-3-yl.

In certain embodiments of formula I or formula II, R^3 is 2,6-dimethyltetrahydro-2H-pyran-4-yl.

In certain embodiments of formula I or formula II, R^3 is tetrahydro-2H-pyran-3-yl).

In certain embodiments of formula I or formula II, R^3 is phenyl.

In certain embodiments of formula I or formula II, R^3 is 4-(methylsulfonyl)phenyl).

In certain embodiments of formula I or formula II, R^3 is 4-cyano-phenyl.

In certain embodiments of formula I or formula II, R^3 is 4-fluoro-phenyl.

In certain embodiments of formula Iv, R^3 is 4-chloro-phenyl.

In certain embodiments of formula I or formula II, R^3 is 3,5-difluorophenyl.

In certain embodiments of formula I or formula II, R^3 is 4-(dimethylamino-carbonyl)-phenyl).

In certain embodiments of formula I or formula II, R^3 is 4-(cyclopropylsulfonyl)phenyl.

In certain embodiments of formula I or formula II, R^3 is 2,2,2-trifluoroethyl.

In certain embodiments of formula I or formula II, R^3 is 2-fluoroethyl.

In certain embodiments of formula I or formula II, R^3 is difluoromethyl.

In certain embodiments of formula I or formula II, R^3 is 2-dimethyl-1,3-dioxan-5-yl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-cyclopropyl-carbonyl.

In certain embodiments of formula I or formula II, R^3 is 3-methylpyridin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 2-methylpyridin-4-yl.

In certain embodiments of formula I or formula II, R^3 is pyridin-2-yl.

In certain embodiments of formula I or formula II, R^3 is pyrimidin-2-yl.

In certain embodiments of formula I or formula II, R^3 is pyrimidin-5-yl.

In certain embodiments of formula I or formula II, R^3 is pyridin-2-ylmethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(pyridin-2-yl)ethyl.

In certain embodiments of formula I or formula II, R^3 is cyclopropylsulfonyl.

In certain embodiments of formula I or formula II, R^3 is 1-cyano-1-methyl-ethyl (also called 2-cyano-propan-2-yl).

In certain embodiments of formula I or formula II, R^3 is 2-cyano-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-cyano-ethyl.

In certain embodiments of formula I or formula II, R^3 is 2-cyano-2-methyl-propyl.

In certain embodiments of formula I or formula II, R^3 is 1-(2,2,2-trifluoroethyl)piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(methylsulfonyl)azetidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is (3-methyloxetan-3-yl)methyl.

In certain embodiments of formula I or formula II, R^3 is (1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(oxetan-3-yl)piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-acetyl-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(cyclopropyl-carbonyl)-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-2-oxo-piperidin-5-yl.

In certain embodiments of formula I or formula II, R^3 is 2-oxo-piperidin-5-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(isopropyl-carbonyl)-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(oxetan-3-yl)azetidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(cyclopropyl-carbonyl)-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 2-methoxycyclopentyl.

In certain embodiments of formula I or formula II, R^3 is 3-methoxycyclopentyl.

In certain embodiments of formula I or formula II, R^3 is 1-methoxy-2-methylpropan-2-yl.

In certain embodiments of formula I or formula II, R^3 is tetrahydro-2H-1,1-dioxo-thiopyran-4-yl.

In certain embodiments of formula I or formula II, R^3 is 3-fluoro-1-(oxetan-3-yl)piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-methoxypropan-2-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(2,2,2-trifluoroethyl)azetidin-3-yl).

In certain embodiments of formula I or formula II, R^3 is 1-(oxetan-3-yl)pyrrolidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is 1-isopropylazetidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is 3-fluoro-1-methylpiperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-ethyl-3-fluoropiperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-methylpyrrolidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is 2-methoxyethyl)piperidin-4-yl).

In certain embodiments of formula I or formula II, R^3 is 1-methyl-1-(methylamino-carbonyl)ethyl.

In certain embodiments of formula I or formula II, R^3 is 2-methyl-2-morpholino-propyl.

In certain embodiments of formula I or formula II, R^3 is 4,4-difluorocyclohexyl.

In certain embodiments of formula I or formula II, R^3 is dimethylamino-carbonyl-methyl.

In certain embodiments of formula I or formula II, R^3 is methylamino-carbonyl-methyl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-1-(dimethylamino-carbonyl)-ethyl.

In certain embodiments of formula I or formula II, R^3 is pyrrolidin-1-yl-carbonyl.

In certain embodiments of formula I or formula II, R^3 is 1-cyano-cyclopropyl.

In certain embodiments of formula I or formula II, R^3 is 1-(pyrrolidin-1-yl-carbonyl)-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(dimethylamino-carbonyl)-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(methoxy-carbonyl)-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(tert-butylamino-carbonyl)-1-methyl-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(2,2,2-trifluoroethyllamino-carbonyl)-1-methyl-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(ethylamino-carbonyl)-1-methyl-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(cyclopropylmethylamino-carbonyl)-1-methyl-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-(ethylamino-carbonyl)-cyclobutyl.

In certain embodiments of formula I or formula II, R^3 is 1-(isopropylamino-carbonyl)-1-methyl-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-cyano-cyclobutyl.

In certain embodiments of formula I or formula II, R^3 is dimethyl-[1,3]dioxan-5-yl.

In certain embodiments of formula I or formula II, R^3 is 2-methoxy-2-methyl-propan-1-yl.

In certain embodiments of formula I or formula II, R^3 is 2-methoxy-1-methyl-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-1-(methoxy-carbonyl)-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-oxetan-3-yl-pyrrolidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is isopropylsulfonyl.

In certain embodiments of formula I or formula II, R^3 is butane-2-sulfonyl.

In certain embodiments of formula I or formula II, R^3 is 1-(2-fluoroethyl)-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 3-fluoro-1-methyl-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-ethyl-3-fluoro-piperidin-4-yl.In certain embodiments of formula I or formula II, R^3 is pyridin-3-ylmethyl.

In certain embodiments of formula I or formula II, R^3 is 6-methyl-pyridin-2-ylmethyl.

In certain embodiments of formula I or formula II, R^3 is 2-(morpholin-1-yl)-1,1,dimethyl-ethyl.

In certain embodiments of formula I or formula II, R^3 is pyrimdin-2-yl-methyl.

In certain embodiments of formula I or formula II, R^3 is 3-fluoro-1-(oxetan-3-yl)-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is 1-(oxetan-3-yl)-piperidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is 1-([1,3]Dioxolan-2-ylmethyl)-piperidin-4-yl.

In certain embodiments of formula I or formula II, R^3 is pyridazin-3-ylmethyl.

In certain embodiments of formula I or formula II, R^3 is piperidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is pyrazin-2-ylmethyl.

In certain embodiments of formula I or formula II, R^3 is 2-hydroxy-3-methyl-butan-1-yl.

In certain embodiments of formula I or formula II, R^3 is 1-([1,3]dioxolan-2-ylmethyl)-pyrrolidin-3-yl.

In certain embodiments of formula I or formula II, R^3 is pyrimidin-4-ylmethyl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-1H-pyrazol-3-ylmethyl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl.

In certain embodiments of formula I or formula II, R^3 is 3-fluoro-piperidin-4-yl; 2-hydroxy-cyclopentyl.

In certain embodiments of formula I or formula II, R^3 is 2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl.

In certain embodiments of formula I or formula II, R^3 is 2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl.

In certain embodiments of formula I or formula II, R^3 is 2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl.

In certain embodiments of formula I or formula II, R^3 is 2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl.

In certain embodiments of formula I or formula II, R^3 is 2-(1-methyl-1H-pyrazol-5-yl.

In certain embodiments of formula I or formula II, R^3 is 2-(4H-1,2,4-triazol-3-yl)propan-2-yl.

In certain embodiments of formula I or formula II, R^3 is 1-methyl-1H-pyrazole-4-yl.

In embodiments of formula I or formula II wherein R^3 is aryl, such aryl may be unsubstituted phenyl or phenyl substituted one or more times with R^8, or in certain embodiments, once, twice or three times with a group or groups independently selected from C_{1-6}alkyl, halo, halo-C_{1-6}alkyl, C_{1-6}alkoxy, hydroxy or cyano.

In embodiments of formula I or formula II wherein R^3 is heteroaryl or heteroaryl-C_{1-6}alkyl, such heteroaryl moiety may be pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, isoxazolyl, isothiazolyl, triazolyl, oxadiaolyl, thiadiazolyl or tetrazolyl, each being unsubstituted or substituted once or twice with R^8, or in certain embodiments, substituted once or twice with C_{1-6}alkyl.

In embodiments of formula I or formula II wherein R^3 is heteroaryl or heteroaryl-C_{1-6}alkyl, such heteroaryl moiety may be pyrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl or oxadiaolyl each being unsubstituted or substituted once or twice with R^8, or in certain embodiments, substituted once or twice with C_{1-6}alkyl.

In embodiments of formula I or formula II wherein R^3 is heteroaryl or heteroaryl-C_{1-6}alkyl, such heteroaryl moiety may be pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl,

pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl, each being unsubstituted or substituted one or more times with R^8.

In embodiments of formula I or formula II wherein R^3 is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R^7.

In embodiments of formula I or formula II wherein R^3 is heterocyclyl-C_{1-6}alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R^7.

In certain embodiments of formula I or formula II, R^3 is -Y-C(O)-R^d.

In certain embodiments of formula I or formula II, Y is a bond.

In certain embodiments of formula I or formula II, Y is C_{2-6}alkylene.

In certain embodiments of formula I or formula II, Y is isopropylidine.

In certain embodiments of formula I or formula II, Y is methylene.

In certain embodiments of formula I or formula II, Y is ethylene.

In certain embodiments of formula I or formula II, Y is -$C(CH_3)_2$-.

In certain embodiments of formula I or formula II, Y is -CH_2-.

In certain embodiments of formula I or formula II, Y is -$CH(CH_3)$-.

In certain embodiments of formula I or formula II, Y is -CH_2-$C(CH_3)_2$-.

In certain embodiments of formula I or formula II, Y is -$C(CH_3)_2$-CH_2-.

In certain embodiments of formula I or formula II, R^d is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^d is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^d is C_{1-6}alkoxy.

In certain embodiments of formula I or formula II, R^d is amino.

In certain embodiments of formula I or formula II, R^d is halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^d is hydroxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^d is C_{1-6}alkoxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^d is cyano-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^d is C_{1-6}alkylsulfonylC_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^d is amino-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^d is C_{3-6}cycloalkyl optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^d is C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^d is heterocyclyl optionally substituted one or more times with R^7.

In certain embodiments of formula I or formula II, R^d is heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7.

In certain embodiments of formula I or formula II, R^d is 1-methyl-cyclopropyl; methylamino; dimethylamino; pyrrolidin-1-yl; methoxy; cyclopropyl-methyl; ethyl; 2,2,2-trifluoro-ethyl; tert-butyl; or isopropyl.

In certain embodiments of formula I or formula II, R^d is 1-methyl-cyclopropyl.

In certain embodiments of formula I or formula II, R^d is methylamino.

In certain embodiments of formula I or formula II, R^d is dimethylamino.

In certain embodiments of formula I or formula II, R^d is pyrrolidin-1-yl.

In certain embodiments of formula I or formula II, R^d is methoxy.

In certain embodiments of formula I or formula II, R^d is cyclopropyl-methyl.

In certain embodiments of formula I or formula II, R^d is ethyl.

In certain embodiments of formula I or formula II, R^d is 2,2,2-trifluoro-ethyl.

In certain embodiments of formula I or formula II, R^d is tert-butyl.

In certain embodiments of formula I or formula II, R^d is isopropyl.

In embodiments of formula I or formula II wherein R^d is heterocyclyl or heterocyclyl-C_{1-6}alkyl, such heterocyclyl may be piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, pyrrolidinyl, azetidinyl, tetrahydrofuranyl or oxetanyl, each optionally substituted one or more times, or one or two times, with R^7 as defined herein.

In embodiments of formula I or formula II wherein R^d is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R^7.

In embodiments of formula I or formula II wherein R^d is heterocyclyl-C_{1-6}alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R^7.

In certain embodiments of formula I or formula II, R^4 is: hydrogen; C_{1-6}alkyl; halo; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^4 is: C_{1-6}alkyl; halo; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^4 is: hydrogen; C_{1-6}alkyl; halo; C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^4 is: hydrogen; C_{1-6}alkyl; halo; or C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is hydrogen or C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is hydrogen.

In certain embodiments of formula I or formula II, R^4 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is halo.

In certain embodiments of formula I or formula II, R^4 is cyano.

In certain embodiments of formula I or formula II, R^4 is halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is C_{1-6}alkoxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is hydroxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is hydrogen or methyl.

In certain embodiments of formula I or formula II, R^4 is C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^4 is -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl.

In certain embodiments of formula I or formula II, R^4 is -C(O)-R^c wherein R^c is heterocyclyl.

In embodiments of formula I or formula II wherein R^c is heterocyclyl, such heterocyclyl may be pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl.

In embodiments of formula I or formula II wherein R^c is heterocyclyl, such heterocyclyl may be piperidinyl, piperazinyl or morpholinyl.

In certain embodiments of formula I or formula II, R^4 is: hydrogen; methyl; isopropyl; cyclopropyl; chloro; or morpholin-4-yl-carbonyl.

In certain embodiments of formula I or formula II, R^4 is: hydrogen; methyl; isopropyl; cyclopropyl; or chloro.

In certain embodiments of formula I or formula II, R^4 is hydrogen.

In certain embodiments of formula I or formula II, R^4 is methyl.

In certain embodiments of formula I or formula II, R^4 is isopropyl.

In certain embodiments of formula I or formula II, R^4 is cyclopropyl.

In certain embodiments of formula I or formula II, R^4 is chloro.

In certain embodiments of formula I or formula II, R^4 is morpholin-4-yl-carbonyl.

In certain embodiments of formula I or formula II, R^4 is 2-fluoro-ethyl.

In certain embodiments of formula I or formula II, R^4 is C_{3-6}cycloalkyl optionally substituted one or more times, or one or two times, with R^6.

In certain embodiments of formula I or formula II, R^4 is C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times, or one or two times, with R^6.

In certain embodiments of formula I or formula II, R^4 is-Y-C(O)-R^d.

In certain embodiments of formula I or formula II, or R^3 and R^4 together with the atoms to which they are attached may form a 5- or 6-membered ring that optionally includes a heteroatom selected from O, N and S.

In certain embodiments of formula I or formula II, R^5 is hydrogen.

In certain embodiments of formula I or formula II, R^5 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^5 is methyl.

In certain embodiments of formula I or formula II, each R^6 is independently C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy; cyano; or halo.

In certain embodiments of formula I or formula II, R^6 is C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy; or halo.

In certain embodiments of formula I or formula II, R^6 is C_{1-6}alkyl; halo-C_{1-6}alkyl; or halo.

In certain embodiments of formula I or formula II, R^6 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^6 is halo-C_{1-6}alkyl.In certain embodiments of formula I or formula II, R^6 is C_{1-6}alkoxy.

In certain embodiments of formula I or formula II, R^6 is cyano.

In certain embodiments of formula I or formula II, R^6 is halo.

In certain embodiments of formula I or formula II, R^6 is Y-C(O)-R^d.

In certain embodiments of formula I or formula II, R^6 is oxo.

In certain embodiments of formula I or formula II, each R^7 is independently C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; C_{1-6}alkylsulfonyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; heterocyclyl; or C_{3-6}cycloalkylsulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^7 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^7 is halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^7 is halo.

In certain embodiments of formula I or formula II, R^7 is C_{1-6}alkylsulfonyl.

In certain embodiments of formula I or formula II, R^7 is C_{1-6}alkoxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^7 is cyano.

In certain embodiments of formula I or formula II, R^7 is -Y-C(O)-R^d.

In certain embodiments of formula I or formula II, R^7 is heterocyclyl.

In certain embodiments of formula I or formula II, R^7 is C_{3-6}cycloalkylsulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^7 is oxo.

In certain embodiments of formula I or formula II, R^7 is C_{1-6}alkoxy.

In certain embodiments of formula I or formula II, R^7 is heterocyclyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^7 is C_{3-6}cycloalkyl.

In certain embodiments of formula I or formula II, R^7 is C_{3-6}cycloalkyl-C_{1-6}alkyl.

In embodiments of formula I or formula II wherein R^7 is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl.

In embodiments of formula I or formula II wherein R^7 is heterocyclyl-C_{1-6}alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl.

In certain embodiments of formula I or formula II, each R^8 is independently oxo; C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; C_{1-6}alkoxy; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; C_{3-6}cycloalkyl optionally substituted one or more times with R^6, C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl

portion is optionally substituted one or more times with R^6, or C_{3-6}cycloalkyl-sulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^8 is oxo.In certain embodiments of formula I or formula II, R^7 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^7 is halo-C_{1-6}alkyl

In certain embodiments of formula I or formula II, R^7 is halo.

In certain embodiments of formula I or formula II, R^7 is C_{1-6}alkoxy.

In certain embodiments of formula I or formula II, R^7 is C_{1-6}alkoxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^7 is cyano.

In certain embodiments of formula I or formula II, R^7 is heterocyclyl.

In certain embodiments of formula I or formula II, R^7 is -Y-C(O)-R^d.

In certain embodiments of formula I or formula II, R^7 is C_{3-6}cycloalkyl optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^7 is C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^7 is C_{3-6}cycloalkyl-sulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6.

In certain embodiments of formula I or formula II, R^8 is oxo.

In certain embodiments of formula I or formula II, R^8 is C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^8 is halo-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^8 is halo.

In certain embodiments of formula I or formula II, R^8 is C_{1-6}alkyl-sulfonyl.

In certain embodiments of formula I or formula II, R^8 is C_{1-6}alkoxy.

In certain embodiments of formula I or formula II, R^8 is C_{1-6}alkoxy-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^8 is cyano; heterocylyl.

In certain embodiments of formula I or formula II, R^8 is heterocyclyl-C_{1-6}alkyl.

In certain embodiments of formula I or formula II, R^8 is -Y-C(O)-R^d.

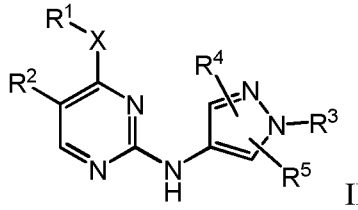
In certain embodiments of formula I or formula II, R^8 is C_{3-6}cycloalkyl.

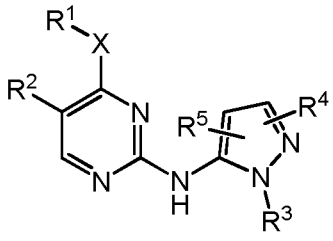
In certain embodiments of formula I or formula II, R^8 is C_{3-6}cycloalkyl-C_{1-6}alkyl, C_{3-6}cycloalkyl-sulfonyl.

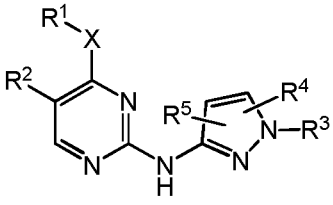
In embodiments of formula I or formula II wherein R^8 is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl.

In embodiments of formula I or formula II wherein R^8 is heterocyclyl-C_{1-6}alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidinyl, [1,3]dioxolanyl or tetrahydrothiopyranyl.

In certain embodiments of the invention, compounds of formulas III, IV and V are provided:


III;


IV;


V;

wherein X, R^1, R, R^2, R^3, R^4 and R^5 are as defined herein.

In certain embodiments of the invention, the subject compounds are of formula III.

In certain embodiments of the invention, the subject compounds are of formula IV.

In certain embodiments of the invention, the subject compounds are of formula V.

Where any of R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8 R^a, R^b, R^c and R^d is alkyl or contains an alkyl moiety, such alkyl can be lower alkyl, i.e. C_1-C_6alkyl, and in many embodiments may be C_1-C_4alkyl.

In a certain embodiment, the invention relates to the compound as described herein, which is selected from the group consisting of

N^2-(1-isopropyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1,5-dimethyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N^2-(1-isopropyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1,3-dimethyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amine,

N^4-methyl-5-(trifluoromethyl)-N^2-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-isopropyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amine,

5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(pyrrolidin-1-yl)-5-(trifluoromethyl)pyrimidin-2-amine,

N^2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1,3-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

N^4-methyl-N^2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(5-chloro-1-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-4-methoxy-N-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-Chloro-4-methoxy-N-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-chloro-4-methoxy-N-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-Chloro-N-(5-chloro-1-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,

2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-chloro-pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,

N^2-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^4-methyl-N^2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N^2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^2-(1,3-dimethyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

5-Chloro-N^2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

N^4-methyl-N^2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(2-Ethyl-2H-pyrazol-3-yl)-5-fluoro-N^4-methyl-pyrimidine-2,4-diamine,

5-Fluoro-N^4-methyl-N^2-(2-methyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,

5-Fluoro-N^4-methyl-N^4-(2-propyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,

N^2-(2,5-Dimethyl-2H-pyrazol-3-yl)-5-fluoro-N^4-methyl-pyrimidine-2,4-diamine,

N^2-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,

N^2-(3-Cyclopropyl-1-methyl-1H-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^2-(5-isopropyl-2-methyl-2H-pyrazol-3-yl)-N^4-methyl-pyrimidine-2,4-diamine,

5-Chloro-4-methoxy-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-Chloro-N^4-methyl-N^2-(1,3,5-trimethyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine,

5-Chloro-N^2-(5-cyclopropyl-2-methyl-2H-pyrazol-3-yl)-N^4-methyl-pyrimidine-2,4-diamine,

N^4-Methyl-N^2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N^2-(1-isopropyl-1H-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

N^2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N^2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

5-chloro-N^2-(1-isopropyl-1H-pyrazol-5-yl)-N^4-methylpyrimidine-2,4-diamine,

5-chloro-N-(1-isopropyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,

5-chloro-4-methoxy-N-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

N^2-(1-ethyl-1H-pyrazol-3-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-4-methoxy-N-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

N^2-(1-isopropyl-1H-pyrazol-3-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-4-methoxy-N-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

N^4-ethyl-N^2-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(oxetan-3-yloxy)pyrimidin-2-amine,

5-chloro-4-(2,2-difluoroethoxy)-N-(1,5-dimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(2,2,2-trifluoroethoxy)pyrimidin-2-amine,

5-chloro-4-methoxy-N-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

(4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone,

(4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone,

4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)benzonitrile,

5-chloro-4-methoxy-N-(3-methyl-1-(3-methylpyridin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-chloro-N-(1-(cyclopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-chloro-N-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

2-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

5-chloro-4-ethoxy-N-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine,

(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine,

(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(5-methyl-1-phenyl-1H-pyrazol-4-yl)-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-(1-methanesulfonyl-3-methyl-1H-pyrazol-4-yl)-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-methyl-1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine,

4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide,

4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide,

4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-benzonitrile,

N^2-(5-Methoxy-1-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-chloro-1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoro-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-amine,

N^2-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl]-N^4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N^2-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-N^4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

N^2-(1,3-Dimethyl-1H-pyrazol-4-yl)-5-iodo-N^4-methyl-pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(1-methyl-1H-pyrazol-5-yl)pyrimidine-2,4-diamine,

2-methyl-1-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,

5-chloro-N4-methyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N2-(1-(difluoromethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(difluoromethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-ethyl-N2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N2-(1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(1-methyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(methylsulfonyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-propyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-chloro-N4-methyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N2-(1-(3,5-difluorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

5-bromo-N2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

5-bromo-N2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

N2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-((1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-butyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyrimidin-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-fluoroethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-fluoroethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone,

cyclopropyl(4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

cyclopropyl(4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone,

N2-(5-chloro-1-isopropyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-ethyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyrimidin-5-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(4-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-cyclopropyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitrile,

4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitrile,

N4-methyl-N2-(3-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one,

5-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one,

5-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-one,

5-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-one,

N2-(1-isopropyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N,N-dimethyl-4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide,

4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamide,

N4-ethyl-N2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(4-(cyclopropylsulfonyl)phenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)benzonitrile,

N4-ethyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N,N-dimethyl-4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide,

N2-(1-(cyclopropylmethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(4-(cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N4-(2,2-difluoroethyl)-N2-(1,5-dimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-chloro-4-methyl-N-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

N2-(1-(4-(cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-methyl-1-(4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)propan-1-one,

N4-ethyl-N2-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)-2-methylpropan-1-one,

N4-ethyl-N2-(3-methyl-1-(1-(oxetan-3-yl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

N4-ethyl-N2-(1-ethyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(S)-N2-(1-(2-methoxypropyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(S)-N2-(1-(2-methoxypropyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-methoxy-2-methylpropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2,6-dimethyltetrahydro-2H-pyran-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N2-(1-(2-methoxypropyl)-5-methyl-1H-pyrazol -4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N2-(1-(3-methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(1-methyl-5-(methylamino)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(tetrahydro-2H-1,1-dioxo-thiopyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

2-methyl-1-(4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-(trifluoromethyl)-1H-pyrazol-1-yl)propan-2-ol,

2-methyl-1-(4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-(trifluoromethyl)-1H-pyrazol-1-yl)propan-2-ol,

N2-(1-(3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N2-(1-(1-methoxypropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(3-tert-butyl-4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-methoxy-2-methylpropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(3-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

(R)-N2-(1-(1-methoxypropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(4-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(5-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-isopropylazetidin-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazole-5-carbonitrile,

N4-ethyl-N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(isopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(sec-butylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(sec-butylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-isopropyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

N2-(1-(3-fluoro-1-methylpiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(3-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(3-cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-((tetrahydro-2H-pyran-4-yl) methyl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(5-chloro-4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

1-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

1-(3-cyclopropyl-4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N,2-dimethylpropanamide,

N2-(1-(1-(2-methoxyethyl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-(2-methoxyethyl)piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(5-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(3-fluoro-1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(1-ethyl-3-fluoropiperidin-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(1-(ethylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-methyl-2-morpholinopropyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-ethyl-3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-(dimethylamino)-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-1-ol,

N^2-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propan-2-ol,

N2-[1-(2-Methoxy-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(2-Methoxy-ethyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[3-methyl-1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1-difluoromethyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1-difluoromethyl-3-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-ethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-[1-(4-fluoro-phenyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-pyrimidine-2,4-diamine,

5-Bromo-N4-methyl-N2-(5-methyl-1-propyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine,

5-Bromo-N2-[1-(4-chloro-phenyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-pyrimidine-2,4-diamine,

N2-(1,5-Dimethyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-2-one,

4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide,

N2-[1-(4-Cyclopropanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-benzonitrile,

N4-Ethyl-N2-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

1-{4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-piperidin-1-yl}-2-methyl-propan-1-one,

1-{4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-1-yl}-2-methyl-propan-1-one,

N4-Methyl-N2-[3-methyl-1-(3-methyl-pyridin-4-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-((R)-2-Methoxy-propyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(2,6-Dimethyl-tetrahydro-pyran-4-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1,1-Dioxo-hexahydro-1$l%6&-thiopyran-4-yl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-((R)-2-Methoxy-1-methyl-ethyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-((S)-2-Methoxy-1-methyl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[3-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[5-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1-Isopropyl-azetidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[5-methyl-1-(propane-2-sulfonyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(5-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(3-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-{1-[1-(2-methoxy-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-{1-[1-(2-methoxy-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-{1-[1-(2-Fluoro-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-{1-[1-(2-Fluoro-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[5-Chloro-1-(3-fluoro-1-methyl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(1-Ethanesulfonyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[5-methyl-1-(2-methyl-2-morpholin-4-yl-propyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(1-Cyclopropanesulfonyl-3-cyclopropyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoro-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-amine,

N4-Methyl-N2-[3-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[1-(2-methoxy-ethyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[1-(2-methoxy-ethyl)-5-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

1-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-2-methyl-propan-2-ol,

1-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propan-2-ol,

N2-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Cyclopropyl-N2-(1-methanesulfonyl-3-methyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Cyclopropyl-N2-(1-methanesulfonyl-5-methyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

1-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2-methyl-propan-2-ol,

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

N4-Methyl-N2-(3-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[5-Chloro-1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[5-Chloro-1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[5-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[3-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[5-methyl-1-((S)-1-methyl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[3-methyl-1-((S)-1-methyl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-[5-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile,

N4-Methyl-N2-[5-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-[5-Chloro-4-(4-ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile,

N4-Ethyl-N2-[1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-Methyl-1-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-butan-2-ol,

3-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-butan-2-ol,

N2-[1-(1-[1,3]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[5-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[3-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile,

N4-Ethyl-N2-{3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1-[1,3]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(5-Fluoromethyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-{3-methyl-1-[1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-{3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[1-(3-fluoro-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol,

2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol,

N4-ethyl-N2-(3-methyl-1-(2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N2-(1',5-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1',3-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-(4H-1,2,4-triazol-3-yl)propan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1,3-Dimethyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidine-5-carbonitrile,

2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-isopropyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-ethyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(ethylamino)pyrimidine-5-carbonitrile,

2-(1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(difluoromethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-propyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

4-(ethylamino)-2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

4-(ethylamino)-2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

4-(ethylamino)-2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

2-(1-isopropyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile,

2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethylamino)pyrimidine-5-carbonitrile,

2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile,

4-(2,2-difluoroethylamino)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethoxy)pyrimidine-5-carbonitrile,

2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile,

2-(1-(4,4-difluorocyclohexyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile,

2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethylamino)pyrimidine-5-carbonitrile,

2-(5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile,

2-(1-Difluoromethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidine-5-carbonitrile,

2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-ethylamino-pyrimidine-5-carbonitrile,

2-[1-(4-Fluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,

4-Methylamino-2-(3-methyl-1-propyl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

4-Methylamino-2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

4-Methylamino-2-(3-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

2-[1-(3,5-Difluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,

4-(2,2-Difluoro-ethoxy)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

2-[1-(4,4-Difluoro-cyclohexyl)-3-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,

(5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)(morpholino)methanone,

2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N,N-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N,N,2-trimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,

(R)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

(R)-N,N-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

(S)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

3-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

3-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

methyl 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate,

methyl 2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate,

2-(3-ethyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile,

(R)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

(R)-N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

(S)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

(S)-N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

(S)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

(S)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

2-(4-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2,2-dimethyl-3-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

2,2-dimethyl-3-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,

N-tert-butyl-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-(2,2,2-trifluoroethyl)propanamide,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-ethyl-2-methyl propanamide,

N-(cyclopropylmethyl)-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

N-(cyclopropylmethyl)-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

N-ethyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarboxamide,

N-isopropyl-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarbonitrile,

2-(4-(4-(cyclopropylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

N,2-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,

2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester,

2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester,

(S)-N,N-Dimethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionamide,

R)-2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile,

2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-cyclopropyl-pyrazol-1-yl]-2-methyl-propionitrile,

(R)-2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile,

N-Ethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

N-Ethyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarboxylic acid ethylamide,

2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-N-(2,2,2-trifluoro-ethyl)-isobutyramide,

N-Isopropyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

N-Methyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarbonitrile,

N-tert-Butyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

2-[4-(4-Cyclopropylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

2-[4-(4-Cyclopropylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propionitrile,

2-(3-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile, and

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

or a pharmaceutically acceptable salt thereof.

In a certain embodiment, the invention relates to the compound as described herein for use as medicament.

In a certain embodiment, the invention relates to the compound as described herein for use in the therapeutic and/or prophylactic treatment of Parkinson's disease.

In a certain embodiment, the invention relates to the use of a compound as described herein for the preparation of medicaments for the therapeutic and/or prophylactic treatment of Parkinson's disease.

In a certain embodiment, the invention relates to a composition comprising:

(a) a pharmaceutically acceptable carrier; and

(b) a compound as described herein.

In a certain embodiment, the invention relates to a method for treating Parkinson's disease, said method comprising administering to a subject in need thereof an effective amount of a compound as described herein.

The invention also provides a method for treating a disease or condition mediated by or otherwise associated with the LRRK2 receptor, the method comprising administering to a subject in need thereof an effective amount of a compound of the invention.

The disease may be a neurodegenerative disease such as Parkinson's disease, Huntington's disease or Lewie body dementia.

The disease may be a CNS disorder such as Alzheimer's disease or L-Dopa induced dyskinesia.

The disease may be a cancer or proliferative disorder such as kidney, breast, prostate, blood, papillary or lung cancer, acute myelogenous leukemia, or multiple myeloma.

The disease may be an inflammatory disease such as leprosy, Crohn's disease, amyotrophic lateral sclerosis, rheumatoid arthritis, or ankylosing spondylytis.

The invention also provides a method for enhancing cognitive memory, the method comprising administering to a subject in need thereof an effective amount of a compound of the invention.

Representative compounds in accordance with the methods of the invention are shown in the experimental examples below.

Synthesis

Compounds of the present invention can be made by a variety of methods depicted in the illustrative synthetic reaction schemes shown and described below.

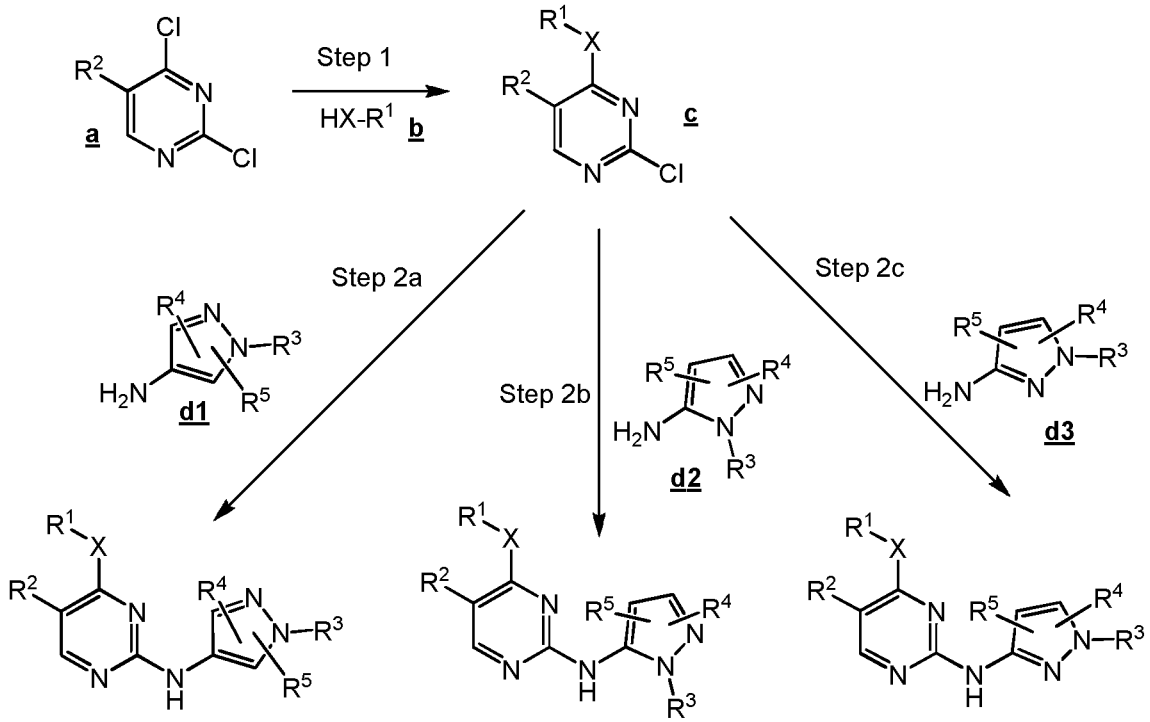
The starting materials and reagents used in preparing these compounds generally are either available from commercial suppliers, such as Aldrich Chemical Co., or are prepared by methods known to those skilled in the art following procedures set forth in references such as *Fieser and Fieser's Reagents for Organic Synthesis*; Wiley & Sons: New York, **1991**, Volumes 1-15; *Rodd's Chemistry of Carbon Compounds*, Elsevier Science Publishers, 1989, Volumes 1-5

and Supplementals; and *Organic Reactions*, Wiley & Sons: New York, **1991**, Volumes 1-40. The following synthetic reaction schemes are merely illustrative of some methods by which the compounds of the present invention can be synthesized, and various modifications to these synthetic reaction schemes can be made and will be suggested to one skilled in the art having referred to the disclosure contained in this Application.

The starting materials and the intermediates of the synthetic reaction schemes can be isolated and purified if desired using conventional techniques, including but not limited to, filtration, distillation, crystallization, chromatography, and the like. Such materials can be characterized using conventional means, including physical constants and spectral data.

Unless specified to the contrary, the reactions described herein may be conducted under an inert atmosphere at atmospheric pressure at a reaction temperature range of from about -78 °C to about 150 °C, for example, from about 0 °C to about 125 °C, or conveniently at about room (or ambient) temperature, e.g., about 20 °C.

Scheme A below illustrates one synthetic procedure usable to prepare specific compounds of formula I, wherein X, R^1, R^2, R^3, R^4 and R^5 are as defined herein.



SCHEME A

In step 1 of Scheme A, dichloropyrimidine compound a is reacted with reagent b to afford pyrimidine compound c. The reaction of step 1 may take place under polar solvent conditions. In embodiments of the invention where X is -O- (reagent b is an alcohol), the reaction of step 1 may be carried out in the presence of base.

Following step 1, one of steps 2a, 2b and 2c is carried out. In step 2a, pyrimidine compound c undergoes reaction with 4-amino-pyrazole compound d1 to provide an

aminopyrimidine compound of formula III. In step 2b, pyrimidine compound c is reacted with 5-amino-pyrazole compound d2 to afford an aminopyrimidine compound of formula IV. In step 2c, pyrimidine compound c is treated with 3-amino-pyrazole compound d3 to yield an aminopyrimidine compound of formula V. The reaction of steps 2a-2c may take place in polar protic solvent and in the presence of acid such as HCl.

Many variations on the procedure of Scheme A are possible and will suggest themselves to those skilled in the art. Specific details for producing compounds of the invention are described in the Examples below.

Administration and Pharmaceutical Composition

The invention includes pharmaceutical compositions comprising at least one compound of the present invention, or an individual isomer, racemic or non-racemic mixture of isomers or a pharmaceutically acceptable salt or solvate thereof, together with at least one pharmaceutically acceptable carrier, and optionally other therapeutic and/or prophylactic ingredients.

In general, the compounds of the invention will be administered in a therapeutically effective amount by any of the accepted modes of administration for agents that serve similar utilities. Suitable dosage ranges are typically 1-500 mg daily, for example 1-100 mg daily, and in some embodiments 1-30 mg daily, depending upon numerous factors such as the severity of the disease to be treated, the age and relative health of the subject, the potency of the compound used, the route and form of administration, the indication towards which the administration is directed, and the preferences and experience of the medical practitioner involved. One of ordinary skill in the art of treating such diseases will be able, without undue experimentation and in reliance upon personal knowledge and the disclosure of this Application, to ascertain a therapeutically effective amount of the compounds of the present invention for a given disease.

Compounds of the invention may be administered as pharmaceutical formulations including those suitable for oral (including buccal and sub-lingual), rectal, nasal, topical, pulmonary, vaginal, or parenteral (including intramuscular, intraarterial, intrathecal, subcutaneous and intravenous) administration or in a form suitable for administration by inhalation or insufflation. A particular manner of administration is generally oral using a convenient daily dosage regimen which can be adjusted according to the degree of affliction.

A compound or compounds of the invention, together with one or more conventional adjuvants, carriers, or diluents, may be placed into the form of pharmaceutical compositions and unit dosages. The pharmaceutical compositions and unit dosage forms may be comprised of conventional ingredients in conventional proportions, with or without additional active compounds or principles, and the unit dosage forms may contain any suitable effective amount of the active ingredient commensurate with the intended daily dosage range to be employed. The pharmaceutical compositions may be employed as solids, such as tablets or filled capsules, semisolids, powders, sustained release formulations, or liquids such as solutions, suspensions, emulsions, elixirs, or filled capsules for oral use; or in the form of suppositories for rectal or

vaginal administration; or in the form of sterile injectable solutions for parenteral use. Formulations containing about one (1) milligram of active ingredient or, more broadly, about 0.01 to about one hundred (100) milligrams, per tablet, are accordingly suitable representative unit dosage forms.

The compounds of the invention may be formulated in a wide variety of oral administration dosage forms. The pharmaceutical compositions and dosage forms may comprise a compound or compounds of the present invention or pharmaceutically acceptable salts thereof as the active component. The pharmaceutically acceptable carriers may be either solid or liquid. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. A solid carrier may be one or more substances which may also act as diluents, flavouring agents, solubilizers, lubricants, suspending agents, binders, preservatives, tablet disintegrating agents, or an encapsulating material. In powders, the carrier generally is a finely divided solid which is a mixture with the finely divided active component. In tablets, the active component generally is mixed with the carrier having the necessary binding capacity in suitable proportions and compacted in the shape and size desired. The powders and tablets may contain from about one (1) to about seventy (70) percent of the active compound. Suitable carriers include but are not limited to magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatine, tragacanth, methylcellulose, sodium carboxymethylcellulose, a low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as carrier, providing a capsule in which the active component, with or without carriers, is surrounded by a carrier, which is in association with it. Similarly, cachets and lozenges are included. Tablets, powders, capsules, pills, cachets, and lozenges may be as solid forms suitable for oral administration.

Other forms suitable for oral administration include liquid form preparations including emulsions, syrups, elixirs, aqueous solutions, aqueous suspensions, or solid form preparations which are intended to be converted shortly before use to liquid form preparations. Emulsions may be prepared in solutions, for example, in aqueous propylene glycol solutions or may contain emulsifying agents, for example, such as lecithin, sorbitan monooleate, or acacia. Aqueous solutions can be prepared by dissolving the active component in water and adding suitable colorants, flavors, stabilizers, and thickening agents. Aqueous suspensions can be prepared by dispersing the finely divided active component in water with viscous material, such as natural or synthetic gums, resins, methylcellulose, sodium carboxymethylcellulose, and other well known suspending agents. Solid form preparations include solutions, suspensions, and emulsions, and may contain, in addition to the active component, colorants, flavors, stabilizers, buffers, artificial and natural sweeteners, dispersants, thickeners, solubilizing agents, and the like.

The compounds of the invention may be formulated for parenteral administration (e.g., by injection, for example bolus injection or continuous infusion) and may be presented in unit dose form in ampoules, pre-filled syringes, small volume infusion or in multi-dose containers

with an added preservative. The compositions may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, for example solutions in aqueous polyethylene glycol. Examples of oily or nonaqueous carriers, diluents, solvents or vehicles include propylene glycol, polyethylene glycol, vegetable oils (e.g., olive oil), and injectable organic esters (e.g., ethyl oleate), and may contain formulatory agents such as preserving, wetting, emulsifying or suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredient may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilization from solution for constitution before use with a suitable vehicle, e.g., sterile, pyrogen-free water.

The compounds of the invention may be formulated for topical administration to the epidermis as ointments, creams or lotions, or as a transdermal patch. Ointments and creams may, for example, be formulated with an aqueous or oily base with the addition of suitable thickening and/or gelling agents. Lotions may be formulated with an aqueous or oily base and will in general also containing one or more emulsifying agents, stabilizing agents, dispersing agents, suspending agents, thickening agents, or coloring agents. Formulations suitable for topical administration in the mouth include lozenges comprising active agents in a flavored base, usually sucrose and acacia or tragacanth; pastilles comprising the active ingredient in an inert base such as gelatine and glycerine or sucrose and acacia; and mouthwashes comprising the active ingredient in a suitable liquid carrier.

The compounds of the invention may be formulated for administration as suppositories. A low melting wax, such as a mixture of fatty acid glycerides or cocoa butter is first melted and the active component is dispersed homogeneously, for example, by stirring. The molten homogeneous mixture is then poured into convenient sized molds, allowed to cool, and to solidify.

The compounds of the invention may be formulated for vaginal administration. Pessaries, tampons, creams, gels, pastes, foams or sprays containing in addition to the active ingredient such carriers as are known in the art to be appropriate.

The subject compounds may be formulated for nasal administration. The solutions or suspensions are applied directly to the nasal cavity by conventional means, for example, with a dropper, pipette or spray. The formulations may be provided in a single or multidose form. In the latter case of a dropper or pipette, this may be achieved by the patient administering an appropriate, predetermined volume of the solution or suspension. In the case of a spray, this may be achieved for example by means of a metering atomizing spray pump.

The compounds of the invention may be formulated for aerosol administration, particularly to the respiratory tract and including intranasal administration. The compound will generally have a small particle size for example of the order of five (5) microns or less. Such a particle size may be obtained by means known in the art, for example by micronization. The active ingredient is provided in a pressurized pack with a suitable propellant such as a chlorofluorocarbon (CFC), for example, dichlorodifluoromethane, trichlorofluoromethane, or

dichlorotetrafluoroethane, or carbon dioxide or other suitable gas. The aerosol may conveniently also contain a surfactant such as lecithin. The dose of drug may be controlled by a metered valve. Alternatively the active ingredients may be provided in a form of a dry powder, for example a powder mix of the compound in a suitable powder base such as lactose, starch, starch derivatives such as hydroxypropylmethyl cellulose and polyvinylpyrrolidine (PVP). The powder carrier will form a gel in the nasal cavity. The powder composition may be presented in unit dose form for example in capsules or cartridges of e.g., gelatine or blister packs from which the powder may be administered by means of an inhaler.

When desired, formulations can be prepared with enteric coatings adapted for sustained or controlled release administration of the active ingredient. For example, the compounds of the present invention can be formulated in transdermal or subcutaneous drug delivery devices. These delivery systems are advantageous when sustained release of the compound is necessary and when patient compliance with a treatment regimen is crucial. Compounds in transdermal delivery systems are frequently attached to an skin-adhesive solid support. The compound of interest can also be combined with a penetration enhancer, e.g., Azone (1-dodecylazacycloheptan-2-one). Sustained release delivery systems are inserted subcutaneously into the subdermal layer by surgery or injection. The subdermal implants encapsulate the compound in a lipid soluble membrane, e.g., silicone rubber, or a biodegradable polymer, e.g., polylactic acid.

The pharmaceutical preparations may be in unit dosage forms. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete quantities of preparation, such as packeted tablets, capsules, and powders in vials or ampoules. Also, the unit dosage form can be a capsule, tablet, cachet, or lozenge itself, or it can be the appropriate number of any of these in packaged form.

Other suitable pharmaceutical carriers and their formulations are described in *Remington: The Science and Practice of Pharmacy* **1995,** edited by E. W. Martin, Mack Publishing Company, 19th edition, Easton, Pennsylvania. Representative pharmaceutical formulations containing a compound of the present invention are described below.

Utility

The compounds of the invention are useful for treatment of LRRK2-mediated diseases or conditions, including neurodegenerative diseases such as Parkinson's disease, Lewy body dementia and Huntington's disease, and for enhancemenent of cognitive memory generally in subjects in need thereof.

Examples

The following preparations and examples are given to enable those skilled in the art to more clearly understand and to practice the present invention. They should not be considered as limiting the scope of the invention, but merely as being illustrative and representative thereof.

Unless otherwise stated, all temperatures including melting points (i.e., MP) are in degrees celsius (°C). It should be appreciated that the reaction which produces the indicated and/or the desired product may not necessarily result directly from the combination of two reagents which were initially added, i.e., there may be one or more intermediates which are produced in the mixture which ultimately leads to the formation of the indicated and/or the desired product. The following abbreviations may be used in the Preparations and Examples.

Abbreviations

AcOH	Acetic acid
AIBN	2,2'-Azobis(2-methylpropionitrile)
Atm.	Atmosphere
$(BOC)_2O$	di-*tert*-Butyl dicarbonate
dba	tris(dibenzylideneacetone)
DCM	Dichloromethane/Methylene chloride
DIAD	Diisopropyl azodicarboxylate
DIPEA	Diisopropylethylamine
DMAP	4-Dimethylaminopyridine
DME	1,2-Dimethoxyethane
DMF	*N,N*-Dimethylformamide
DMSO	Dimethyl sulfoxide
DPPF	1,1'-Bis(diphenylphosphino)ferrocene
Et_2O	Diethyl ether
EtOH	Ethanol/Ethyl alcohol
EtOAc	Ethyl acetate
HATU	2-(1H-7-Azabenzotriazol-1-yl)--1,1,3,3-tetramethyl uronium hexafluorophosphate Methanaminium
HBTU	*O*-Benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium hexafluorophosphate
HOBT	1-Hydroxybenzotriazole
HPLC	High pressure liquid chromatography
RP HPLC	Reverse phase high pressure liquid chromatography

i-PrOH	Isopropanol/isopropyl alcohol
LCMS	Liquid Chromatograph/Mass Spectroscopy
MeOH	Methanol/Methyl alcohol
MW	Microwaves
NBS	*N*-Bromosuccinimide
NMP	1-Methyl-2-pyrrolidinone
PSI	Pound per square inch
RT	Room temperature
SFC	Supercritical fluid chromatography
TBDMS	*tert*-Butyldimethylsilyl
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin layer chromatography
Xphos	2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl

Liquid Chromatography-Mass Spectrometry Method A

LC-MS was performed on an Agilent 1200 Series LC coupled to an Agilent 6140 quadrupole mass spectrometer using an Agilent SD-C18 column (1.8 μm, 2.1 x 30 mm) with a linear gradient of 3-95% acetonitrile/water (with 0.05% trifluoroacetic acid in each mobile phase) within 8.5 minutes and held at 95% for 2.5 minutes.

Liquid Chromatography-Mass Spectrometry Method B

LC-MS was performed on a Waters 2795 Alliance HT HPLC with Waters 2996 Diode Array Detector coupled to a Micromass ZQ, single quadrapole mass spectrometer using a Phenomenex Luna C18 (2) column (5 um, 100 x 4.6mm plus guard cartridge) with a linear gradient of 5-95% acetonitrile/water (with 0.1% formic acid in each mobile phase) within 3.5 minutes and held at 95% for 2.0 minutes.

Liquid Chromatography-Mass Spectrometry Method C

LC-MS was performed on a Waters 2795 Alliance HT HPLC with Waters 2996 Diode Array Detector coupled to a Micromass ZQ, single quadrapole mass spectrometer using a Waters Xterra MS C18 column (5 um, 100 x 4.6mm plus guard cartridge) being initially held at 5% acetonitrile/water (with 10mM ammonium bicarbonate in the aqueous mobile phase) for 0.5 minutes, followed by a linear gradient of 5-95% within 3.5 minutes and then held at 95% for 1.5 minutes.

Analytical Methods

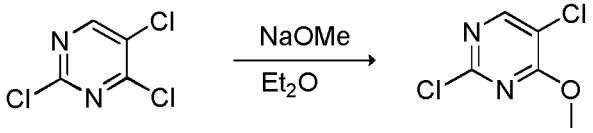
^{1}H Nuclear magnetic resonance (NMR) spectroscopy was carried out using a Bruker instrument operating at 400 or 500 MHz using the stated solvent at around room temperature unless otherwise stated. In all cases, NMR data were consistent with the proposed structures. Characteristic chemical shifts (δ) are given in parts-per-million using conventional abbreviations for designation of major peaks: e.g. s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; br, broad. Where thin layer chromatography (TLC) has been used it refers to silica gel TLC using silica gel MK6F 60Å plates, R_f is the distance travelled by the compound divided by the distance travelled by the solvent on a TLC plate. Flash chromatography refers to silica gel chromatography and is carried out using an SP4 or an Isolara 4 MPLC system (manufactured by Biotage); pre-packed silica gel cartridges (supplied by Biotage); or using conventional glass column chromatography.

Compound preparation

Where the preparation of starting materials is not described, these are commercially available, known in the literature, or readily obtainable by those skilled in the art using standard procedures. Where it is stated that compounds were prepared analogously to earlier examples or intermediates, it will be appreciated by the skilled person that the reaction time, number of equivalents of reagents and temperature can be modified for each specific reaction and that it may be necessary or desirable to employ different work-up or purification techniques. Where reactions are carried out using microwave irradiation, the microwave used is an Initiator 60 supplied by Biotage. The actual power supplied varies during the course of the reaction in order to maintain a constant temperature.

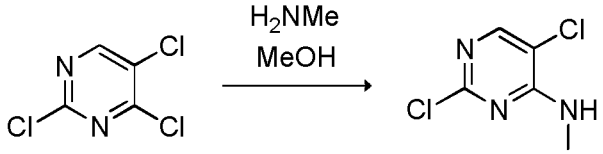
Compounds made in the following examples are summarized in the Tables below, which shows affinity values for LRRK2 (Ki, micromolar) for representative compounds together with LCMS method (M), LC retention time (RT) in minutes, and Mass Spec m/z values (molecular weight).

Intermediate 1 2,5-Dichloro-4-methoxypyrimidine



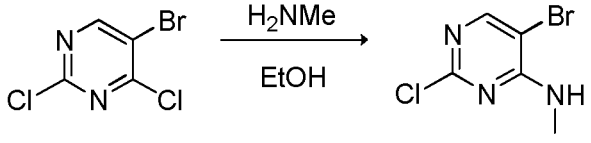
To a 250 mL round bottom flask equipped with a stir bar was added 2,4,5-trichloro-pyrimidine (1 g), and diethyl ether (15 mL). The mixture was cooled to 0°C in an ice bath and then 1 equivalent of sodium methoxide in methanol (prepared from reacting 120 mg of sodium with 4 mL of methanol at room temperature) was slowly added. The reaction was stirred over night at room temperature and checked by LCMS. The white precipitate was filtered and the solid washed with cold methanol. After drying, 0.98 g of pure 2,5-dichloro-4-methoxypyrimidine was obtained and this material was used without further purification. ^{1}H-NMR (DMSO): δ 8.61 (s, 1H), 4.05 (s, 3H).

Intermediate 2 2,5-Dichloro-N-methylpyrimidin-4-amine



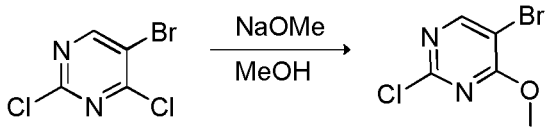
To a cooled (0 °C) solution of 2,4,5-trichloropyrimidine (2.0 g, 11 mmol) in methanol (30 mL) was added dropwise a 2 M solution of methylamine in methanol (6.3 mL). The reaction was allowed to warm to room temperature and stirred overnight. The reaction was then concentrated and redissolved in DCM. The solution was washed with sat. $NaHCO_3$, brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (0-40% EtOAc in heptane) to give 2,5-dichloro-N-methylpyrimidin-4-amine (0.9 g, 50%). ^{1}H-NMR (DMSO): δ 8.13 (s, 1H), 7.89 (s, 1H), 2.86 (d, J = 4.5, 3H).

Intermediate 3 5-Bromo-2-chloro-N-methylpyrimidin-4-amine



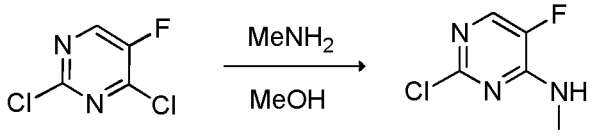
To a cooled (0 °C) solution of 5-bromo-2,4-dichloropyrimidine (5.0 g, 22 mmol) in methanol (42 mL) was added dropwise a 33 wt% solution of methylamine in ethanol (3.3 mL). The reaction was allowed to warm to room temperature. The reaction was then concentrated. The crude product was purified by column chromatography (0-10% methanol in DCM) to give 5-bromo-2-chloro-N-methylpyrimidin-4-amine (1.8 g, 39%). ^{1}H-NMR (DMSO): δ 8.22 (s, 1H), 7.75 (s, 1H), 2.85 (d, J = 3.9, 3H).

Intermediate 4 5-Bromo-2-chloro-4-methoxypyrimidine



To a cooled (-78 °C) solution of 5-bromo-2,4-dichloropyrimidine (1.7 g, 7.3 mmol) in THF (30mL) was added dropwise a 25 wt% solution of methylamine in ethanol (1.7 mL). The reaction was allowed to warm to 0 °C and stirred for 1 h. The reaction was then concentrated and re-dissolved in EtOAc. The solution was washed with brine, dried over Na_2SO_4, filtered and concentrated to give 5-bromo-2-chloro-4-methoxypyrimidine (1.25 g, 76%). ^{1}H-NMR ($CDCl_3$): δ 8.43 (s, 1H), 4.10 (s, 3H).

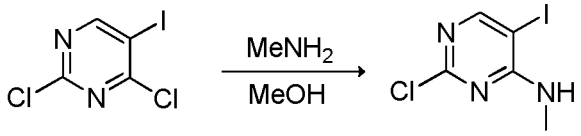
Intermediate 5 2-chloro-5-fluoro-N-methylpyrimidin-4-amine



To a 250mL round bottom flask equipped with a stir bar was added 5-fluoro-2,4-dichloro- pyrimidine (9 g), methanol (40 mL) and 8M methylamine in ethanol (15 mL). The reaction heated up (mild exo-therm) and was allowed to stir at room temperature for 30 minutes.

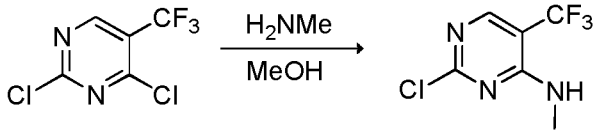
A check by TLC (1:1 EtOAc: heptane) and LCMS showed complete reaction. The reaction was concentrated down to give 9.77g crude material which was purified on a silica column running a gradient of 1% to 10% MeOH in DCM over 35 minutes to give 2-chloro-5-fluoro-N-methylpyrimidin-4-amine (6.77 g).

Intermediate 6 2-Chloro-5-iodo-N-methylpyrimidin-4-amine



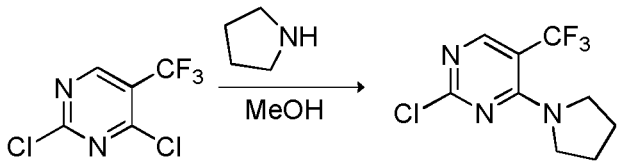
2-chloro-5-iodo-N-methylpyrimidin-4-amine was prepared following the procedure of Intermediate 5 but using 2,4-dichloro-5-iodopyrimidine. ^{1}H-NMR (DMSO): δ 8.26 (s, 1H), 5.47 (s, 1H), 3.07 (d, J = 4.9, 3H).

Intermediate 7 2-Chloro-N-methyl-5-(trifluoromethyl)pyrimidin-4-amine



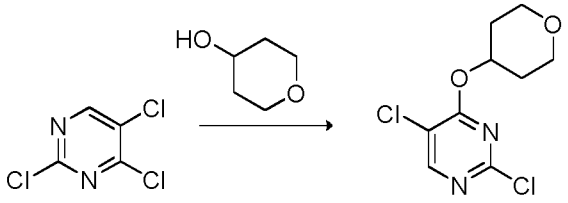
To a cooled (-10 °C) solution of 2,4-dichloro-5-trifluoromethylpyrimidine (20 g, 0.089 mol) in methanol (100 mL) was added triethylamine (12.5 mL, 0.089 mol) and a 2 M solution of methylamine in methanol (45 mL). The reaction was allowed to warm to room temperature and stirred overnight. The reaction was then concentrated and re-dissolved in ethyl acetate. The solution was washed with sat. $NaHCO_3$, brine, dried over $MgSO_4$, filtered and concentrated. The crude product was purified by column chromatography (5-25% EtOAc in heptane) to give 2-chloro-N-methyl-5-(trifluoromethyl)pyrimidin-4-amine (8.6 g, 45%). ^{1}H-NMR (DMSO): δ 8.37 (s, 1H), 7.90 (s, 1H), 2.90 (s, 3H).

Intermediate 8 2-chloro-4-(pyrrolidin-1-yl)-5-(trifluoromethyl)pyrimidine



2-Chloro-4-(pyrrolidin-1-yl)-5-(trifluoromethyl)pyrimidine was prepared according to the procedure described for intermediate 7 using pyrrolidine.

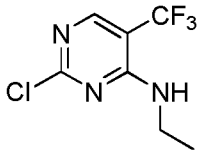
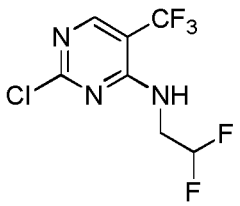
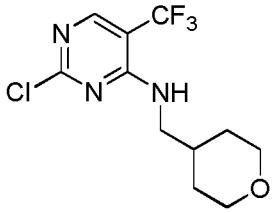
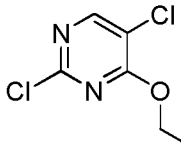
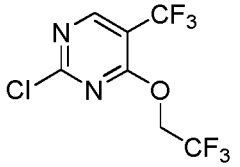
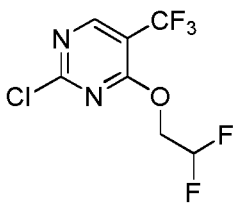
Intermediate 9 2,5-Dichloro-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidine

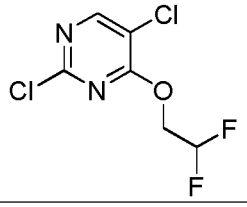
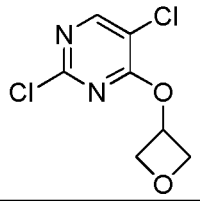
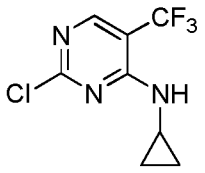


To a solution of tetrahydro-4-pyranol (0.36 g, 3.54 mmol) in DMF (5 mL) was added sodium hydride (60% dispersion, 0.17 g, 4.25 mmol). The resulting mixture was added to a solution of 2,4,5-trichloropyrimidine (650 mg, 3.5 mmol) in THF at 0 °C. The combined mixture was then allowed to warm to room temperature. To the reaction was then added water and the product was extracted with a 1:1 EtOAc-Heptane mixture. The extract was then dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatrography (0-30% EtOAc in heptane) to give 2,5-dichloro-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidine. ^{1}H-NMR ($CDCl_3$): δ 8.33(s, 1H), 5.42 (m, 1H), 4.09 – 3.90 (m, 2H), 3.65 (m, 2H), 2.19-1.99 (m, 2H), 1.87 (m, 2H).

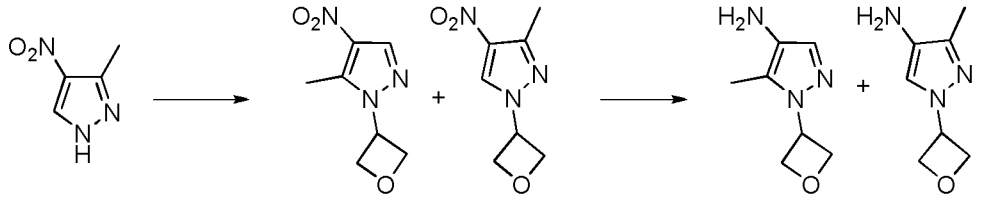
Additional intermediates prepared using similar methods as described above are listed in Table 1 below:

Table 1

10	2-chloro-N-ethyl-5-(trifluoromethyl)pyrimidin-4-amine	
11	2-chloro-N-(2,2-difluoroethyl)-5-(trifluoromethyl)pyrimidin-4-amine	
12	2-chloro-N-((tetrahydro-2H-pyran-4-yl)methyl)-5-(trifluoromethyl)pyrimidin-4-amine	
13	2,5-dichloro-4-ethoxypyrimidine	
14	2-chloro-4-(2,2,2-trifluoroethoxy)-5-(trifluoromethyl)pyrimidine	
15	2-chloro-4-(2,2-difluoroethoxy)-5-(trifluoromethyl)pyrimidine	

16	2,5-dichloro-4-(2,2-difluoroethoxy)pyrimidine	
17	2,5-dichloro-4-(oxetan-3-yloxy)pyrimidine	
18	2-chloro-N-cyclopropyl-5-(trifluoromethyl)pyrimidin-4-amine	

Intermediates 19 and 20 5-Methyl-1-(oxetan-3-yl)-1H-pyrazol-4-amine and 3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-amine



Step 1 5-Methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole and 3-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole

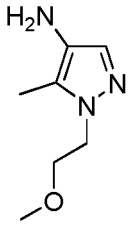
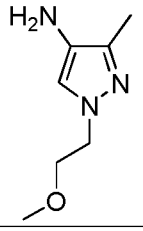
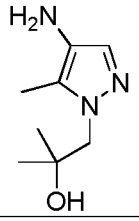
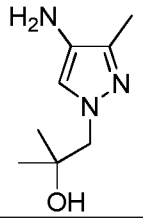
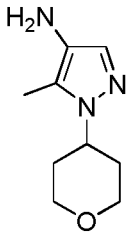
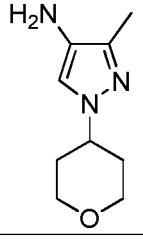
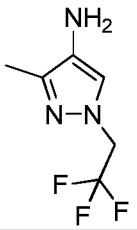
To a mixture of 3-methyl-4-nitro-pyrazole (0.80 g, 6.3 mmol), cesium carbonate (4.1 g, 12 mmol) in DMF (10 mL) was added 3-iodo-oxetane (3.47 g, 19 mmol). The mixture was stirred at 100 °C for 3 h. The reaction was diluted with water and extracted with ethyl acetate (3x). The combined extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatrography (20-100% EtOAc-heptane) to give a mixture of 5-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole and 3-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole (0.85 g, 74%).

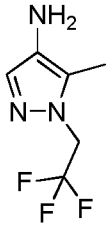
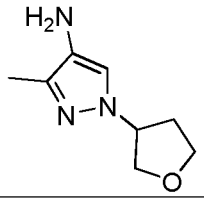
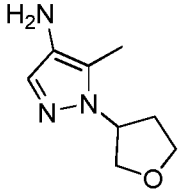
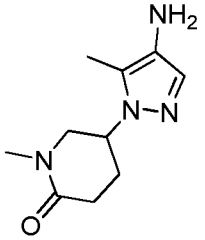
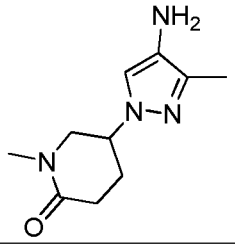
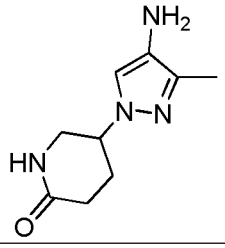
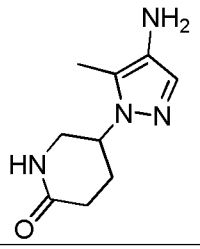
Step 2 5-Methyl-1-(oxetan-3-yl)-1H-pyrazol-4-amine and 3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-amine

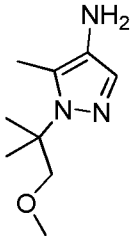
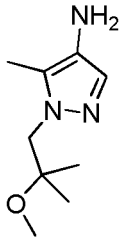
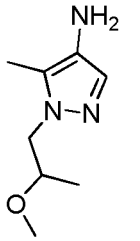
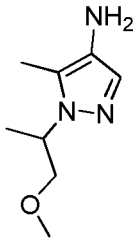
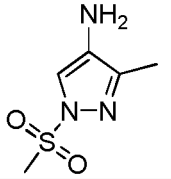
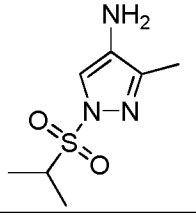
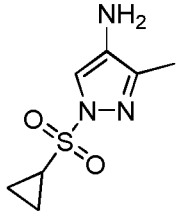
To a solution of 5-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole and 3-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole (0.137 g, 0.75 mmol) in ethanol (2 mL) was added Pd-C (10 wt%, 0.10 g). The mixture was stirred under a hydrogen atmosphere for 24 hours. The reaction was filtered through Celite® and concentrated to give a mixture of 5-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-amine and 3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-amine (83 mg, 73%), which were used together in the following Examples.

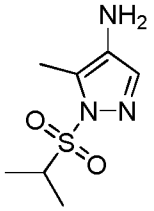
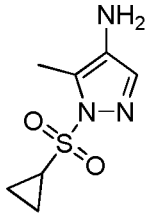
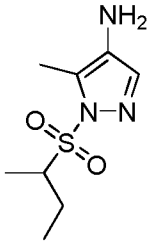
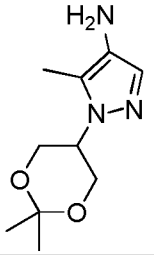
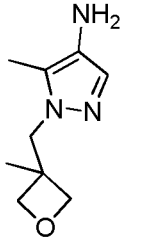
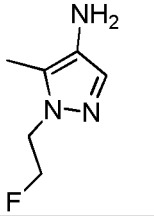
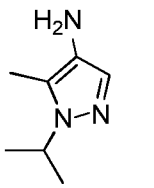
Additional intermediates made using the above procedure are shown in Table 2 below.

Table 2

21	1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-amine	
22	1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-amine	
23	1-(4-Amino-5-methyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol	
24	1-(4-amino-3-methyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol	
25	5-Methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-amine	
26	3-Methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-amine	
27	3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-amine	

28	5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-amine	
29	3-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-amine	
30	5-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-amine	
31	5-(4-amino-5-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one	
32	5-(4-amino-3-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one	
33	5-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-2-one	
34	5-(4-amino-5-methyl-1H-pyrazol-1-yl)piperidin-2-one	

35	1-(1-methoxy-2-methylpropan-2-yl)-5-methyl-1H-pyrazol-4-amine	
36	1-(2-methoxy-2-methylpropyl)-5-methyl-1H-pyrazol-4-amine	
37	1-(2-methoxypropyl)-5-methyl-1H-pyrazol-4-amine	
38	1-(1-methoxypropan-2-yl)-5-methyl-1H-pyrazol-4-amine	
39	3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-amine	
40	1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-amine	
41	1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-amine	

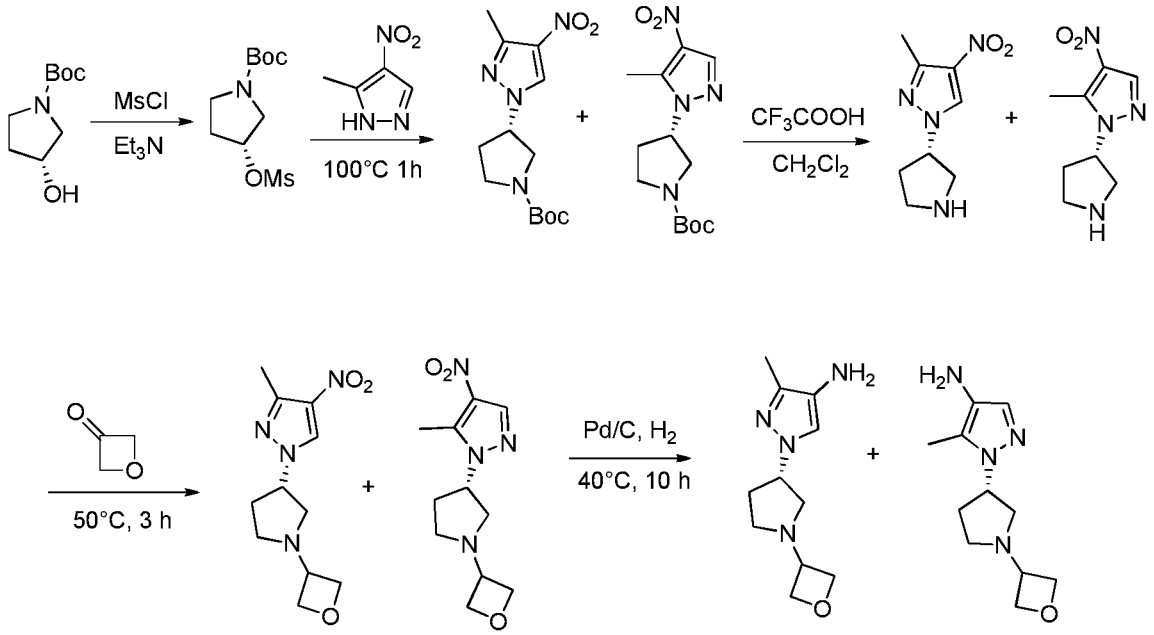
42	1-(isopropylsulfonyl)-5-methyl-1H-pyrazol-4-amine	
43	1-(cyclopropylsulfonyl)-5-methyl-1H-pyrazol-4-amine	
44	1-(sec-butylsulfonyl)-5-methyl-1H-pyrazol-4-amine	
45	1-(2,2-dimethyl-1,3-dioxan-5-yl)-5-methyl-1H-pyrazol-4-amine	
46	5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-amine	
47	1-(2-fluoroethyl)-5-methyl-1H-pyrazol-4-amine	
48	1-isopropyl-5-methyl-1H-pyrazol-4-amine	

Intermediate 49 5-Chloro-1-methyl-1H-pyrazol-4-amine



To a suspension of 5-chloro-1-methyl-1H-pyrazole-4-carboxylic acid (1.0 g, 6.2 mmol) in toluene (15 mL) was added triethylamine (1.7 mL, 12 mmol) and diphenylphosphonic azide (2 mL, 9.3 mmol). The resulting solution was stirred at room temperature for 30 minutes before heating at 95 °C for 1 h. After cooling to room temperature, the reaction was diluted with water and extracted with ethyl acetate (3x). The combined extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated to give a yellow syrup. The crude product was purified by column chromatography (0-50% EtOAc in heptane) to give 5-chloro-1-methyl-1H-pyrazol-4-amine. ^{1}H-NMR ($CDCl_3$): δ 7.90 (s, 1H), 3.88 (s, 2H), 1.55 (s, 3H).

Intermediates 50 and 51 (S)-3-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-amine and (S)-5-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-amine



Step 1: (R)-tert-butyl 3-(methylsulfonyloxy)pyrrolidine-1-carboxylate

(R)-tert-butyl 3-hydroxypyrrolidine-1-carboxylate (5.0 g, 26.7 mmol) and Et_3N (8.0 g, 80.2 mmol) were dissolved in dichloromethane (50 mL). The mixture was stirred at 0°C for 30 minutes, then methanesulfonyl chloride (4.5 g, 40.1 mmol) was added dropwise. It was stirred at room temperature for 2 h and concentrated under reduced pressure. DCM (50 mL) and water (50 mL) were added. The organic phase was washed with saturated $NaHCO_3$ (30 mL) and H_2O (2 x 30 mL), and concentrated to afford the title compound as oil (6 g, 100%).

Step 2: (S)-tert-butyl 3-(3-methyl-4-nitro-1H-pyrazol-1-yl)pyrrolidine-1-carboxylate and (S)-tert-butyl 3-(5-methyl-4-nitro-1H-pyrazol-1-yl)pyrrolidine-1-carboxylate

A microwave vial equipped with a magnetic stirrer was charged with (R)-tert-butyl 3-(methylsulfonyloxy)pyrrolidine-1-carboxylate (6.0 g, 22.5 mmol), 5-methyl-4-nitro-1H-pyrazole

(2 g, 15.1 mmol), K_2CO_3 (6.2g, 45.3 mmol) and DMF (50 mL). The reaction mixture was heated at 100 °C for 1 h under microwave irradiation. It was then filtered to get rid of K_2CO_3 and the filtrate was concentrated. The residue was purified by silica gel chromatography eluting with petroleum ether/ethyl acetate (2: 1) to afford the mixture of the two title compounds as brown oil (5 g, 100%). m/z (ES+APCI)$^+$: [M+H]+ 241.

Alternatively, (S)-tert-butyl 3-(3-methyl-4-nitro-1H-pyrazol-1-yl)pyrrolidine-1-carboxylate (049-3) and (S)-tert-butyl 3-(5-methyl-4-nitro-1H-pyrazol-1-yl)pyrrolidine-1-carboxylate or related analogs, such as tert-butyl 3-fluoro-4-(3-methyl-4-nitro-1H-pyrazol-1-yl)piperidine-1-carboxylate, can be prepared by the following procedure: To a solution of 5-methyl-4-nitro-1H-pyrazole (0.99 g, 7.8 mmol), tert-butyl 3-fluoro-4-hydroxypiperidine-1-carboxylate (1.7 g, 7.8 mmol) and triphenylphosphine (2.3 g, 8.5 mmol) in THF (8 mL) was added diisopropyl azodicarboxylate (2 g, 9.3 mmol). The reaction was stirred at room temperature for 2 hours before being diluted with water and extracted with EtOAc (4x). The organic extracts were washed with brine, dried over sodium sulfate, filtered and concentrated. The crude product was purified by chromatography to give tert-butyl 3-fluoro-4-(3-methyl-4-nitro-1H-pyrazol-1-yl)piperidine-1-carboxylate (2.25 g, 88%).

Step 3: (S)-3-methyl-4-nitro-1-(pyrrolidin-3-yl)-1H-pyrazole and (S)-5-methyl-4-nitro-1-(pyrrolidin-3-yl)-1H-pyrazole

The mixture of (S)-tert-butyl 3-(3-methyl-4-nitro-1H-pyrazol-1-yl)pyrrolidine-1-carboxylate and (S)-tert-butyl 3-(5-methyl-4-nitro-1H-pyrazol-1-yl)pyrrolidine-1-carboxylate (5 g, 16.9 mmol) was dissolved in dichloromethane (40 mL). CF_3COOH (10 mL) was added and the mixture was stirred at room temperature for overnight. The solvent was removed under reduced pressure to afford the mixture of the two title compounds as brown oil (4.0 g, 100%). m/z (ES+APCI)$^+$: [M+H]+ 197.

Step 4: (S)-3-methyl-4-nitro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazole and (S)-5-methyl-4-nitro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazole

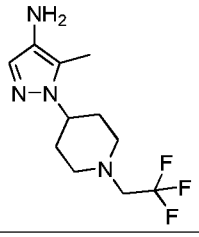
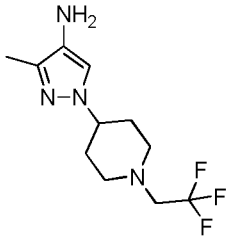
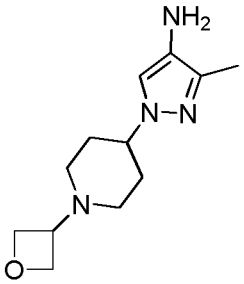
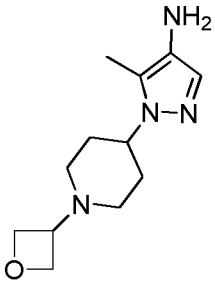
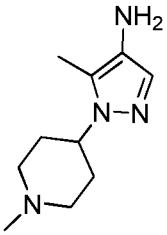
To the mixture of (S)-3-methyl-4-nitro-1-(pyrrolidin-3-yl)-1H-pyrazole and (S)-5-methyl-4-nitro-1-(pyrrolidin-3-yl)-1H-pyrazole (4 g, 20.4 mmol), oxetan-3-one (4.4 g, 61.2 mmol), and $ZnCl_2$ (8.3 g, 61.2 mmol) in MeOH (50 mL) was added $NaBH_4$ (3.8 g, 61.2 mmol). The mixture was stirred at 50°C for 5 h. Then the solvent was removed in vacuum. Dichloromethane (100 mL) was added and the mixture was washed with water (2 x 50 mL). It was then concentrated in *vacuo* and purified by silica gel chromatography eluting with dichloromethane/methanol (25/ 1) to afford the mixture of the two title compounds as yellow oil (3.8 g, 75%). m/z (ES+APCI)$^+$: [M+H]+ 253.

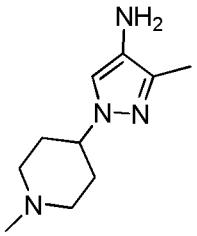
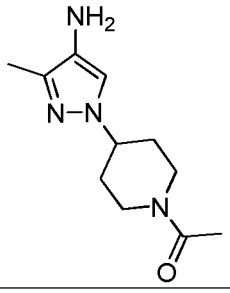
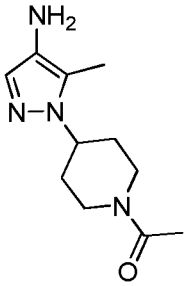
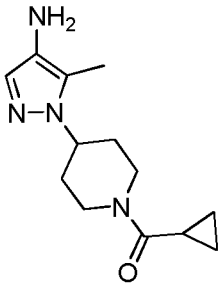
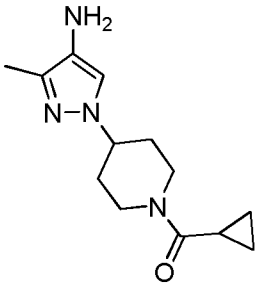
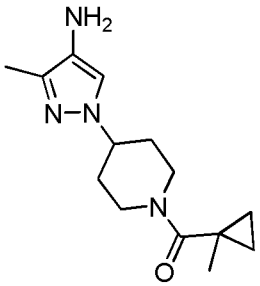
Step 5: (S)-3-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-amineand (S)-5-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-amine

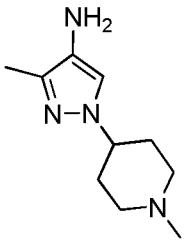
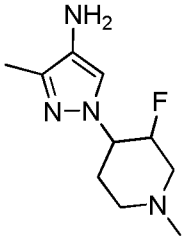
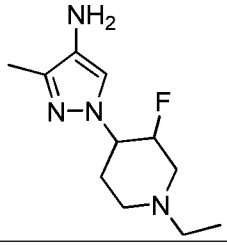
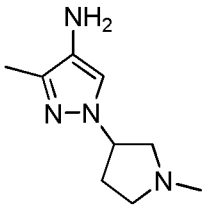
To the mixture of (S)-3-methyl-4-nitro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazole and (S)-5-methyl-4-nitro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazole (500 mg, 1.98 mmol), and Zn (506 mg, 7.94 mmol) in methanol (20 mL) was added THF (20 mL) and NH_4Cl (841 mg, 15.9 mmol). The mixture was stirred at 50°C for 2 h. It was then concentrated and purified by reverse-phase prep-HPLC to afford the mixture of the two title compounds as yellow solid (200 mg, 45%). m/z (ES+APCI)$^+$: [M+H]+ 223.

Additional intermediates made using the above procedure are shown in Table 3 below.

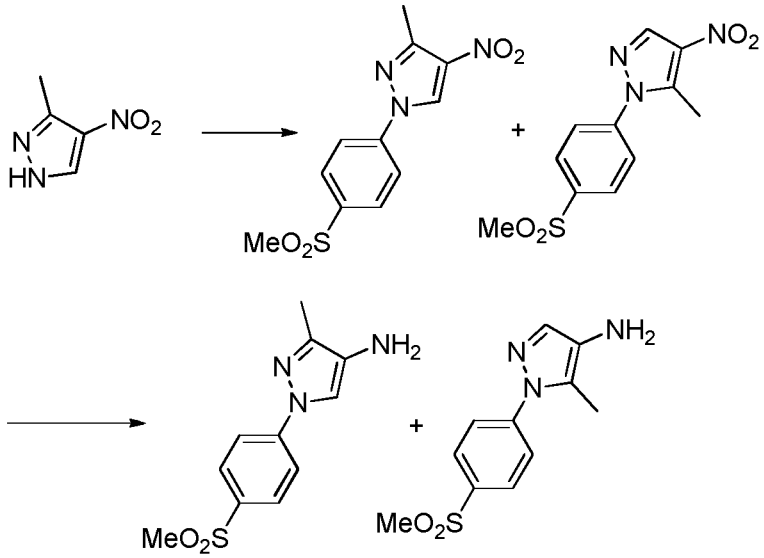
Table 3

52	5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-amine	
53	3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-amine	
54	3-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-amine	
55	5-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-amine	
56	5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	

57	3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
58	1-(4-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone	
59	1-(4-(4-amino-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone	
60	(4-(4-amino-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(cyclopropyl)methanone	
61	(4-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(cyclopropyl)methanone	
62	(4-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone	

63	3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
64	1-(3-fluoro-1-methylpiperidin-4-yl)-3-methyl-1H-pyrazol-4-amine	
65	1-(1-ethyl-3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-amine	
66	3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-amine	

Intermediates 67 and 68 : 3-Methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole compound with 5-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole



Step 1: 3-Methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole compound and 5-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole

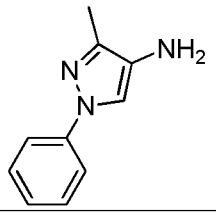
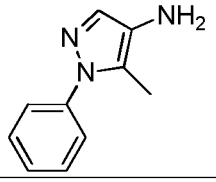
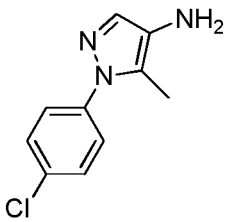
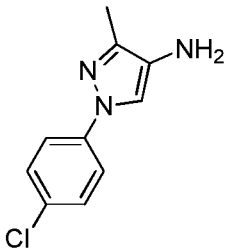
A mixture of 3-methyl-4-nitro-1H-pyrazole (2.1 g, 17 mmol) and 4-methylsulfonylphenylboronic acid (5.0 g, 25 mmol), copper (II) acetate monohydrate (0.91 g, 5.0 mmol) and pyridine (0.5 g, 6.6 mmol) in DMF was stirred at 95 °C under an oxygen atmosphere for 7 hours. The reaction was diluted with water, extracted with EtOAc (3x). The combined extracts were washed with brine, dried over sodium sulfate, filtered and concentrated. The crude product was purified by flash chromatography to give a mixture of 3-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole compound and 5-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole (1.3 g, 28%).

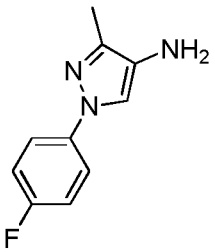
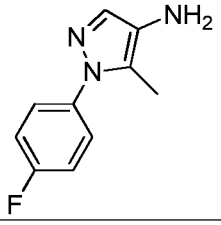
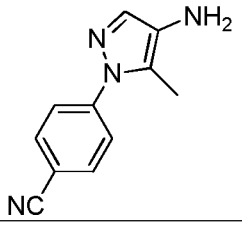
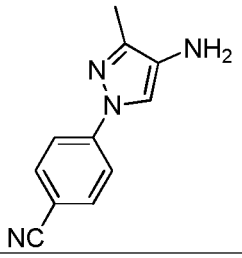
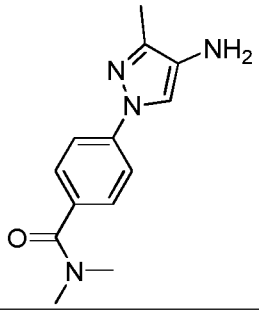
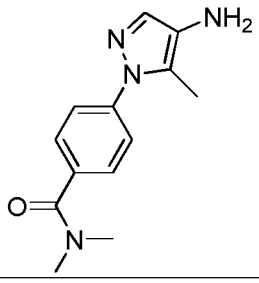
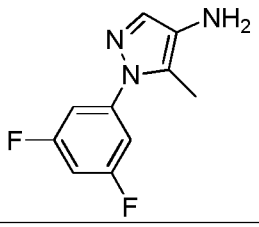
Step 2: 3-Methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole compound with 5-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole

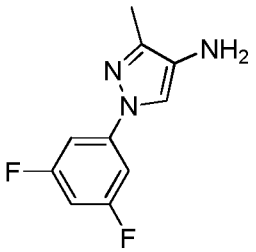
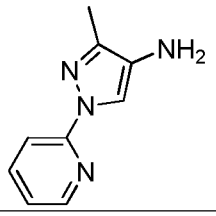
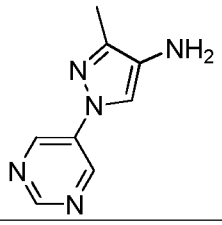
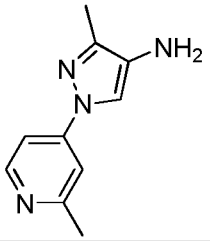
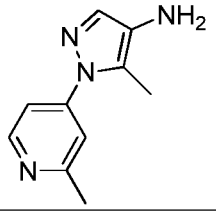
A suspension of 3-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole compound and 5-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole (0.57 g, 2.0 mmol) and palladium on carbon (10 wt%, 0.2 g) in ethanol was stirred under a hydrogen atmosphere at 55 °C for 18 hours. The reaction mixture was filtered through celite and concentrated to give the title compounds as a mixture of regioisomers (446 mg, 87%).

Additional intermediates made using the above procedure are shown in Table 4 below

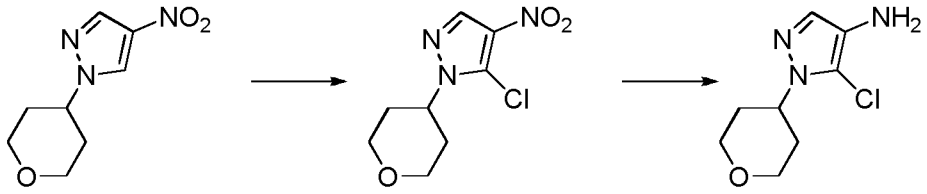
Table 4

69	3-methyl-1-phenyl-1H-pyrazol-4-amine	
70	5-methyl-1-phenyl-1H-pyrazol-4-amine	
71	1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-amine	
72	1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-amine	

73	1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-amine	
74	1-(4-fluorophenyl)-5-methyl-1H-pyrazol-4-amine	
75	4-(4-amino-5-methyl-1H-pyrazol-1-yl)benzonitrile	
76	4-(4-amino-3-methyl-1H-pyrazol-1-yl)benzonitrile	
77	4-(4-amino-3-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamide	
78	4-(4-amino-5-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamide	
79	1-(3,5-difluorophenyl)-5-methyl-1H-pyrazol-4-amine	

80	1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-amine	
81	3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-amine	
82	3-methyl-1-(pyrimidin-5-yl)-1H-pyrazol-4-amine	
83	3-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-amine	
84	5-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-amine	

Intermediate 85: 5-Chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-amine



Step 1: 5-Chloro-4-nitro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazole

To a solution of 4-nitro-1-tetrahydropyran-4-yl-pyrazole (1.32 g; 6.69 mmol) in THF (15 mL) was added dropwise LHMDS (1 mol/L) in THF (2.0 equiv.; 13.4 mmol) at -78°C. The reaction was stirred at -78°C for 30 minutes before the addition of hexachloroethane (2.4 g, 10 mmol) in THF (5 mL). The reaction was stirred at -78°C before warming to room temperature. The reaction was diluted with sat. NaCl and extracted with EtOAc (3x). The combined extracts were washed with brine, dried over sodium sulfate, filtered and concentrated.

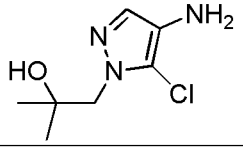
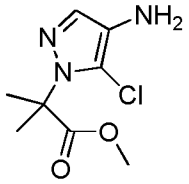
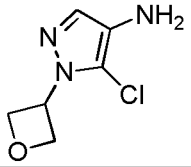
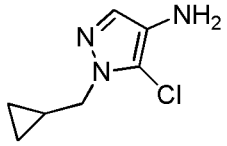
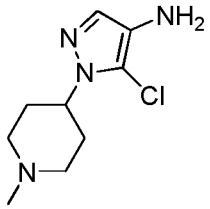
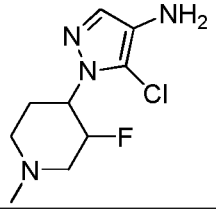
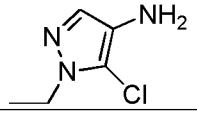
The crude product was purified by flash chromatography to give 5-chloro-4-nitro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazole (0.98 g, 63%).

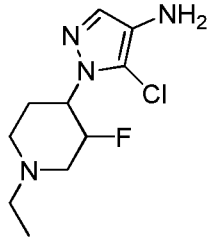
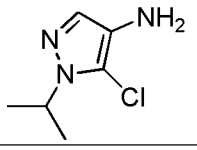
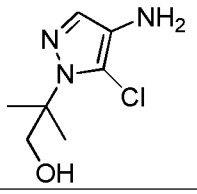
Step 2: 5-Chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-amine

To a solution of 5-chloro-4-nitro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazole (0.4 g, 2 mmol) in ethanol (10 mL) was added ammonium chloride (0.3 g, 5 mmol) and iron (0.3 g). The reaction was stirred at 90 °C for 30 minutes before filtered through Celite® and concentrated. The residue was titurated in EtOAc and filtered. The filtrated was concentrated to give the title compound (0.34 g, quant.)

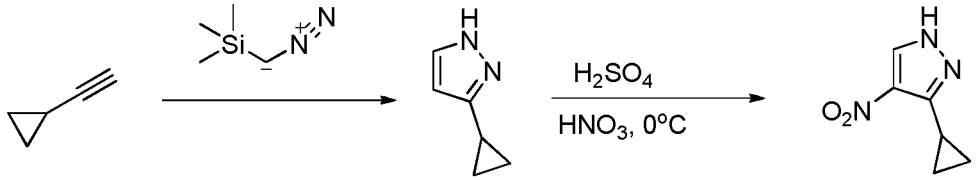
Additional intermediates made using the above procedure are shown in Table 5 below.

Table 5

86	1-(4-amino-5-chloro-1H-pyrazol-1-yl)-2-methylpropan-2-ol	
87	methyl 2-(4-amino-5-chloro-1H-pyrazol-1-yl)-2-methylpropanoate	
88	5-chloro-1-(oxetan-3-yl)-1H-pyrazol-4-amine	
89	5-chloro-1-(cyclopropylmethyl)-1H-pyrazol-4-amine	
90	5-chloro-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
91	5-chloro-1-(3-fluoro-1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
92	5-chloro-1-ethyl-1H-pyrazol-4-amine	

93	5-chloro-1-(1-ethyl-3-fluoropiperidin-4-yl)-1H-pyrazol-4-amine	
94	5-chloro-1-isopropyl-1H-pyrazol-4-amine	
95	2-(4-amino-5-chloro-1H-pyrazol-1-yl)-2-methylpropan-1-ol	

Intermediates 96: 3-Cyclopropyl-4-nitro-1H-pyrazole



Step 1: 3-cyclopropyl-1H-pyrazole

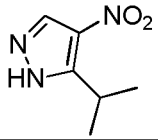
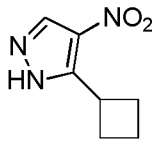
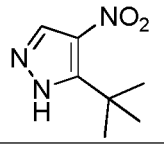
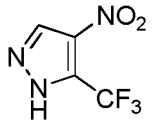
Ethynylcyclopropane (660 mg, 10 mmol) mixed with (diazomethyl)trimethylsilane (5 mL, 2M in hexane) in a 30 mL microwave tube was microwaved at 135 °C for 1 h. Then this reaction was concentrated in vacuo to give a light yellow oil product (1.02 g, 94%). This product was pure enough to be used to the next step reaction without further purification. MS: $[M+H]^+$ 109.

Step 2: 3-Cyclopropyl-4-nitro-1H-pyrazole

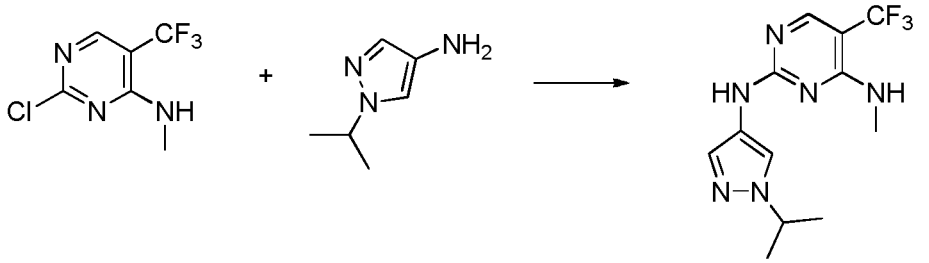
To a cooling (0 °C) solution of 3-cyclopropyl-1H-pyrazole (1.5 g, 13.89mmol) in concentrated H_2SO_4 (20 mL, 98%) was added concentrated HNO_3 (20 mL, 65%) over 2 min. The reaction mixture was stirred over 1 hr at this temperature. It was then diluted with ice-water and extracted with EA (30 mL X 4). The organic phase was combined and washed with saturated sodium bicarbonate (50 mL). It was dried over Na_2SO_4 and concentrated in vacuo to give a crude product (1.5 g, 70%). This crude product was pure enough to be delivered or used to the next step reaction. MS: $[M+H]^+$ 154. ^1H NMR (500 MHz, CDCl3) δ 0.97 (m, 2H), 1.22(m, 2H), 2.66 (m, 1H), 8.20(s, 1H), 8.38 (s, 1H).

Intermediates made using the above procedure are shown in Table 6 below

Table 6

97	5-isopropyl-4-nitro-1H-pyrazole	
98	5-cyclobutyl-4-nitro-1H-pyrazole	
99	5-tert-butyl-4-nitro-1H-pyrazole	
100	4-nitro-5-(trifluoromethyl)-1H-pyrazole	

Example 1 N^2-(1-isopropyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine

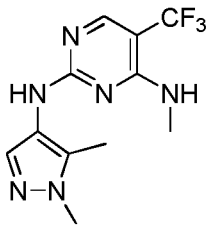
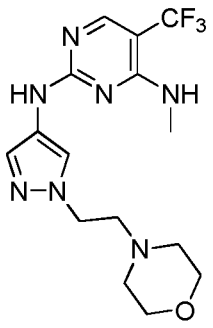
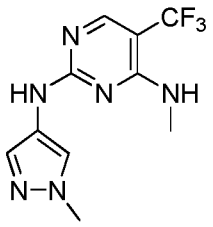
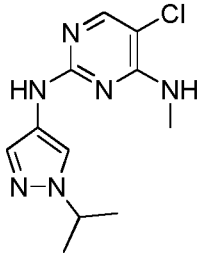
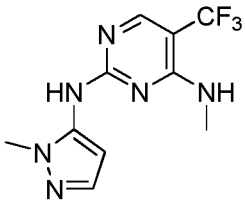


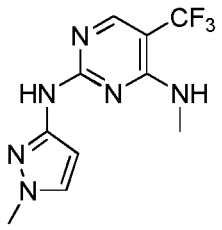
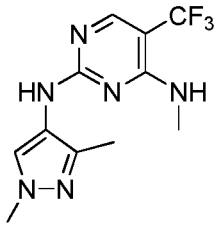
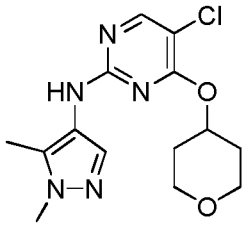
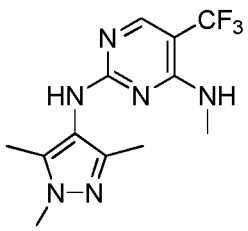
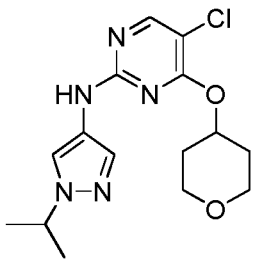
To a microwave tube was added 2-chloro-N-methyl-5-(trifluoromethyl)pyrimidin-4-amine (112 mg, 0.53 mmol), 1-isopropyl-1H-pyrazol-4-amine (55 mg, 0.44 mmol), cesium carbonate (0.287 g, 0.88 mmol), XPhos (21 mg, 0.044 mmol), $Pd_2(dba)_3$ (20 mg, 0.02 mmol) and dioxane (2.5 mL). The tube was sealed and the reaction was irradiated in the microwave at 140 °C for 30 minutes. The reaction mixture was then filtered and concentrated. The crude product was purified by reverse phase HPLC to give N^2-(1-isopropyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine (22 mg, 16%). LCMS (Method A): [MH^+] = 301.1 at 3.2 min. ^{1}H-NMR (DMSO): δ 9.43 (m, 2H), 8.08 (s, 1H), 7.89 (s, 1H), 7.54 (s, 1H), 6.96 (m, 2H), 4.43 (m, 1H), 2.92 (d, J = 8.0, 3H), 1.39 (d, J = 6.6, 6H).

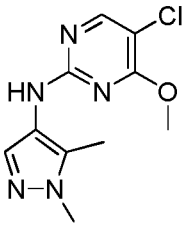
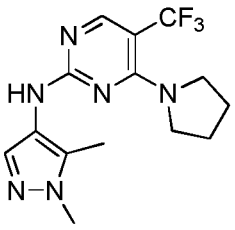
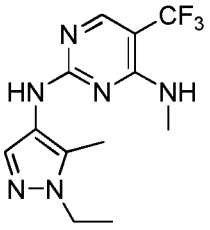
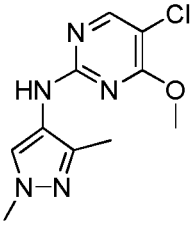
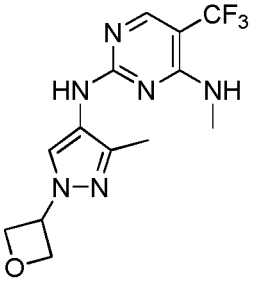
Compounds made using the above procedure are shown in Table 7 below, together with low resolution mass spectrometry (M+H), proton NMR, and LRRK2 K_i (micromolar) data for selected compounds determined from the assay described below.

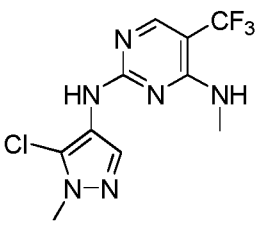
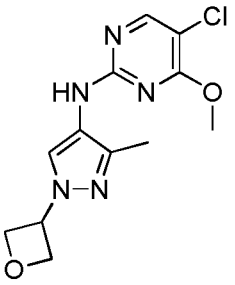
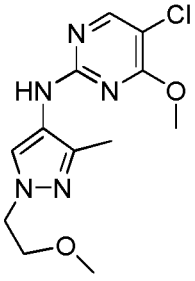
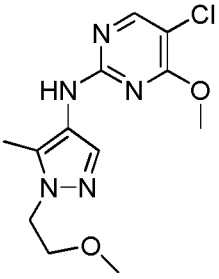
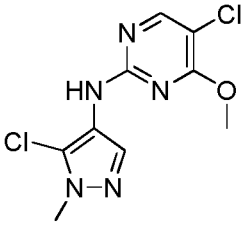
Table 7

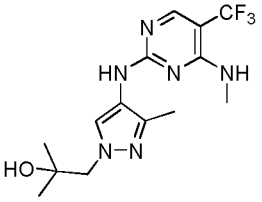
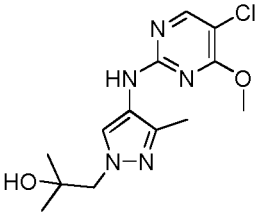
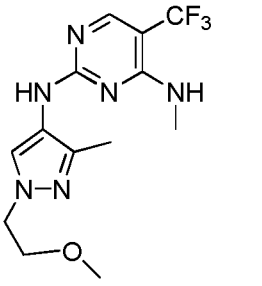
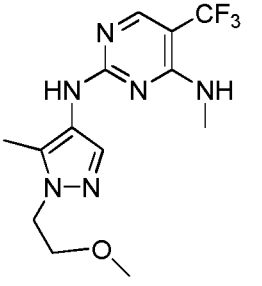
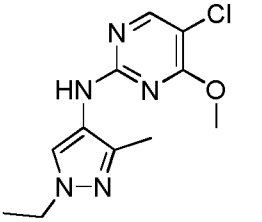
	Name	Structure	^{1}H NMR	M+H^+	K_I

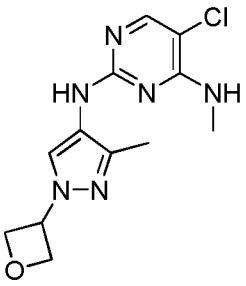
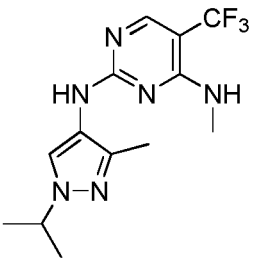
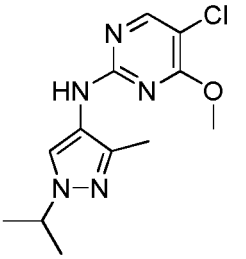
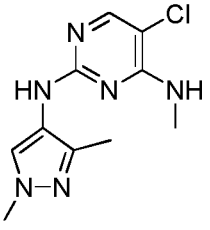
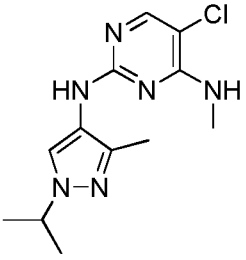
2	N^2-(1,5-dimethyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.87 (s, 1H), 8.04 (s, 1H), 7.64 (s, 1H), 6.90 (s, 2H), 3.69 (s, 3H), 2.84 (s, 3H), 2.17 (s, 3H).	287.0	
3	N^4-methyl-N^2-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.53 (s, 1H), 8.08 (s, 1H), 7.88 (s, 1H), 7.55 (s, 1H), 7.04 (s, 1H), 4.17 (t, *J* = 6.0, 2H), 3.61-3.49 (m, 4H), 2.96 (s, 3H), 2.67 (t, *J* = 6.4, 2H), 2.39 (s, 3H).	372.1	0.015
4	N^4-methyl-N^2-(1-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.53 (s, 1H), 8.08 (s, 1H), 7.81 (s, 1H), 7.53 (s, 1H), 7.06 (s, 1H), 3.79 (s, 3H), 2.95 (s, 3H).	273.0	0.0097
5	5-chloro-N^2-(1-isopropyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.00 (s, 1H), 7.5 (s, 2H), 7.47 (s, 1H), 7.06 (s, 1H), 4.47-4.32 (m, 1H), 2.91 (s, 3H), 1.38 (d, *J* = 6.6, 6H).	267.0	
6	N^4-methyl-N^2-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.40 (s, 1H), 8.14 (s, 1H), 7.32 (s, 1H), 7.13 (s, 1H), 6.23 (s, 1H), 3.66 (s, 3H), 2.84 (d, *J* = 3.8, 3H).	273.0	0.016

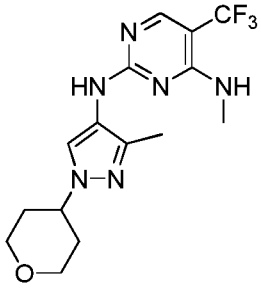
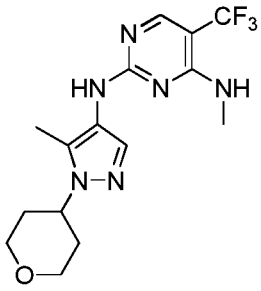
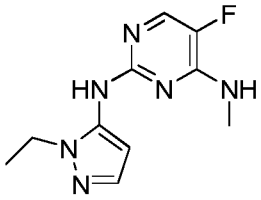
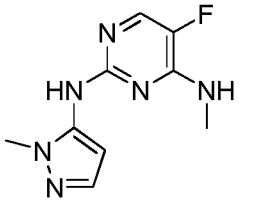
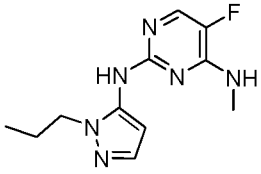
7	N^4-methyl-N^2-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.69 (s, 1H), 8.10 (s, 1H), 7.53 (s, 1H), 7.02 (s, 1H), 6.60 (s, 1H), 3.73 (s, 3H), 2.91 (s, 3H).	273.0	0.018
8	N^2-(1,3-dimethyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.86 (s, 1H), 8.07 (s, 1H), 7.79 (s, 1H), 6.94 (s, 1H), 3.72 (s, 3H), 2.88 (s, 3H), 2.10 (s, 3H).	287.0	
9	5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.78 (s, 1H), 8.15 (s, 1H), 7.44 (s, 1H), 5.20 (s, 1H), 3.85 (m, 2H), 3.69 (s, 3H), 3.47 (m, 2H), 2.15 (s, 3H), 1.98 (s, 2H), 1.66 (m, 2H).	324.1	0.039
10	N^4-methyl-5-(trifluoromethyl)-N^2-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.39 (m, 1H), 7.99 (s, 1H), 6.79 (s, 1H), 3.62 (s, 3H), 2.78 (m, 3H), 2.03 (s, 3H), 1.94 (s, 3H).	301.1	0.096
11	5-Chloro-N-(1-isopropyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amine		^{1}H-NMR (DMSO): δ 9.49 (s, 1H), 8.23 (s, 1H), 7.80 (s, 1H), 7.47 (s, 1H), 5.31 (m, 1H), 4.45 (m, 1H), 3.88 (m, 2H), 3.53 (m, 2H), 2.06 (m, 2H), 1.70 (m, 2H), 1.40 (d, 6H).	338.1	0.033

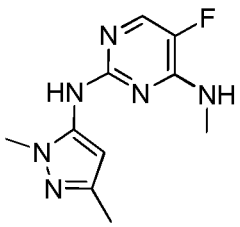
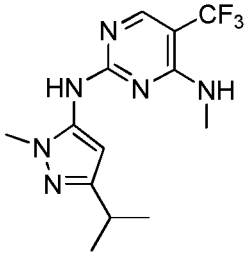
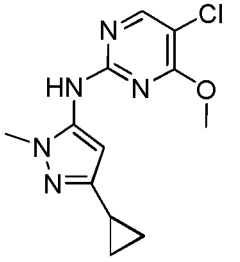
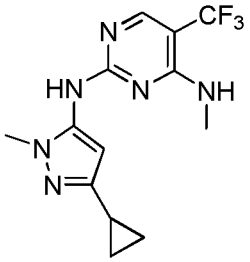
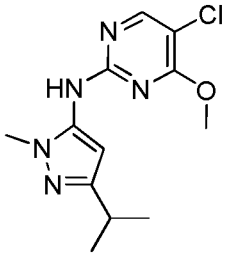
12	5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.82 (s, 1H), 8.13 (s, 1H), 7.48 (s, 1H), 3.91 (s, 3H), 3.69 (s, 3H), 2.15 (s, 3H).	254.0	0.0091
13	N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(pyrrolidin-1-yl)-5-(trifluoromethyl)pyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.88 (s, 1H), 8.22 (s, 1H), 7.61 (s, 1H), 3.69 (s, 3H), 3.51 (s, 4H), 2.17 (s, 3H), 1.87 (s, 4H).	327.1	0.012
14	N^2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.90 (s, 1H), 8.05 (s, 1H), 7.67 (s, 1H), 6.95 (s, 1H), 4.01 (m, 2H), 2.82 (s, 3H), 2.19 (s, 3H), 1.27 (t, *J* = 7.2, 3H).	301.1	0.024
15	5-Chloro-N-(1,3-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.87 (s, 1H), 8.17 (s, 1H), 7.77 (s, 1H), 3.95 (s, 3H), 3.72 (s, 3H), 2.09 (s, 3H).	254.0	0.0144
16	N^4-methyl-N^2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.97 (s, 1H), 8.08 (m, 2H), 6.96 (s, 1H), 5.44 (m, 1H), 4.85 (m, 4H), 2.89 (d, *J* = 4.4, 3H), 2.18 (s, 3H).	329.1	

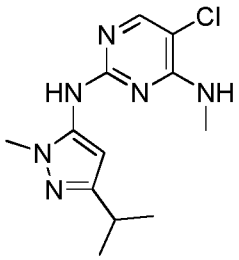
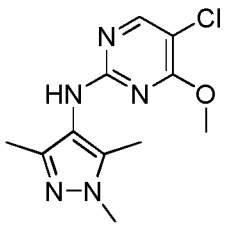
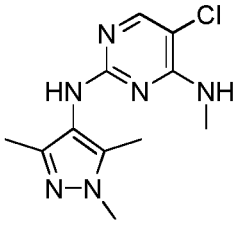
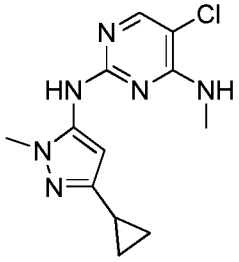
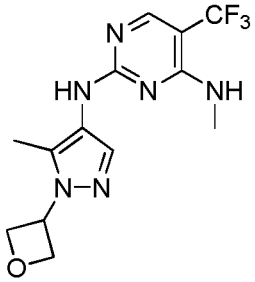
17	N^2-(5-chloro-1-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.87 (s, 1H), 8.07 (s, 1H), 7.71 (s, 1H), 6.98 (s, 1H), 3.77 (s, 3H), 2.83 (s, 3H).	307.0	
18	5-Chloro-4-methoxy-N-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.97 (s, 1H), 8.19 (s, 1H), 7.98 (s, 1H), 5.46 (s, 1H), 4.85 (s, 4H), 3.96 (s, 3H), 2.18 (s, 3H).	296.0	0.022
19	5-Chloro-4-methoxy-N-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)pyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.81 (s, 1H), 8.13 (s, 1H), 7.53 (s, 1H), 4.14 (t, *J* = 5.4, 2H), 3.90 (s, 3H), 3.63 (t, *J* = 5.4, 2H), 3.21 (s, 3H), 2.16 (s, 3H)	298.0	0.015
20	5-chloro-4-methoxy-N-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)pyrimidin-2-amine		1H-NMR (DMSO): δ 8.90 (s, 1H), 8.17 (s, 1H), 7.83 (s, 1H), 4.13 (t, *J* = 5.2, 2H), 3.95 (s, 3H), 3.63 (t, *J* = 5.3, 2H), 3.22 (s, 3H), 2.11 s, 3H).	298.0	0.019
21	5-Chloro-N-(5-chloro-1-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.99 (s, 1H), 8.18 (s, 1H), 7.67 (s, 1H), 3.91 (s, 3H), 3.78 (s, 3H).	274.0	0.020

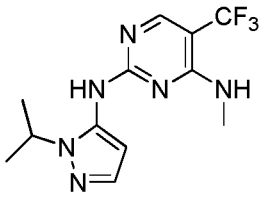
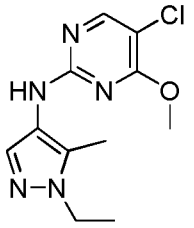
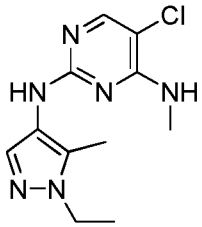
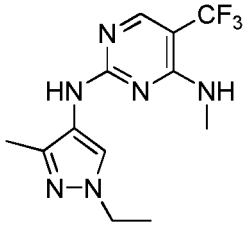
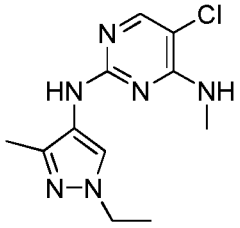
22	2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol		^{1}H-NMR (DMSO): δ 8.89 (s, 1H), 8.07 (s, 1H), 7.95 (s, 1H), 6.93 (s, 1H), 4.60 (s, 1H), 3.88 (s, 2H), 2.87 (d, *J* = 4.1, 3H), 2.13 (s, 3H), 1.05 (s, 6H).	345.1	
23	2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-chloro-pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol		^{1}H-NMR (DMSO): δ 8.92 (s, 1H), 8.18 (s, 1H), 7.86 (s, 1H), 4.61 (s, 1H), 3.94 (s, 3H), 3.89 (s, 2H), 2.12 (s, 3H), 1.05 (s, 6H).	312.1	0.027
24	N^2-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.82 (s, 1H), 8.04 (s, 1H), 7.64 (s, 1H), 6.88 (s, 1H), 4.13 (t, *J* = 5.4, 2H), 3.63 (t, *J* = 5.4, 2H), 3.21 (s, 3H), 2.83 (s, 3H), 2.17 (s, 3H)	331.1	0.019
25	N^2-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.89 (s, 1H), 8.07 (s, 1H), 7.91 (s, 1H), 6.94 (s, 1H), 4.12 (t, *J* = 5.2, 2H), 3.63 (t, *J* = 5.3, 2H), 3.22 (s, 3H), 2.88 (d, *J* = 4.4, 3H), 2.12 (s, 3H).	331.1	
26	5-Chloro-N-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-		^{1}H-NMR (DMSO): δ 8.87 (s, 1H), 8.17 (s, 1H), 7.81 (s, 1H), 4.01 (q, *J* = 7.3, 2H), 3.95 (s, 3H), 2.10 (s,	268.0	0.013

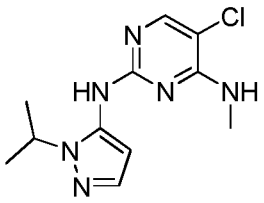
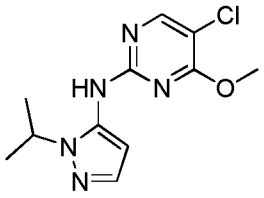
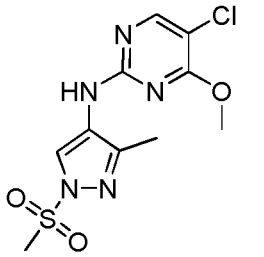
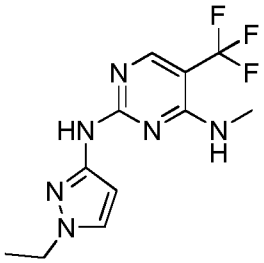
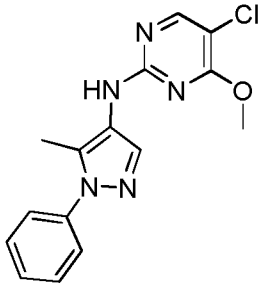
	methoxypyrimidin-2-amine		3H), 1.32 (t, *J* = 7.3, 3H).		
27	5-Chloro-N^4-methyl-N^2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.36 (s, 1H), 7.97 (s, 1H), 7.82 (s, 1H), 7.01 (d, *J* = 4.5, 1H), 5.43 (m, 1H), 4.85 (m, 4H), 2.88 (d, *J* = 4.6, 3H), 2.17 (s, 3H).	295.0	0.0088
28	N^2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.89 (s, 1H), 8.07 (s, 1H), 7.93 (s, 1H), 6.95 (s, 1H), 4.34 (m, 1H), 2.88 (d, *J* = 4.4, 3H), 2.12 (s, 3H), 1.37 (d, *J* = 6.7, 6H).	315.1	
29	5-Chloro-N-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.87 (s, 1H), 8.17 (s, 1H), 7.84 (s, 1H), 4.36 (m, 1H), 3.95 (s, 3H), 2.11 (s, 3H), 1.37 (d, *J* = 6.7, 6H).	282.1	0.022
30	5-Chloro-N^2-(1,3-dimethyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.25 (s, 1H), 7.80 (s, 1H), 7.74 (s, 1H), 6.98 (d, *J* = 4.5, 1H), 3.70 (s, 3H), 2.87 (d, *J* = 4.6, 3H), 2.08 (s, 3H).	253.0	
31	5-Chloro-N^2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.26 (s, 1H), 7.83 (s, 1H), 7.80 (s, 1H), 6.98 (d, *J* = 4.3, 1H), 4.33 (m, 1H), 2.87 (d, *J* = 4.6, 3H), 2.10 (s, 3H), 1.36 (d, *J* = 6.7, 7H).	281.1	0.012

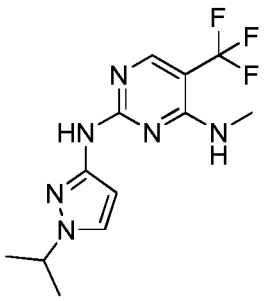
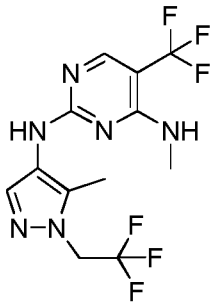
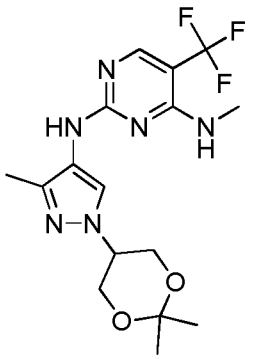
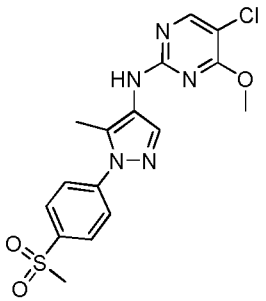
32	N^4-methyl-N^2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.90 (s, 1H), 8.07 (s, 1H), 7.96 (s, 1H), 6.95 (s, 1H), 4.24 (s, 1H), 3.93 (d, *J* = 10.9, 2H), 3.44 (t, *J* = 12.5, 2H), 2.89 (d, *J* = 4.3, 3H), 2.13 (s, 3H), 1.92 (s, 4H).	357.2	0.024
33	N^4-methyl-N^2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.83 (s, 1H), 8.04 (s, 1H), 7.65 (s, 1H), 6.89 (s, 1H), 4.33 (m, 1H), 3.95 (m, 2H), 3.47 (t, *J* = 11.2, 2H), 2.84 (s, 3H), 2.21 (s, 3H), 2.02 (m, 2H), 1.82-1.67 (m, 2H).	357.2	
34	N^2-(2-Ethyl-2H-pyrazol-3-yl)-5-fluoro-N^4-methyl-pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.75 (s, 1H), 7.78 (d, 1H), 7.39 (s, 1H), 7.30 (s, 1H), 3.17 (s, 1H), 3.99 (q, 2H), 2.82 (d, 3H), 1.26 (t, 3H).	237.1	
35	5-Fluoro-N^4-methyl-N^2-(2-methyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.77 (s, 1H), 7.78 (s, 1H), 7.37 (s, 1H), 7.26 (s, 1H), 6.17 (s, 1H), 3.64 (s, 3H), 2.82 (d, 3H).	223.1	0.267
36	5-Fluoro-N^4-methyl-N^4-(2-propyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.79 (s, 1H), 7.78 (s, 1H), 7.41 (s, 1H), 7.29 (s, 1H), 6.19 (s, 1H), 3.94 (t, 2H), 2.82 (d, 3H), 1.69 (m, 2H), 0.80 (t, 3H).	251.0	

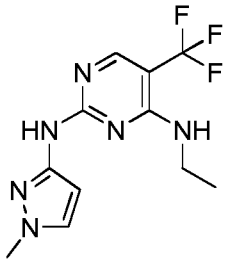
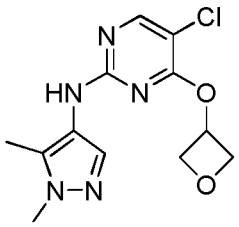
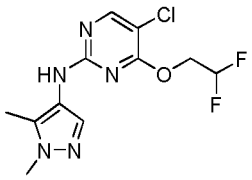
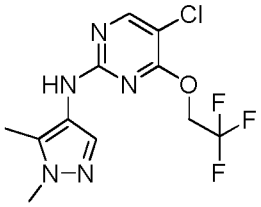
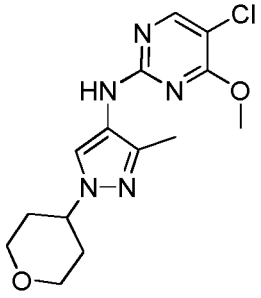
37	N^2-(2,5-Dimethyl-2H-pyrazol-3-yl)-5-fluoro-N^4-methyl-pyrimidine-2,4-diamine			237.0	
38	N^2-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.36 (s, 1 H), 8.14 (s, 1 H), 7.13 (d, *J* = 5.2, 1 H), 6.08 (s, 1 H), 3.59 (s, 3 H), 2.86 (d, *J* = 4.3, 3 H), 2.84-2.73 (m, 1 H), 1.17 (d, *J* = 6.9, 6 H).	315	0.012
39	5-Chloro-N-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine		^{1}H-NMR ($CDCl_3$): δ 8.11 (s, 1 H), 6.64 (s, 1 H), 5.94 (s, 1 H), 3.98 (s, 3 H), 3.69 (s, 3 H), 1.93-1.84 (m, 1 H), 0.94-0.84 (m, 2 H), 0.76-0.68 (m, 2 H).	280	0.059
40	N^2-(3-Cyclopropyl-1-methyl-1*H*-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.35 (s, 1 H), 8.13 (s, 1 H), 7.13 (d, *J* = 5.2, 1 H), 5.94 (s, 1 H), 3.56 (s, 3 H), 2.85 (d, *J* = 4.3, 3 H), 1.78 (tt, *J* = 8.4, *J* = 5.0, 1 H), 0.84-0.74 (m, 2 H), 0.63-0.55 (m, 2 H).	313	
41	5-Chloro-N-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine		^{1}H-NMR ($CDCl_3$): δ 8.12 (s, 1 H), 6.65 (s, 1 H), 6.11 (s, 1 H), 3.98 (s, 3 H), 3.72 (s, 3 H), 2.98-2.88 (m, 1 H), 1.27 (d, *J* = 6.9, 6 H).	282	0.070

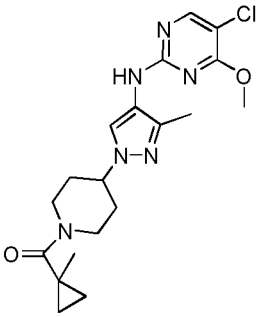
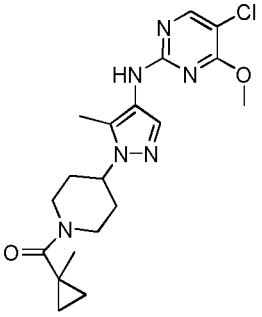
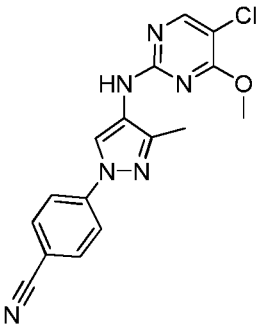
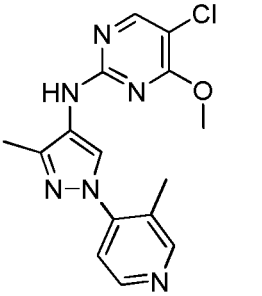
42	5-Chloro-N^2-(5-isopropyl-2-methyl-2H-pyrazol-3-yl)-N^4-methyl-pyrimidine-2,4-diamine		^{1}H-NMR ($CDCl_3$): δ 7.87 (s, 1 H), 6.44 (s, 1 H), 6.13 (s, 1 H), 5.29 (s, 1 H), 3.71 (s, 3 H), 3.01 (d, *J* = 4.9, 3 H), 2.97-2.89 (m, 1 H), 1.27 (d, *J* = 6.9, 6 H).	281	0.016
43	5-Chloro-4-methoxy-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine		^{1}H-NMR ($CDCl_3$): δ 8.04 (s, 1 H), 6.04 (s, 1 H), 3.93 (s, 3 H), 3.73 (s, 3 H), 2.13 (d, *J* = 5.39, 6 H).	268	
44	5-Chloro-N^4-methyl-N^2-(1,3,5-trimethyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine		^{1}H-NMR ($CDCl_3$): δ 7.80 (s, 1 H), 5.94 (s, 1 H), 5.18 (s, 1 H), 3.72 (s, 3 H), 2.97 (d, *J* = 4.9, 3 H), 2.14 (d, *J* = 2.9, 6 H).	267	
45	5-Chloro-N^2-(5-cyclopropyl-2-methyl-2H-pyrazol-3-yl)-N^4-methyl-pyrimidine-2,4-diamine		^{1}H-NMR ($CDCl_3$): δ 7.86 (s, 1 H), 6.41 (s, 1 H), 5.95 (s, 1 H), 5.29 (s, 1 H), 3.69 (s, 3 H), 3.01 (d, *J* = 4.9, 3H), 1.92-1.85 (m, 1 H), 0.91-0.85 (m, 2 H), 0.73-0.68 (m, 2 H).	279	0.0134
46	N^4-Methyl-N^2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.91 (s, 1H), 8.05 (s, 1H), 7.86 (s, 1H), 6.94 (s, 1H), 5.53 (m, 1H), 4.93 (m, 2H), 4.90-4.83 (m, 2H), 2.85 (s, 3H), 2.14 (s, 3H).	329	

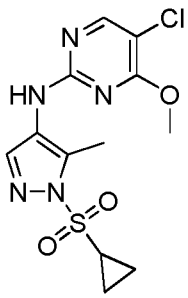
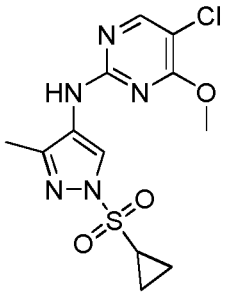
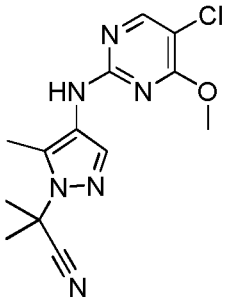
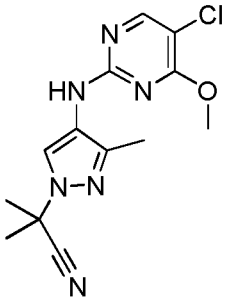
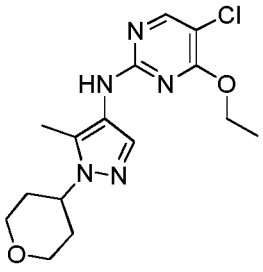
47	N^2-(1-isopropyl-1*H*-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 9.27 (s, 1 H), 8.12 (s, 1 H), 7.38 (d, *J* = 1.8, 1 H), 7.11 (d, *J* = 5.2, 1 H), 6.17 (s, 1 H), 4.54-4.46 (m, 1 H), 2.81 (d, *J* = 4.3, 3 H), 1.32 (d, *J* = 6.6, 6 H).	301	0.112
48	5-Chloro-N-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine		^{1}H-NMR (DMSO): δ 8.81 (s, 1H), 8.14 (s, 1H), 7.51 (s, 1H), 4.02 (q, *J* = 7.1, 2H), 3.91 (s, 3H), 2.17 (s, 3H), 1.28 (t, *J* = 7.1, 4H).	268.1	
49	5-Chloro-N^2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.21 (s, 1H), 7.76 (s, 1H), 7.51 (s, 1H), 6.94 (s, 1H), 4.0 (q, *J* = 7.1, 2H), 2.83 (d, *J* = 3.7, 3H), 2.15 (s, 3H), 1.27 (t, *J* = 7.2, 3H).	267.1	
50	N^2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.88 (s, 1H), 8.07 (s, 1H), 7.89 (s, 1H), 6.94 (s, 1H), 4.00 (q, *J* = 7.1, 2H), 2.88 (d, *J* = 3.9, 3H), 2.11 (s, 3H), 1.32 (t, *J* = 7.2, 3H).	301.1	
51	5-Chloro-N^2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.26 (s, 1H), 7.80 (s, 2H), 6.99 (s, 1H), 3.98 (q, 2H), 2.86 (s, 3H), 2.10 (s, 3H), 1.32 (t, 3H).	267.1	

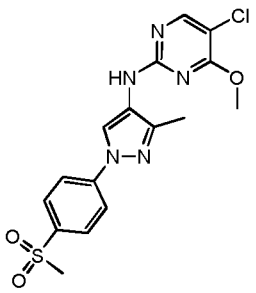
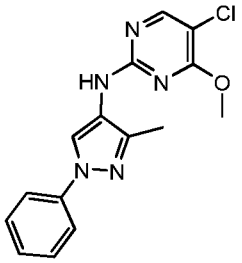
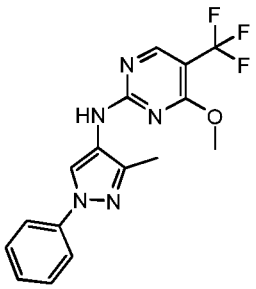
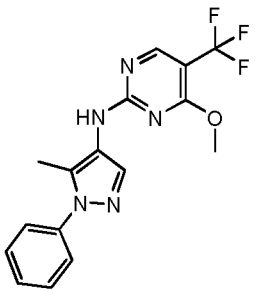
52	5-chloro-N^2-(1-isopropyl-1H-pyrazol-5-yl)-N^4-methylpyrimidine-2,4-diamine				
53	5-chloro-N-(1-isopropyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine				
54	5-chloro-4-methoxy-N-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidin-2-amine		1H NMR (400 MHz, DMSO) δ 9.44 (s, 1H), 8.41 (s, 1H), 8.34 (s, 1H), 4.01 (s, 3H), 3.42 (s, 3H), 2.32 (s, 3H).		0.0078
55	N^2-(1-ethyl-1H-pyrazol-3-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine				
56	5-chloro-4-methoxy-N-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine		1H NMR (400 MHz, DMSO) δ 9.17 (s, 1H), 8.57 (s, 1H), 8.25 (s, 1H), 7.73 (d, J = 7.9, 2H), 7.46 (t, J = 7.9, 2H), 7.23 (t, J = 7.4, 1H), 4.01 (s, 3H), 2.26 (s, 3H).	316.1	0.027

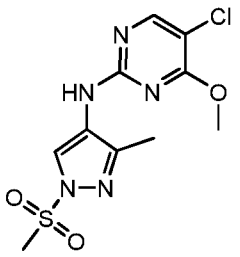
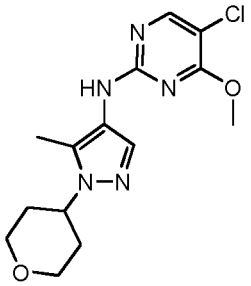
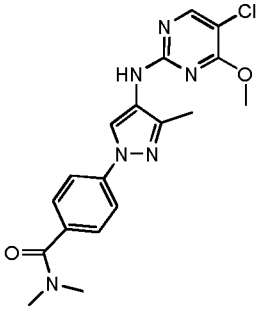
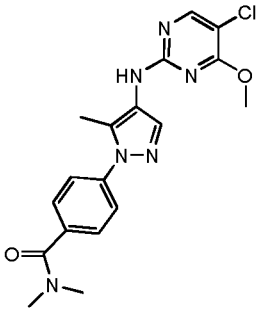
57	N^2-(1-isopropyl-1H-pyrazol-3-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			0.0025	
58	N^4-methyl-N^2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.88 (s, 1H), 8.06 (s, 1H), 7.74 (s, 1H), 6.93 (s, 1H), 5.01 (q, J = 9.2, 2H), 2.82 (s, 3H), 2.22 (s, 3H).		0.0036
59	N^2-(1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			387	
60	5-chloro-4-methoxy-N-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine				0.015

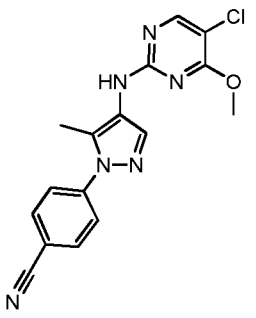
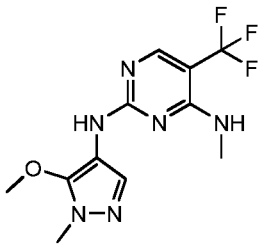
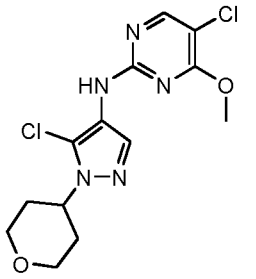
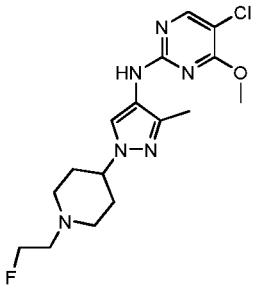
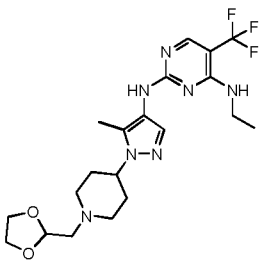
61	N^4-ethyl-N^2-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.0046
62	5-chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(oxetan-3-yloxy)pyrimidin-2-amine				0.039
63	5-chloro-4-(2,2-difluoroethoxy)-N-(1,5-dimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine				0.024
64	5-chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(2,2,2-trifluoroethoxy)pyrimidin-2-amine				0.0586
65	5-chloro-4-methoxy-N-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine		1H NMR (400 MHz, DMSO) δ 8.82 (s, 1H), 8.14 (s, 1H), 7.57 (s, 1H), 4.41 – 4.26 (m, 1H), 4.03 – 3.82 (m, 5H), 3.47 (t, J = 11.3, 2H), 2.20 (s, 3H), 2.01 (qd, J = 12.4, 4.5, 2H), 1.76 (dd, J = 12.5, 2.1, 2H).		0.0029

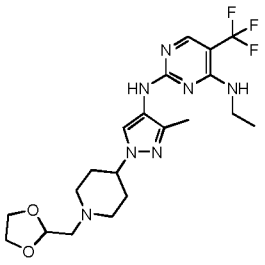
66	(4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone		1H NMR (400 MHz, DMSO) δ 8.82 (s, 1H), 8.14 (s, 1H), 7.58 (s, 1H), 4.36 (m, 3H), 3.91 (s, 2H), 3.01 (s, 2H), 2.21 (s, 3H), 1.87 (m, 4H), 0.80 (m, 2H), 0.55 (m, 2H).		0.066
67	(4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone		1H NMR (400 MHz, DMSO) δ 8.88 (s, 1H), 8.17 (s, 1H), 7.89 (s, 1H), 4.39 – 4.24 (m, 4H), 2.96 (s, 2H), 2.11 (s, 3H), 2.01 (m, 3H), 1.74 (m, 3H), 1.24 (s, 4H), 0.81 (t, J = 5.1, 2H), 0.54 (m, 2H).		0.0089
68	4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)benzonitrile		1H NMR (400 MHz, DMSO) δ 9.29 (s, 1H), 8.71 (s, 1H), 8.27 (s, 1H), 7.98 – 7.86 (m, 4H), 4.02 (s, 3H), 2.29 (s, 3H).		0.0024
69	5-chloro-4-methoxy-N-(3-methyl-1-(3-methylpyridin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine		1H NMR (400 MHz, DMSO) δ 9.25 (s, 1H), 8.53 (s, 1H), 8.46 (d, J = 5.4, 1H), 8.43 (s, 1H), 8.26 (s, 1H), 7.47 (d, J = 5.4, 1H), 4.01 (s, 3H), 2.45 (s, 3H), 2.29 (s, 3H).		0.055

70	5-chloro-N-(1-(cyclopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine			334.0	0.015
71	5-chloro-N-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine		1H NMR (400 MHz, DMSO) δ 9.44 (s, 1H), 8.39 (s, 1H), 8.34 (s, 1H), 4.01 (s, 3H), 3.10 – 2.95 (m, 1H), 2.31 (s, 3H), 1.17 (m, 4H).		0.020
72	2-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile		1H NMR (400 MHz, DMSO) δ 8.98 (s, 1H), 7.69 (s, 1H), 7.06 (s, 1H), 3.91 (s, 3H), 2.40 (s, 3H), 1.95 (s, 6H).		0.016
73	2-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile		1H NMR (400 MHz, DMSO) δ 9.11 (s, 1H), 8.14 (s, 1H), 7.07 (s, 1H), 3.98 (s, 3H), 2.18 (s, 3H), 1.93 (s, 7H).		0.014
74	5-chloro-4-ethoxy-N-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-		1H NMR (400 MHz, DMSO) δ 8.84 (s, 1H), 8.17 (s, 1H), 7.84 (s, 1H), 4.41 (q, J = 7.0, 2H), 4.31 – 4.16 (m, 1H), 4.06 – 3.84 (m, 2H), 3.44 (td, J = 11.5, 2.7, 2H), 2.11 (s, 3H),	338.1	

	amine		1.98 – 1.77 (m, 4H), 1.34 (t, J = 7.1, 3H).		
75	(5-Chloro-4-methoxy-pyrimidin-2-yl)-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-amine				0.0022
76	(5-Chloro-4-methoxy-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine				0.0023
77	(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine				0.0016
78	(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(5-methyl-1-phenyl-1H-pyrazol-4-yl)-amine				0.0381

79	(5-Chloro-4-methoxy-pyrimidin-2-yl)-(1-methanesulfonyl-3-methyl-1H-pyrazol-4-yl)-amine				0.0078
80	(5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-methyl-1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine				0.0663
81	4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide				0.0022
82	4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide				0.63

83	4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-benzonitrile				0.0090
84	N^2-(5-Methoxy-1-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0742
85	(5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-chloro-1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine				0.0066
86	(5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoro-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-amine				0.183
87	N^2-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl]-N^4-ethyl-5-trifluoromethyl-				0.0008

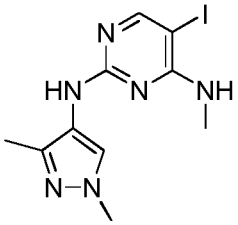
	pyrimidine-2,4-diamine				
88	N^2-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-N^4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0094

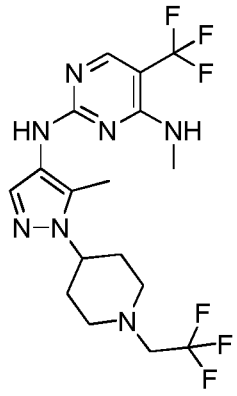
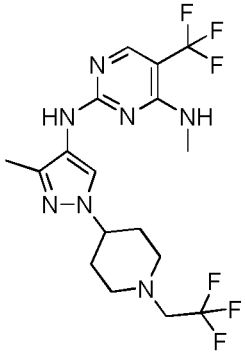
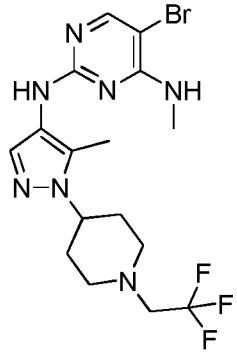
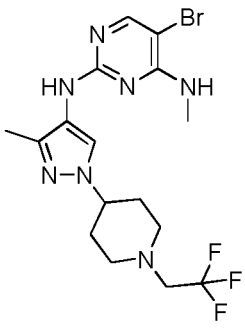
Example 89 5-Bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine

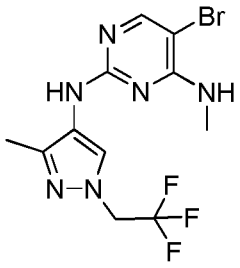
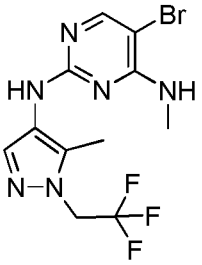
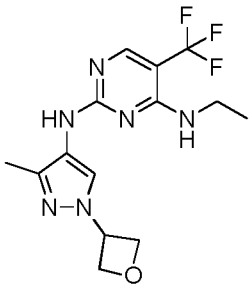
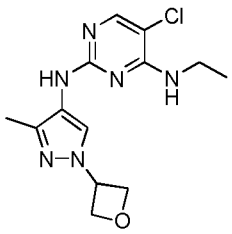
To a mixture of 5-bromo-2-chloro-N-methylpyrimidin-4-amine (0.201 g, 0.903 mmol) and 1,5-dimethyl-1H-pyrazol-4-amine (0.12 g, 1.08 mmol) in 2-methoxyethanol (2 mL) was added TFA (0.070 mL, 0.9 mmol). The reaction was stirred in a sealed tube at 100 °C for 90 minutes. The resulting precipitate was collected by filtration. The isolated solid was further purified by reverse phase HPLC to give 5-bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine (46 mg, 17%). LCMS (Method A): [MH+] = 297.0 at 2.57 min. 1H-NMR (DMSO): δ 8.28 (s, 1H), 7.84 (s, 1H), 7.49 (s, 1H), 6.79 (d, J = 3.4, 1H), 3.67 (s, 3H), 2.82 (d, J = 3.6, 3H), 2.14 (s, 3H). Ki = 0.017 μM.

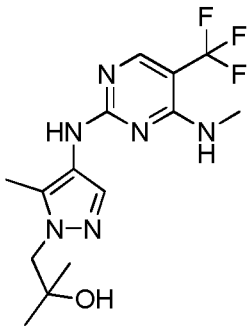
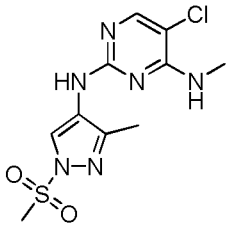
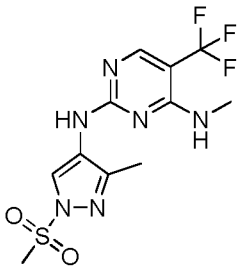
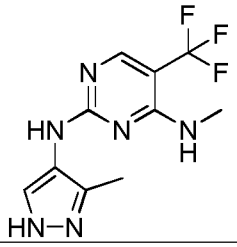
Compounds made using the above procedure are shown in Table 8 below, together with low resolution mass spectrometry (M+H), proton NMR, and LRRK2 Ki (micromolar) data for selected compounds determined from the assay described below.

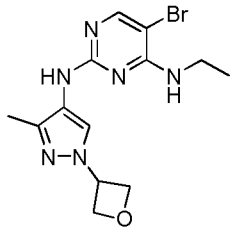
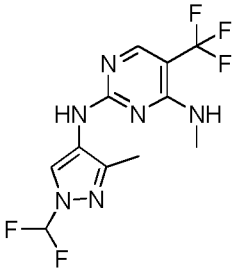
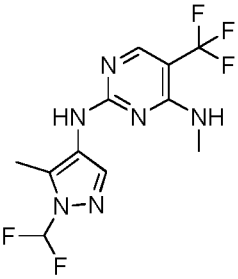
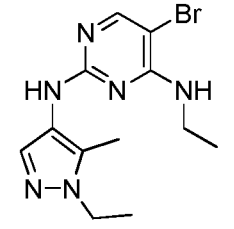
Table 8

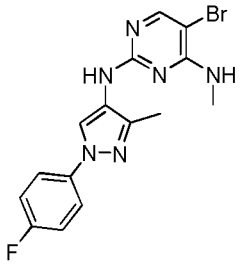
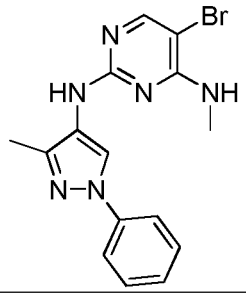
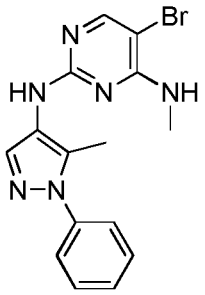
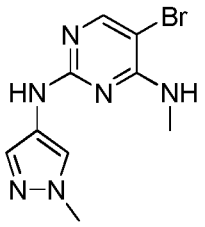
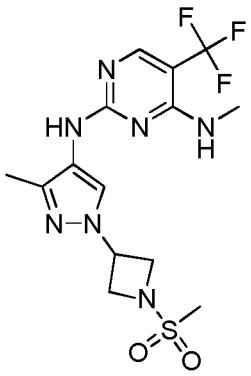
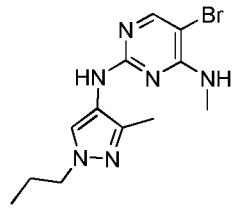
	Name	Structure	^{1}H NMR	M+H$^+$	K_I
90	N^2-(1,3-Dimethyl-1H-pyrazol-4-yl)-5-iodo-N^4-methyl-pyrimidine-2,4-diamine		^{1}H-NMR (DMSO): δ 8.24 (s, 1H), 7.98 (s, 1H), 7.73 (s, 1H), 6.46 (d, *J* = 4.3, 1H), 3.70 (s, 3H), 2.85 (d, *J* = 4.6, 3H), 2.08 (s, 3H).	345.0	

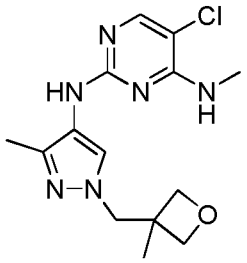
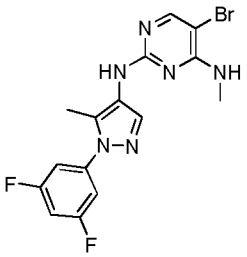
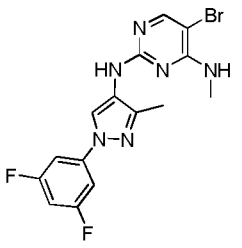
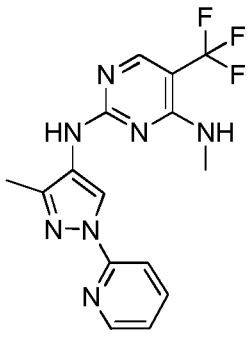
91	N4-methyl-N2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine			438.2	0.0041
92	N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine			438.2	0.046
93	5-bromo-N4-methyl-N2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.22 (s, 1H), 7.84 (s, 1H), 7.56 (s, 1H), 6.76 (d, J = 4.6, 1H), 4.12 – 4.00 (m, 1H), 3.22 (q, J = 10.2, 2H), 3.00 (d, J = 11.9, 2H), 2.82 (d, J = 4.5, 3H), 2.56 (d, J = 11.9, 2H), 2.01 (qd, J = 12.3, 3.7, 2H), 1.75 (d, J = 13.4, 2H).		0.0014
94	5-bromo-N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.28 (s, 1H), 7.86 (d, J = 13.2, 2H), 6.80 (d, J = 4.6, 1H), 4.05 – 3.93 (m, 1H), 3.21 (dd, J = 20.6, 10.3, 5H), 2.98 (d, J = 12.0, 2H), 2.86 (d, J = 4.6, 3H), 2.00 – 1.80 (m, 5H).		0.013

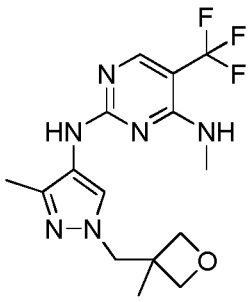
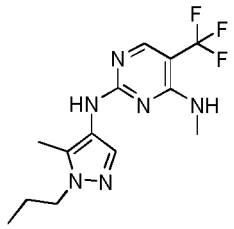
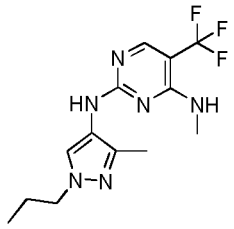
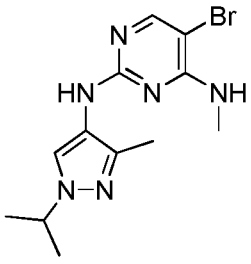
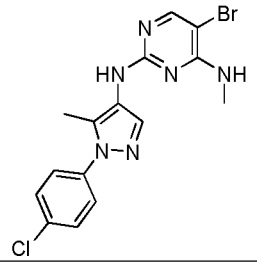
95	5-bromo-N4-methyl-N2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.45 (s, 1H), 7.98 (s, 1H), 7.91 (s, 1H), 6.86 (d, J = 4.4, 1H), 4.96 (q, J = 9.2, 2H), 2.87 (d, J = 4.6, 3H), 2.15 (s, 3H).		0.0012
96	5-bromo-N4-methyl-N2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.35 (s, 1H), 7.86 (s, 1H), 7.68 (s, 1H), 6.80 (d, J = 4.5, 1H), 4.99 (q, J = 9.2, 2H), 2.81 (d, J = 4.5, 3H), 2.20 (s, 3H).		0.0011
97	N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.06* (br s, 1H), 8.69† (br s, 1H), 8.33† (s, 1H), 8.13* (s, 1H), 8.09* (br s, 1H), 7.94† (br s, 1H), 7.09* (br s, 1H), 6.95† (br s, 1H), 5.47 (p, J = 7.0, 1H), 4.92-4.85 (m, 4H), 3.68-3.30 (m, 2H), 2.21 (s, 3H), 1.17 (t, J = 7.0, 3H). [* and † denote rotameric peaks.]	343	0.0016
98	5-chloro-N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.44 (br s, 1H), 8.01 (s, 1H), 7.87 (s, 1H), 7.10 (s, 1H), 5.46 (t, J = 7.0, 1H), 4.89 (dt, J = 22.1, 6.7, 4H), 3.44 (p, J = 6.7, 2H), 2.20 (s, 3H), 1.18 (t, J = 7.1, 3H).	309	0.0031

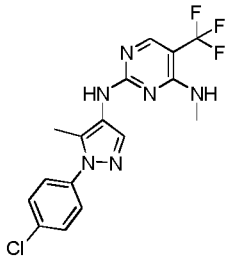
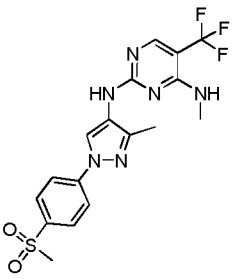
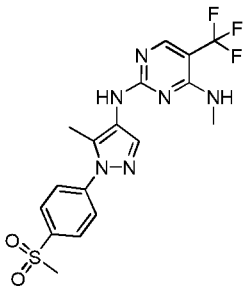
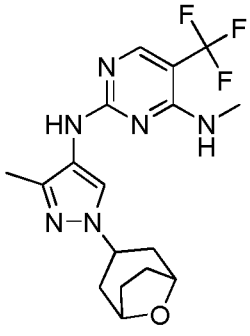
99	5-bromo-N4-methyl-N2-(1-methyl-1H-pyrazol-5-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.04 (s, 1H), 8.29 (s, 1H), 7.99 (s, 1H), 7.32 (d, J = 2.0, 1H), 7.05 (q, J = 4.7, 1H), 6.23 (d, J = 2.0, 1H), 3.68 (s, 3H), 2.86 (d, J = 4.7, 3H). Note: formic acid salt.	283	0.0054
100	2-methyl-1-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol		1H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.76 (br s, 1H), 6.69 (br s, 1H), 5.15 (s, 1H), 4.49 (s, 1H), 3.97 (s, 2H), 2.98 (d, J = 4.6, 3H), 2.21 (s, 3H), 1.18 (s, 6H).	345	0.0085
101	5-chloro-N4-methyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.88 (s, 1H), 8.43 (s, 1H), 7.95 (s, 1H), 7.22 (d, J = 4.3, 1H), 3.38 (s, 3H), 2.91 (d, J = 4.6, 3H), 2.31 (s, 3H).		0.0088
102	N4-methyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.35 (s, 1H), 8.47 (s, 1H), 8.20 (s, 1H), 7.17 (s, 1H), 3.41 (s, 3H), 2.93 (d, J = 4.4, 3H), 2.32 (s, 3H).		0.0029
103	N4-methyl-N2-(3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-		1H NMR (400 MHz, DMSO) δ 12.20 (d, J = 43.0, 1H), 8.81 (s, 1H), 8.06 (s, 1H), 7.79 (d, J = 67.1, 1H), 6.90 (s, 1H),		0.0090

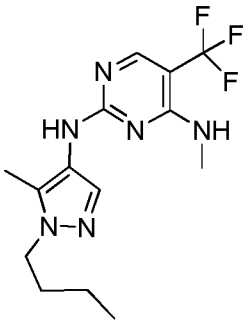
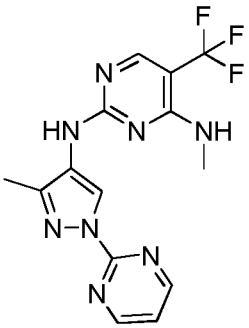
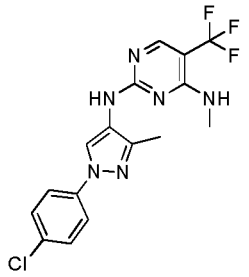
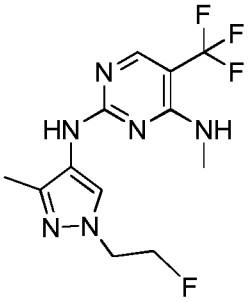
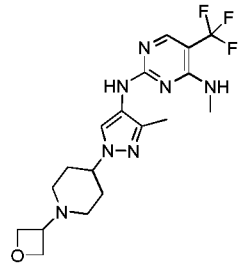
	diamine		2.86 (s, 3H), 2.15 (s, 3H).		
104	5-bromo-N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.46 (br s, 1H), 8.00 (s, 1H), 7.94 (s, 1H), 6.90 (s, 1H), 5.47-5.45 (m, 1H), 4.89 (dt, J = 22.8, 6.7, 4H), 3.44 (p, J = 6.7, 2H), 2.20 (s, 3H), 1.18 (t, J = 7.1, 3H).	353	0.0014
105	N2-(1-(difluoromethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.04 (s, 1H), 8.09 (s, 1H), 7.98 (s, 1H), 7.71 (t, J = 58.1, 1H), 7.01 (s, 1H), 2.84 (s, 3H), 2.34 (s, 3H).		0.0055
106	N2-(1-(difluoromethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.20 (s, 1H), 8.31 (s, 1H), 8.15 (s, 1H), 7.66 (t, J = 59.5, 1H), 7.15 (s, 1H), 2.91 (d, J = 4.4, 3H), 2.24 (s, 3H).		0.0019
107	5-bromo-N4-ethyl-N2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.20 (s, 1H), 7.85 (s, 1H), 7.49 (s, 1H), 6.72 (t, J = 5.5, 1H), 4.00 (q, J = 7.2, 2H), 3.35 (p, J = 6.9, 2H), 2.15 (s, 3H), 1.27 (t, J = 7.2, 3H), 1.10 (t, J = 7.1, 3H).		0.0004 3

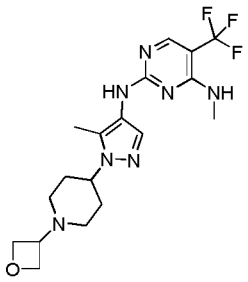
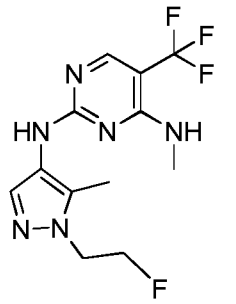
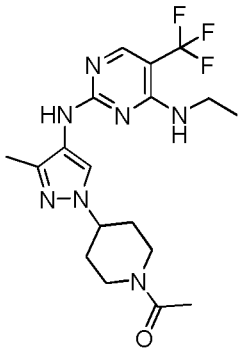
108	5-bromo-N2-(1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.47 (s, 1H), 7.88 (m, 2H), 7.60 – 7.49 (m, 2H), 7.34 (t, J = 8.4, 2H), 6.84 (s, 1H), 2.86 (d, J = 3.8, 3H), 2.23 (s, 3H).		0.0003
109	5-bromo-N4-methyl-N2-(3-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine			360	0.0084
110	5-bromo-N4-methyl-N2-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine			360	
111	5-bromo-N4-methyl-N2-(1-methyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine				
112	N4-methyl-N2-(3-methyl-1-(1-(methylsulfonyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (300MHz, CD_3OD) δ 8.12 (s, 1H), 7.93 (s, 1H), 5.22-5.13 (m, 1H), 4.35-4.30 (m, 4H), , 3.31 (s, 3H), 3.31 (s, 3H), 2.24 (s, 3H)		
113	5-bromo-N4-methyl-N2-(3-methyl-1-propyl-1H-pyrazol-4-yl)pyrimidine-		1H NMR (400 MHz, DMSO) δ 8.22 (s, 1H), 7.84 (s, 1H), 7.51 (s, 1H), 6.75 (d, J = 4.0, 1H), 3.92 (t, J = 7.0, 2H), 2.81 (d, J =		0.012

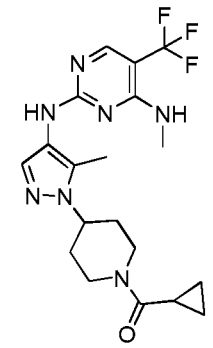
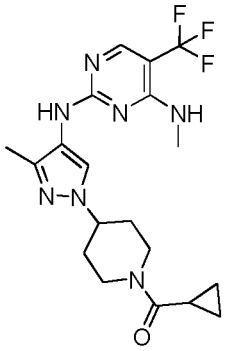
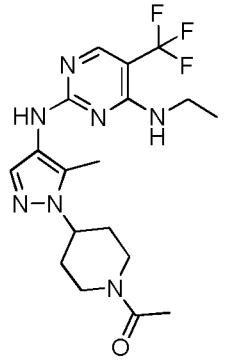
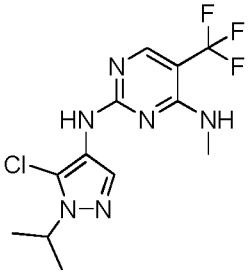
	2,4-diamine		4.3, 3H), 2.15 (s, 3H), 1.70 (h, J = 7.2, 2H), 0.83 (t, J = 7.4, 3H).		
114	5-chloro-N4-methyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.36 (s, 1H), 7.84 (s, 1H), 7.82 (s, 1H), 7.04 (q, J = 4.7, 1H), 4.57 (d, J = 5.8, 2H), 4.20 (d, J = 6.0, 3H), 3.44 (br s, 2H), 2.86 (d, J = 4.6, 3H), 2.11 (s, 2H), 1.14 (s, 3H).	323	0.019
115	5-bromo-N2-(1-(3,5-difluorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.67 (s, 1H), 8.61 (s, 1H), 7.96 (s, 1H), 7.45 (d, J = 8.2, 2H), 7.06 (t, J = 9.2, 1H), 6.93 (d, J = 4.3, 1H), 2.91 (d, J = 4.5, 3H), 2.25 (s, 3H).		0.031
116	5-bromo-N2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.55 (s, 1H), 7.96 (s, 1H), 7.90 (s, 1H), 7.40 – 7.20 (m, 3H), 6.86 (d, J = 4.4, 1H), 2.86 (d, J = 4.5, 3H), 2.34 (s, 3H).		0.0003
117	N4-methyl-N2-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.20 (s, 2H), 8.40 (d, J = 4.7, 1H), 8.18 (s, 1H), 7.91 (t, J = 7.8, 1H), 7.83 (d, J = 8.2, 1H), 7.29 – 7.19 (m, 1H), 7.08 (s, 1H), 2.96 (d, J = 3.9, 3H), 2.32 (s, 3H).		0.0067

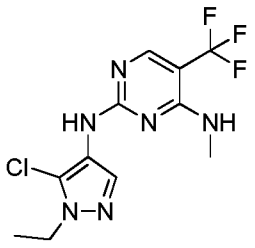
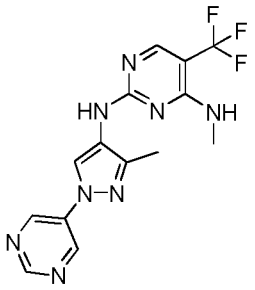
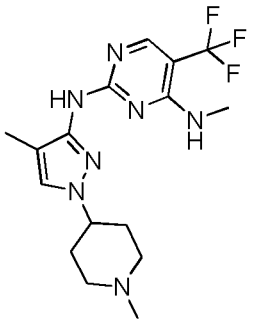
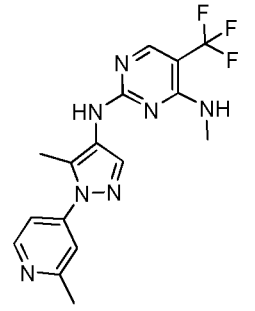
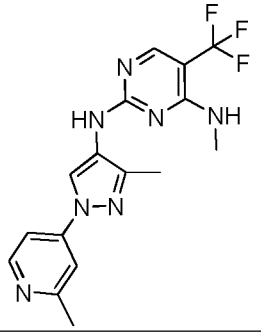
118	N4-methyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.83 (s, 1H), 6.59 (br s, 1H), 5.18 (br s, 1H), 4.69 (d, J = 6.1, 2H), 4.39 (d, J = 6.1, 2H), 4.24 (s, 2H), 3.05 (d, J = 4.7, 3H), 2.24 (s, 3H), 1.28 (s, 3H).	357	0.0072
119	N4-methyl-N2-(5-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.86 (s, 1H), 8.07 (s, 1H), 7.85 (s, 1H), 6.93 (s, 1H), 3.92 (t, J = 6.8, 2H), 2.87 (d, J = 4.0, 3H), 2.11 (s, 3H), 1.73 (h, J = 7.1, 2H), 0.82 (t, J = 7.3, 3H).		0.0056
120	N4-methyl-N2-(3-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.80 (s, 1H), 8.04 (s, 1H), 7.61 (s, 1H), 6.88 (s, 1H), 3.94 (t, J = 7.0, 2H), 2.82 (s, 3H), 2.12 (d, J = 39.3, 3H), 1.71 (h, J = 7.3, 2H), 0.84 (t, J = 7.3, 3H).		0.0006
121	5-bromo-N2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine -2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.28 (s, 1H), 7.88 (s, 1H), 7.83 (s, 1H), 6.80 (d, J = 4.3, 1H), 4.39 – 4.26 (m, 1H), 2.86 (d, J = 4.6, 3H), 2.10 (s, 3H), 1.36 (d, J = 6.7, 6H).		0.0031
122	5-bromo-N2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine		1H NMR (400 MHz, DMSO) δ 8.64 (s, 1H), 8.55 (s, 1H), 7.95 (s, 1H), 7.72 (d, J = 8.9, 2H), 7.49 (d, J = 8.9, 2H), 6.92 (d, J		0.014

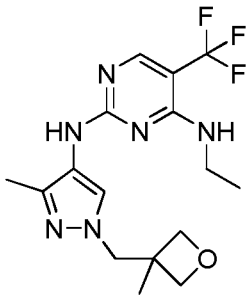
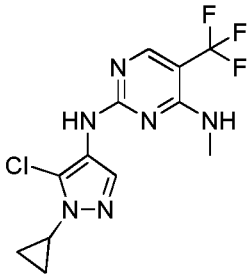
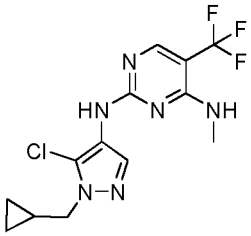
	-2,4-diamine		= 4.4, 1H), 2.91 (d, J = 4.5, 3H), 2.25 (s, 3H).		
123	N2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.03 (s, 1H), 8.05 (d, J = 33.8, 2H), 7.57 (s, 4H), 6.76 (d, J = 171.5, 2H), 2.88 (d, J = 3.9, 3H), 2.28 (s, 3H).		0.0003
124	N4-methyl-N2-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.12 (s, 1H), 8.07 (t, J = 13.9, 3H), 7.84 (d, J = 11.0, 2H), 7.00 (s, 1H), 3.28 (s, 3H), 2.88 (d, J = 4.0, 3H), 2.37 (s, 3H).		0.0003
125	N4-methyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.24 (s, 1H), 8.75 (s, 1H), 8.16 (s, 1H), 8.02 – 7.91 (m, 4H), 7.09 (s, 1H), 3.23 (s, 3H), 2.95 (d, J = 4.3, 3H), 2.31 (s, 3H).		0.0047
126	N2-(1-((1S,5S)-8-oxabicyclo[3.2.1] octan-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (300 MHz, CD_3OD) δ 8.05 (s, 2H), 4.37-4.46 (m, 3H), 3.00 (s, 3H), 2.45-2.42 (m, 4H), 2.25 (s, 3H), 1.79-1.77 (m, 4H)		0.113

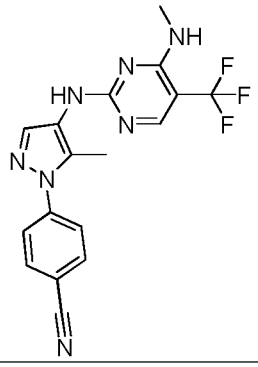
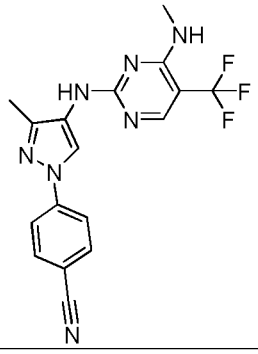
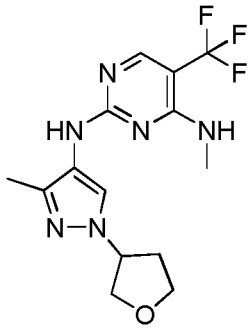
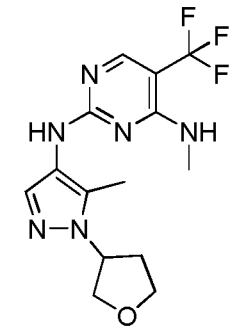
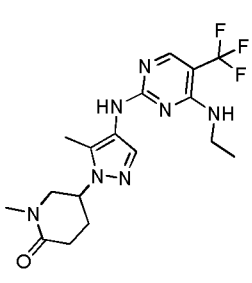
127	N2-(1-butyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			329.2	0.0003
128	N4-methyl-N2-(3-methyl-1-(pyrimidin-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.28 (s, 1H), 8.96 (s, 1H), 8.78 (d, J = 4.8, 2H), 8.19 (s, 1H), 7.35 (t, J = 4.8, 1H), 7.11 (s, 1H), 2.97 (d, J = 4.0, 3H), 2.33 (s, 3H).		0.0114
129	N2-(1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.16 (s, 1H), 8.60 (s, 1H), 8.14 (s, 1H), 7.74 (d, J = 8.8, 2H), 7.50 (d, J = 8.9, 2H), 7.05 (s, 1H), 2.93 (d, J = 4.4, 3H), 2.26 (s, 3H).		0.028
130	N2-(1-(2-fluoroethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.97 (s, 1H), 8.08 (s, 1H), 7.93 (s, 1H), 7.25 – 6.91 (m, 1H), 4.77 (t, J = 4.7, 1H), 4.65 (t, J = 4.7, 1H), 4.33 (t, J = 4.7, 1H), 4.26 (t, J = 4.7, 1H), 2.88 (d, J = 4.3, 3H), 2.13 (s, 3H).		0.0011
131	N4-methyl-N2-(3-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-		1H NMR (400 MHz, DMSO) δ 8.90 (s, 1H), 8.07 (s, 1H), 7.93 (s, 1H), 6.95 (s, 1H), 4.54 (t, J = 6.5, 2H), 4.43 (t, J = 6.1, 2H), 4.00 (s, 1H), 3.49 –		0.0374

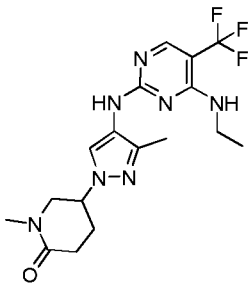
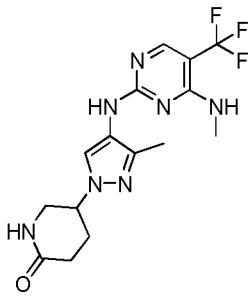
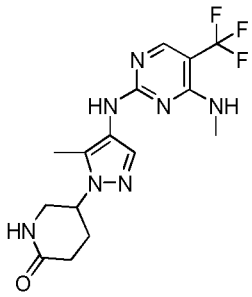
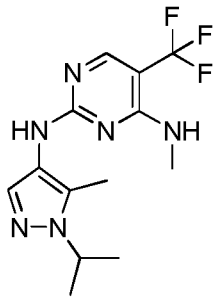
	(trifluoromethyl) pyrimidine-2,4-diamine		3.38 (m, 1H), 2.88 (d, J = 4.4, 3H), 2.76 (d, J = 9.5, 2H), 2.12 (s, 3H), 2.04 – 1.72 (m, 6H).		
132	N4-methyl-N2-(5-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.84 (s, 1H), 8.04 (s, 1H), 7.71 (s, 1H), 6.89 (s, 1H), 4.55 (t, J = 6.3, 2H), 4.45 (t, J = 5.5, 2H), 4.07 (s, 1H), 3.54 – 3.37 (m, 1H), 2.84 (t, J = 19.1, 5H), 2.19 (s, 3H), 1.99 (td, J = 23.4, 11.5, 4H), 1.80 (d, J = 11.5, 2H).		
133	N2-(1-(2-fluoroethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.87 (s, 1H), 8.05 (s, 1H), 7.69 (s, 1H), 6.91 (s, 1H), 4.77 (t, J = 4.8, 1H), 4.66 (t, J = 4.8, 1H), 4.35 (t, J = 4.8, 1H), 4.28 (t, J = 4.8, 1H), 2.84 (s, 3H), 2.18 (s, 3H).		0.0018
134	1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone		1H NMR (400 MHz, DMSO) δ 8.78 (s, 1H), 8.05 (s, 1H), 7.61 (s, 1H), 6.87 (s, 1H), 4.47 (d, J = 13.6, 1H), 4.42 – 4.25 (m, 1H), 3.92 (d, J = 13.6, 1H), 3.38 (m, 2H), 3.20 (t, J = 11.5, 1H), 2.70 (m, 1H), 2.27 (d, J = 46.8, 3H), 1.83 (m, 4H), 1.08 (m, 3H).		0.0022

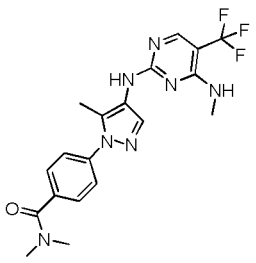
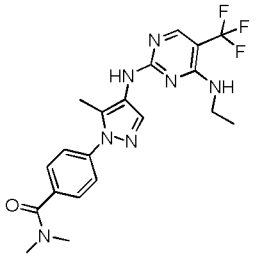
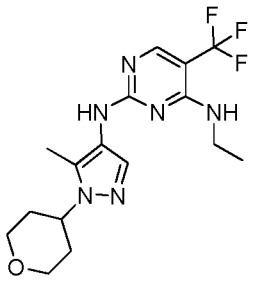
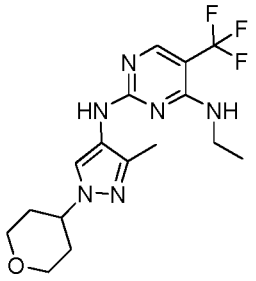
135	cyclopropyl(4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanone		1H NMR (400 MHz, DMSO) δ 8.85 (s, 1H), 8.05 (s, 1H), 7.71 (s, 1H), 6.89 (s, 1H), 4.55 – 4.23 (m, 3H), 2.84 (s, 4H), 2.22 (s, 3H), 1.91 (m, 5H), 0.79 – 0.62 (m, 4H).		0.0010
136	cyclopropyl(4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanone		1H NMR (400 MHz, DMSO) δ 8.90 (s, 1H), 8.10 (s, 1H), 7.95 (s, 1H), 6.95 (s, 1H), 4.35 (m, 3H), 3.24 (m, 1H), 2.88 (d, J = 4.3, 3H), 2.74 (m, 1H), 2.04 (m, 6H), 1.75 (m, 2H), 0.72 (m, 4H).		0.0093
137	1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone		1H NMR (400 MHz, DMSO) δ 8.78 (s, 1H), 8.05 (s, 1H), 7.61 (s, 1H), 6.87 (s, 1H), 4.47 (d, J = 13.6, 1H), 4.42 – 4.25 (m, 1H), 3.92 (d, J = 13.6, 1H), 3.38 (m, 2H), 3.20 (t, J = 11.5, 1H), 2.70 (m, 1H), 2.27 (d, J = 46.8, 3H), 1.83 (m, 4H), 1.08 (m, 3H).		0.0004
138	N2-(5-chloro-1-isopropyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.98 (br s, 1H), 8.12 (s, 1H), 7.85 (s, 1H), 7.05 (s, 1H), 4.65 (p, J = 6.6, 1H), 2.86 (s, 3H), 1.42 (d, J = 6.6, 6H).	335	0.0011

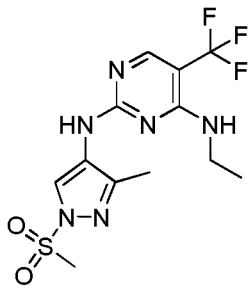
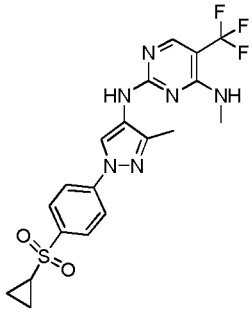
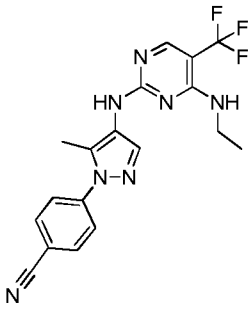
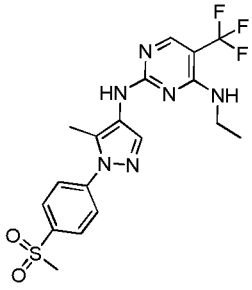
139	N2-(5-chloro-1-ethyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.08 (s, 1H), 6.68 (br s, 1H), 5.21 (s, 1H), 4.18 (q, J = 7.3, 2H), 3.07 (d, J = 4.7, 3H), 1.44 (t, J = 7.3, 3H).	321	0.0020
140	N4-methyl-N2-(3-methyl-1-(pyrimidin-5-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.19 (m, 3H), 9.06 (s, 1H), 8.76 (s, 1H), 8.16 (s, 1H), 7.10 (s, 1H), 2.96 (d, J = 4.3, 3H), 2.31 (s, 3H).		0.0061
141	N4-methyl-N2-(4-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-3-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine			370.2	0.041
142	N4-methyl-N2-(5-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.11 (s, 1H), 8.52 (d, J = 5.5, 1H), 8.10 (s, 2H), 7.50 (s, 1H), 7.43 (dd, J = 5.5, 1.9, 1H), 6.99 (s, 1H), 2.87 (d, J = 3.5, 3H), 2.54 (s, 3H), 2.40 (s, 3H).		0.0003
143	N4-methyl-N2-(3-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)		1H NMR (400 MHz, DMSO) δ 9.19 (s, 1H), 8.72 (s, 1H), 8.42 (d, J = 5.6, 1H), 8.16 (s, 1H), 7.59 (s, 1H), 7.49 (d, J = 4.7, 1H), 7.09 (s, 1H), 2.95 (d, J		0.0069

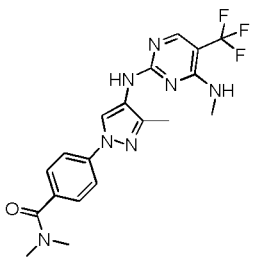
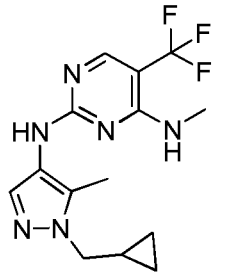
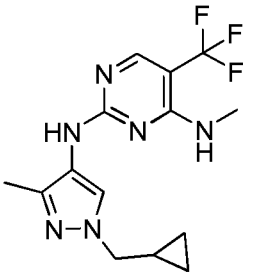
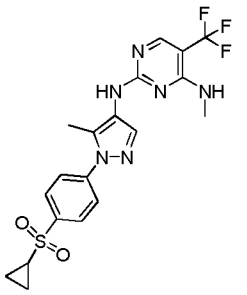
	pyrimidine-2,4-diamine		= 4.3, 3H), 2.29 (s, 3H).		
144	N4-ethyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.79 (s, 1H), 6.58 (br s, 1H), 5.10 (br s, 1H), 4.69 (d, J = 6.0, 2H), 4.39 (d, J = 6.0, 2H), 4.24 (s, 2H), 3.52 (p, J = 6.6, 2H), 2.23 (s, 3H), 1.28 (s, 3H), 1.28 (t, J = 6.6, 3H).	371	0.0009
145	N2-(5-chloro-1-cyclopropyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.04 (s, 1H), 6.76 (br s, 1H), 5.21 (s, 1H), 3.48-3.42 (m, 1H), 3.06 (d, J = 4.7, 3H), 1.23-1.19 (m, 2H), 1.10-1.04 (m, 2H).	333	0.0017
146	N2-(5-chloro-1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.10 (s, 1H), 6.72 (br s, 1H), 5.21 (s, 1H), 4.00 (d, J = 7.0, 2H), 3.07 (d, J = 4.7, 3H), 1.34-1.25 (m, 1H), 0.62-0.56 (m, 2H), 0.44-0.39 (m, 2H).	347	0.0003

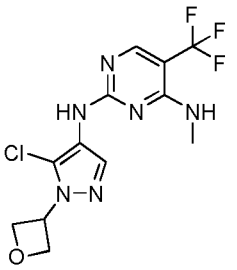
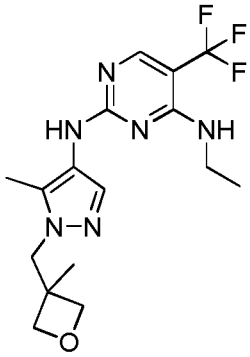
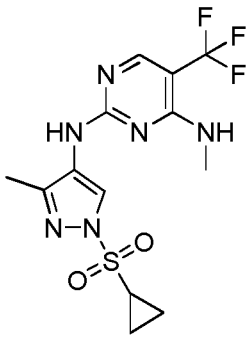
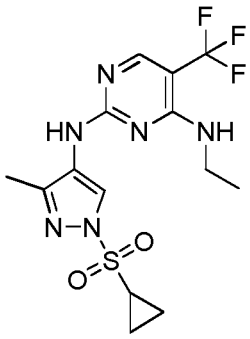
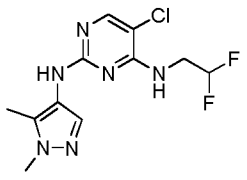
147	4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitrile		1H NMR (400 MHz, DMSO) δ 9.20 (s, 1H), 8.73 (s, 1H), 8.16 (s, 1H), 7.91 (s, 4H), 7.09 (s, 1H), 2.94 (d, J = 4.3, 3H), 2.29 (s, 3H).		0.017
148	4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitrile		1H NMR (400 MHz, DMSO) δ 9.07 (s, 1H), 8.10 (s, 1H), 7.98 (d, J = 8.6, 2H), 7.78 (d, J = 8.6, 1H), 6.99 (s, 1H), 2.88 (d, J = 3.8, 2H), 2.36 (s, 2H).		0.0003
149	N4-methyl-N2-(3-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.95 (s, 1H), 8.08 (s, 1H), 7.99 (s, 1H), 6.96 (s, 1H), 4.88 (m, 1H), 3.99 – 3.74 (m, 4H), 2.89 (d, J = 4.4, 3H), 2.33 (m, 1H), 2.13 (m, 4H).		0.0068
150	N4-methyl-N2-(5-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.87 (s, 1H), 8.05 (s, 1H), 7.61 (d, J = 92.3, 1H), 6.90 (s, 1H), 5.10 – 4.58 (m, 1H), 4.19 – 3.69 (m, 4H), 2.84 (m, 3H), 2.42 – 2.04 (m, 5H).		0.0051
151	5-(4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-1-		1H NMR (400 MHz, DMSO) δ 8.84 (s, 1H), 8.05 (s, 1H), 7.66 (s, 1H), 6.89 (s, 1H), 4.81 – 4.63 (m, 1H), 3.61 (m, 1H), 3.50 (m, 1H), 3.38 (m, 2H), 2.82 (m, 3H), 2.49 – 2.09 (m,		0.0011

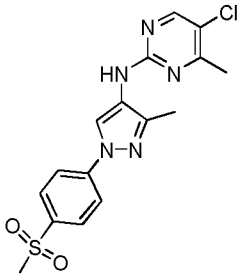
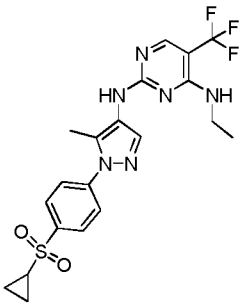
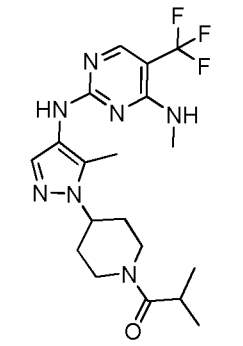
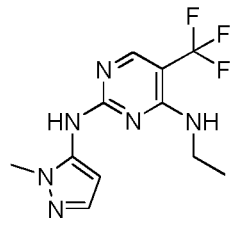
	methylpiperidin-2-one		6H), 1.99 (m, 1H), 1.08 (m, 3H).		
152	5-(4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one		1H NMR (400 MHz, DMSO) δ 8.90 (s, 1H), 8.08 (s, 1H), 7.90 (s, 1H), 6.95 (s, 1H), 4.58 (m, 1H), 3.68 – 3.53 (m, 2H), 3.42 (m, 2H), 2.82 (m, 3H), 2.45 – 2.18 (m, 3H), 2.13 (m, 4H), 1.12 (m, 3H).		0.0073
153	5-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-one		1H NMR (400 MHz, DMSO) δ 8.95 (s, 1H), 8.05 (d, J = 23.6, 2H), 7.50 (s, 1H), 6.97 (s, 1H), 4.49 (m, 1H), 3.47 (m, 2H), 2.88 (d, J = 4.3, 3H), 2.39 – 1.97 (m, 7H).		0.0097
154	5-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-one		1H NMR (400 MHz, DMSO) δ 8.87 (s, 1H), 8.05 (s, 1H), 7.62 (d, J = 96.3, 2H), 6.90 (s, 1H), 4.59 (m, 1H), 3.55 – 3.42 (m, 1H), 3.36 (m, 1H), 2.84 (m, 3H), 2.30 (m, 6H), 1.99 (m, 1H).		0.0022
155	N2-(1-isopropyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (500 MHz, DMSO) δ 8.08 (s, 1H), 7.88 (s, 1H), 6.80 (s, 1H), 5.15 (s, 1H), 4.39-4.44 (m, 1H), 3.01 (d, *J* = 5, 3H), 2.22 (s, 3H), 1.49 (d, *J* = 6.5, 6H).	315	0.0025

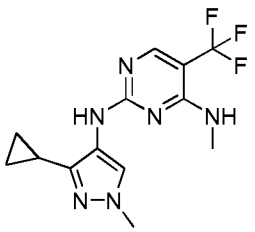
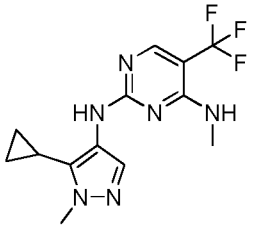
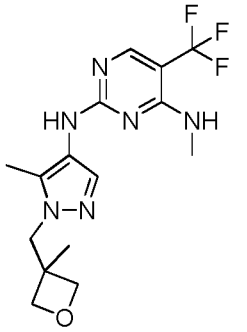
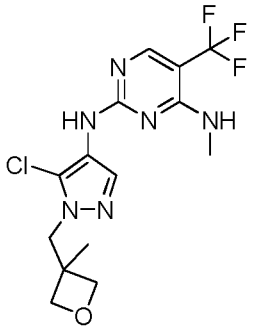
156	N,N-dimethyl-4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide		1H NMR (400 MHz, DMSO) δ 9.07 (s, 1H), 8.10 (s, 1H), 7.57 (q, J = 8.5, 4H), 6.98 (s, 1H), 2.99 (s, 6H), 2.88 (d, J = 4.0, 3H), 2.31 (s, 3H).		0.0003
157	4-(4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamide		1H NMR (400 MHz, DMSO) δ 9.00 (s, 1H), 8.24 – 7.78 (m, 2H), 7.57 (q, J = 8.5, 4H), 6.95 (s, 1H), 3.43 (s, 2H), 2.99 (s, 6H), 2.31 (s, 3H), 1.12 (t, J = 6.7, 3H).		0.0003
`58	N4-ethyl-N2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.80 (s, 1H), 8.05 (s, 1H), 7.63 (s, 1H), 6.87 (s, 1H), 4.41 – 4.24 (m, 1H), 3.95 (dd, J = 11.2, 4.0, 2H), 3.47 (t, J = 11.2, 2H), 3.38 (s, 2H), 2.20 (s, 3H), 2.01 (qd, J = 12.4, 4.5, 2H), 1.85 – 1.64 (m, 2H), 1.08 (s, 3H).		0.0003
159	N4-ethyl-N2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.88 (s, 1H), 8.08 (s, 1H), 7.87 (s, 1H), 6.98 (s, 1H), 4.42 – 4.15 (m, 1H), 3.94 (d, J = 11.0, 2H), 3.44 (t, J = 11.0, 3H), 2.12 (s, 2H), 1.89 (s, 3H), 1.21 – 1.00 (m, 2H).		0.0039

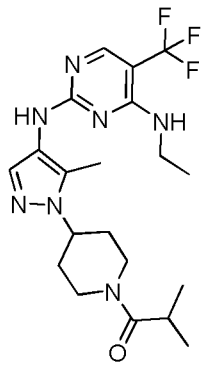
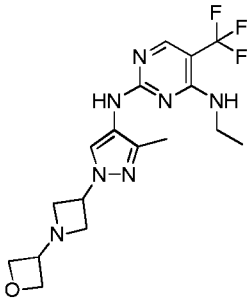
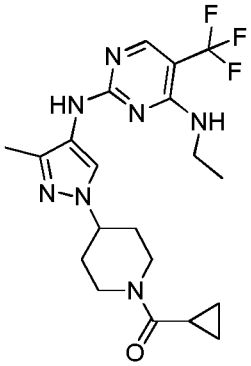
160	N4-ethyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.38 (s, 1H), 8.44 (s, 1H), 8.20 (s, 1H), 7.24 (s, 1H), 3.47 (p, J = 6.8, 2H), 3.40 (s, 3H), 2.32 (s, 3H), 1.21 – 1.09 (m, 3H).		0.0003
161	N2-(1-(4-(cyclopropylsulfonyl)phenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.12 (s, 1H), 8.11 (s, 1H), 8.02 (d, J = 8.6, 3H), 7.84 (d, J = 8.6, 2H), 7.00 (s, 1H), 3.01 – 2.82 (m, 4H), 2.37 (s, 3H), 1.22 – 1.14 (m, 2H), 1.14 – 0.94 (m, 2H).		0.0003
162	4-(4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)benzonitrile		1H NMR (400 MHz, DMSO) δ 9.06 (s, 1H), 8.10 (s, 1H), 7.99 (d, J = 8.6, 2H), 7.78 (d, J = 8.6, 2H), 6.97 (s, 1H), 3.43 (s, 2H), 2.36 (s, 3H), 1.12 (t, J = 6.8, 3H).		0.0003
163	N4-ethyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.09 (s, 1H), 8.15 – 8.02 (m, 3H), 7.84 (d, J = 8.7, 2H), 6.97 (s, 1H), 3.43 (s, 2H), 2.37 (s, 3H), 1.12 (t, J = 7.0, 3H).		0.0003

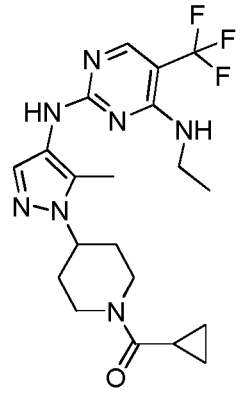
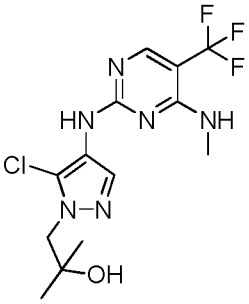
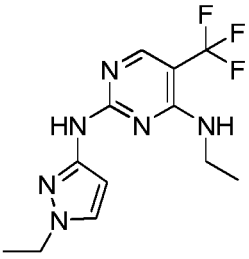
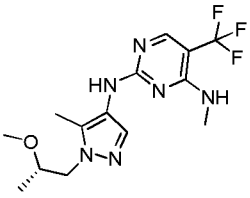
164	N,N-dimethyl-4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide		1H NMR (400 MHz, DMSO) δ 9.17 (s, 1H), 8.65 (s, 1H), 8.14 (s, 1H), 7.76 (d, J = 8.5, 2H), 7.50 (d, J = 8.6, 2H), 7.06 (s, 1H), 3.06 – 2.86 (m, 9H), 2.28 (s, 3H).		0.0057
165	N2-(1-(cyclopropylmethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 8.41 (d, *J* = 16.0, 1H), 8.04 (s, 1H), 6.59 (s, 1H), 6.59 (s, 1H), 3.89 (m, *J* = 11.0, 2H), 3.85 (d, *J* = 7.5, 3H), 2.17 (s, 1H), 1.13-1.18 (m, 1H), 0.44-0.50 (m, 2H), 0.28-0.32 (s, 2H).	327	0.0012
166	N2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 8.46 (d, *J* = 2.0, 1H), 8.14 (s, 1H), 8.04 (s, 1H), 6.65 (s, 1H), 3.82-3.84 (m, 2H), 2.90 (d, *J* = 7.5, 3H), 1.89 (s, 1H), 1.15-1.20 (m, 1H), 0.47-0.53 (m, 2H), 0.28-0.33 (s, 2H).		0.0045
167	N2-(1-(4-(cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.24 (s, 1H), 8.75 (s, 1H), 8.16 (s, 1H), 8.02 – 7.87 (m, 4H), 7.09 (s, 1H), 2.96 (d, J = 4.3, 3H), 2.92 – 2.81 (m, 1H), 2.31 (s, 3H), 1.21 – 1.11 (m, 2H), 1.10 – 0.97 (m, 2H).		0.0188

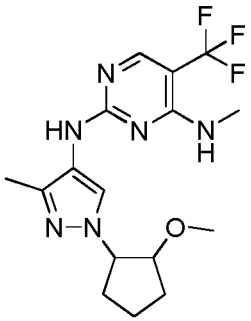
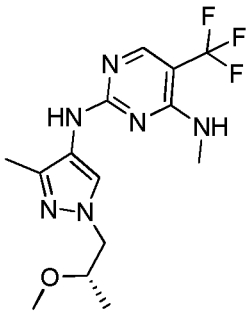
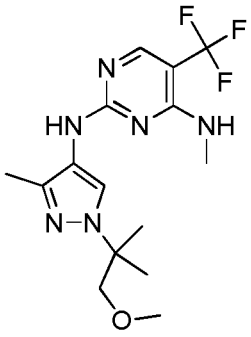
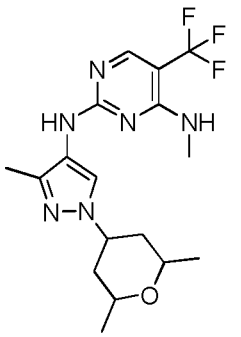
168	N2-(5-chloro-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.13 (s, 1H), 6.89 (br s, 1H), 5.56 (p, J = 7.1, 1H), 5.25 (s, 1H), 5.19 (t, J = 6.6, 2H), 5.00 (t, J = 7.2, 2H), 3.08 (d, J = 4.7, 3H).	349	0.0095
169	N4-ethyl-N2-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.70 (br s, 1H), 6.41 (br s, 1H), 5.04 (s, 1H), 4.78 (d, J = 6.1, 2H), 4.40 (d, J = 6.1, 2H), 4.22 (s, 2H), 3.46 (p, J = 6.6, 2H), 2.20 (s, 3H), 1.25 (s, 3H), 1.21 (t, J = 7.0, 3H).	371	0.0022
170	N2-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.36 (s, 1H), 8.44 (s, 1H), 8.19 (s, 1H), 7.18 (s, 1H), 3.07 – 2.96 (m, 1H), 2.92 (d, J = 4.4, 3H), 2.32 (s, 3H), 1.24 – 1.07 (m, 4H).		0.002
171	N2-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.36 (s, 1H), 8.41 (s, 1H), 8.19 (s, 1H), 7.23 (s, 1H), 3.47 (m, 2H), 2.99 (m, 1H), 2.32 (s, 3H), 1.23 – 1.04 (m, 7H).		0.0009
172	5-chloro-N4-(2,2-difluoroethyl)-N2-(1,5-dimethyl-1H-				0.0070

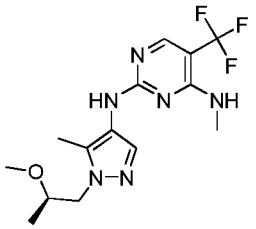
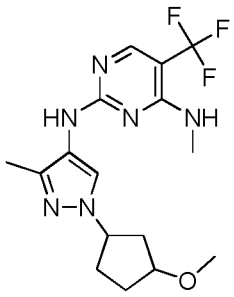
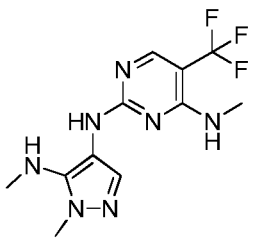
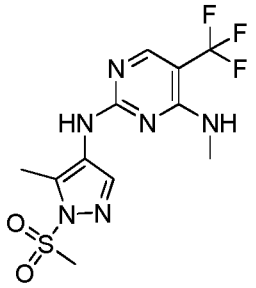
	pyrazol-4-yl)pyrimidine-2,4-diamine				
173	5-chloro-4-methyl-N-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine		1H NMR (400 MHz, DMSO) δ 9.10 (s, 1H), 8.31 (s, 1H), 8.06 (d, J = 8.6, 2H), 7.93 (s, 1H), 7.85 (d, J = 8.6, 2H), 3.28 (s, 6H), 2.40 (s, 3H), 2.34 (s, 3H).		0.484
174	N2-(1-(4-(cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.21 (s, 1H), 8.68 (s, 1H), 8.17 (s, 1H), 7.95 (q, J = 9.0, 4H), 7.09 (s, 1H), 3.58 – 3.43 (m, 2H), 2.95 – 2.79 (m, 1H), 2.31 (s, 3H), 1.12 (ddd, J = 34.8, 14.3, 8.6, 7H).		0.0011
175	2-methyl-1-(4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)propan-1-one			426	0.0068
176	N4-ethyl-N2-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.011

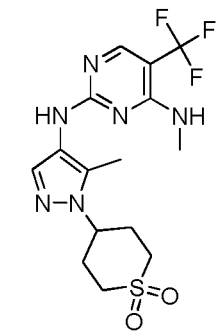
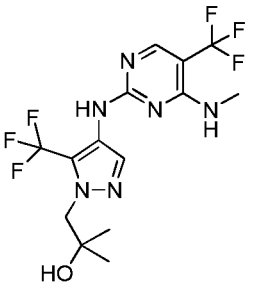
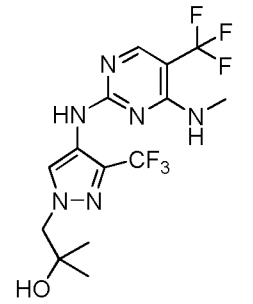
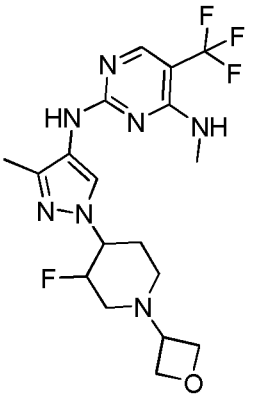
177	N2-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.0067
178	N2-(5-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.012
179	N4-methyl-N2-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.73 (br s, 1H), 6.50 (br s, 1H), 5.13 (s, 1H), 4.78 (d, J = 6.1, 2H), 4.40 (d, J = 6.1, 2H), 4.22 (s, 2H), 2.99 (d, J = 4.7, 3H), 2.20 (s, 3H), 1.25 (s, 3H).	357	0.0090
180	N2-(5-chloro-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 8.11 (s, 1H), 6.68 (br s, 1H), 5.22 (s, 1H), 4.78 (d, J = 6.2, 2H), 4.40 (d, J = 6.2, 2H), 4.33 (s, 2H), 3.06 (d, J = 4.7, 3H), 1.28 (s, 3H).	377	0.0056

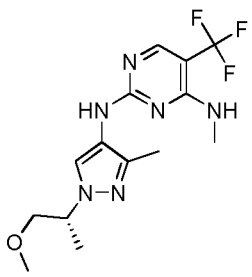
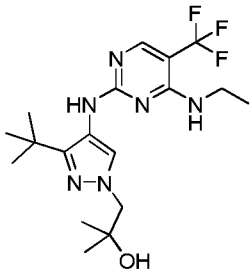
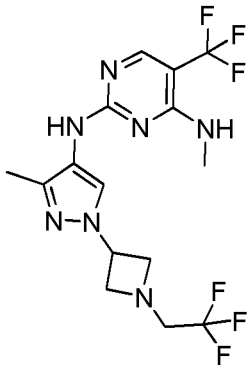
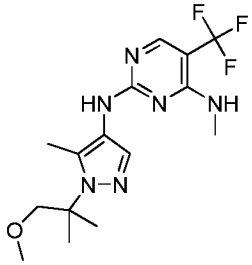
181	1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)-2-methylpropan-1-one		1H NMR (400 MHz, DMSO) δ 8.78 (s, 1H), 8.05 (s, 1H), 7.62 (s, 1H), 6.88 (s, 1H), 4.51 (d, J = 11.9, 1H), 4.45 – 4.30 (m, 1H), 4.06 (d, J = 12.8, 1H), 3.37 (s, 2H), 3.20 (m, 1H), 2.92 (m, 1H), 2.80 – 2.60 (m, 1H), 2.21 (s, 3H), 1.88 (m, 4H), 1.02 (m, 8H).		0.00082
182	N4-ethyl-N2-(3-methyl-1-(1-(oxetan-3-yl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.83 (s, 1H), 8.05 (s, 1H), 7.73 (s, 1H), 6.87 (s, 1H), 4.98 (p, J = 7.2, 1H), 4.60 (t, J = 6.6, 2H), 4.43 (t, J = 5.8, 2H), 3.88 – 3.77 (m, 1H), 3.70 (t, J = 7.3, 2H), 3.56 (t, J = 7.3, 2H), 3.39 (s, 2H), 2.16 (s, 3H), 1.09 (s, 3H).		0.0015
183	cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)methanone			438.3	0.0006

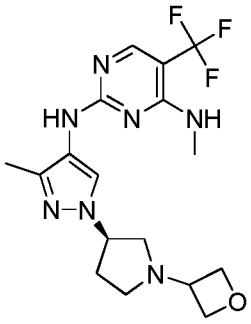
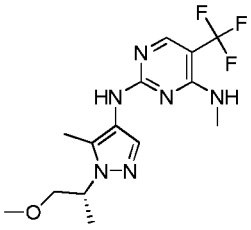
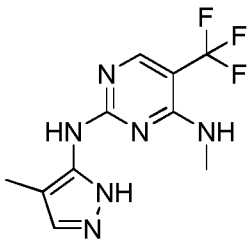
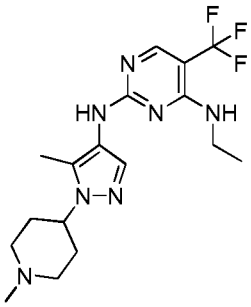
184	cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)methanone			438.3	0.0047
185	1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol		1H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 8.13 (s, 1H), 6.81 (br s, 1H), 5.23 (s, 1H), 4.09 (s, 2H), 3.99 (s, 1H), 3.06 (d, J = 4.7, 3H), 1.19 (s, 6H).	365	0.0069
186	N4-ethyl-N2-(1-ethyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.66 (s, 1H), 8.10 (s, 1H), 7.58 (d, J = 2.0, 1H), 7.02 (s, 0H), 7.00 (s, 1H), 6.54 (d, J = 2.0, 1H), 4.02 (q, J = 7.2, 2H), 3.57 – 3.37 (m, 2H), 1.35 (t, J = 7.2, 3H), 1.15 (t, J = 7.1, 3H).		0.0019
187	(S)-N2-(1-(2-methoxypropyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			345	0.0188

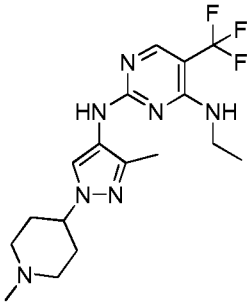
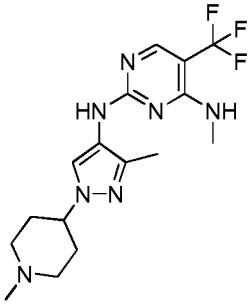
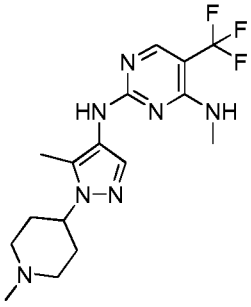
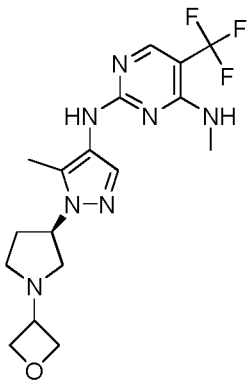
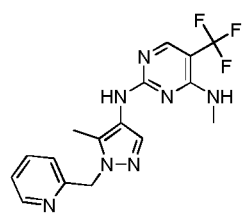
188	N2-(1-(2-methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 8.49 (s, 1H), 8.07 (s, 1H), 6.68 (d, *J* = 2.5, 1H), 4.41 (m, 1H), 3.95 (m, 1H), 3.18 (s, 1H), 2.91 (d, *J* = 8.0, 3H), 2.09 (s, 3H), 1.64-192 (m, 6H).		0.012
189	(S)-N2-(1-(2-methoxypropyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 8.11 (s, 1H), 7.90 (s, 1H), 6.71 (s, 1H), 5.20 (s, 1H), 3.00~4.07 (m, 2H), 3.68~3.74 (m, 1H), 3.32 (s, 3H), 3.00~3.06 (t, *J* = 3 Hz, 3H), 2.25 (d, *J* = 3 Hz, 3H), 1.14~1.18 (m, 3H).		0.0118
190	N2-(1-(1-methoxy-2-methylpropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, MeOD) δ 8.01 (s, 1H), 7.79 (s, 1H), 3.58 (s, 2H), 3.27 (s, 3H), 2.99 (s, 3H), 2.22 (s, 3H), 1.55 (s, 6H).		0.0069
191	N2-(1-(2,6-dimethyltetrahydro-2H-pyran-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, CDCl3) δ 8.54 (s, 1H),8.08 (s, 1H), 7.98 (s, 1H), 6.70 (s, 1H), 4.47 (s, 1H), 3.70-3.80 (m, 2H), 2.90 (d, *J* = 7.5, 3H), 2.13-2.24 (m, 5H), 1.56-1.66 (m, 2H), 1.16 (d, *J* = 6.5, 6H).		0.0846

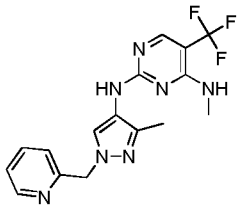
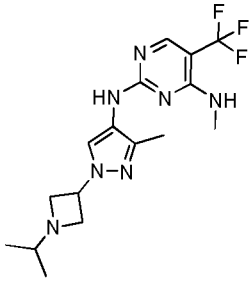
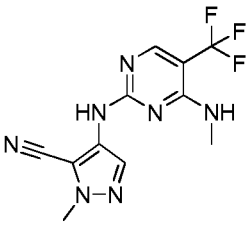
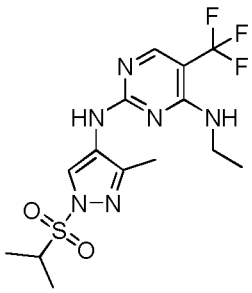
192	(R)-N2-(1-(2-methoxypropyl)-5-methyl-1H-pyrazol -4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			345	0.0063
193	N2-(1-(3-methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H-NMR (500 MHz, DMSO) δ 8.46 (brs, 1H), 8.04 (s, 1H), 7.85 (s, 1H), 6.85 (brs, 1H), 4.48-4.54 (m, 1H), 3.80-3.84 (m, 1H), 3.20 (s, 3H), 2.89 (d, *J* = 7.0, 3H), 2.35-2.45 (m, 1H), 2.10 (s, 3H), 1.84-2.08 (m, 3H), 1.74-1.81 (m, 2H).		0.019
194	N4-methyl-N2-(1-methyl-5-(methylamino)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.75-8.24 (m, 1H), 8.06 (s, 1H), 7.56-7.06 (m, 1H), 7.01-6.82 (m, 1H), 4.89-4.66 (m, 1H), 3.59 (s, 3H), 2.87 (br s, 3H), 2.68 (d, J = 5.1, 3H).	302	0.0522
195	N4-methyl-N2-(5-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.43 (s, 1H), 8.47 (s, 1H), 8.20 (s, 1H), 7.20 (s, 1H), 3.41 (s, 3H), 2.93 (d, J = 4.4, 3H), 2.32 (s, 3H).		0.010

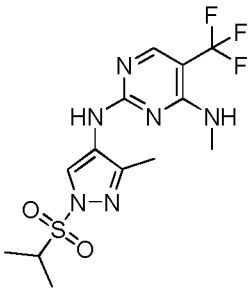
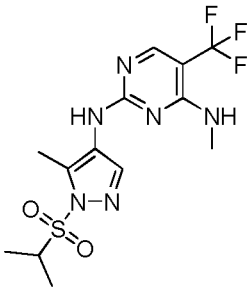
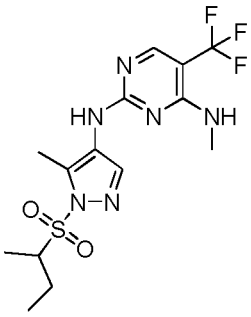
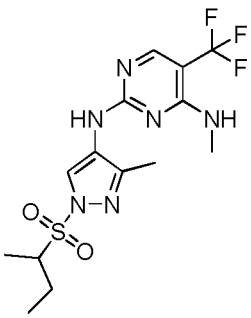
196	N4-methyl-N2-(5-methyl-1-(tetrahydro-2H-1,1-dioxo-thiopyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (500 MHz, DMSO) δ 8.45 (d, *J* = 12, 1H), 8.01 (d, *J* = 7.5, 1H), 7.59 (s, 1H), 6.59-6.64 (m, 1H), 4.49-4.56 (m, 1H), 3.26-3.35 (t, *J* = 20.5, 2H), 3.16 (d, *J* = 20.5, 2H), 2.82 (d, *J* = 6.0, 3H), 2.34-2.45 (m, 2H), 2.11-2.17 (m, 5H).		0.047
197	2-methyl-1-(4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-5-(trifluoromethyl)-1H-pyrazol-1-yl)propan-2-ol			399.1	0.026
198	2-methyl-1-(4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-3-(trifluoromethyl)-1H-pyrazol-1-yl)propan-2-ol			399.1	0.027
199	N2-(1-(3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			430.2	0.0022

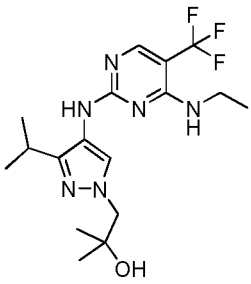
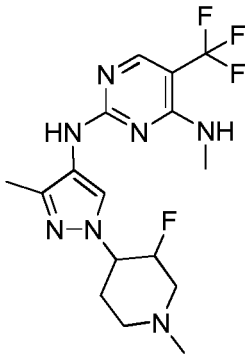
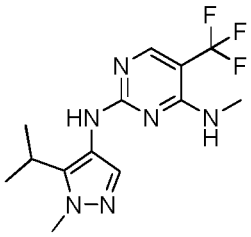
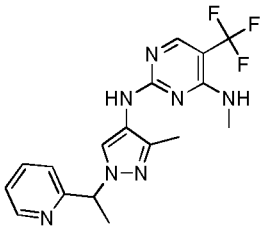
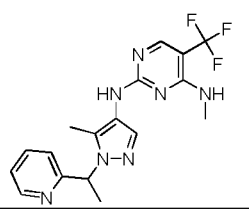
200	(R)-N2-(1-(1-methoxypropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			345	0.0128
201	1-(3-tert-butyl-4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol			401.2	0.42
202	N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.01 (s, 1H), 8.13 (d, J = 36.8, 2H), 7.01 (s, 2H), 4.93 (p, J = 6.9, 1H), 3.82 (t, J = 7.6, 2H), 3.58 (d, J = 6.9, 2H), 2.90 (d, J = 4.4, 3H), 2.15 (s, 4H).		0.034
203	N2-(1-(1-methoxy-2-methylpropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, MeOD) δ 7.97 (s, 1H), 7.49 (s, 1H), 3.67 (s, 2H), 3.31 (s, 3H), 2.96 (s, 3H), 2.36 (s, 3H), 1.65 (s, 6H).		0.042

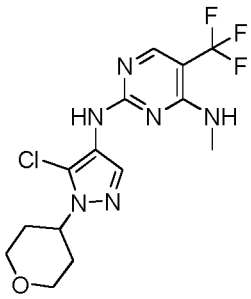
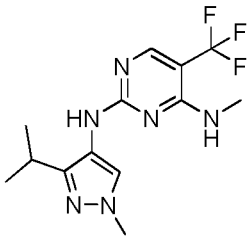
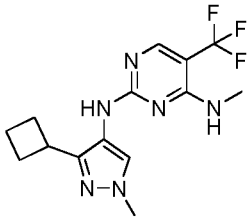
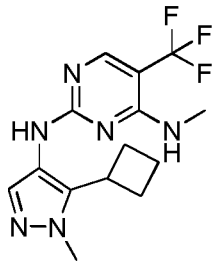
204	(R)-N4-methyl-N2-(3-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 9.01 (s, 1H), 8.12 (d, J = 19.5 Hz, 2H), 7.04 (s, 1H), 4.75~4.80 (m, 1H), 4.55~4.59 (m, 2H), 4.42~4.47 (m, 2H), 3.61 (t, *J* = 6.0Hz, 1H), 2.92 (s, 3H), 2.75 (s, 3H), 2.32-2.42 (m, 2H), 1.97~2.14 (m, 4H).		0.029
205	(R)-N2-(1-(1-methoxypropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H-NMR (Bruker, 500 MHz, MeOD) *δ* 7.98 (s, 1H), 4.54-4.58 (m, 1H), 3.60-3.72 (m, 2H), 3.342 (s, 3H), 2.96 (s, 3H), 2.23 (s, 3H), 1.45 (d, *J* = 6.5, 3H).		0.019
206	N4-methyl-N2-(4-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.33 (s, 1H), 5.33 (s, 1H), 3.08 (d, J = 4.8, 3H), 2.05 (s, 3H).	273	0.2324
207	N4-ethyl-N2-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.80 (s, 1H), 8.04 (s, 1H), 7.61 (s, 1H), 6.90 (s, 1H), 4.02 (m, 1H), 3.39 (m, 2H), 2.93 – 2.76 (m, 2H), 2.20 (m, 6H), 2.10 – 1.93 (m, 4H), 1.75 (m, 2H), 1.07 (m, 3H).		0.0026

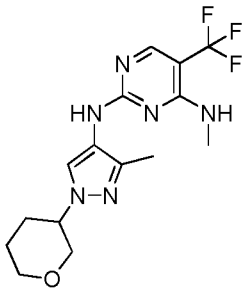
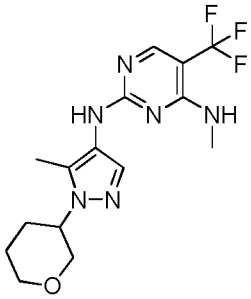
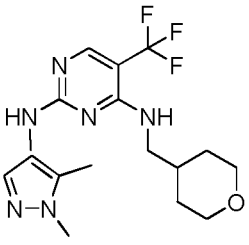
208	N4-ethyl-N2-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.90 (s, 1H), 8.08 (s, 1H), 7.88 (s, 1H), 7.02 (s, 1H), 4.01 – 3.83 (m, 1H), 3.43 (s, 2H), 2.82 (d, J = 11.6, 2H), 2.16 – 1.76 (m, 9H), 1.12 (t, J = 7.0, 3H).		0.0102
209	N4-methyl-N2-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine			370.2	0.041
210	N4-methyl-N2-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine			370.2	0.0071
211	(R)-N4-methyl-N2-(5-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 9.00 (s, 1H), 8.12 (d, *J* = 18, 1H), 7.85 (s, 1H), 7.05 (s, 1H), 4.77-4.80 (m, 1H), 4.46-4.59 (m, 2H), 4.43-4.48 (m, 2H), 3.62 (t, *J* = 5.5, 1H), 2.93 (s, 3H), 2.76 (s, 3H), 2.44 (s, 1H), 2.36 (t, *J* = 2, 1H), 1.99-2.15 (m, 4H).		0.0033
212	N4-methyl-N2-(5-methyl-1-(pyridin-2-ylmethyl)-1H-		^{1}H NMR (500 MHz, DMSO) δ 8.57 (d, *J* = 5, 8.11 (s, 1H), 7.97 (s, 1H), 7.62-7.66 (m, 1H), 7.21 (t,		0.0029

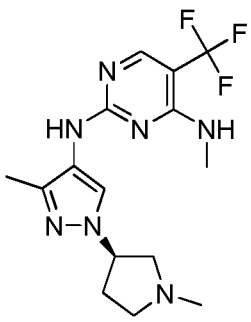
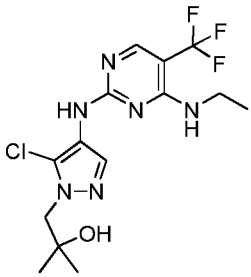
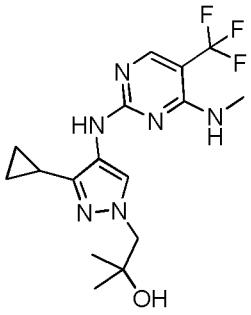
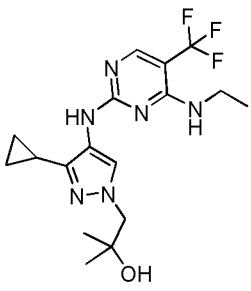
	pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		*J* = 1.5, 1H), 7.04 (d, *J* = 8, 1H), 6.62 (s, 1H), 5.37 (s, 2H), 5.16 (d, *J*= 4.5, 1H), 2.98 (s, 3H), 2.29 (s, 3H).		
213	N4-methyl-N2-(3-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 8.56 (d, *J* = 4.5 Hz), 8.09 (s, 1H), 7.82-7.85 (m, 1H), 7.60-7.64 (m, 1H), 7.19-7.21 (m, 1H), 7.89 (3, 1H), 6.62 (s, 1H), 5.42 (s, 2H), 5.14 (s, 1H), 2.98 (d, *J* = 4, 3H), 2.18 (s, 3H).		0.0029
214	N2-(1-(1-isopropylazetidin-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.91 (s, 1H), 8.05 (s, 1H), 7.78 (s, 1H), 6.93 (s, 1H), 4.82 (dd, J = 14.4, 7.2, 1H), 3.64 (t, J = 7.2, 2H), 2.84 (s, 2H), 2.36 (dt, J = 12.4, 6.2, 1H), 2.16 (s, 3H).		0.064
215	1-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazole-5-carbonitrile		1H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.14 (s, 1H), 7.20 (br s, 1H), 5.29 (s, 1H), 4.01 (s, 3H), 3.09 (d, J = 4.7, 3H).	298	0.0032
216	N4-ethyl-N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.41 (s, 1H), 8.44 (s, 1H), 8.19 (s, 1H), 7.26 (s, 1H), 3.76 (m, 1H), 3.54 – 3.39 (m, 2H), 2.31 (s, 3H), 1.24 – 1.10 (m, 10H).		0.0039

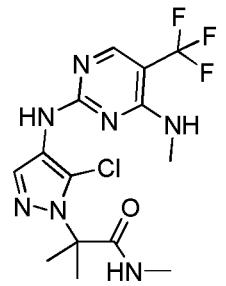
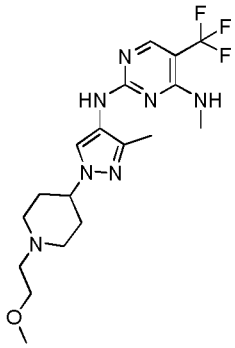
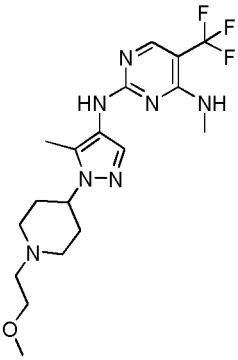
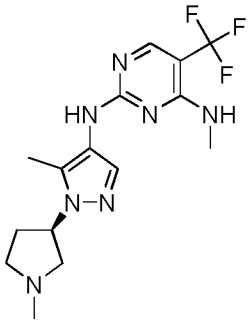
217	N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.39 (s, 1H), 8.47 (s, 1H), 8.20 (s, 1H), 7.20 (s, 1H), 3.77 (dq, J = 13.6, 6.8, 1H), 2.90 (d, J = 4.4, 3H), 2.31 (s, 3H), 1.19 (d, J = 6.8, 6H).		0.0099
218	N2-(1-(isopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.08 (s, 1H), 8.14 (d, J = 21.1, 2H), 7.06 (s, 1H), 3.85 – 3.74 (m, 1H), 2.82 (s, 3H), 2.39 (s, 3H), 1.20 (d, J = 6.8, 6H).		0.0081
219	N2-(1-(sec-butylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.08 (s, 1H), 8.13 (d, J = 14.5, 2H), 7.06 (s, 1H), 3.70 – 3.57 (m, 1H), 2.82 (s, 3H), 1.84 – 1.69 (m, 1H), 1.56 – 1.41 (m, 1H), 1.16 (d, J = 6.8, 3H), 0.93 (t, J = 7.5, 3H).		0.0067
220	N2-(1-(sec-butylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.39 (s, 1H), 8.47 (s, 1H), 8.19 (s, 1H), 7.20 (s, 1H), 3.60 (dq, J = 13.7, 6.9, 1H), 2.90 (d, J = 4.3, 3H), 2.31 (s, 3H), 1.87 – 1.70 (m, 1H), 1.45 (dt, J = 14.0, 7.7, 1H), 1.16 (d, J = 6.9, 3H), 0.92 (t, J = 7.5, 3H).		0.0117

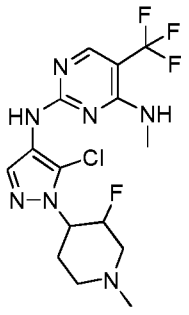
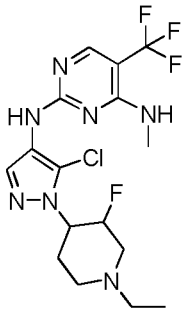
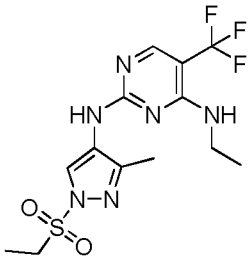
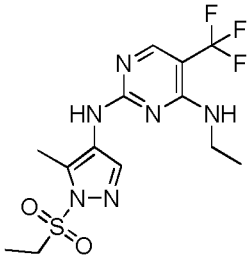
221	1-(4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-3-isopropyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol				0.0061
222	N2-(1-(3-fluoro-1-methylpiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.88 (s, 1H), 8.05 (s, 1H), 7.78 (s, 1H), 6.93 (s, 1H), 4.91 (m, 1H), 4.77 (m, 1H), 4.35 – 4.05 (m, 1H), 3.26 – 3.10 (m, 1H), 2.83 (s, 4H), 2.28 (m, 3H), 2.26 – 2.00 (m, 5H), 1.86 (m, 1H).		0.0016
223	N2-(5-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			315.1	0.014
224	N4-methyl-N2-(3-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H-NMR (500 MHz, CDCl3) δ 8.54 (d, *J* = 4.0, 1H), 7.97-8.12 (m, 2H), 7.78-7.81 (m, 1H), 7.32-7.35 (m, 1H), 7.12 (d, *J* = 7.5, 1H), 5.53-5.57 (m, 1H), 5.90-5.91 (m, 3H), 2.23 (s, 3H), 1.91 (d, *J* = 7.0, 3H).		0.0024
225	N4-methyl-N2-(5-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-		1H-NMR (500 MHz, CDCl3) δ 8.53 (t, *J* = 4.0, 1H), 7.98 (s, 1H), 7.72-7.78 (m, 2H), 7.31-7.34		0.0038

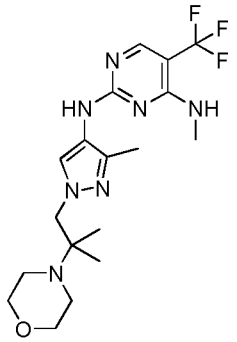
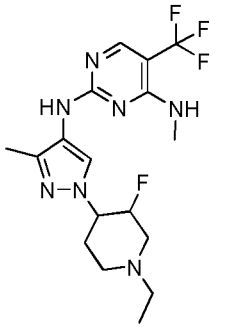
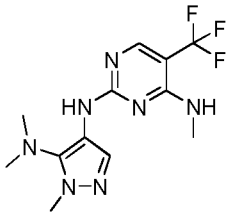
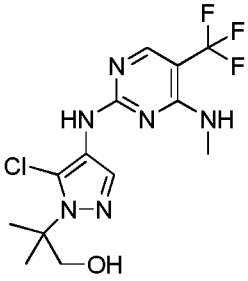
	pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		(m, 1H), 6.96 (s, 1H), 5.62-5.67 (m, 1H), 2.86-2.96 (m, 3H), 2.15 (s, 3H), 1.95 (d, *J* = 7.5, 3H).		
226	N2-(5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.91 (s, 1H), 8.08 (s, 1H), 7.82 (s, 1H), 7.00 (s, 1H), 4.50 (tt, J = 11.4, 4.3, 1H), 3.97 (dd, J = 11.3, 4.0, 2H), 3.49 (t, J = 11.4, 2H), 2.83 (s, 3H), 2.01 (qd, J = 12.4, 4.6, 2H), 1.81 (dd, J = 12.8, 2.4, 2H).		0.0007
227	N2-(3-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			315.1	0.069
228	N2-(3-cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			327.1	0.0034
229	N2-(5-cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.21 – 7.98 (s, 1H), 7.82 – 7.34 (s, 1H), 6.58 – 6.18 (s, 1H), 5.22 – 5.01 (s, 1H), 3.82 – 3.70 (s, 3H), 3.67 – 3.50 (m, 1H), 3.06 – 2.94 (d, J = 4.7 Hz, 3H), 2.54 – 2.26 (m, 4H),	327.1	0.011

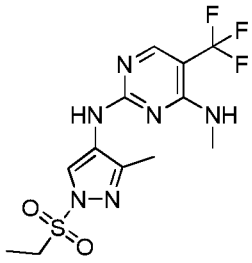
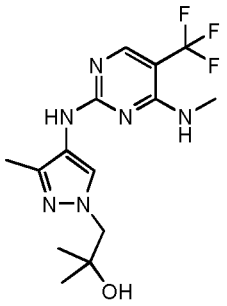
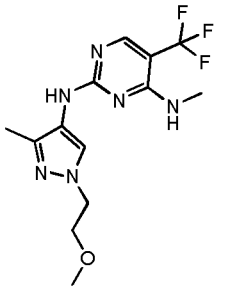
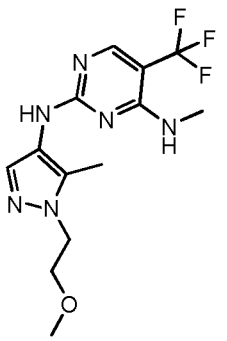
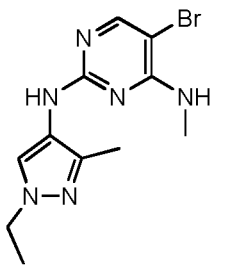
			2.16 – 1.99 (m, 1H), 1.97 – 1.81 (m, 1H)		
230	N4-methyl-N2-(3-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.95 (s, 1H), 8.08 (s, 2H), 6.98 (s, 1H), 4.22 – 4.07 (m, 1H), 3.92 (dd, J = 10.9, 3.6, 1H), 3.77 (d, J = 11.1, 1H), 3.55 (t, J = 9.8, 1H), 3.41 (t, J = 9.7, 1H), 2.89 (d, J = 4.4, 3H), 2.21 – 1.92 (m, 5H), 1.79 – 1.53 (m, 2H).		0.0096
231	N4-methyl-N2-(5-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.89 (s, 1H), 8.05 (s, 1H), 7.73 (s, 1H), 6.92 (s, 1H), 4.26 – 4.11 (m, 1H), 3.86 (dd, J = 10.7, 2.4, 2H), 3.51 (t, J = 10.6, 1H), 2.83 (s, 3H), 2.21 (s, 3H), 2.12 – 1.94 (m, 2H), 1.85 – 1.58 (m, 2H).		0.0018
232	N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-((tetrahydro-2H-pyran-4-yl) methyl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.0096

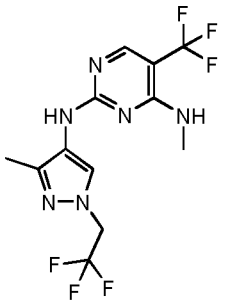
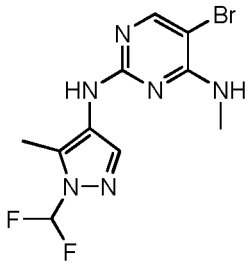
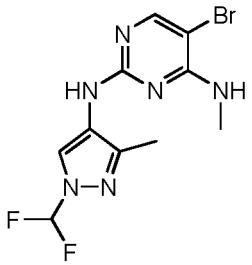
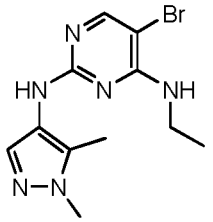
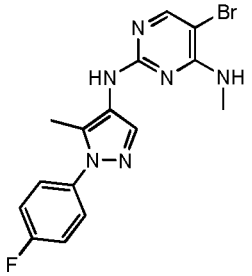
233	(R)-N4-methyl-N2-(3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		^{1}H NMR (500 MHz, DMSO) δ 9.00 (s, 1H), 8.13 (s, 1H), 8.08 (s, 1H), 7.03 (s, 1H), 4.74 (m, 1H), 2.90 (d, *J* = 4.5 Hz, 3H), 2.75-2.80 (m, 3H), 2.30 (m, 5H), 2.14 (s, 3H), 1.96 (s, 2H).		0.061
234	1-(5-chloro-4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol		1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 8.02 (s, 1H), 6.81 (br s, 1H), 5.62 (br s, 1H), 4.10 (s, 2H), 3.84 (s, 1H), 3.59 (p, J = 6.6, 2H), 1.31 (t, J = 7.2, 3H), 1.19 (s, 6H).	379	0.0031
235	1-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol		1H NMR (400 MHz, $CDCl_3$) δ 8.18 – 8.09 (s, 1H), 7.93 – 7.82 (s, 1H), 3.98 – 3.92 (s, 2H), 3.10 – 3.01 (d, J = 4.7 Hz, 3H), 1.80 – 1.68 (td, J = 8.3, 4.2 Hz, 1H), 1.19 – 1.09 (s, 6H), 0.98 – 0.77 (m, 4H)	371.2	0.0051
236	1-(3-cyclopropyl-4-(4-(ethylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol		1H NMR (400 MHz, $CDCl_3$) δ 8.15 – 8.10 (s, 1H), 7.86 – 7.81 (s, 1H), 3.95 – 3.92 (s, 2H), 3.59 – 3.49 (m, 2H), 1.77 – 1.67 (td, J = 8.3, 4.1 Hz, 1H), 1.32 – 1.23 (t, J = 7.2 Hz, 3H), 1.18 – 1.12 (s,6H), 0.95- 0.75 (m, 4H)	385.2	0.0015

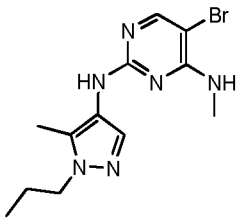
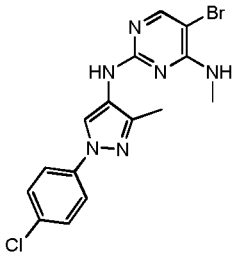
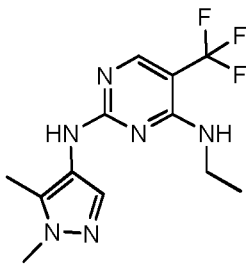
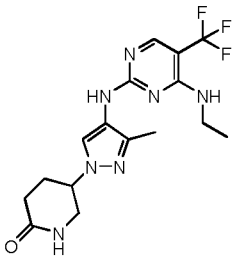
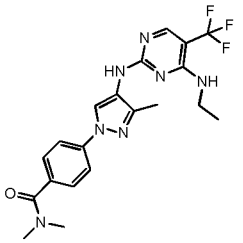
237	2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N,2-dimethylpropanamide		1H NMR (400 MHz, DMSO) δ 8.90 (s, 1H), 8.09 (s, 1H), 7.85 (s, 1H), 7.67 (d, J = 4.4, 1H), 7.02 (s, 1H), 2.84 (d, J = 3.8, 3H), 2.60 (d, J = 4.5, 3H), 1.66 (s, 6H).		0.045
238	N2-(1-(1-(2-methoxyethyl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.92 (s, 1H), 8.07 (s, 1H), 7.94 (s, 1H), 6.97 (s, 1H), 3.95 (dt, J = 15.5, 5.6, 1H), 3.43 (t, J = 5.8, 2H), 3.24 (s, 3H), 2.93 (d, J = 11.8, 2H), 2.88 (d, J = 4.4, 3H), 2.10 (d, J = 11.8, 5H), 2.02 – 1.72 (m, 4H).		0.016
239	N2-(1-(1-(2-methoxyethyl)piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.86 (s, 1H), 8.04 (s, 1H), 7.71 (s, 1H), 6.91 (s, 1H), 4.12 – 3.88 (m, 1H), 3.44 (t, J = 5.9, 2H), 3.24 (s, 3H), 2.96 (d, J = 11.6, 2H), 2.84 (s, 3H), 2.15 (dd, J = 22.8, 10.9, 4H), 1.98 (qd, J = 12.2, 3.4, 2H), 1.75 (d, J = 12.3, 2H).		0.006
240	(R)-N4-methyl-N2-(5-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				

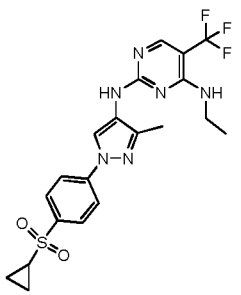
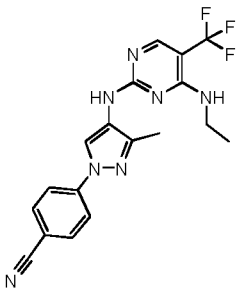
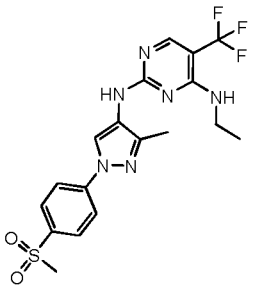
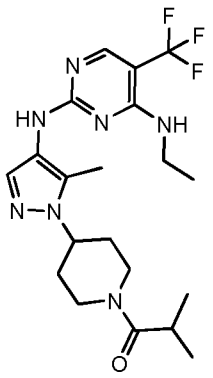
241	N2-(5-chloro-1-(3-fluoro-1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.94 (s, 1H), 8.08 (s, 1H), 7.85 (s, 1H), 7.00 (s, 1H), 4.87 (dtd, J = 49.9, 9.8, 5.1, 1H), 4.34 (qd, J = 11.2, 4.9, 1H), 3.27 – 3.15 (m, 1H), 2.82 (s, 4H), 2.22 – 2.04 (m, 3H), 1.91 (s, 1H).		0.0018
242	N2-(5-chloro-1-(1-ethyl-3-fluoropiperidin-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.95 (s, 1H), 8.08 (s, 1H), 7.87 (s, 1H), 7.00 (s, 1H), 4.86 (m, 1H), 4.36 (m, 1H), 3.08 – 2.71 (m, 4H), 2.25 – 1.81 (m, 5H), 1.03 (t, J = 7.1, 3H).		0.0021
243	N4-ethyl-N2-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.40 (s, 1H), 8.45 (s, 1H), 8.20 (s, 1H), 7.28 (s, 1H), 3.58 (q, J = 7.3, 2H), 3.53 – 3.37 (m, 2H), 2.31 (s, 3H), 1.16 (t, J = 7.0, 3H), 1.07 (t, J = 7.3, 3H).		0.0005
244	N4-ethyl-N2-(1-(ethylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.07 (s, 1H), 8.11 (s, 2H), 7.05 (s, 1H), 3.62 (q, J = 7.3, 2H), 3.37 (s, 2H), 2.39 (s, 3H), 1.09 (t, J = 7.3, 6H).		0.0047

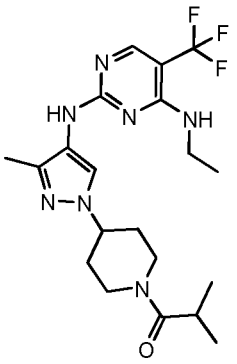
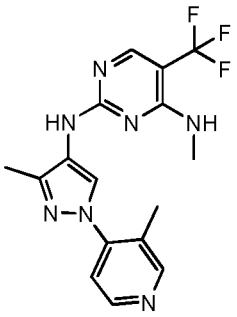
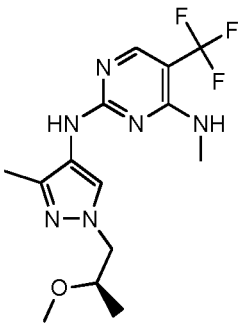
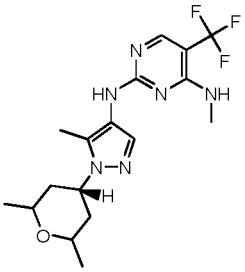
245	N4-methyl-N2-(3-methyl-1-(2-methyl-2-morpholinopropyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine			414.2	
246	N2-(1-(1-ethyl-3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.92 (s, 1H), 8.05 (s, 1H), 7.79 (s, 1H), 6.95 (s, 1H), 5.22 – 4.55 (m, 1H), 4.22 (dd, J = 21.0, 11.1, 1H), 2.85 (d, J = 21.1, 3H), 2.33 – 1.97 (m, 5H), 1.03 (t, J = 7.1, 3H).	402.2	
247	N2-(5-(dimethylamino)-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.74 (br s, 1H), 6.52 (br s, 1H), 5.13 (s, 1H), 3.74 (s, 3H), 3.02 (d, J = 4.7, 3H), 2.80 (s, 6H).	316	0.0779
248	2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-1-ol		1H NMR (400 MHz, DMSO) δ 8.75 (s, 1H), 8.08 (s, 1H), 7.73 (s, 1H), 6.99 (s, 1H), 4.92 (t, J = 5.7, 1H), 3.77 (d, J = 5.6, 2H), 2.83 (d, J = 3.0, 3H), 1.57 (s, 6H).	365.1	

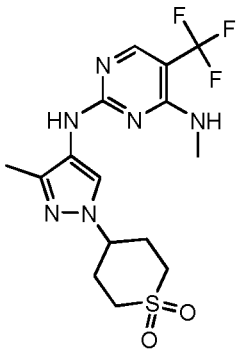
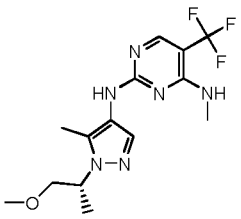
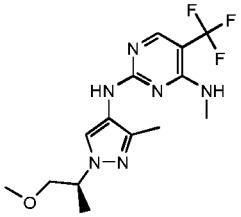
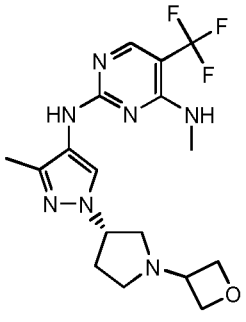
249	N^2-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.41 (s, 1H), 8.48 (s, 1H), 8.20 (s, 1H), 7.20 (s, 1H), 3.58 (q, J = 7.3, 2H), 2.91 (d, J = 4.4, 3H), 2.31 (s, 3H), 1.08 (t, J = 7.3, 3H).	365.1	0.0033
250	2-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propan-2-ol				0.0122
251	N2-[1-(2-Methoxy-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0026
252	N2-[1-(2-Methoxy-ethyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0061
253	5-Bromo-N2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine				0.0022

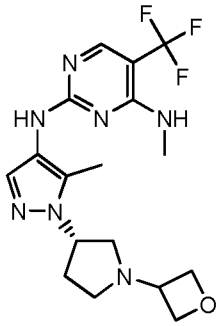
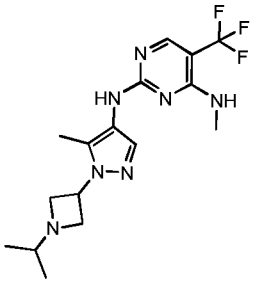
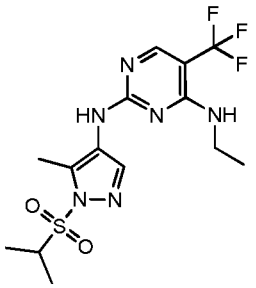
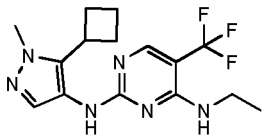
254	N4-Methyl-N2-[3-methyl-1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0077
255	5-Bromo-N2-(1-difluoromethyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine				0.0007
256	5-Bromo-N2-(1-difluoromethyl-3-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine				0.0022
257	5-Bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-ethyl-pyrimidine-2,4-diamine				0.0015
258	5-Bromo-N2-[1-(4-fluoro-phenyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-pyrimidine-2,4-diamine				

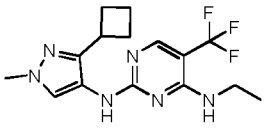
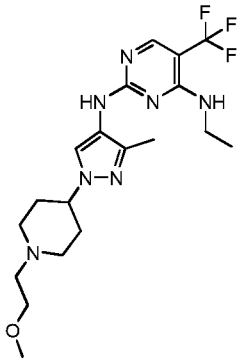
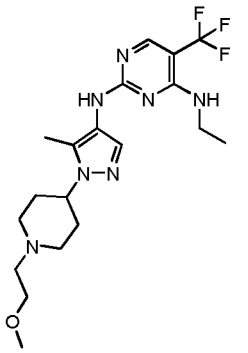
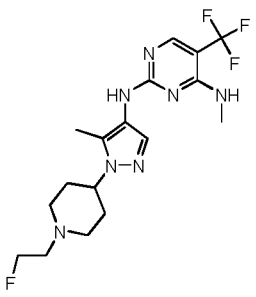
259	5-Bromo-N4-methyl-N2-(5-methyl-1-propyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine				0.0057
260	5-Bromo-N2-[1-(4-chloro-phenyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-pyrimidine-2,4-diamine				0.0003
261	N2-(1,5-Dimethyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0013
262	5-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-2-one				0.0013
263	4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide				0.0018

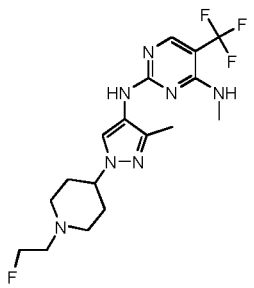
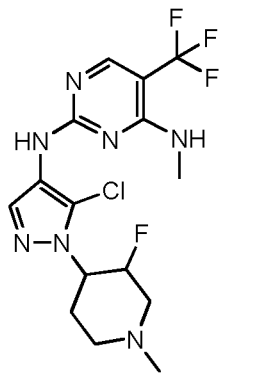
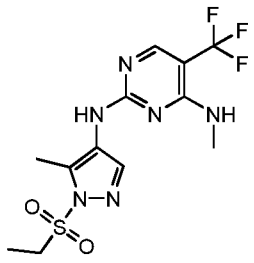
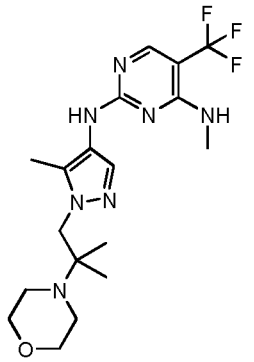
264	N2-[1-(4-Cyclopropanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0032
265	4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-benzonitrile				0.0048
266	N4-Ethyl-N2-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0021
267	1-{4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-piperidin-1-yl}-2-methyl-propan-1-one				0.0008

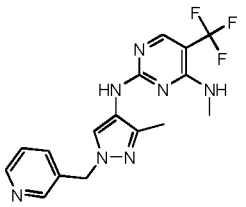
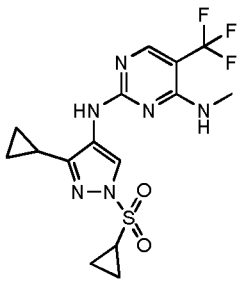
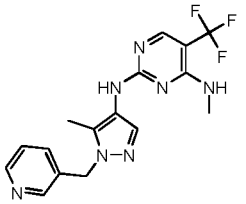
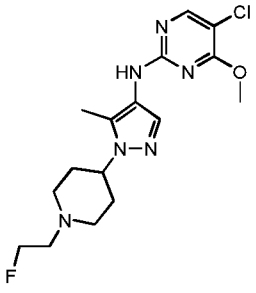
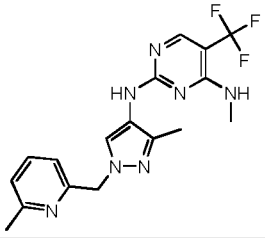
268	1-{4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-1-yl}-2-methyl-propan-1-one				0.0077
269	N4-Methyl-N2-[3-methyl-1-(3-methyl-pyridin-4-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0091
270	N2-[1-((R)-2-Methoxy-propyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.017
272	N2-[1-(2,6-Dimethyl-tetrahydro-pyran-4-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0051

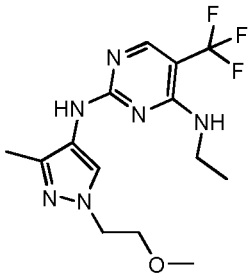
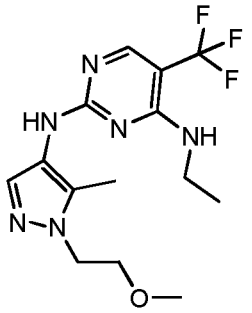
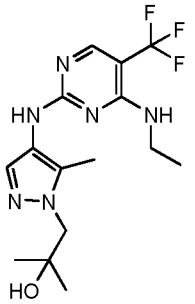
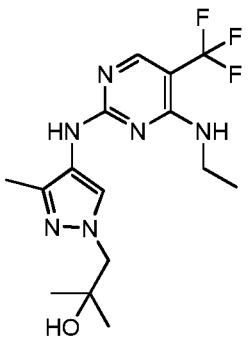
273	N2-[1-(1,1-Dioxo-hexahydro-1$l%6&-thiopyran-4-yl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.037
274	N2-[1-((R)-2-Methoxy-1-methyl-ethyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0185
275	N2-[1-((S)-2-Methoxy-1-methyl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0089
276	N4-Methyl-N2-[3-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0039

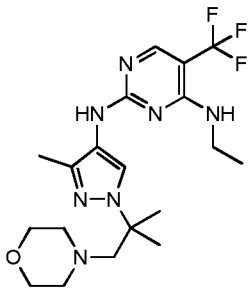
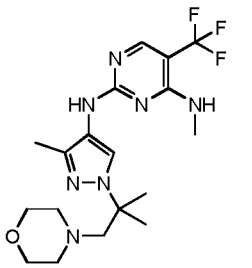
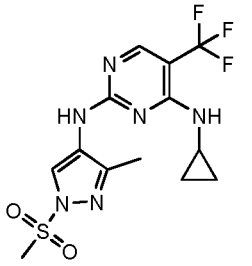
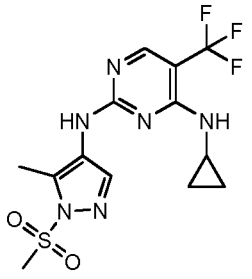
277	N4-Methyl-N2-[5-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.058
278	N2-[1-(1-Isopropyl-azetidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0012
279	N4-Ethyl-N2-[5-methyl-1-(propane-2-sulfonyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0047
280	N2-(5-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0036

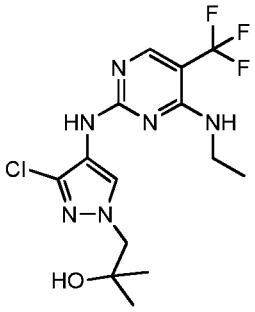
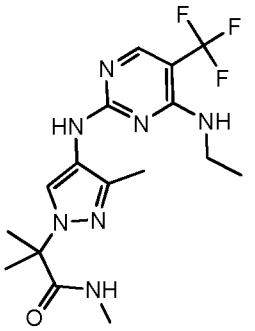
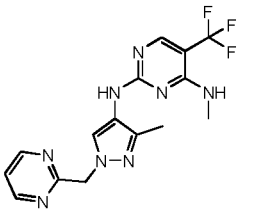
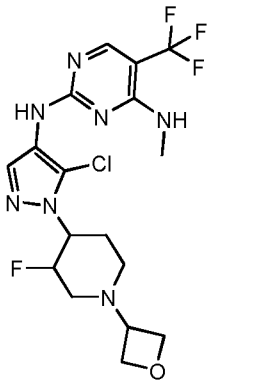
281	N2-(3-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0013
282	N4-Ethyl-N2-{1-[1-(2-methoxy-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0054
283	N4-Ethyl-N2-{1-[1-(2-methoxy-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine				0.002
284	N2-{1-[1-(2-Fluoro-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0042

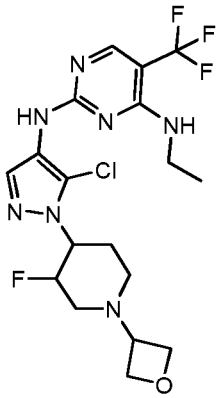
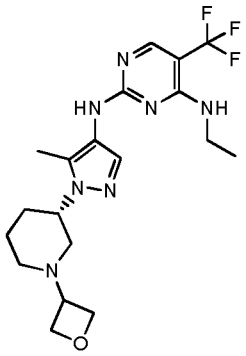
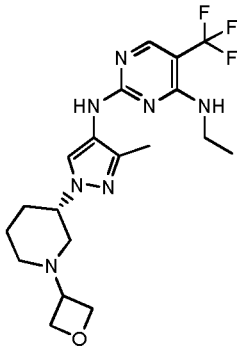
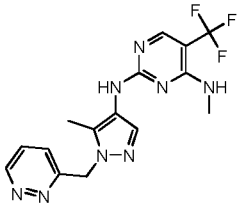
285	N2-{1-[1-(2-Fluoro-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0283
286	N2-[5-Chloro-1-(3-fluoro-1-methyl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.95 (s, 1H), 8.08 (s, 1H), 7.88 (s, 1H), 7.00 (s, 1H), 4.87 (dtd, J = 49.9, 9.8, 5.1, 1H), 4.34 (qd, J = 11.3, 4.9, 1H), 3.29 – 3.13 (m, 1H), 2.82 (s, 4H), 2.28 (s, 3H), 2.25 – 1.99 (m, 3H), 1.92 (d, J = 6.8, 1H).		0.0018
287	N2-(1-Ethanesulfonyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0072
288	N4-Methyl-N2-[5-methyl-1-(2-methyl-2-morpholin-4-yl-propyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0077

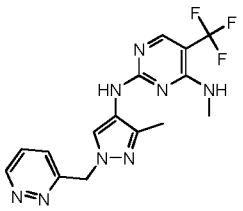
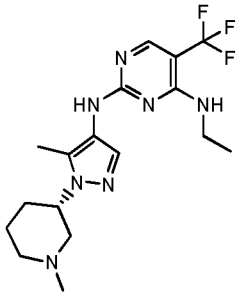
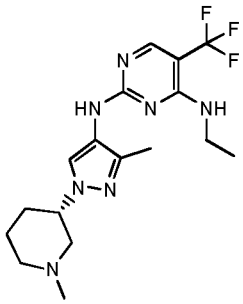
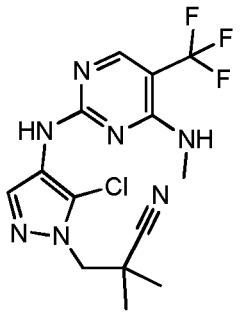
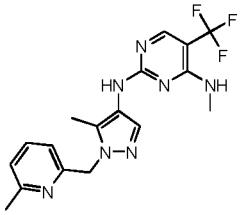
289	N4-Methyl-N2-(3-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.025
290	N2-(1-Cyclopropanesulfonyl-3-cyclopropyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				
291	N4-Methyl-N2-(5-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				
292	(5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoro-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-amine				0.0042
293	N4-Methyl-N2-[3-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-				0.0006

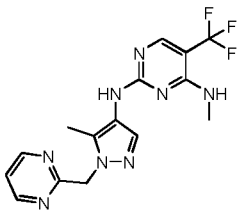
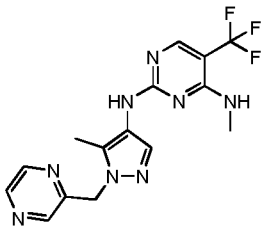
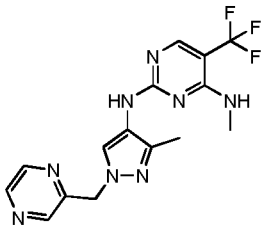
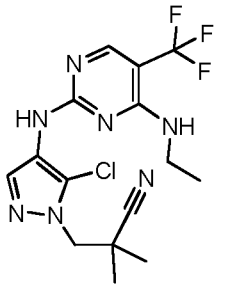
	trifluoromethyl-pyrimidine-2,4-diamine				
294	N4-Ethyl-N2-[1-(2-methoxy-ethyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0011
295	N4-Ethyl-N2-[1-(2-methoxy-ethyl)-5-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0004
296	1-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-2-methyl-propan-2-ol		1H NMR (400 MHz, DMSO) δ 8.75 (s, 1H), 8.05 (s, 1H), 7.57 (s, 1H), 6.86 (s, 1H), 4.63 (s, 1H), 3.90 (s, 2H), 3.36 (s, 2H), 2.19 (s, 3H), 1.08 (s, 7H).		0.0023
297	1-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propan-2-ol		1H NMR (400 MHz, DMSO) δ 8.83 (s, 1H), 8.07 (s, 1H), 7.85 (s, 1H), 6.91 (s, 1H), 4.60 (s, 1H), 3.79 (d, J = 64.3, 2H), 3.42 (s, 2H), 2.27 – 1.82 (m, 3H), 1.35 – 1.05 (m, 3H), 0.97 (d, J = 63.4, 6H).		0.0021

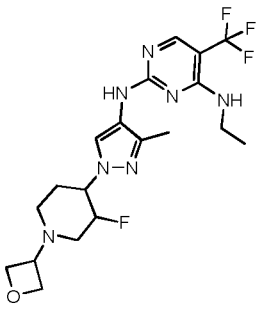
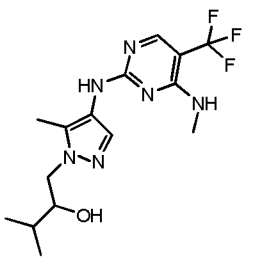
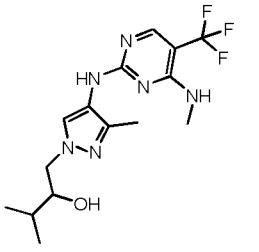
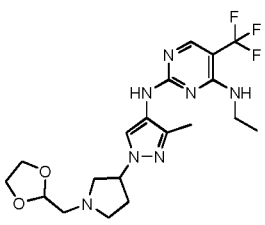
298	N2-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0506
299	N2-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.228
300	N4-Cyclopropyl-N2-(1-methanesulfonyl-3-methyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.55 (s, 1H), 8.83 (s, 1H), 8.22 (s, 1H), 7.27 (s, 1H), 3.39 (s, 3H), 2.79 (s, 1H), 2.34 (s, 3H), 0.95 – 0.58 (m, 4H).		0.0004
301	N4-Cyclopropyl-N2-(1-methanesulfonyl-5-methyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.25 (s, 1H), 8.40 (s, 1H), 8.14 (s, 1H), 7.04 (s, 1H), 3.46 (s, 3H), 2.79 (s, 1H), 2.43 (s, 3H), 0.68 (dd, J = 13.9, 9.3, 4H).		0.0021

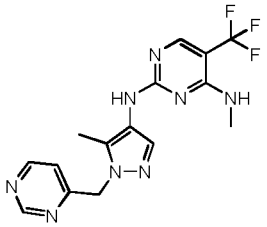
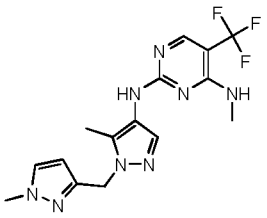
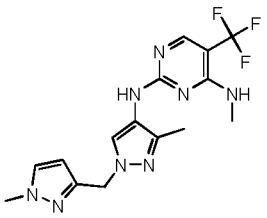
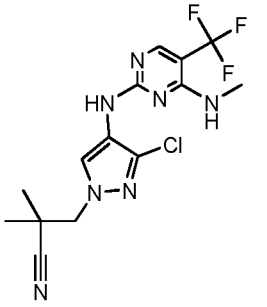
302	1-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2-methyl-propan-2-ol				0.016
303	2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide				0.0013
304	N4-Methyl-N2-(3-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0051
305	N2-[5-Chloro-1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.91 (s, 1H), 8.08 (s, 1H), 7.86 (s, 1H), 7.00 (s, 1H), 4.97 (td, J = 9.8, 5.0, 0H), 4.90 – 4.74 (m, 1H), 4.63 – 4.52 (m, 2H), 4.46 (dt, J = 21.3, 7.5, 3H), 3.71 – 3.53 (m, 1H), 3.26 – 3.11 (m, 1H), 2.94 – 2.71 (m, 4H), 2.16 – 1.85 (m, 4H).		0.0022

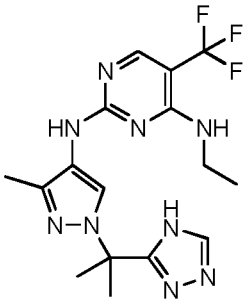
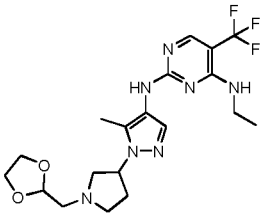
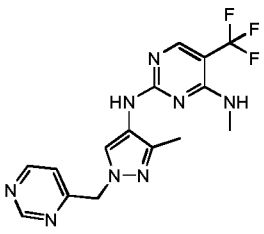
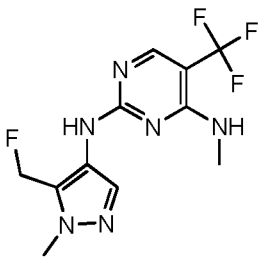
306	N2-[5-Chloro-1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.84 (s, 1H), 8.08 (s, 1H), 7.80 (s, 1H), 6.98 (s, 1H), 5.02 – 4.79 (m, 1H), 4.56 (t, J = 6.5, 3H), 4.46 (dt, J = 20.4, 7.0, 4H), 3.65 – 3.53 (m, 2H), 3.24 – 3.15 (m, 1H), 2.77 (s, 1H), 2.20 – 1.85 (m, 5H), 1.05 (s, 4H).		0.0006
307	N4-Ethyl-N2-[5-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0003
308	N4-Ethyl-N2-[3-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0085
309	N4-Methyl-N2-(5-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0028

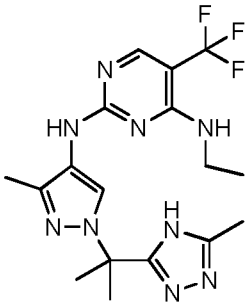
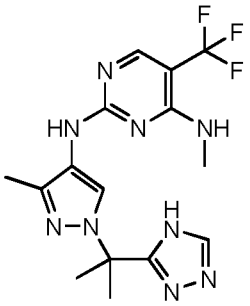
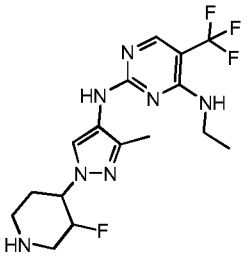
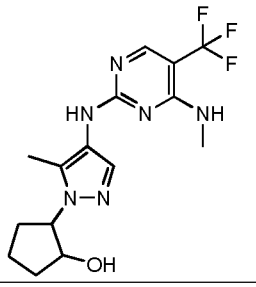
310	N4-Methyl-N2-(3-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0093
311	N4-Ethyl-N2-[5-methyl-1-((S)-1-methyl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0012
312	N4-Ethyl-N2-[3-methyl-1-((S)-1-methyl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0156
313	3-[5-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile		1H NMR (400 MHz, DMSO) δ 8.92 (s, 1H), 8.09 (s, 1H), 7.86 (s, 1H), 7.00 (s, 1H), 4.29 (s, 2H), 2.82 (s, 3H), 1.38 (s, 6H).		0.0017
314	N4-Methyl-N2-[5-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-				0.0015

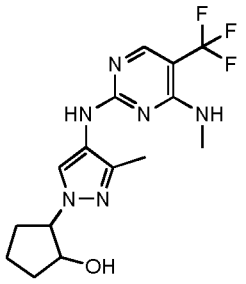
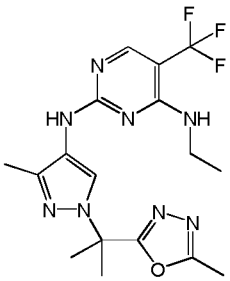
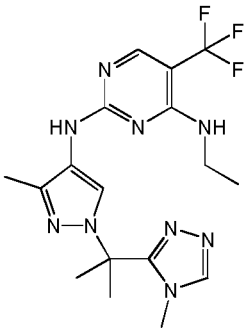
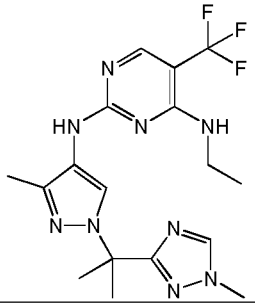
	pyrimidine-2,4-diamine				
315	N4-Methyl-N2-(5-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0014
316	N4-Methyl-N2-(5-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0026
317	N4-Methyl-N2-(3-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0012
318	3-[5-Chloro-4-(4-ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile		1H NMR (400 MHz, DMSO) δ 8.87 (s, 1H), 8.09 (s, 1H), 7.80 (s, 1H), 6.98 (s, 1H), 4.30 (s, 2H), 3.35 (s, 2H), 1.38 (s, 6H), 1.05 (s, 3H).		0.0007

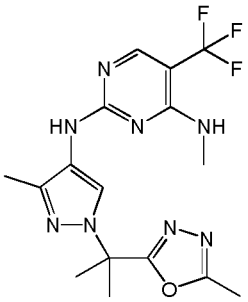
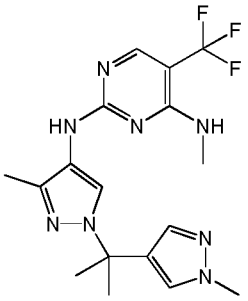
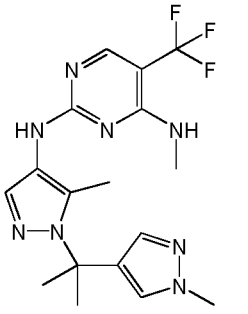
319	N4-Ethyl-N2-[1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 8.79 (s, 1H), 8.05 (s, 1H), 7.67 (s, 1H), 6.87 (s, 1H), 5.06 – 4.73 (m, 1H), 4.56 (td, J = 6.5, 2.5, 2H), 4.46 (dt, J = 12.0, 6.1, 2H), 4.26 (dd, J = 21.1, 11.2, 1H), 3.58 (p, J = 6.3, 1H), 3.38 (s, 2H), 3.22 – 3.07 (m, 1H), 2.77 (d, J = 9.0, 1H), 2.26 – 1.99 (m, 6H), 1.90 (s, 1H), 1.08 (s, 3H).		0.0003
320	3-Methyl-1-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-butan-2-ol		1H NMR (400 MHz, DMSO) δ 8.82 (s, 1H), 8.04 (s, 1H), 7.65 (s, 1H), 6.88 (s, 1H), 4.71 (d, J = 5.2, 1H), 3.93 (ddd, J = 21.6, 14.0, 6.1, 2H), 3.59 (dd, J = 7.4, 4.5, 1H), 2.83 (s, 3H), 2.19 (s, 3H), 1.58 (dd, J = 12.0, 6.5, 1H), 0.90 (t, J = 7.0, 6H).		0.0030
321	3-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-butan-2-ol				0.0108
322	N2-[1-(1-[1,3]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-				0.0049

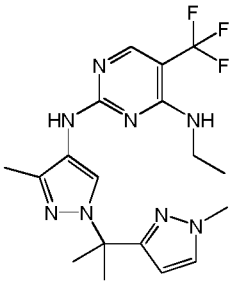
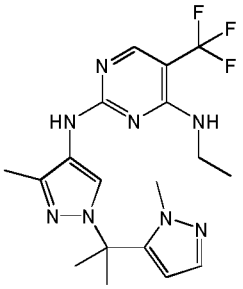
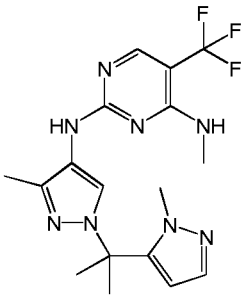
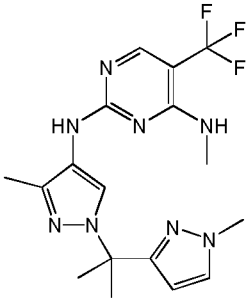
	trifluoromethyl-pyrimidine-2,4-diamine				
323	N4-Methyl-N2-(5-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0022
324	N4-Methyl-N2-[5-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0006
325	N4-Methyl-N2-[3-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0038
326	3-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-				0.0082

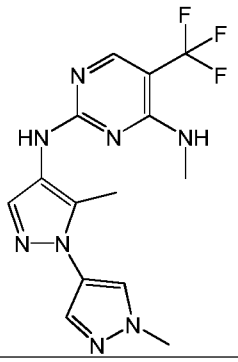
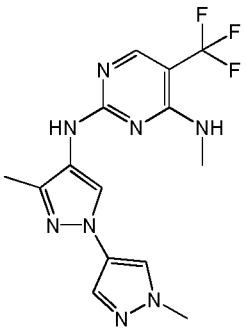
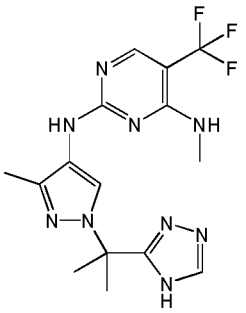
	propionitrile				
327	N4-Ethyl-N2-{3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0005
328	N2-[1-(1-[1,3]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0004
329	N4-Methyl-N2-(3-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0052
330	N2-(5-Fluoromethyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-				0.0245

	pyrimidine-2,4-diamine				
331	N4-Ethyl-N2-{3-methyl-1-[1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 13.49 (d, J = 53.3, 1H), 8.89 (s, 1H), 8.07 (s, 1H), 7.78 (s, 1H), 6.96 (s, 1H), 2.31 (s, 3H), 2.13 (s, 3H), 1.83 (s, 6H), 1.06 (s, 3H).		0.0008
332	N4-Methyl-N2-{3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0023
333	N4-Ethyl-N2-[1-(3-fluoro-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0007
334	2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-				0.0063

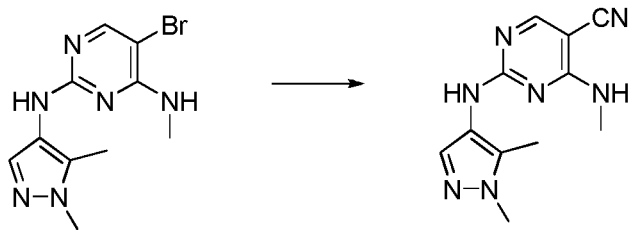
	cyclopentanol				
335	2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol				0.0033
336	N4-ethyl-N2-(3-methyl-1-(2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.0012
337	N4-ethyl-N2-(3-methyl-1-(2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.0076
338	N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-				0.0003

	5-(trifluoromethyl)pyrimidine-2,4-diamine				
339	N4-methyl-N2-(3-methyl-1-(2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.0117
340	N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.0003
341	N4-methyl-N2-(5-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.0061

342	N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.0217
343	N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.0003
344	N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				0.0014
345	N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)				0.115

	pyrimidine-2,4-diamine				
346	N2-(1',5-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine				
347	N2-(1',3-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine				
348	N2-(1-(2-(4H-1,2,4-triazol-3-yl)propan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine				

Example 349 2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile

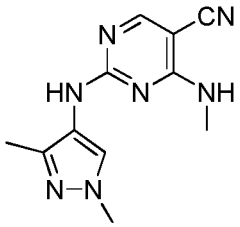
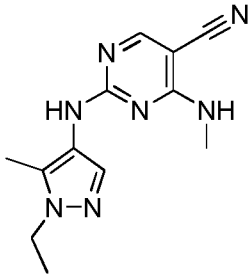
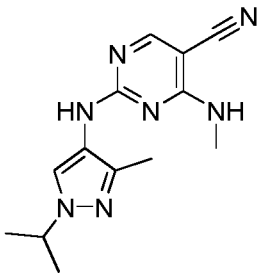
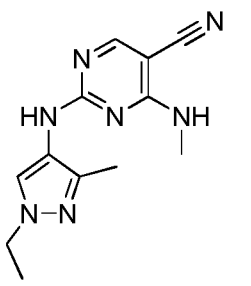


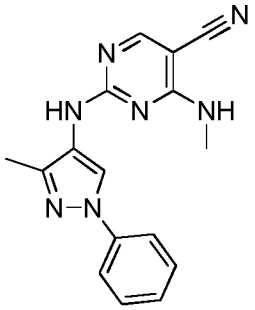
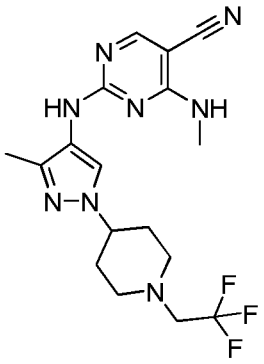
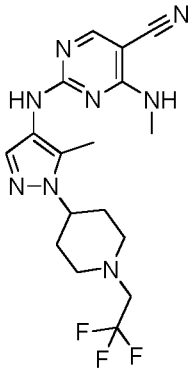
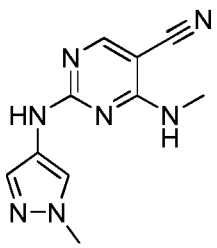
To a mixture of 5-bromo-N^2-(1,5-dimethyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine (95 mg, 0.32 mmol), zinc cyanide (70 mg, 0.60 mmol), $Pd_2(dba)_3$ (11 mg, 0.012 mmol),

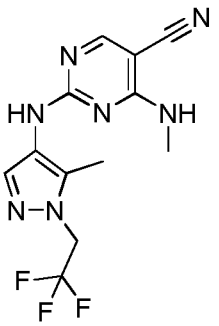
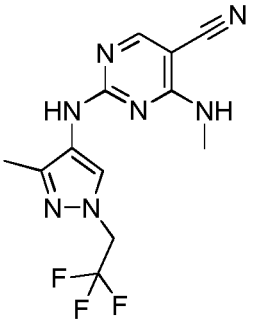
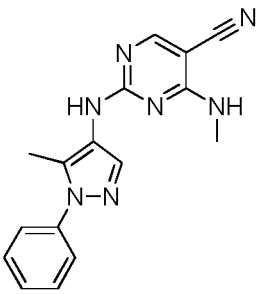
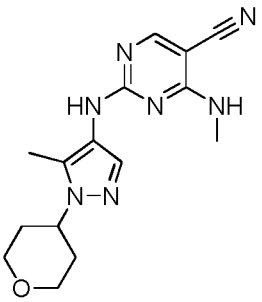
DPPF (13 mg, 0.023 mmol) was added DMF (3.5 mL). The reaction was then heated in a sealed tube at 105 °C for 18 h. The reaction mixture was filtered and concentrated. The crude product was purified by reverse phase HPLC to give 2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile (19 mg, 25%). LCMS (Method A): [MH^+] = 244.1 at 2.53 min. ^{1}H-NMR (DMSO): δ 8.96 (m, 1H), 8.21 (m, 1H), 7.49 (m, 2H), 3.69 (s, 3H), 2.84 (m, 3H), 2.14 (m, 3H). K_I = 0.025μM.

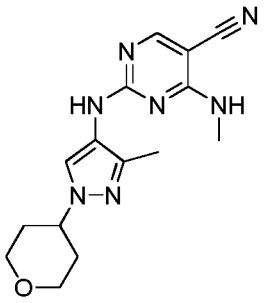
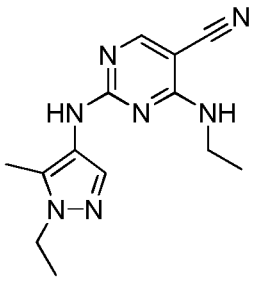
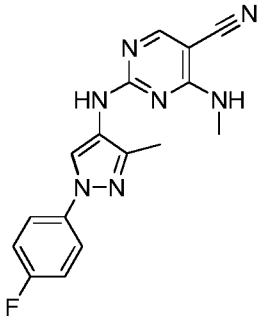
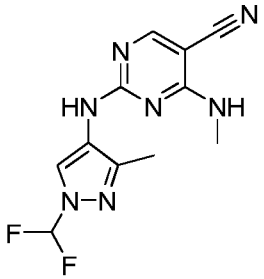
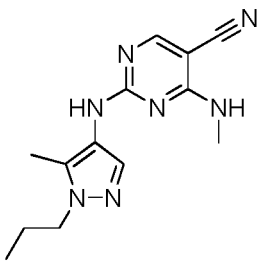
Compounds made using the above procedure are shown in Table 9 below, together with low resolution mass spectrometry (M+H), proton NMR, and LRRK2 K_i (micromolar) data for selected compounds determined from the assay described below.

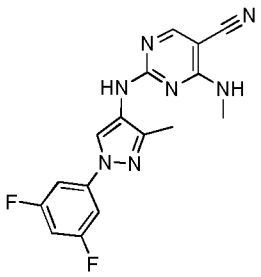
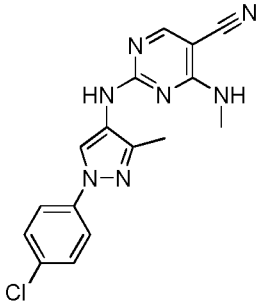
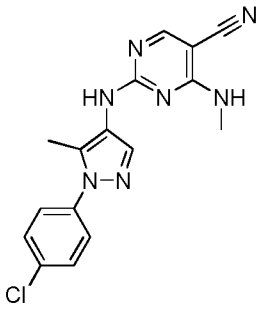
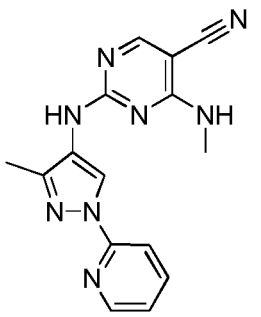
Table 9

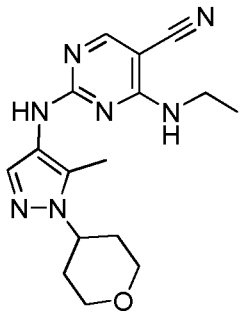
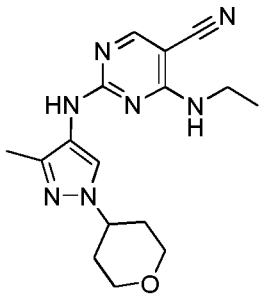
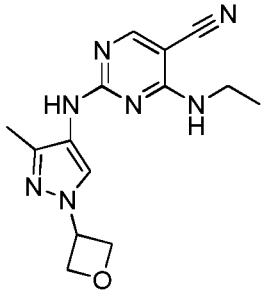
	Name	Structure	^{1}H NMR	M+H$^+$	K_i
350	2-(1,3-Dimethyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidine-5-carbonitrile		^{1}H-NMR (DMSO): δ 9.15 (s, 1H), 8.23 (s, 1H), 7.84 (s, 1H), 7.53 (s, 1H), 3.72 (s, 3H), 2.86 (d, *J* = 4.4, 3H), 2.12 (s, 3H).	244.1	0.029
351	2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.12 (s, 1H), 8.21 (s, 1H), 7.73 – 7.27 (m, 2H), 4.01 (q, J = 7.2, 2H), 2.80 (m, 3H), 2.20 (m, 3H), 1.27 (t, J = 7.2, 3H).		0.0097
352	2-(1-isopropyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.18 (s, 1H), 8.23 (s, 1H), 7.95 (s, 1H), 7.55 (s, 1H), 4.35 (m, 1H), 2.86 (d, J = 4.5, 3H), 2.14 (m, 3H), 1.36 (d, J = 6.6, 6H).		0.048
353	2-(1-ethyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-		1H NMR (400 MHz, DMSO) δ 8.10 (s, 0H), 7.58 (d, J = 2.1, 0H), 7.01 (d, J = 3.6, 0H), 6.60 (s, 0H), 4.02 (q, J = 7.2, 1H), 2.91 (d, J = 4.4, 1H), 1.35		0.036

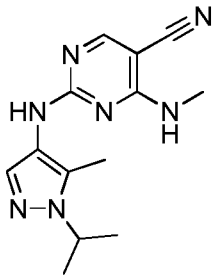
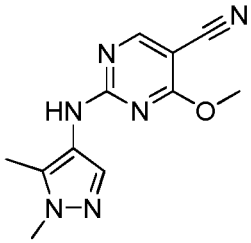
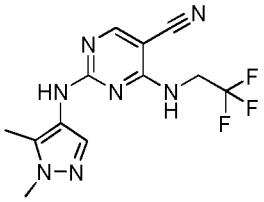
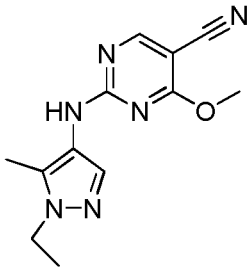
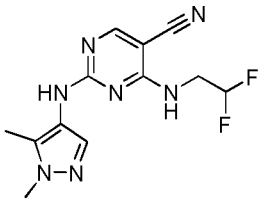
	carbonitrile		(t, J = 7.2, 1H).		
354	2-(3-methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.43 (s, 1H), 8.62 (s, 1H), 8.30 (s, 1H), 7.71 (d, J = 8.0, 2H), 7.46 (t, J = 7.9, 2H), 7.24 (t, J = 7.4, 1H), 2.92 (d, J = 3.5, 3H), 2.27 (s, 3H).		0.12
355	2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile				0.299
356	2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile				0.0225
357	2-(1-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile				

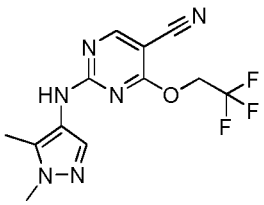
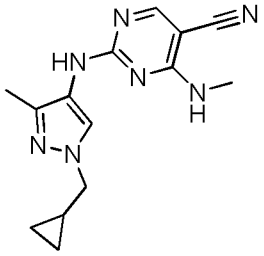
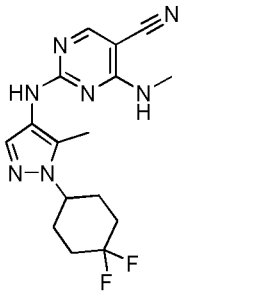
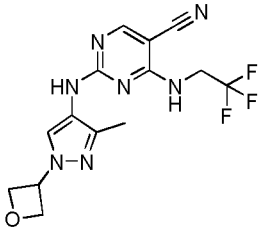
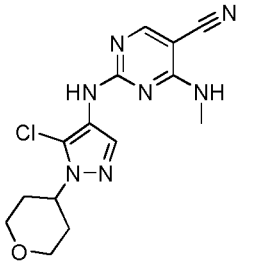
358	2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.18 (s, 1H), 8.23 (s, 1H), 7.78 (s, 1H), 7.53 (s, 1H), 5.02 (q, J = 9.2, 2H), 2.79 (s, 3H), 2.23 (s, 3H).		0.032
359	2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.28 (s, 1H), 8.26 (s, 1H), 8.06 (s, 1H), 7.59 (s, 1H), 5.00 (q, J = 9.0, 2H), 2.86 (d, J = 4.0, 3H), 2.17 (s, 3H).		0.053
360	2-(5-methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.32 (s, 1H), 8.26 (s, 1H), 7.84 (d, J = 116.0, 1H), 7.46 (d, J = 37.7, 6H), 2.86 (s, 3H), 2.28 (s, 3H).		0.0013
361	2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 8.96 (d, J = 136.9, 1H), 8.20 (d, J = 5.4, 1H), 7.73 (s, 1H), 7.44 (d, J = 34.8, 1H), 4.41 – 4.24 (m, 1H), 3.95 (dd, J = 11.3, 3.8, 2H), 3.47 (t, J = 11.4, 2H), 2.81 (s, 3H), 2.19 (d, J = 30.4, 3H), 2.07 – 1.93 (m, 2H), 1.75 (d, J = 12.7, 2H).		0.0087

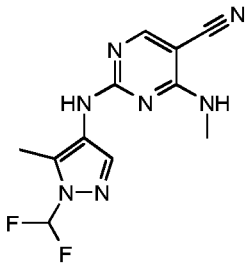
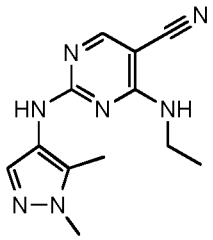
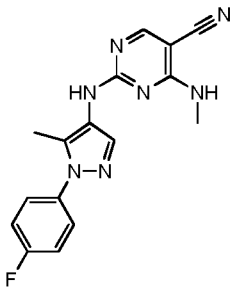
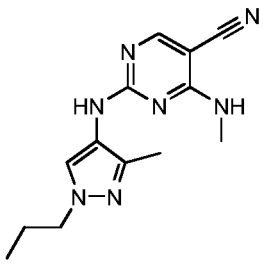
362	2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			314.1	0.086
363	2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(ethylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.08 (m, 1H), 8.21 (m, 1H), 7.70 – 7.28 (m, 2H), 4.01 (q, J = 7.2, 2H), 3.33 (m, 2H), 2.19 (m, 3H), 1.27 (t, J = 7.2, 3H), 1.08 (m, 3H).		0.0060
364	2-(1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.17 (d, J = 125.4, 1H), 8.12 (d, J = 107.0, 2H), 7.55 (s, 3H), 7.35 (t, J = 8.7, 2H), 2.86 (s, 3H), 2.26 (s, 3H).		0.0019
365	2-(1-(difluoromethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			280.1	0.035
366	2-(5-methyl-1-propyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			272.2	0.0054

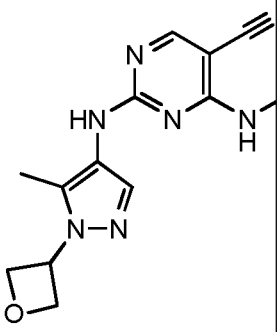
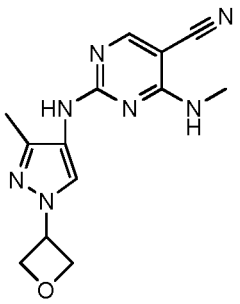
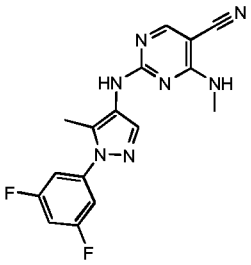
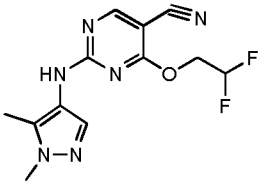
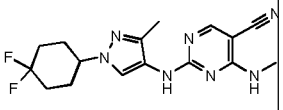
367	2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			342.2	0.0018
368	2-(1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.45 (s, 1H), 8.62 (s, 1H), 8.30 (s, 1H), 7.75 (d, J = 8.6, 2H), 7.67 (s, 1H), 7.50 (d, J = 8.9, 2H), 2.91 (d, J = 4.4, 3H), 2.26 (s, 3H).		0.082
369	2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			340.1	0.0025
370	2-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.51 (s, 1H), 8.94 (s, 1H), 8.53 – 8.24 (m, 2H), 7.92 (t, J = 7.7, 1H), 7.84 (t, J = 6.7, 1H), 7.69 (s, 1H), 7.32 – 7.21 (m, 1H), 2.93 (s, 3H), 2.31 (s, 3H).		0.0415

371	4-(ethylamino)-2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 8.92 (d, J = 137.5, 1H), 8.21 (s, 1H), 7.77 – 7.30 (m, 2H), 4.41 – 4.27 (m, 1H), 3.95 (dd, J = 11.2, 4.0, 2H), 3.47 (t, J = 11.3, 2H), 2.23 (s, 3H), 2.00 (qd, J = 12.4, 4.5, 2H), 1.75 (dd, J = 12.6, 2.2, 2H), 1.08 (s, 3H).		0.0052
372	4-(ethylamino)-2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 8.97 (d, J = 158.8, 1H), 8.24 (s, 1H), 7.84 (d, J = 58.8, 1H), 7.52 (d, J = 79.5, 1H), 4.31 – 4.17 (m, 1H), 4.01 – 3.86 (m, 2H), 3.43 (dd, J = 23.6, 12.1, 4H), 2.10 (d, J = 27.9, 3H), 1.89 (dt, J = 20.4, 11.9, 4H), 1.13 (t, J = 7.1, 3H).		0.024
373	4-(ethylamino)-2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.32* (s, 1H), 8.94† (s, 1H), 8.29 (s, 1H), 8.10* (s, 1H), 7.89† (s, 1H), 7.71* (s, 1H), 7.54† (s, 1H), 5.48 (p, J = 7.0, 1H), 4.90-4.87 (m, 4H), 3.43 (br s, 2H), 2.28-2.11 (m, 3H), 1.17 (t, J = 7.1, 3H). [* and † denote rotameric peaks.]	300	0.0228

374	2-(1-isopropyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		^{1}H NMR (500 MHz, DMSO) δ 8.68 (s, 1H), 8.15 (s, 1H), 7.54 (s, 1H), 7.17-7.19 (m, 1H), 4.40-4.47 (m, 1H), 2.84 (d, *J* = 7.5, 3H), 2.16 (s, 3H), 1.29-1.36 (m, 6H).		0.0158
375	2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile				0.145
376	2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethylamino)pyrimidine-5-carbonitrile			312	0.0275
377	2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile			259	0.075
378	4-(2,2-difluoroethylamino)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile			294	0.033

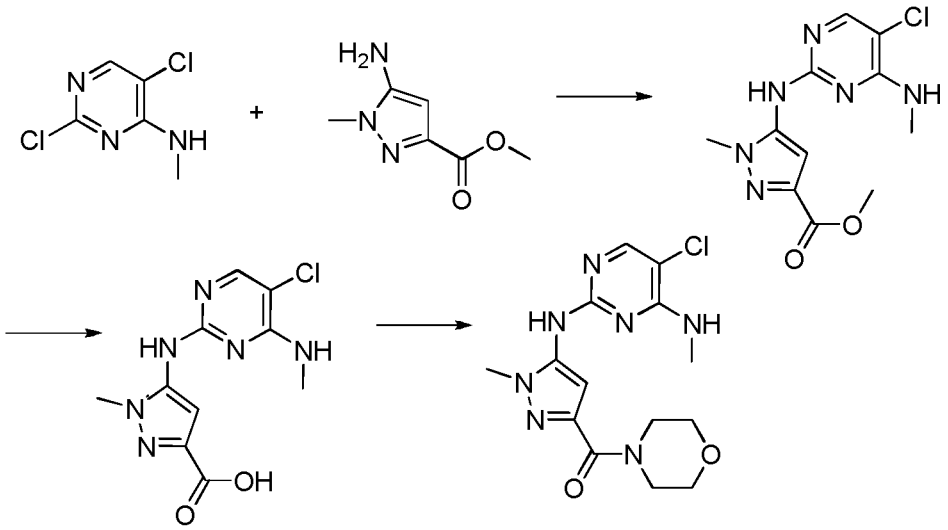
378	2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethoxy)pyrimidine-5-carbonitrile				0.54
380	2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile		H NMR (500 MHz, DMSO) δ 8.74 (s, 1H), 8.21 (s, 1H), 7.85 (s, 1H), 7.23 (s, 1H), 3.90 (d, *J* = 11.5, 2H), 2.89 (d, *J* = 7.5, 2H), 2.17 (s, 3H), 1.14-1.22 (m, 1H), 0.48-0.54 (m, 2H), 0.28-0.33 (m, 2H).		0.045
381	2-(1-(4,4-difluorocyclohexyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile		^{1}H NMR (500 MHz, DMSO) δ 8.71 (m, 1H), 8.32 (s, 1H), 7.58 (s, 1H), 7.19 (m,1H), 4.33 (m, 1H), 2.83 (d, *J* = 8.0, 3H), 1.90-2.19 (m, 11H).		0.011
382	2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethylamino)pyrimidine-5-carbonitrile			354.1	0.066
383	2-(5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)		1H NMR (400 MHz, DMSO) δ 9.12 (m, 1H), 8.25 (s, 1H), 7.73 (m, 2H), 4.59 – 4.41 (m, 1H), 3.96 (m, 2H), 3.49 (m, 2H), 2.80 (s, 3H), 2.13 – 1.92		0.0096

	pyrimidine-5-carbonitrile		(m, 2H), 1.81 (m, 2H).		
384	2-(1-Difluoromethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidine-5-carbonitrile				0.0191
385	2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-ethylamino-pyrimidine-5-carbonitrile				0.0127
386	2-[1-(4-Fluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile				0.0959
387	4-Methylamino-2-(3-methyl-1-propyl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile				0.0054

388	4-Methylamino-2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile				0.0322
389	4-Methylamino-2-(3-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile				0.0372
390	2-[1-(3,5-Difluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile				0.241
391	4-(2,2-Difluoro-ethoxy)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile				0.211
392	2-[1-(4,4-Difluoro-cyclohexyl)-3-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-				0.266

	carbonitrile				

Example 393 (5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)(morpholino)methanone



Step 1 Methyl 5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylate

To a 30 mL microwave vial was added 0.98 g of 2,5-dichloro-N-methylpyrimidin-4-amine, 0.78 g of methyl 5-amino-1-methyl-1H-pyrazole-3-carboxylate, 10 mL of 1-butanol and 0.13 mL of 4M hydrogen chloride in dioxane. The vial was capped and the reaction was heated in a microwave for 30 minutes at 130°C. As the reaction cooled, a precipitate fell out. Filter the precipitate and rinse with a small amount of n-butanol. Drying the cake yielded 0.964 g of methyl 5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylate which was used without further purification.

Step 2 5-(5-Chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylic acid

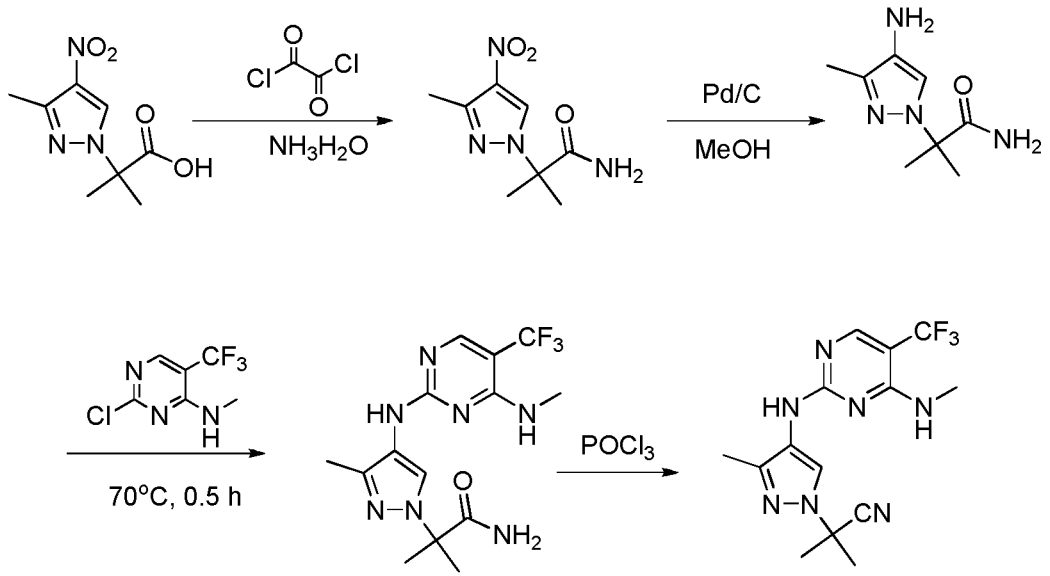
To a 100 mL round bottom flask equipped with a stir bar was added 0.964 g of methyl 5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylate, 0.28 g of LiOH, 15 mL of tetrahydrofuran and 10 mL of water. The reaction was stirred at room temperature for 18 hours. The tetrahydrofuran was removed *in vacuo* and the aqueous layer was acidified to pH 5 with 1N HCl. The aqueous layer was partitioned with ethyl acetate and the organic layer washed with brine, dried over $MgSO_4$, filtered and concentrated to give 0.58 g of 5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylic acid which was used without further purification.

Step 3 (5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)(morpholino)methanone

To a 100 mL round bottom flask equipped with a stir bar was added 0.116 g of 5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylic acid, 0.19 g

of o-benzotriazol-1-yl-tetramethyluronium hexafluorophosphate, 0.14 mL of diisopropylethylamine and 2 mL of dimethylformamide. After pre-activating for 10 minutes, 0.05 mL of morpholine was added and the reaction stirred at room temperature for 2 hours. The reaction was concentrated and purified by preparative reverse phase HPLC to yield 53.2 mg of (5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)(morpholino)methanone. LCMS (Method A): $[MH^+]$ = 352.0 at 2.80 min. ^{1}H-NMR (DMSO): δ 9.47 (s, 1H), 7.86 (s, 1H), 7.15 (s, 1H), 6.78 (s, 1H), 3.74 (s, 3H), 3.61 (m, 8H), 2.88 (d, 3H). K_I = 0.16μM.

Example 394 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H- pyrazol-1-yl)propanenitrile



Step 1: 2-methyl-2-(3-methyl-4-nitro-1H-pyrazol-1-yl)propanamide.

To a solution of 2-methyl-2-(3-methyl-4-nitro-1H-pyrazol-1-yl)propanoic acid (2.5 g, 11.7 mmol) in CH_2Cl_2 (50 mL) was added dropwise of oxalyl chloride (2.97 g, 23.4 mmol). The reaction was stirred at ambient temperature for about 2 hours, then concentrated under reduced pressure to remove the solvent, the remained solid was dissolved in THF (30 mL) and was added dropwise into NH_4OH (50 mL), the reaction was stirred at ambient temperature for 1 hour. The solution was concentrated under reduced pressure and portioned between EtOAc (50 mL) and water (100 mL), the aqueous phase was extracted with EtOAc, and the combined organic was washed with sat. NH_4Cl (50 mL), dried over anhydrous Na_2SO_4, filleted and concentrated to give crude 2-methyl-2-(3-methyl-4-nitro-1H-pyrazol-1-yl)propanamide (2.5 g, 100%) as white solid which was used in the next step without further purification.

Step 2: 2-(4-amino-3-methyl-1H-pyrazol-1-yl)-2-methylpropanamide.

To a solution of 2-methyl-2-(3-methyl-4-nitro-1H-pyrazol-1-yl)propanamide (2.5g, 11.7 mmol) in MeOH (50 mL) was added Pd/C (1 g), exchanged with nitrogen for three times then with hydrogen, and the reaction was stirred at hydrogen atmosphere (1 atm) for 1 h at ambient temperature. The solution was filtered and the filtrate was concentrated under reduced pressure

to give crude 2-(4-amino-3-methyl-1H-pyrazol-1-yl)-2-methylpropanamide (2.0 g, 93%) which was used in the next step without further purification.

Step 3: 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide

To a solution of 2-(4-amino-3-methyl-1H-pyrazol-1-yl)-2-methylpropanamide (250 mg, 1.37 mmol) in 2-methoxyethanol (5 mL) was added 2-chloro-N-methyl-5-(trifluoromethyl)pyrimidin-4-amine (290 mg, 1.37 mmol) and trifluoroaceticacid (156 mg, 1.37 mmol), the reaction was stirred at 70 °C for about 0.5 h. The reaction mixture was cooled to ambient temperature followed with the addition of water (10 mL) and the pH of solution was adjusted to 8 with sat. Na_2CO_3 The aqueous phase was extracted with ethyl acetate (10 mL x 3), the combined organic phase was dried over anhydrous sodium sulfate, filtered and concentrated to dry to give a residue which was purified by column chromatography on silica gel (CH_2Cl_2:MeOH = 20: 1) to give 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H- pyrazol-1-yl)propanamide (250mg, 51%) as white solid. LCMS (m/z) ES+ 358 (m+H).

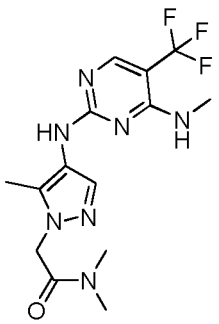
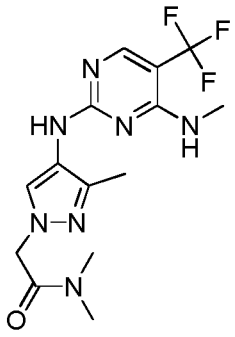
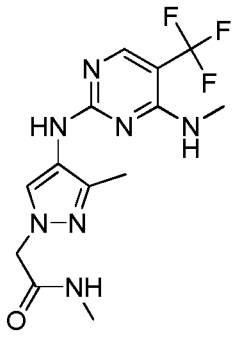
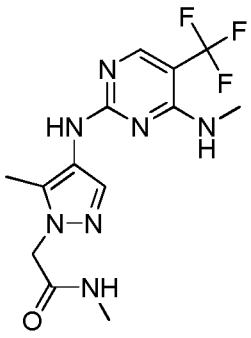
Step 4: 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile

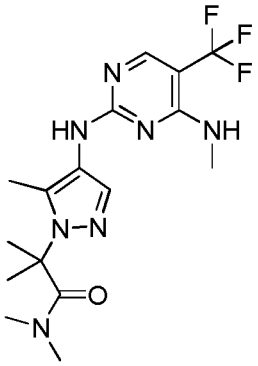
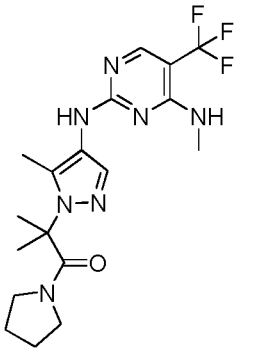
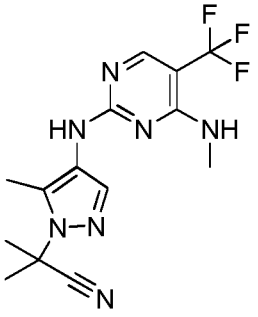
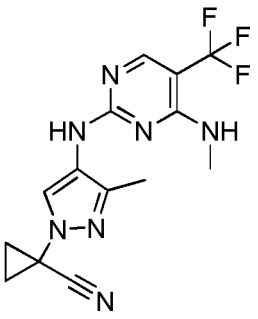
A stirred solution of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H- pyrazol-1-yl)propanamide (250 mg, 0.7 mmol) in $POCl_3$ (5 mL) was stirred at 90 °C for 1 hour. $POCl_3$ was removed by evaporation, the mixture was added into ice/H_2O(10 ml) and the pH of the solution was adjusted to 8 with sat.Na_2CO_3, the aqueous phase was extracted with ethyl acetate (5 mL x 3). he combined organic phase was washed with sat. sodium chloride (10 mL), dried over anhydrous sodium sulfate, filtered and concentrated to dry to give a residue which was purified by recrystallization to give 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H- pyrazol-1-yl)propanenitrile (100 mg, 42%) as a white solid. 1H-NMR (300 MHz, DMSO-d_6) δ ppm 9.18 (s, 1H), 8.29 (s, 1H), 8.14 (s, 1H), 7.10 (s, 1H), 2.91 (d, 3H), 2.22 (s, 3H), 1.94 (s, 2H). LCMS (m/z) ES+ 340 (m+1). Purity, 99.3% (HPLC at 214 nm); K_i = 0.0005μM.

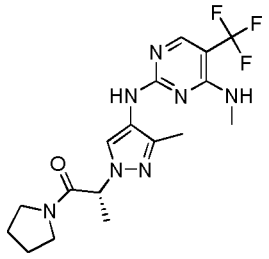
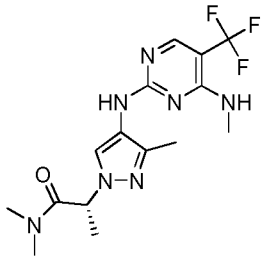
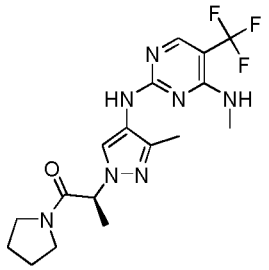
Compounds made using the above procedure are shown in Table 10 below, together with low resolution mass spectrometry (M+H), proton NMR, and LRRK2 K_i (micromolar) data for selected compounds determined from the assay described below.

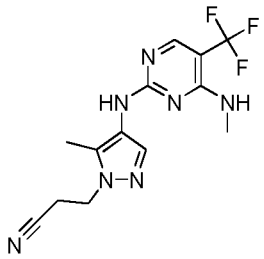
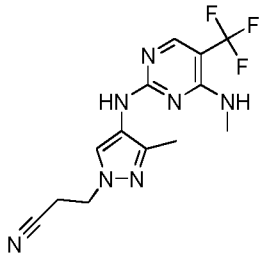
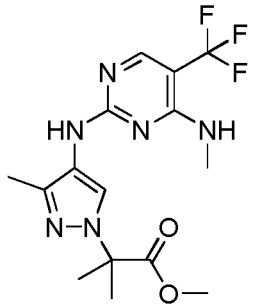
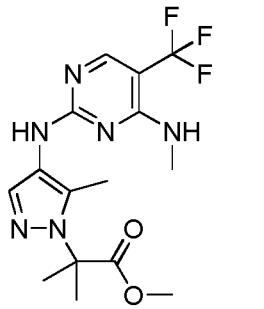
Table 10

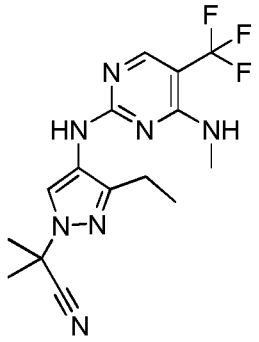
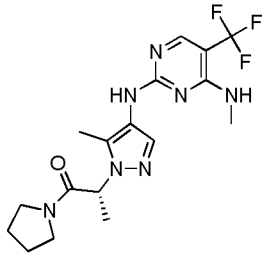
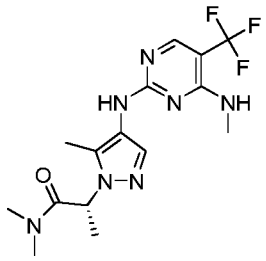
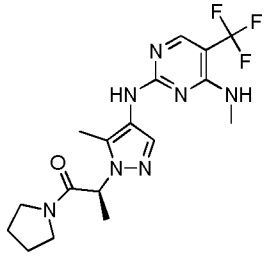
	Name	Structure	^{1}H NMR	M+H$^+$	K_i

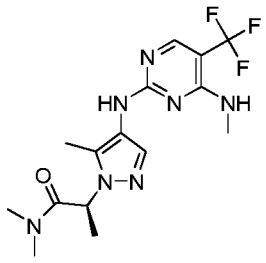
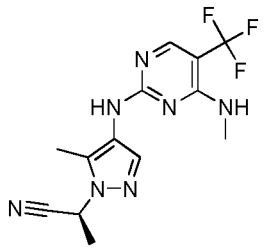
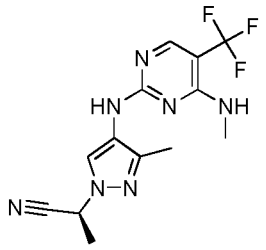
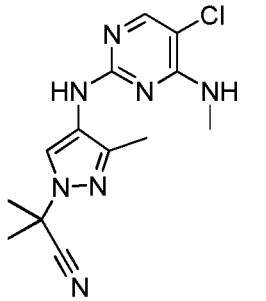
395	N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide		^{1}H NMR (300 MHz, CD_3OD) δ ppm 8.08 (s, 1H), 7.79 (br s, 1H), 5.24 (br s, 1H), 4.92 (s, 2H), 3.12 (s, 3H), 3.04 (s, 3H), 3.00 (s, 3H), 2.24 (s, 3 H)		0.015
396	N,N-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide		^{1}H NMR (300 MHz, CD_3OD) δ ppm 8.11 (s, 1H), 7.96 (s, 1H), 5.23 (b rs, 1H), 4.90 (s, 2H), 3.08 (s, 3H), 3.07(s, 3H), 2.99 (s, 3H), 2.27 (s, 3 H)		0.004
397	N-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide		^{1}H NMR (300 MHz, CD_3OD) δ ppm 8.14 (s, 1H), 7.94 (s, 1 H), 6.19 (brs, 1 H), 5.26 (brs, 1 H), 4.73 (s, 2 H), 3.07 (d, J = 4.8 Hz, 3 H), 2.81 (d, J = 4.8 Hz, 3 H), 2.32 (s, 3 H)		0.0095
398	N-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide		^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 2H), 6.17 (s, 1H), 5.26 (s, 1H), 3.07 (d, J = 4.6 Hz, 3H), 2.73 (d, J = 4.8 Hz, 3H), 2.32 (s, 3H), 1.84 (s, 6H)		0.003

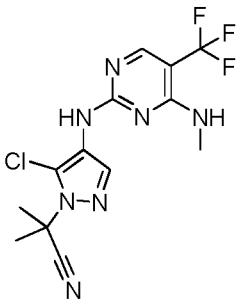
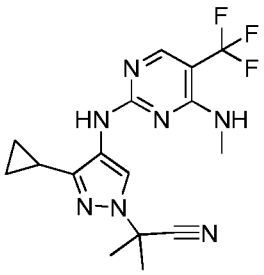
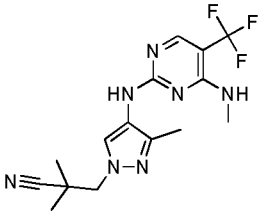
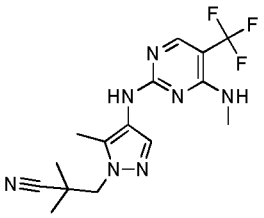
399	N,N,2-trimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide		1H NMR (400 MHz, DMSO) δ 8.79 (s, 1H), 8.06 (s, 1H), 7.68 (s, 1H), 6.85 (s, 1H), 2.84 (s, 6H), 2.38 (s, 3H), 2.02 (s, 3H), 1.67 (s, 6H).		0.314
400	2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one		1H NMR (400 MHz, DMSO) δ 8.77 (s, 1H), 8.04 (s, 1H), 7.69 (s, 1H), 6.92 (s, 1H), 3.35 (t, J = 6.6, 2H), 2.81 (s, 3H), 2.53 (s, 1H), 2.03 (s, 3H).		0.404
401	2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile		^{1}H-NMR (300 MHz, DMSO-d_6) δ ppm 9.18 (s, 1H), 8.29 (s, 1H), 8.14 (s, 1H), 7.10 (s, 1H), 2.91 (d, 3H), 2.22 (s, 3H), 1.94 (s, 2H)		0.0007
402	1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanec		1H NMR (400 MHz, DMSO) δ 9.09 (s, 1H), 8.12 (s, 2H), 7.03 (s, 1H), 2.91 (d, J = 4.4, 3H), 2.16 (s, 3H), 1.87 – 1.78 (m, 2H), 1.78 – 1.70 (m, 2H).		0.0037

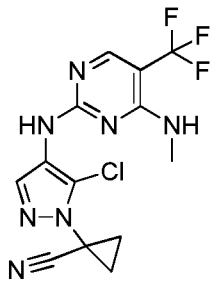
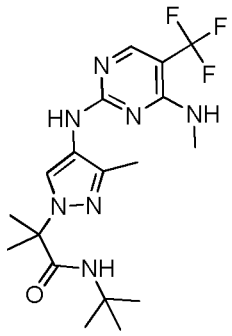
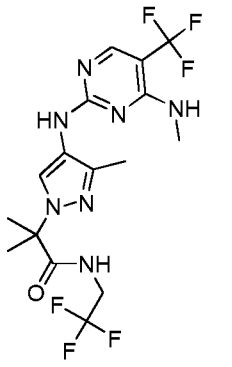
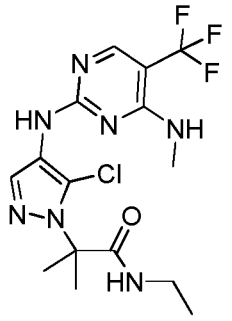
	arbonitrile				
403	(R)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one			398	0.016
404	(R)-N,N-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide		^{1}H-NMR (500 MHz, DMSO) δ 9.04 (s, 1H), 8.09 (s, 1H), 8.01 (s, 1H), 7.04 (s, 1H), 5.39 (q, *J* = 6.5 Hz, 1H), 2.97 (s, 3H), 2.87 (s, 3H), 2.82 (s, 3H), 2.14 (s, 3H), 1.45 (d, *J* = 6.5 Hz, 3H).		0.018
405	(S)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one		^{1}H NMR (500 MHz, DMSO) δ 9.08 (s, 1H), 8.09 (s, 1H), 8.04 (s, 1H), 7.02 (s, 1H), 5.16-5.20 (m, 1H), 3.53-3.57 (m, 1H), 3.23-3.31 (m, 3H), 2.88 (d, *J* = 4.0, 3H), 2.13 (s, 3H), 1.83-1.88 (m, 2H), 1.67-1.79 (m, 2H), 1.48 (d, *J* = 6.5, 3H).		0.022

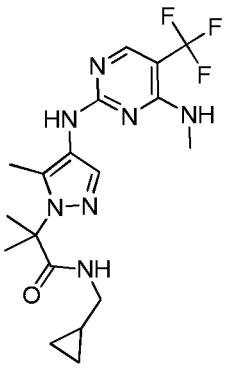
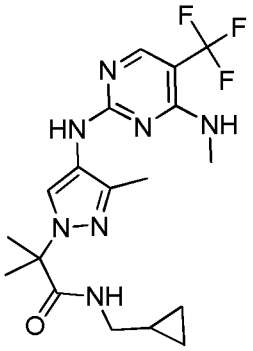
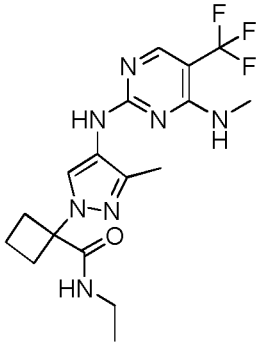
406	3-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile		^{1}H NMR (500 MHz, MeOD) δ 7.96 (s, 1H), 7.67 (s, 1H), 4.34-4.37 (m, 2H), 2.96-2.99 (m, 2H), 2.91 (s, 3H), 2.27 (s, 3H).		0.0073
407	3-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile		^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.97 (s, 1H), 4.30-4.33 (m, 2H), 3.07 (s, 3H), 2.90-2.93 (m, 2H), 2.26 (s, 3H), 1.64 (s, 2H).		0.0054
408	methyl 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate		1H NMR (400 MHz, DMSO) δ 9.02 (s, 1H), 8.14 (s, 1H), 8.10 (s, 1H), 7.03 (s, 1H), 3.61 (s, 3H), 2.89 (d, J = 4.4, 3H), 2.14 (s, 3H), 1.71 (s, 6H).		0.0047
409	methyl 2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate		1H NMR (400 MHz, DMSO) δ 8.86 (s, 1H), 8.06 (s, 1H), 7.69 (s, 1H), 6.94 (s, 1H), 3.70 (s, 3H), 2.83 (s, 3H), 2.05 (s, 3H), 1.71 (s, 6H).		0.0076

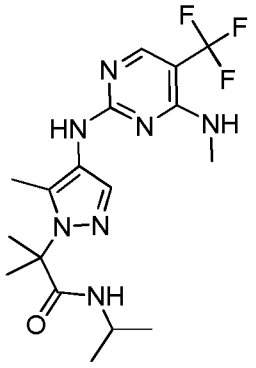
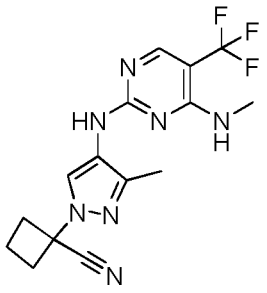
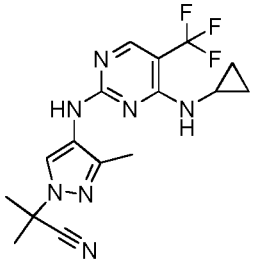
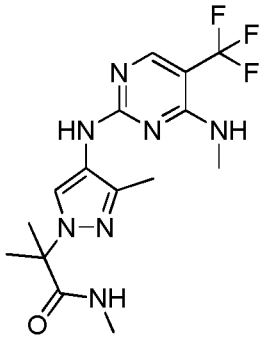
410	2-(3-ethyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile		1H NMR (400 MHz, DMSO) δ 8.93 (s, 1H), 8.07 (s, 1H), 7.80 (s, 1H), 6.98 (s, 1H), 2.97 (s, 2H), 2.84 (s, 3H), 1.95 (s, 6H), 1.13 (t, J = 7.4, 3H).		0.010
411	(R)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one		^{1}H-NMR (500 MHz, MeOD) δ 7.88 (s, 1H), 7.53 (s, 1H), 7.49-5.19 (m, 1H), 3.35-3.39 (m, 1H), 2.77-2.81 (m, 3H), 2.69-2.71 (m, 1H), 2.13 (s, 3H), 1.75-1.84 (m, 3H), 1.66-1.71 (m, 1H), 1.50 (d, *J* = 7.0, 1H).		0.039
412	(R)-N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide		^{1}H-NMR (500 MHz, DMSO) δ 8.88 (s, 1H), 8.06 (s, 1H), 7.67 (s, 1H), 6.95 (s, 1H), 5.37 (q, *J* = 6.0 Hz, 1H), 2.79 (s, 6H), 2.74 (s, 3H), 2.15 (s, 3H), 1.43 (d, *J* = 6.0 Hz, 3H).		0.0284
413	(S)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-		^{1}H NMR (500 MHz, DMSO) δ 8.08 (s, 1H), 7.79 (d, *J* = 10.0, 1H), 6.56-6.52 (m, 1H), 5.15 (s, 1H), 5.08-5.12 (m, 1H), 3.48-3.56 (m, 2H), 3.27-3.32 (m, 1H), 2.99 (d, *J* = 4.5, 3H), 2.84 (d, *J* = 4.0, 1H), 2.21 (t, *J* = 9.5, 3H), 1.81-1.88 (m, 4H),		0.040

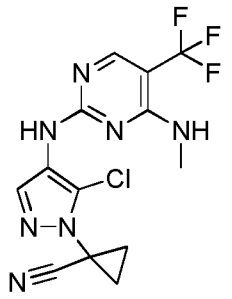
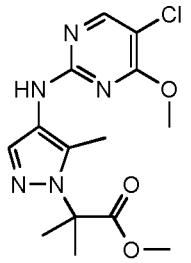
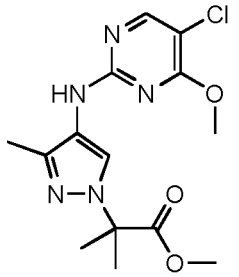
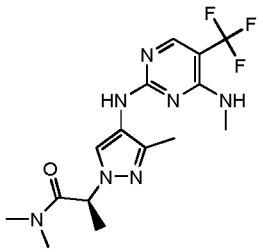
	yl)propan-1-one		1.74-1.79 (m, 3H).		
414	(S)-N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide		^{1}H NMR (500 MHz, DMSO) δ 8.48 (s, 1H), 8.06 (s, 1H), 7.57 (s, 1H), 6.64-6.66 (m, 1H), 5.33-5.36 (m, 1H), 2.77-2.85 (m, 9H), 2.16 (s, 3H), 1.48-1.51 (m, 3H).		0.030
415	(S)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile		^{1}H NMR (500 MHz, DMSO) δ 8.60 (s, 1H), 8.06 (s, 1H), 7.75 (s, 1H), 6.71 (s, 1H), 5.73-5.75 (m, 1H), 2.87-2.98 (m, 3H), 2.26 (s, 3H), 1.75-1.78 (s, 3H).		0.0095
416	(S)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile		^{1}H NMR (500 MHz, DMSO) δ 8.25-8.26 (m, 1H), 8.10 (s, 1H), 8.03 (s, 1H), 6.75 (s, 1H), 5.68-5.69 (m, 1H), 2.92-2.93 (m, 3H), 2.19 (s, 3H), 1.76-1.78 (m, 3H).		0.0019
417	2-(4-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile		1H NMR (400 MHz, DMSO) δ 8.53 (s, 1H), 8.15 (s, 1H), 7.85 (s, 1H), 7.09 (d, J = 4.5, 1H), 2.89 (d, J = 4.6, 3H), 2.18 (s, 3H), 1.91 (s, 6H).		0.0021

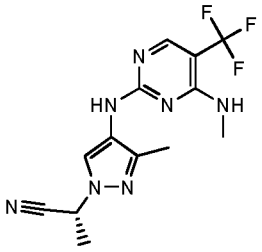
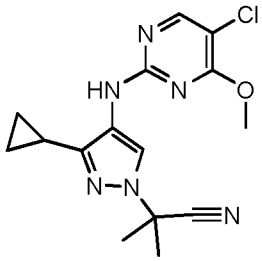
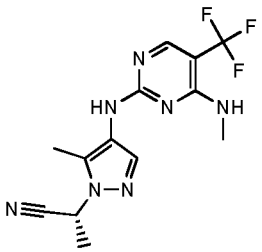
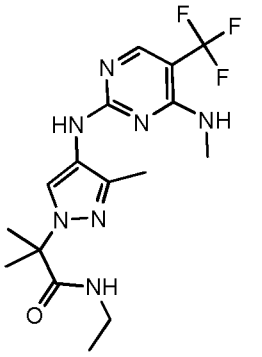
418	2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile		1H NMR (400 MHz, DMSO) δ 9.05 (s, 1H), 8.11 (s, 1H), 7.92 (s, 1H), 7.06 (s, 1H), 2.83 (s, 3H), 2.01 (s, 6H).		0.0019
419	2-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile		1H NMR (400 MHz, DMSO) δ 9.19 (s, 1H), 8.22 (s, 1H), 8.12 (s, 1H), 7.05 (s, 1H), 2.91 (d, J = 4.4, 3H), 2.12 (s, 1H), 1.89 (s, 6H), 0.92 – 0.80 (m, 2H), 0.80 – 0.64 (m, 2H).		0.0010
420	2,2-dimethyl-3-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile		^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.03 (s, 2H), 7.05 (br, s, 1H), 5.20 (d, J = 1.5Hz, 1H), 4.08 (s, 2H), 3.01 (s, 3H), 2.18 (s, 3H), 1.40 (m, 6H)		0.0028
421	2,2-dimethyl-3-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile		^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.73 (br, s, 1H), 5.10 (s, 1H), 4.09 (s, 2H), 2.93 (d, J = 4.5 Hz, 3H), 2.27 (s, 3H), 1.40 (s, 6H)		0.0068

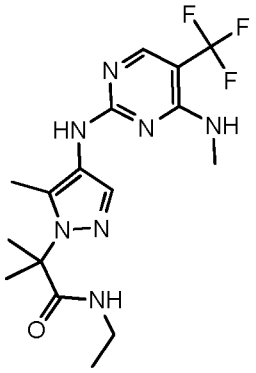
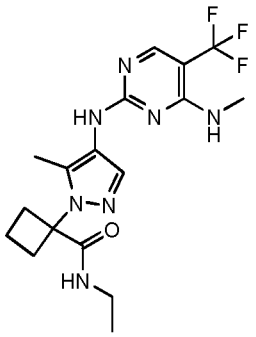
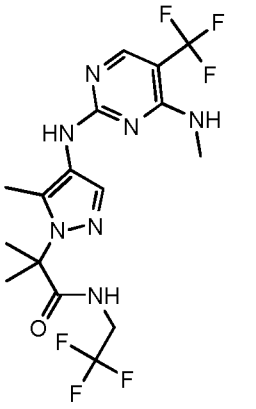
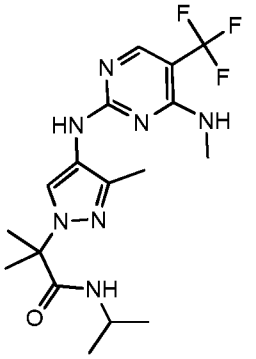
422	1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile		1H NMR (400 MHz, DMSO) δ 9.12 (s, 1H), 8.11 (s, 1H), 7.94 (s, 1H), 7.06 (t, J = 6.9, 1H), 2.84 (s, 2H), 2.10 – 1.98 (m, 1H), 1.89 – 1.76 (m, 1H).		0.0023
423	N-tert-butyl-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide		1H-NMR (500 MHz, DMSO) δ 9.101 (s, 1H), 8.081-8.143 (m, 2H), 7.025-7.049 (m, 1H), 6.348 (s, 1H), 2.877 (d, *J* = 4.0, 3H), 2.193 (s, 3H), 1.644 (s, 6H), 1.177 (s, 9H).		0.073
424	2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-(2,2,2-trifluoroethyl)propanamide				0.0063
425	2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-		1H NMR (400 MHz, DMSO) δ 8.35 (d, J = 9.1, 1H), 8.22 (s, 1H), 8.16 (s, 1H), 7.34 (d, J = 8.5, 2H), 6.32 (t, J = 9.5, 1H), 3.54 (s, 3H), 2.94 (d, J = 4.4, 3H).		0.0355

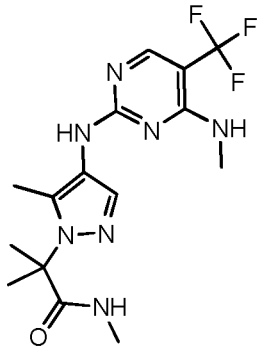
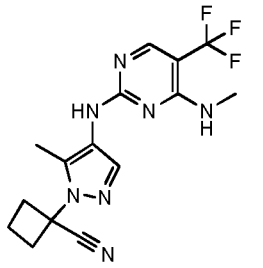
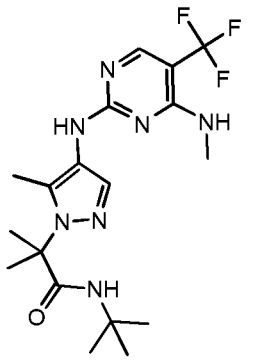
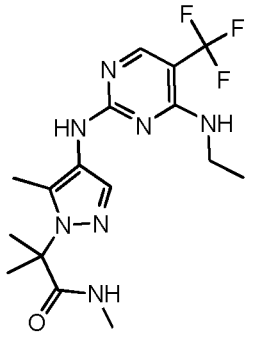
	ethyl-2-methyl propanamide				
426	N-(cyclopropylmethyl)-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide		1H-NMR (500 MHz, MeOD) δ 7.50-8.10 (m, 2H), 3.05 (d, *J* = 7.0 Hz, 3H), 2.97 (s, 3H), 2.16 (s, 3H), 1.76 (s, 6H), 0.99-1.23 (m, 1H), 0.43-0.47 (m, 2H), 0.19-0.22 (m, 2H).		0.009
427	N-(cyclopropylmethyl)-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide		1H-NMR (500 MHz, MeOD) δ 7.82-8.20 (m, 2H), 3.03 (d, *J* = 6.5 Hz, 3H), 2.98 (s, 3H), 2.20 (s, 3H), 1.76 (s, 6H), 0.93-0.94 (m, 1H), 0.39-0.44 (m, 2H), 0.13-0.18 (m, 2H).		0.052
428	N-ethyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarboxamide			398.2	0.024

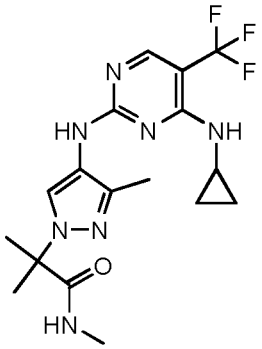
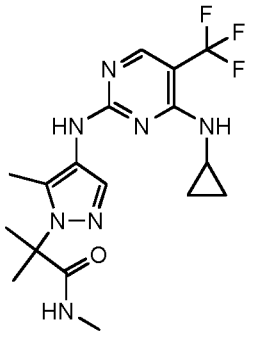
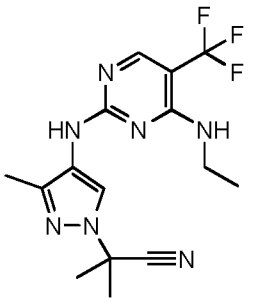
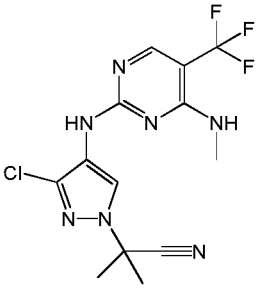
429	N-isopropyl-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide				
430	1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarbonitrile			352.1	
431	2-(4-(4-(cyclopropylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile				
432	N,2-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-		1H NMR (400 MHz, DMSO) δ 9.04 (s, 1H), 8.13 (s, 1H), 8.10 (s, 1H), 7.17 (s, 1H), 7.01 (s, 1H), 2.93 (d, 3H), 2.55 (d, 3H), 2.17 (s, 3H). 1.64 (s, 6H).	372.1	0.0184

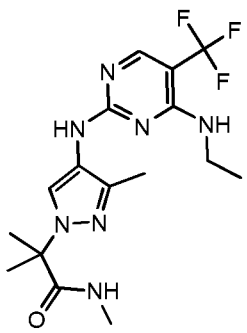
	yl)propanamide				
433	1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile			358.1	
434	2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester				0.0122
435	2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester				0.0355
436	(S)-N,N-Dimethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionamide				0.0303

437	R)-2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile				0.0065
438	2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-cyclopropyl-pyrazol-1-yl]-2-methyl-propionitrile				0.0058
439	(R)-2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile				0.0016
440	N-Ethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0095

441	N-Ethyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0237
442	1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarboxylic acid ethylamide				0.0156
443	2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-N-(2,2,2-trifluoro-ethyl)-isobutyramide				0.0666
444	N-Isopropyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0246

445	N-Methyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0926
446	1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarbonitrile				0.0024
447	N-tert-Butyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.067
448	2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N-methyl-isobutyramide				0.0153

449	2-[4-(4-Cyclopropylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide		1H NMR (400 MHz, DMSO) δ 9.10 (s, 1H), 8.22 (s, 1H), 8.13 (s, 1H), 7.21 (d, J = 4.1, 1H), 6.98 (s, 1H), 2.83 (s, 1H), 2.54 (d, J = 4.3, 3H), 2.20 (s, 3H), 1.61 (s, 6H), 0.69 (dd, J = 35.4, 4.3, 4H).		0.0013
450	2-[4-(4-Cyclopropylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N-methyl-isobutyramide				0.0071
451	2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propionitrile		1H NMR (400 MHz, DMSO) δ 9.07 (s, 1H), 8.15 (d, J = 26.9, 2H), 7.05 (s, 1H), 3.51 – 3.42 (m, 2H), 2.19 (s, 3H), 1.92 (s, 6H), 1.13 (t, J = 7.1, 3H).		0.0003
452	2-(3-chloro-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile				

453	2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide				0.0092

Example 454: *In Vitro* LRRK2 Lanthascreen binding Assay

This assay was used to determine a compound's potency in inhibiting activity of LRRK2 by determining, Ki_{app}, IC_{50}, or percent inhibition values. In 384 well proxiplates F black, shallow well plates LRRK2, Eu-anti-GST-antibody, Alexa Fluor® Kinase tracer 236 and test compound were incubated together.

Binding of the Alexa Fluor® "tracer" to a kinase is detected by addition of a Eu-labeled anti-GST antibody. Binding of the tracer and antibody to a kinase results in a high degree of FRET, whereas displacement of the tracer with a kinase inhibitor results in a loss of FRET.

Assay conditions and materials used were as follows:

Final Assay Conditions:

GST-LRRK2 G2019S	10 nM
Eu-anti-GST-antibody	2nM
Kinase tracer 236	8.5 nM
Kinase reaction time:	1 hour
Temperature:	ambient
Total volume:	15 µl
DMSO	1%

Materials:

384 well proxiplates F black shallow well Perkin Elmer cat# 6008260

Kinase: LRRK2 G2019S,	Invitrogen cat # PV4882(LOT 567054A).
Eu-labeled anti-GST antibody	Invitrogen cat # PV5594
Alexa Fluor® Kinase tracer 236	Invitrogen cat #PV5592
TRIS- HCl	Sigma cat # T3253

EGTA	Sigma cat # E3889
Brij-35:	Sigma cat # B4184(30% w/v)
DMSO:	Sigma cat # D8418
$MgCl_2$	Sigma cat # M9272

Reaction Buffer:H_2O/50 mM Tris, pH 7.4/10mM $MgCl_2$/1 mM EGTA/0.01% Brij 35

Compound Plate Preparation:

Serially dilute test compounds (10mM stock) 1:3.16 (20ul + 43.2ul) in 100% DMSO. 12pt curve. Dilute each concentration 1:33.3 (3ul +97ul) in reaction buffer. Stamp 5ul to assay plate. Final top test concentration 100uM

Total and Blank Preparation:

In Reaction Buffer,5ul of DMSO(3%) was added to total and blank wells and 5ul of Eu-labeled anti-GST antibody(6nM) was added to blank wells. Add 5ul LRRK2(30nM)/ Eu-labeled anti-GST antibody (6nM) mix to compound and total wells.

Assay Procedure:

Add 5ul kinase tracer (25.5nM) to all wells. Incubate plates at room temperature for 1 hour on a plate shaker (gentle shaking). Read on Perkin Elmer EnVision reader HTRF protocol

Data Handling:

Calculate ratio : (665/620)*10000. Substract mean background values from all data points. Calculate % of control for each test value. Plot % of control vs Compound concentration. Calculate Ki Value (xlfit curve fitting- Morrison equation). Results expressed as a Ki in μM.Equation for Ki:

Y=V0*(1-((x+Ki*(1+S/Km)+Et)/(2*Et)-(((x+Ki*(1+S/Km)+Et)^2-(4*Et*x))^0.5)/(2*Et)))

Where Et = 4nM

kd (Tracer) = 8.5nM

Tracer concentration (S) = 8.5nM

Example 455: *In Vitro* LRRK2 Assay

This assay was used to determine a compound's potency in inhibiting activity of LRRK2 by determining, Ki_{app}, IC_{50}, or percent inhibition values. In a polypropylene plate, LRRK2, fluorescently-labeled peptide substrate, ATP and test compound were incubated together. Using a LabChip 3000 (Caliper Life Sciences), after the reaction the substrate was separated by capillary electrophoresis into two populations: phosphorylated and unphosphorylated. The relative amounts of each were quantitated by fluorescence intensity. LRRK2 Ki was determined according to the equation:

Y=V0*(1-((x+Ki*(1+S/Km)+Et)/(2*Et)-(((x+Ki*(1+S/Km)+Et)^2-(4*Et*x))^0.5)/(2*Et))).

Ki values in Table 4 and elsewhere herein are shown in μM.

Assay conditions and materials used were as follows:

Final Assay Conditions:

LRRK2 G2019S in 5 mM $MgCl_2$:	5.2 nM (Invitrogen lot # 567054A)
LRRK2 G2019S in 1 mM $MnCl_2$:	11 nM (Invitrogen lot # 567054A)
LRRK2 Wild type in 5 mM $MgCl_2$:	15 nM (Invitrogen lot # 500607F)
LRRK2 I2020T in 5 mM $MgCl_2$:	25 nM (Invitrogen lot # 43594)
Substrate:	1 μM
ATP:	130 μM
Kinase reaction time:	2 hours
Temperature:	ambient
Total volume:	20 μl

ATP^{app} Kms:

G2019S in 5 mM $MgCl_2$:	130 μM
G2019S in 1 mM $MnCl_2$:	1 μM
Wild type in 5 mM $MgCl_2$:	80 μM
I2020T in 5 mM $MgCl_2$:	14 μM

Materials:

Solid Support: Black 50 μL volume polypropylene 384 well plate (MatriCal cat # MP101-1-PP)

Kinase: LRRK2 G2019S (Invitrogen cat # PV4882).

LRRK2 Wild type (Invitrogen cat # PV4874).

Substrate: 5FAM-GAGRLGRDKYKTLRQIRQ-$CONH_2$

Non-binding plate: 384 well clear V-bottom polypropylene plates (Greiner cat # 781280).

ATP: 10 mM ATP (Cell Signaling cat # 9804).

Triton X-100: Triton X-100.

Brij-35: Brij-35 (Pierce cat # 20150).

Coating Reagent #3: Coating Reagent #3 (Caliper).

DMSO: DMSO (Sigma cat # 34869-100ML).

Complete Reaction Buffer: H_2O/25 mM Tris, pH 8.0/5 mM $MgCl_2$/2 mM DTT/0.01% Triton X-100.

Stop Solution: H_2O/100 mM HEPES, pH 7.2/0.015% Brij-35/0.2% Coating Reagent #3/20 mM EDTA.

Separation Buffer: H_2O/100 mM HEPES, pH 7.2/0.015% Brij-35/0.1% Coating Reagent #3/1:200 Coating Reagent #8/10 mM EDTA/5% DMSO.

Compound Plate Preparation:

For serial dilutions, 34.6 µl DMSO was added to columns 3-24. For the assay controls, 37.5 µl DMSO was added to columns 1 and 2 of rows A and P. a,d and 50 µl 25 µM G-028831 (Staurosporine) was added to columns 1 and 2, row B. For the samples: to start at 100 µM, 37.5 µl DMSO was to columns 1 and 2, then 12.5 µl 10 mM compound; to start at 10 µM, 78 µl DMSO was added to columns 1 & 2, then 2 µl 10 mM compound; and to start at 1 µM, 25 µM compound (2 µl 10 mM cmpd + 798 µl DMSO) was added to empty columns 1 and 2. A Precision instrument was used to perform 1:3.16 serial dilutions ("PLK_BM_serial_halflog").

ATP Preparation:

ATP was diluted to 282.1 µM in Complete Kinase Buffer (final concentration was 130 µM).

Total and Blank Preparation:

In Complete Reaction Buffer, substrate was diluted to 4 µM. Equal volumes of Complete Reaction Buffer and 4 µM substrate were combined to obtain the blank. Equal volumes of Complete Reaction Buffer and 4 µM substrate were combined and to the combined solution was added 2X final LRRK2 concentration.

Assay Procedure:

To a 50 µl polypropylene plate, 5 µl/well buffer/substrate was added by hand to Blank wells. A Biomek FX was used to start the kinase reaction ("PLK SAR 23 ATP"). The following were added to the appropriate wells:

2 µl compound + 23 µl ATP;

5 µl/well compound/ATP in Assay Plate;

5 µl/well kinase/substrate in Assay Plate;

The plate was incubated for 2 hours in the dark. Biomek FX was used to stop the kinase reaction ("PLK Stop"), and 10 µl/well Stop solution was added to the Assay Plate. Results were read on the LabChip 3000.

Lab Chip 3000 Protocol:

The LabChip 3000 was run using the job "LRRK2 IC50" with the following job settings:

Pressure:	-1.4 psi
Downstream voltage:	-500 V
Upstream voltage:	-2350 V
Post sample buffer sip time:	75 seconds
Post dye buffer sip time:	75 seconds
Final delay time:	200 seconds

Example 456 Parkinson's disease mouse model

Parkinson's disease can be replicated in mice and in primates by administration of 1-methyl-4-phenyul tetrahydropyridine (MPTP), a selective nigrostriatal dopaminergic neurotoxin that produces a loss of striatal dopamine (DA) nerve terminal markers. Compounds of the invention may be evaluated for effectiveness in treatment of Parkinson's disease using MPTP induced neurodegeneration following generally the protocol described by Saporito et al., *J. Pharmacology* (1999) Vol. 288, pp. 421-427.

Briefly, MPTP is dissolved in PBS at concentrations of 2-4 mg/ml, and mice (male C57 weighing 20-25 g) are given a subcutaneous injection of 20 to 40 mg/kg. Compounds of the invention are solubilized with polyethylene glycol hydroxystearate and dissolved in PBS. Mice are administered 10 ml/kg of compound solution by subcutaneous injection 4 to 6 h before MPTP administration, and then daily for 7 days. On the day of the last injection, mice are sacrificed and the midbrain blocked and postfixed in paraformaldehyde. Striata are dissected free, weighed, and stored at −70°C.

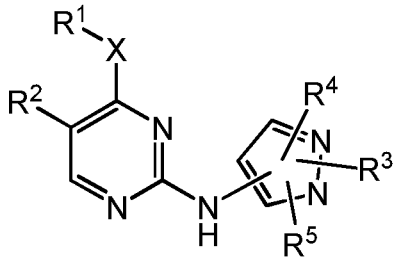
The striata thus collected are evaluated for content of dopamine and its metabolites dihydroxyphenylacetic acid and homovanillic acid, by HPLC with electrochemical detection as described by Sonsalla et al., *J.Pharmacol. Exp. Ther.* (1987) Vol. 242, pp. 850-857. The striata may also be evaluated using the tyrosine hydroxylase assay of Okunu et al., *Anal Biochem* (1987) Vol. *129*, pp. 405–411 by measuring $^{14}CO_2$ evolution associated with tyrosine hydroxylase-mediated conversion of labeled tyrosine to L-dopa. The striata may further be

evaluated using the Monoamine oxidase-B assay as described by White et al., *Life Sci.* (1984), Vol. 35, pp. 827-833, and by monitoring dopamine uptake as described by Saporito et al.,(1992) Vol. 260, pp. 1400-1409.

While the present invention has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the invention. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective spirit and scope of the present invention. All such modifications are intended to be within the scope of the claims appended hereto.

CLAIMS

1. A compound of the formula I:



I

or a pharmaceutically acceptable salt thereof,

wherein:

X is: -NR^a-; or -O- wherein R^a is hydrogen or C_{1-6}alkyl;

R^1 is: C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with C_{1-6}alkyl; heterocyclyl optionally substituted one or more times with R^7; or heterocyclyl-C_{1-6}alkyl optionally substituted one or more times with R^7;

or X and R^1 together form C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6;

or R^1 and R^a together with the atoms to which they are attached may form a three- to six-membered heterocyclic ring optionally substituted one or more times with R^7;

R^2 is: C_{1-6}alkyl; halo; C_{1-6}alkoxy; cyano; C_{2-6}alkynyl; C_{2-6}alkenyl; halo-C_{1-6}alkyl; halo-C_{1-6}alkoxy; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; -OR^b wherein R^b is C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted one or more times with R^6, or C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; or -C(O)-R^c wherein R^c is C_{1-6}alkyl, C_{1-6}alkoxy, amino, or heterocyclyl optionally substituted one or more times with R^7;

R^3 is: hydrogen; C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano-C_{1-6}alkyl; C_{1-6}alkylsulfonyl; C_{1-6}alkylsulfonylC_{1-6}alkyl; amino-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-sulfonyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; heterocyclyl optionally substituted one or more times with R^7; heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7; aryl

optionally substituted one or more times with R^8; aryl-C_{1-6}alkyl wherein the aryl portion is optionally substituted one or more times with R^8; heteroaryl optionally substituted one or more times with R^8; heteroaryl-C_{1-6}alkyl wherein the heteroaryl portion is optionally substituted one or more times with R^8;or -Y-C(O)-R^d;

Y is C_{2-6}alkylene or a bond;

R^d is C_{1-6}alkyl, C_{1-6}alkoxy, amino, C_{1-6}alkyl-amino, di-C_{1-6}alkyl-amino, halo-C_{1-6}alkyl-amino, di-halo-C_{1-6}alkyl-amino, halo-C_{1-6}alkyl, hydroxy-C_{1-6}alkyl, hydroxy, C_{1-6}alkoxy-C_{1-6}alkyl, cyano-C_{1-6}alkyl, C_{1-6}alkylsulfonylC_{1-6}alkyl, amino-C_{1-6}alkyl, C_{3-6}cycloalkyl optionally substituted one or more times with R^6, C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6, heterocyclyl optionally substituted one or more times with R^7, or heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7;

R^4 is: hydrogen; C_{1-6}alkyl; halo; cyano; halo-C_{1-6}alkyl; C_{2-6}alkenyl; C_{2-6}alkynyl; C_{1-6}alkoxy; C_{1-6}alkoxy-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally substituted one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; or -Y-C(O)-R^d;

R^5 is: hydrogen; or C_{1-6}alkyl;

each R^6 is independently: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy; oxo; cyano; halo; or Y-C(O)-R^d;

each R^7 is independently: C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; oxo; C_{1-6}alkoxy; C_{1-6}alkylsulfonyl; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; -Y-C(O)-R^d; heterocyclyl; heterocyclyl-C_{1-6}alkyl; C_{3-6}cycloalkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl; or C_{3-6}cycloalkylsulfonyl; and

each R^8 is independently: oxo; C_{1-6}alkyl; halo-C_{1-6}alkyl; halo; C_{1-6}alkyl-sulfonyl; C_{1-6}alkoxy; C_{1-6}alkoxy-C_{1-6}alkyl; cyano; hetoeryclyl; heterocyclyl-C_{1-6}alkyl; -Y-C(O)-R^d; C_{3-6}cycloalkyl, C_{3-6}cycloalkyl-C_{1-6}alkyl, or C_{3-6}cycloalkyl-sulfonyl.

2. The compound of claim 1, wherein X is -NH-or -O-.

3. The compound of any of claims 1-2, wherein R^1 is: C_{1-6}alkyl; halo-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; amino-C_{1-6}alkyl; C_{1-6}alkylsulfonyl-C_{1-6}alkyl; C_{3-6}cycloalkyl; or C_{3-6}cycloalkyl-C_{1-6}alkyl.

4. The compound of any of claims 1-3, wherein R^1 is C_{1-6}alkyl.

5. The compound of any of claims 1-4, wherein R^2 is: halo; C_{1-6}alkoxy; halo-C_{1-6}alkyl; halo-C_{1-6}alkoxy; C_{3-6}cycloalkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted with C_{1-6}alkyl; tetrahydrofuranyl; tetrahydrofuranyl-C_{1-6}alkyl; oxetanyl; or oxetan-C_{1-6}alkyl.

6. The compound of any of claims 1-5, wherein R^2 is: halo; halo-C_{1-6}alkyl or cyano.

7. The compound of any of claims 1-6, wherein R^2 is: fluoro; bromo; chloro; iodo; trifluoromethyl; or cyano.

8. The compound of any of claims 1-7, wherein R^3 is: C_{1-6}alkyl; halo-C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; C_{3-6}cycloalkyl optionally one or more times with R^6; C_{3-6}cycloalkyl-C_{1-6}alkyl wherein the C_{3-6}cycloalkyl portion is optionally substituted one or more times with R^6; heterocyclyl optionally substituted one or more times with R^7; heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7; or -C(O)-R^d.

9. The compound of any of claims 1-8, wherein R^3 is: C_{1-6}alkyl; hydroxy-C_{1-6}alkyl; C_{1-6}alkoxy-C_{1-6}alkyl; heterocyclyl optionally substituted one or more times with R^7; or heterocyclyl-C_{1-6}alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R^7.

10. The compound of any of claims 1-9, wherein R^3 is: methyl; ethyl; propyl; isopropyl; butyl; cyclopropyl; cyclopropylmethyl; cyclobutyl; methanesulfonyl; ethylsulfonyl; cyclopropylsulfonyl; sec-butylsulfonyl; morpholin-4-yl-ethyl; oxetan-3-yl; 2-methoxyethyl; 2-hydroxy-2-methyl-propyl; 3-hydroxy-2-methyl-propan-2-yl; 2-methoxy-propyl; tetrahydro-2H-pyran-4-yl; tetrahydrofuran-3-yl; 2,6-dimethyltetrahydro-2H-pyran-4-yl; tetrahydro-2H-pyran-3-yl); phenyl; 4-(methylsulfonyl)phenyl); 4-cyano-phenyl; 4-fluoro-phenyl; 4-chloro-phenyl; 3,5-difluorophenyl; 4-(dimethylamino-carbonyl)-phenyl); 4-(cyclopropylsulfonyl)phenyl; 2,2,2-trifluoroethyl; 2-fluoroethyl; difluoromethyl; 2-dimethyl-1,3-dioxan-5-yl; 1-methyl-cyclopropyl-carbonyl; 3-methylpyridin-4-yl; 2-methylpyridin-4-yl; pyridin-2-yl; pyrimidin-2-yl; pyrimidin-5-yl; pyridin-2-ylmethyl; 1-(pyridin-2-yl)ethyl; cyclopropylsulfonyl; 1-cyano-1-methyl-ethyl; 2-cyano-ethyl; 1-cyano-ethyl; 2-cyano-2-methyl-propyl; 1-(2,2,2-trifluoroethyl)piperidin-4-yl; 1-(methylsulfonyl)azetidin-3-yl; (3-methyloxetan-3-yl)methyl; (1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl; 1-(oxetan-3-yl)piperidin-4-yl; 1-acetyl-piperidin-4-yl; 1-(cyclopropyl-carbonyl)-piperidin-4-yl; 1-methyl-piperidin-4-yl; 1-methyl-2-oxo-piperidin-5-yl; 2-oxo-piperidin-5-yl; 1-(isopropyl-carbonyl)-piperidin-4-yl; 1-(oxetan-3-yl)azetidin-3-yl; 1-(cyclopropyl-carbonyl)-piperidin-4-yl; 2-methoxycyclopentyl; 3-methoxycyclopentyl; 1-methoxy-2-methylpropan-2-yl; tetrahydro-2H-1,1-dioxo-thiopyran-4-yl; 3-fluoro-1-(oxetan-3-yl)piperidin-4-yl; 1-methoxypropan-2-yl; 1-(2,2,2-trifluoroethyl)azetidin-3-yl); 1-(oxetan-3-yl)pyrrolidin-3-yl; 1-isopropylazetidin-3-yl; 3-

fluoro-1-methylpiperidin-4-yl; 1-ethyl-3-fluoropiperidin-4-yl; 1-methylpyrrolidin-3-yl; 2-methoxyethyl)piperidin-4-yl); 1-methyl-1-(methylamino-carbonyl)-ethyl; 2-methyl-2-morpholino-propyl; 4,4-difluorocyclohexyl; morpholin-4-yl-carbonyl; dimethylamino-carbonyl-methyl; methylamino-carbonyl-methyl; 1-methyl-1-(dimethylamino-carbonyl)-ethyl; pyrrolidin-1-yl-carbonyl; 1-cyano-cyclopropyl; 1-(pyrrolidin-1-yl-carbonyl)-ethyl; 1-(dimethylamino-carbonyl)-ethyl; 1-(methoxy-carbonyl)-ethyl; 1-(tert-butylamino-carbonyl)-1-methyl-ethyl; 1-(2,2,2-trifluoroethyllamino-carbonyl)-1-methyl-ethyl; 1-(ethylamino-carbonyl)-1-methyl-ethyl; 1-(cyclopropylmethylamino-carbonyl)-1-methyl-ethyl; 1-(ethylamino-carbonyl)-cyclobutyl; 1-(isopropylamino-carbonyl)-1-methyl-ethyl; 1-cyano-cyclobutyl; 2-methoxy-1-methyl-ethyl; 1-methyl-1-(methoxy-carbonyl)-ethyl; 2-methoxy-2-methyl-propan-1-yl; 1-(oxetan-3-yl)-pyrrolidin-3-yl; isopropylsulfonyl; butane-2-sulfonyl; 1-(2-fluoroethyl)-piperidin-4-yl; 3-fluoro-1-methyl-piperidin-4-yl; 1-ethyl-3-fluoro-piperidin-4-yl; pyridin-3-ylmethyl; 6-methyl-pyridin-2-ylmethyl; 2-(morpholin-1-yl)-1,1,dimethyl-ethyl; pyrimdin-2-yl-methyl; 3-fluoro-1-(oxetan-3-yl)-piperidin-4-yl; 1-(oxetan-3-yl)-piperidin-3-yl; 1-([1,3]Dioxolan-2-ylmethyl)-piperidin-4-yl; pyridazin-3-ylmethyl; piperidin-3-yl; pyrazin-2-ylmethyl; 2-hydroxy-3-methyl-butan-1-yl; 1-([1,3]Dioxolan-2-ylmethyl)-pyrrolidin-3-yl; pyrimidin-4-ylmethyl; 1-methyl-1H-pyrazol-3-ylmethyl; 1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl; 1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl; 3-fluoro-piperidin-4-yl; 2-hydroxy-cyclopentyl; dimethyl-[1,3]dioxan-5-yl; 2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl; 2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl; 2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-5-yl; 2-(4H-1,2,4-triazol-3-yl)propan-2-yl; or 1-methyl-1H-pyrazole-4-yl.

11. The compound of any of claims 1-10, wherein R^4 is hydrogen; C_{1-6}alkyl; halo; or C_{3-6}cycloalkyl optionally substituted with C_{1-6}alkyl.

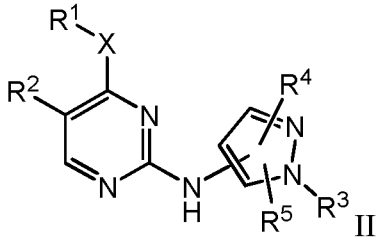
12. The compound of any of claims 1-11, wherein R^4 is hydrogen or C_{1-6}alkyl.

13. The compound of any of claims 1-12, wherein R^4 is chloro or methyl.

14. The compound of any of claims 1-13, wherein R^5 is C_{1-6}alkyl.

15. The compound of any of claims 1-14, wherein R^5 is hydrogen or methyl.

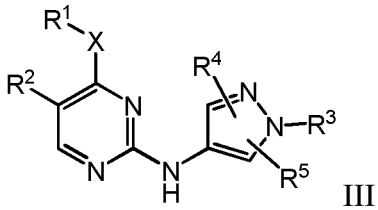
16. The compound of any of claims 1-15, wherein said compounds are of formula II



II

and wherein X, R^1, R^2, R^3, R^4 and R^5 are as recited in any of claims 1-15.

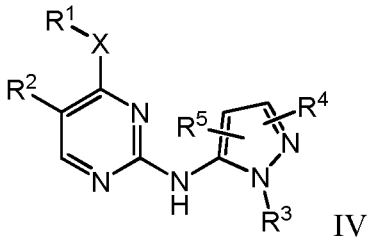
17. The compound of any of claims 1-15, wherein said compound is of formula III



III

and wherein X, R^1, R^2, R^3, R^4 and R^5 are as recited in any of claims 1-15.

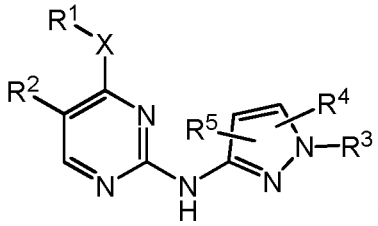
18. The compound of any of claims 1-15, wherein said compound is of formula IV



IV

and wherein X, R^1, R^2, R^3, R^4 and R^5 are as recited in any of claims 1-15.

19. The compound of any of claims 1-15, wherein said compound is of formula V



V

and wherein X, R^1, R^2, R^3, R^4 and R^5 are as recited in any of claims 1-15.

20. The compound of any of claims 1-19, which is selected from the group consisting of N^2-(1-isopropyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1,5-dimethyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N^2-(1-isopropyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1,3-dimethyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amine,

N^4-methyl-5-(trifluoromethyl)-N^2-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-isopropyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amine,

5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(pyrrolidin-1-yl)-5-(trifluoromethyl)pyrimidin-2-amine,

N^2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1,3-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

N^4-methyl-N^2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(5-chloro-1-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-4-methoxy-N-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-Chloro-4-methoxy-N-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-chloro-4-methoxy-N-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-Chloro-N-(5-chloro-1-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,

2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-chloro-pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,

N^2-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^4-methyl-N^2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N^2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^2-(1,3-dimethyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

5-Chloro-N^2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

N^4-methyl-N^2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(2-Ethyl-2H-pyrazol-3-yl)-5-fluoro-N^4-methyl-pyrimidine-2,4-diamine,

5-Fluoro-N^4-methyl-N^2-(2-methyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,

5-Fluoro-N^4-methyl-N^4-(2-propyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,

N^2-(2,5-Dimethyl-2H-pyrazol-3-yl)-5-fluoro-N^4-methyl-pyrimidine-2,4-diamine,

N^2-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,

N^2-(3-Cyclopropyl-1-methyl-1H-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^2-(5-isopropyl-2-methyl-2H-pyrazol-3-yl)-N^4-methyl-pyrimidine-2,4-diamine,

5-Chloro-4-methoxy-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-Chloro-N^4-methyl-N^2-(1,3,5-trimethyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine,

5-Chloro-N^2-(5-cyclopropyl-2-methyl-2H-pyrazol-3-yl)-N^4-methyl-pyrimidine-2,4-diamine,

N^4-Methyl-N^2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N^2-(1-isopropyl-1H-pyrazol-5-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-Chloro-N^2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

N^2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-Chloro-N^2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N^4-methylpyrimidine-2,4-diamine,

5-chloro-N^2-(1-isopropyl-1H-pyrazol-5-yl)-N^4-methylpyrimidine-2,4-diamine,

5-chloro-N-(1-isopropyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,

5-chloro-4-methoxy-N-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

N^2-(1-ethyl-1H-pyrazol-3-yl)-N^4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-4-methoxy-N-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

N^2-(1-isopropyl-1H-pyrazol-3-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^4-methyl-N^2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N^2-(1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-4-methoxy-N-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

N^4-ethyl-N^2-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(oxetan-3-yloxy)pyrimidin-2-amine,

5-chloro-4-(2,2-difluoroethoxy)-N-(1,5-dimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(2,2,2-trifluoroethoxy)pyrimidin-2-amine,

5-chloro-4-methoxy-N-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

(4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone,

(4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone,

4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)benzonitrile,

5-chloro-4-methoxy-N-(3-methyl-1-(3-methylpyridin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

5-chloro-N-(1-(cyclopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

5-chloro-N-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,

2-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

5-chloro-4-ethoxy-N-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine,

(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine,

(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(5-methyl-1-phenyl-1H-pyrazol-4-yl)-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-(1-methanesulfonyl-3-methyl-1H-pyrazol-4-yl)-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-methyl-1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine,

4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide,

4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide,

4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-benzonitrile,

N^2-(5-Methoxy-1-methyl-1H-pyrazol-4-yl)-N^4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-chloro-1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoro-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-amine,

N^2-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl]-N^4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N^2-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-N^4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

N^2-(1,3-Dimethyl-1H-pyrazol-4-yl)-5-iodo-N^4-methyl-pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(1-methyl-1H-pyrazol-5-yl)pyrimidine-2,4-diamine,

2-methyl-1-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,

5-chloro-N4-methyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-ethyl-N2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N2-(1-(difluoromethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(difluoromethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-ethyl-N2-(1-ethyl-5-methyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N2-(1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(1-methyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(methylsulfonyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N4-methyl-N2-(3-methyl-1-propyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-chloro-N4-methyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-bromo-N2-(1-(3,5-difluorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

5-bromo-N2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-bromo-N2-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

5-bromo-N2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine,

N2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-((1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-butyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyrimidin-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-fluoroethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-fluoroethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone,

cyclopropyl(4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

cyclopropyl(4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone,

N2-(5-chloro-1-isopropyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-ethyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyrimidin-5-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(4-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-cyclopropyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitrile,

4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitrile,

N4-methyl-N2-(3-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one,

5-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one,

5-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-one,

5-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-one,

N2-(1-isopropyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N,N-dimethyl-4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide,

4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamide,

N4-ethyl-N2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(4-(cyclopropylsulfonyl)phenyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)benzonitrile,

N4-ethyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N,N-dimethyl-4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide,

N2-(1-(cyclopropylmethyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(4-(cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

5-chloro-N4-(2,2-difluoroethyl)-N2-(1,5-dimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,

5-chloro-4-methyl-N-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,

N2-(1-(4-(cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-methyl-1-(4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)propan-1-one,

N4-ethyl-N2-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)-2-methylpropan-1-one,

N4-ethyl-N2-(3-methyl-1-(1-(oxetan-3-yl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

N4-ethyl-N2-(1-ethyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(S)-N2-(1-(2-methoxypropyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(S)-N2-(1-(2-methoxypropyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-methoxy-2-methylpropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2,6-dimethyltetrahydro-2H-pyran-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N2-(1-(2-methoxypropyl)-5-methyl-1H-pyrazol -4-yl)-N4-methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N2-(1-(3-methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(1-methyl-5-(methylamino)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(tetrahydro-2H-1,1-dioxo-thiopyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

2-methyl-1-(4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-(trifluoromethyl)-1H-pyrazol-1-yl)propan-2-ol,

2-methyl-1-(4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-(trifluoromethyl)-1H-pyrazol-1-yl)propan-2-ol,

N2-(1-(3-fluoro-1-(oxetan-3-yl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N2-(1-(1-methoxypropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(3-tert-butyl-4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-methoxy-2-methylpropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(3-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

(R)-N2-(1-(1-methoxypropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(4-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(5-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-isopropylazetidin-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazole-5-carbonitrile,

N4-ethyl-N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(isopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(sec-butylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(sec-butylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-isopropyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

N2-(1-(3-fluoro-1-methylpiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(3-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(3-cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-((tetrahydro-2H-pyran-4-yl) methyl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

1-(5-chloro-4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

1-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

1-(3-cyclopropyl-4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N,2-dimethylpropanamide,

N2-(1-(1-(2-methoxyethyl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(1-(2-methoxyethyl)piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

(R)-N4-methyl-N2-(5-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(3-fluoro-1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-chloro-1-(1-ethyl-3-fluoropiperidin-4-yl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-ethyl-N2-(1-(ethylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-methyl-2-morpholinopropyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N2-(1-(1-ethyl-3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(5-(dimethylamino)-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-1-ol,

N^2-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propan-2-ol,

N2-[1-(2-Methoxy-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(2-Methoxy-ethyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[3-methyl-1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1-difluoromethyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1-difluoromethyl-3-methyl-1H-pyrazol-4-yl)-N4-methyl-pyrimidine-2,4-diamine,

5-Bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-ethyl-pyrimidine-2,4-diamine,

5-Bromo-N2-[1-(4-fluoro-phenyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-pyrimidine-2,4-diamine,

5-Bromo-N4-methyl-N2-(5-methyl-1-propyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine,

5-Bromo-N2-[1-(4-chloro-phenyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-pyrimidine-2,4-diamine,

N2-(1,5-Dimethyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

5-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-2-one,

4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide,

N2-[1-(4-Cyclopropanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-benzonitrile,

N4-Ethyl-N2-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

1-{4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-piperidin-1-yl}-2-methyl-propan-1-one,

1-{4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-1-yl}-2-methyl-propan-1-one,

N4-Methyl-N2-[3-methyl-1-(3-methyl-pyridin-4-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-((R)-2-Methoxy-propyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(2,6-Dimethyl-tetrahydro-pyran-4-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1,1-Dioxo-hexahydro-1$l%6&-thiopyran-4-yl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-((R)-2-Methoxy-1-methyl-ethyl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-((S)-2-Methoxy-1-methyl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[3-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[5-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1-Isopropyl-azetidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[5-methyl-1-(propane-2-sulfonyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(5-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(3-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-{1-[1-(2-methoxy-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-{1-[1-(2-methoxy-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-{1-[1-(2-Fluoro-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-{1-[1-(2-Fluoro-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[5-Chloro-1-(3-fluoro-1-methyl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(1-Ethanesulfonyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[5-methyl-1-(2-methyl-2-morpholin-4-yl-propyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(1-Cyclopropanesulfonyl-3-cyclopropyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

(5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoro-ethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-amine,

N4-Methyl-N2-[3-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[1-(2-methoxy-ethyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[1-(2-methoxy-ethyl)-5-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

1-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-2-methyl-propan-2-ol,

1-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propan-2-ol,

N2-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Cyclopropyl-N2-(1-methanesulfonyl-3-methyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Cyclopropyl-N2-(1-methanesulfonyl-5-methyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

1-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2-methyl-propan-2-ol,

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

N4-Methyl-N2-(3-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[5-Chloro-1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[5-Chloro-1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[5-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[3-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[5-methyl-1-((S)-1-methyl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[3-methyl-1-((S)-1-methyl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-[5-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile,

N4-Methyl-N2-[5-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-[5-Chloro-4-(4-ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile,

N4-Ethyl-N2-[1-(3-fluoro-1-oxetan-3-yl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-Methyl-1-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-butan-2-ol,

3-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-butan-2-ol,

N2-[1-(1-[1,3]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(5-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[5-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-[3-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

3-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile,

N4-Ethyl-N2-{3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-[1-(1-[1,3]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-(3-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,

N2-(5-Fluoromethyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-{3-methyl-1-[1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Methyl-N2-{3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine,

N4-Ethyl-N2-[1-(3-fluoro-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,

2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol,

2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol,

N4-ethyl-N2-(3-methyl-1-(2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(5-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N4-methyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine,

N2-(1',5-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1',3-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

N2-(1-(2-(4H-1,2,4-triazol-3-yl)propan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1,3-Dimethyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidine-5-carbonitrile,

2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-isopropyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-ethyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(ethylamino)pyrimidine-5-carbonitrile,

2-(1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(difluoromethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(5-methyl-1-propyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

4-(ethylamino)-2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

4-(ethylamino)-2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

4-(ethylamino)-2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

2-(1-isopropyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,

2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile,

2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethylamino)pyrimidine-5-carbonitrile,

2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile,

4-(2,2-difluoroethylamino)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,

2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethoxy)pyrimidine-5-carbonitrile,

2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile,

2-(1-(4,4-difluorocyclohexyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile,

2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluoroethylamino)pyrimidine-5-carbonitrile,

2-(5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile,

2-(1-Difluoromethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidine-5-carbonitrile,

2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-ethylamino-pyrimidine-5-carbonitrile,

2-[1-(4-Fluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,

4-Methylamino-2-(3-methyl-1-propyl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

4-Methylamino-2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

4-Methylamino-2-(3-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

2-[1-(3,5-Difluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,

4-(2,2-Difluoro-ethoxy)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile,

2-[1-(4,4-Difluoro-cyclohexyl)-3-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,

(5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)(morpholino)methanone,

2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N,N-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamide,

N,N,2-trimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,

(R)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

(R)-N,N-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

(S)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

3-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

3-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

methyl 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate,

methyl 2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate,

2-(3-ethyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile,

(R)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

(R)-N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

(S)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

(S)-N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

(S)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

(S)-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

2-(4-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile,

2,2-dimethyl-3-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

2,2-dimethyl-3-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,

1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,

N-tert-butyl-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-(2,2,2-trifluoroethyl)propanamide,

2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-ethyl-2-methyl propanamide,

N-(cyclopropylmethyl)-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

N-(cyclopropylmethyl)-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

N-ethyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarboxamide,

N-isopropyl-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarbonitrile,

2-(4-(4-(cyclopropylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile,

N,2-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,

1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,

2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester,

2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester,

(S)-N,N-Dimethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionamide,

R)-2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile,

2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-cyclopropyl-pyrazol-1-yl]-2-methyl-propionitrile,

(R)-2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile,

N-Ethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

N-Ethyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarboxylic acid ethylamide,

2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-N-(2,2,2-trifluoro-ethyl)-isobutyramide,

N-Isopropyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

N-Methyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarbonitrile,

N-tert-Butyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide,

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

2-[4-(4-Cyclopropylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

2-[4-(4-Cyclopropylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propionitrile,

2-(3-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile, and

2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide,

or a pharmaceutically acceptable salt thereof.

21. The compound of any of claims 1-20 for use as medicament.

22. The compound of any of claims 1-20 for use in the therapeutic and/or prophylactic treatment of Parkinson's disease.

23. The use of a compound of any of claims 1-20 for the preparation of medicaments for the therapeutic and/or prophylactic treatment of Parkinson's disease.

24. A composition comprising:

(a) a pharmaceutically acceptable carrier; and

(b) a compound of any of claims 1-20.

25. A method for treating Parkinson's disease, said method comprising administering to a subject in need thereof an effective amount of a compound of any of claims 1-20.

26. The invention as herein before described.

***