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(54) PYRAZOLE AMINOPYRIMIDINE DERIVATIVES AS LRRK2 MODULATORS

PYRAZOLAMINOPYRIMIDINDERIVATE ALS LRRK2-MODULATOREN

DÉRIVÉS DE PYRAZOLE AMINOPYRIMIDINE EN TANT QUE MODULATEURS DU LRRK2

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Description

FIELD OF THE INVENTION

5 **[0001]** 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

10 **[0002]** 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.

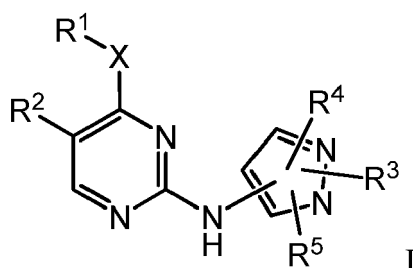
15 **[0003]** The gene encoding the leucine-rich repeat kinase 2 protein (LRRK2) has been identified in association with hereditary Parkinson's disease (Paisan-Ruiz et al., *Neuron*, Vol. 44(4), 2004, pp 595-600; Zimprich et al., *Neuron*, Vol. 44(4), 2004, 601-607). *In-vitro* studies show that Parkinson's 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 Lewy body dementia suggesting that LRRK2 may play an important role in Lewy 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.

20 **[0004]** 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 spondylitis (Danoy et al., *PLoS Genetics*, Vol. 6(12), 2010, e1001195, pp. 1-5).
 25 WO2009127642 describes N2,N4-diphenylpyrimidine-2,4-diamines useful as LRRK2 inhibitors.

30 **[0005]** Accordingly, compounds and compositions effective at modulating LRRK2 activity may provide a treatment for neurodegenerative diseases such as Parkinson's disease and Lewy 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 spondylitis. 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

45 **[0006]** The invention provides compounds of the formula I:



or pharmaceutically acceptable salts thereof,

wherein:

X is: -NR^a-; or -O- wherein R^a is hydrogen;

5 R¹ is: C₁₋₆alkyl;

R² is: halo; cyano; or halo-C₁₋₆alkyl;

10 R³ is: hydrogen; C₁₋₆alkyl; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano-C₁₋₆alkyl; C₁₋₆alkylsulfonyl; C₁₋₆alkylsulfonyl-C₁₋₆alkyl; amino-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-sulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷; heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷; aryl optionally substituted one or more times with R⁸; aryl-C₁₋₆alkyl wherein the aryl portion is optionally substituted one or more times with R⁸; heteroaryl optionally substituted one or more times with R⁸; heteroaryl-C₁₋₆alkyl wherein the heteroaryl portion is optionally substituted one or more times with R⁸; or -Y-C(O)-R^d;

20 Y is C₂₋₆alkylene or a bond;

R^d is C₁₋₆alkyl, C₁₋₆alkoxy, amino, C₁₋₆alkyl-amino, di-C₁₋₆alkyl-amino, halo-C₁₋₆alkylamino, di-halo-C₁₋₆alkyl-amino, halo-C₁₋₆alkyl, hydroxy-C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy-C₁₋₆alkyl, cyano-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, amino-C₁₋₆alkyl, C₃₋₆cycloalkyl optionally substituted one or more times with R⁶, C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷, or heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷;

30 R⁴ is: hydrogen; C₁₋₆alkyl; halo; cyano; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; C₁₋₆alkoxy; C₁₋₆alkoxy-C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; or -Y-C(O)-R^d;

R⁵ is: hydrogen; or C₁₋₆alkyl;

35 each R⁶ is independently: C₁₋₆alkyl; halo-C₁₋₆alkyl; C₁₋₆alkoxy; oxo; cyano; halo; or Y-C(O)-R^d;

each R⁷ is independently: C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; oxo; C₁₋₆alkoxy; C₁₋₆alkylsulfonyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; -Y-C(O)-R^d; heterocyclyl; heterocyclyl-C₁₋₆alkyl; C₃₋₆cycloalkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl; or C₃₋₆cycloalkylsulfonyl; and

40 each R⁸ is independently: oxo; C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; C₁₋₆alkyl-sulfonyl; C₁₋₆alkoxy; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; heterocyclyl; heterocyclyl-C₁₋₆alkyl; -Y-C(O)-R^d; C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, or C₃₋₆cycloalkyl-sulfonyl.

45 **[0007]** The invention also provides pharmaceutical compositions comprising the compounds, the compounds for use as medicament, and methods of preparing the compounds.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

50 **[0008]** 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.

55 **[0009]** "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. C₁₋₆alkyl. 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.

[0010] "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.

[0011] "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.

[0012] "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.

[0013] "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.

[0014] "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.

[0015] "Alkoxyalkoxy" means a group of the formula -O-R-R' wherein R is alkylene and R' is alkoxy as defined herein.

[0016] "Alkylcarbonyl" means a moiety of the formula -C(O)-R, wherein R is alkyl as defined herein.

[0017] "Alkoxycarbonyl" means a group of the formula -C(O)-R wherein R is alkoxy as defined herein.

[0018] "Alkylcarbonylalkyl" means a group of the formula -R-C(O)-R wherein R is alkylene and R' is alkyl as defined herein.

[0019] "Alkoxycarbonylalkyl" means a group of the formula -R-C(O)-R wherein R is alkylene and R' is alkoxy as defined herein.

[0020] "Alkoxycarbonylalkoxy" means a group of the formula -O-R-C(O)-R' wherein R is alkylene and R' is alkoxy as defined herein.

[0021] "Hydroxycarbonylalkoxy" means a group of the formula -O-R-C(O)-OH wherein R is alkylene as defined herein.

[0022] "Alkylaminocarbonylalkoxy" means a group of the formula -O-R-C(O)-NHR' wherein R is alkylene and R' is alkyl as defined herein.

[0023] "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.

[0024] "Alkylaminoalkoxy" means a group of the formula -O-R-NHR' wherein R is alkylene and R' is alkyl as defined herein.

[0025] "Dialkylaminoalkoxy" means a group of the formula -O-R-NR'R' wherein R is alkylene and R' and R" are alkyl as defined herein.

[0026] "Alkylsulfonyl" means a moiety of the formula -SO₂-R, wherein R is alkyl as defined herein.

[0027] "Alkylsulfonylalkyl" means a moiety of the formula -R'-SO₂-R" where where R' is alkylene and R" is alkyl as defined herein.

[0028] "Alkylsulfonylalkoxy" means a group of the formula -O-R-SO₂-R' wherein R is alkylene and R' is alkyl as defined herein.

[0029] "Amino" means a moiety of the formula -NRR' wherein R and R' each independently is hydrogen 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)".

[0030] "Aminocarbonyl" means a group of the formula -C(O)-R wherein R is amino as defined herein.

[0031] "Alkoxyamino" means a moiety of the formula -NR-OR' wherein R is hydrogen or alkyl and R' is alkyl as defined herein.

[0032] "Alkylsulfanyl" means a moiety of the formula -SR wherein R is alkyl as defined herein.

[0033] "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.

[0034] "Aminoalkoxy" means a group -OR-R' wherein R' is amino and R is alkylene as defined herein.

[0035] "Alkylsulfonylamido" means a moiety of the formula -NR'SO₂-R wherein R is alkyl and R' is hydrogen or alkyl.

[0036] "Aminocarbonyloxyalkyl" or "carbonylalkyl" 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.

[0037] "Alkynylalkoxy" means a group of the formula -O-R-R' wherein R is alkylene and R' is alkynyl as defined herein.

[0038] "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, benzodioxyl, benzopyranyl, benzoxazinyl, benzoxazinonyl, benzopiperadiny, benzopiperaziny, benzopyrrolidiny, benzomorpholinyl, methylenedioxyphenyl, ethylenedioxyphenyl, and the like, including partially hydrogenated derivatives thereof, each

being optionally substituted.

[0039] "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.

[0040] "Arylsulfonyl" means a group of the formula $-SO_2-R$ wherein R is aryl as defined herein.

[0041] "Aryloxy" means a group of the formula $-O-R$ wherein R is aryl as defined herein.

[0042] "Aralkyloxy" means a group of the formula $-O-R-R'$ wherein R is alkylene and R' is aryl as defined herein.

[0043] "Carboxy" or "hydroxycarbonyl", which may be used interchangeably, means a group of the formula $-C(O)-OH$.

[0044] "Cyanoalkyl" means a moiety of the formula $-R'-R''$, where R' is alkylene as defined herein and R'' is cyano or nitrile.

[0045] "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.

[0046] "Cycloalkylalkyl" means a moiety of the formula $-R'-R''$, where R' is alkylene and R'' is cycloalkyl as defined herein.

[0047] "Cycloalkylalkoxy" means a group of the formula $-O-R-R'$ wherein R is alkylene and R' is cycloalkyl as defined herein.

[0048] "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-hydroxymethyl-ethyl, 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.

[0049] "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, quinoliziny, naphthyridinyl, pteridinyl, carbazolyl, azepinyl, diazepinyl, acridinyl and the like, including partially hydrogenated derivatives thereof, each optionally substituted.

[0050] "Heteroarylalkyl" or "heteroaralkyl" means a group of the formula $-R-R'$ wherein R is alkylene and R' is heteroaryl as defined herein.

[0051] "Heteroarylsulfonyl" means a group of the formula $-SO_2-R$ wherein R is heteroaryl as defined herein.

[0052] "Heteroaryloxy" means a group of the formula $-O-R$ wherein R is heteroaryl as defined herein.

[0053] "Heteroaralkyloxy" means a group of the formula $-O-R-R'$ wherein R is alkylene and R' is heteroaryl as defined herein.

[0054] The terms "halo", "halogen" and "halide", which may be used interchangeably, refer to a substituent fluoro, chloro, bromo, or iodo.

[0055] "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.

[0056] "Haloalkoxy" means a moiety of the formula $-OR$, wherein R is a haloalkyl moiety as defined herein. An exemplary haloalkoxy is difluoromethoxy.

[0057] "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.

[0058] "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, imidazoliny, imidazolidinyl, pyridinyl, pyridazinyl, pyrimidinyl, oxazolidinyl, isoxazolidinyl, morpholinyl, thiazolidinyl, isothiazolidinyl, quinuclidinyl, quinolinyl, isoquinolinyl,

benzimidazolyl, thiadiazolylidiny, benzothiazolidinyl, benzoazolylidiny, dihydrofuryl, tetrahydrofuryl, dihydropyranyl, tetrahydropyranyl, thiamorpholinyl, thiamorpholinylsulfoxide, thiamorpholinylsulfone, dihydroquinoliny, dihydroisoquinoliny, tetrahydroquinoliny, tetrahydroisoquinoliny, and the like.

[0059] "Heterocyclalalkyl" means a moiety of the formula -R-R' wherein R is alkylene and R' is heterocyclal as defined herein.

[0060] "Heterocyclaloxo" means a moiety of the formula -OR wherein R is heterocyclal as defined herein.

[0061] "Heterocyclalalkoxy" means a moiety of the formula -OR-R' wherein R is alkylene and R' is heterocyclal as defined herein.

[0062] "Hydroxyalkoxy" means a moiety of the formula -OR wherein R is hydroxyalkyl as defined herein.

[0063] "Hydroxyalkylamino" means a moiety of the formula -NR-R' wherein R is hydrogen or alkyl and R' is hydroxyalkyl as defined herein.

[0064] "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.

[0065] "Hydroxycarbonylalkyl" or "carboxyalkyl" means a group of the formula -R-(CO)-OH where R is alkylene as defined herein.

[0066] "Hydroxycarbonylalkoxy" means a group of the formula -O-R-C(O)-OH wherein R is alkylene as defined herein.

[0067] "Hydroxyalkoxyalkyl" or "hydroxyalkoxyalkyl" means a group of the formula -R-C(O)-O-R-OH wherein each R is alkylene and may be the same or different.

[0068] "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

[0069] "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.

[0070] "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.

[0071] "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.

[0072] "Carbamate" means a group of the formula -O-C(O)-NR'R" wherein R' and R" each independently is hydrogen or alkyl.

[0073] "Carboxy" means a group of the formula -O-C(O)-OH.

[0074] "Sulfonamido" means a group of the formula -SO₂-NR'R" wherein R', R" and R"" each independently is hydrogen or alkyl.

[0075] "Optionally substituted", when used in association with "aryl", phenyl", "heteroaryl" "cycloalkyl" or "heterocyclal", means an aryl, phenyl, heteroaryl, cycloalkyl or heterocyclal 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, monoalkylamino, dialkylamino, haloalkyl, haloalkoxy, heteroalkyl, -COR, -SO₂R (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 "heterocyclal" include alkyl, halo, haloalkyl, alkoxy, cyano, amino and alkylsulfonyl. In one embodiment substituents are methyl, fluoro, chloro, trifluoromethyl, methoxy, amino and methanesulfonyl.

[0076] "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 arylsulfonyloxy, such as methanesulfonyloxy, ethanesulfonyloxy, thiomethyl, benzenesulfonyloxy, tosyloxy, and thienyloxy, dihalophosphinoyloxy, optionally substituted benzyloxy, isopropoxy, acyloxy, and the like.

[0077] "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.

[0078] "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.

[0079] "Disease" and "Disease state" means any disease, condition, symptom, disorder or indication.

[0080] "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.

[0081] "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.

[0082] "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, oxalic 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, polyamine 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).

[0083] 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. dioxane 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.

[0084] 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.

[0085] 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*.

[0086] 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 (K_i) using the Cheng-Prusoff equation (Biochem. Pharmacol. (1973) 22:3099). The term "inhibition constant" (K_i) 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. K_i values can be converted logarithmically to pK_i values ($-\log K_i$), in which higher values indicate exponentially greater potency.

[0087] 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.

[0088] 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.

[0089] "Protective group" or "protecting group" means the group which selectively blocks one reactive site in a multi-functional 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.

[0090] "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 H₂O, such combination being able to form one or more hydrate.

[0091] "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).

[0092] "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.

[0093] "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.

[0094] "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.

[0095] 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.

[0096] "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.

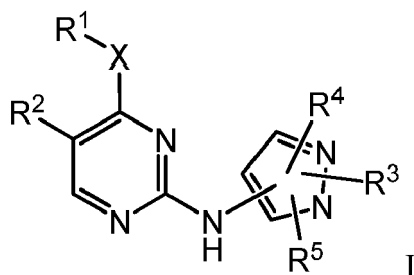
[0097] The terms "treating", "contacting" and "reacting" when referring to a chemical reaction means adding or mixing two or more reagents under appropriate conditions to produce the indicated and/or the desired product. It should be appreciated that the reaction which produces the indicated and/or the 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

[0098] 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 C¹³ and C¹⁴ isotopes.

Compounds of the Invention

[0099] The invention provides compounds of the formula I:



or pharmaceutically acceptable salts thereof,
wherein:

X is: -NR^a-; or -O- wherein R^a is hydrogen;

R¹ is: C₁₋₆alkyl;

R² is: halo; cyano; or halo-C₁₋₆alkyl;

R³ is: hydrogen; C₁₋₆alkyl; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano-C₁₋₆alkyl; C₁₋₆alkylsulfonyl; C₁₋₆alkylsulfonyl-C₁₋₆alkyl; amino-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-sulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷; heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷; aryl optionally substituted one or more times with R⁸; aryl-C₁₋₆alkyl wherein the aryl portion is optionally substituted one or more times with R⁸; heteroaryl optionally substituted one or more times with R⁸; heteroaryl-C₁₋₆alkyl wherein the heteroaryl portion is optionally substituted one or more times with R⁸; or -Y-C(O)-R^d;

Y is C₂₋₆alkylene or a bond;

R^d is C₁₋₆alkyl, C₁₋₆alkoxy, amino, C₁₋₆alkyl-amino, di-C₁₋₆alkyl-amino, halo-C₁₋₆alkylamino, di-halo-C₁₋₆alkyl-amino, halo-C₁₋₆alkyl, hydroxy-C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy-C₁₋₆alkyl, cyano-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, amino-C₁₋₆alkyl, C₃₋₆cycloalkyl optionally substituted one or more times with R⁶, C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷, or heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷;

R⁴ is: hydrogen; C₁₋₆alkyl; halo; cyano; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; C₁₋₆alkoxy; C₁₋₆alkoxy-C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; or -Y-C(O)-R^d;

R⁵ is: hydrogen; or C₁₋₆alkyl;

each R⁶ is independently: C₁₋₆alkyl; halo-C₁₋₆alkyl; C₁₋₆alkoxy; oxo; cyano; halo; or Y-C(O)-R^d;

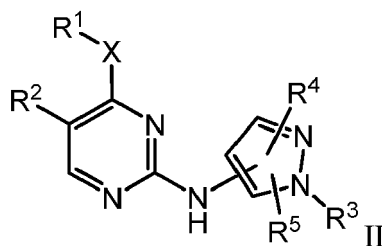
each R⁷ is independently: C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; oxo; C₁₋₆alkoxy; C₁₋₆alkylsulfonyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; -Y-C(O)-R^d; heterocyclyl; heterocyclyl-C₁₋₆alkyl; C₃₋₆cycloalkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl; or C₃₋₆cycloalkylsulfonyl; and

each R⁸ is independently: oxo; C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; C₁₋₆alkyl-sulfonyl; C₁₋₆alkoxy; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; heterocyclyl; heterocyclyl-C₁₋₆alkyl; -Y-C(O)-R^d; C₃₋₆cycloalkyl, C₃₋₆cycloalkyl-C₁₋₆alkyl, or C₃₋₆cycloalkyl-sulfonyl.

[0100] In certain embodiments the invention provides compounds of the formula II:

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or pharmaceutically acceptable salts thereof,
wherein:

- 15 X is: -NR^a-; or -O- wherein R^a is hydrogen;
R¹ is: C₁₋₆alkyl;
R² is: halo; cyano; or halo-C₁₋₆alkyl;
R³ is: hydrogen; C₁₋₆alkyl; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano-
C₁₋₆alkyl; C₁₋₆alkylsulfonyl; C₁₋₆alkylsulfonylalkyl; amino-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted with
20 C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl; hetero-
cyclyl; heterocyclyl-C₁₋₆alkyl; aryl; heteroaryl; or -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl;
R⁴ is: hydrogen; C₁₋₆alkyl; halo; cyano; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; C₁₋₆alkoxy-C₁₋₆alkyl; hydroxy-
C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl
25 portion is optionally substituted with C₁₋₆alkyl; or -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl;
and
R⁵ is: hydrogen; or C₁₋₆alkyl.

[0101] In certain embodiments of formula I or formula II, X is -NR^a- or -O-.

[0102] In certain embodiments of formula I or formula II, X is -NR^a.

30 [0103] In certain embodiments of formula I or formula II, X is -O-.

[0104] In certain embodiments of formula I or formula II, X is -NH- or -O-.

[0105] In certain embodiments of formula I or formula II, X is -NH-.

[0106] In certain embodiments of formula I or formula II, X is -O-.

[0107] In certain embodiments of formula I or formula II, R^a is hydrogen.

35 [0108] In certain embodiments of formula I or formula II, R¹ is C₁₋₆alkyl.

[0109] In certain embodiments of formula I or formula II, R¹ is: methyl; ethyl; n-propyl; isopropyl; or isobutyl.

[0110] In certain embodiments of formula I or formula II, R¹ is methyl or ethyl.

[0111] In certain embodiments of formula I or formula II, R¹ is methyl.

[0112] In certain embodiments of formula I or formula II, R¹ is ethyl.

40 [0113] In certain embodiments of formula I or formula II, R² is: halo; halo-C₁₋₆alkyl or cyano.

[0114] In certain embodiments of formula I or formula II, R² is: fluoro; bromo; chloro; iodo; trifluoromethyl; or cyano.

[0115] In certain embodiments of formula I or formula II, R² is: chloro; trifluoromethyl; or cyano.

[0116] In certain embodiments of formula I or formula II, R² is: halo; or halo-C₁₋₆alkyl.

[0117] In certain embodiments of formula I or formula II, R² is halo.

45 [0118] In certain embodiments of formula I or formula II, R² is halo-C₁₋₆alkyl.

[0119] In certain embodiments of formula I or formula II, R² is fluoro, chloro or bromo.

[0120] In certain embodiments of formula I or formula II, R² is chloro.

[0121] In certain embodiments of formula I or formula II, R² is fluoro.

[0122] In certain embodiments of formula I or formula II, R² is bromo.

50 [0123] In certain embodiments of formula I or formula II, R² is iodo.

[0124] In certain embodiments of formula I or formula II, R² is trifluoromethyl.

[0125] In certain embodiments of formula I or formula II, R² is cyano.

55 [0126] In certain embodiments of formula I or formula II, R³ is: C₁₋₆alkyl; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl;
hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano-C₁₋₆alkyl; C₁₋₆alkylsulfonyl; C₁₋₆alkylsulfonyl-C₁₋₆alkyl; amino-C₁₋₆alkyl;
C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion
is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷;
heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷; aryl optionally
substituted one or more times with R⁸; heteroaryl optionally substituted one or more times with R⁸; or -Y-C(O)-R^d.

- [0127]** In certain embodiments of formula I or formula II, R³ is: hydrogen; C₁₋₆alkyl; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano-C₁₋₆alkyl; C₁₋₆alkylsulfonyl; C₁₋₆alkylsulfonylalkyl; amino-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl; heterocyclyl; heterocyclyl-C₁₋₆alkyl; aryl; heteroaryl; or -C(O)-R^c.
- [0128]** In certain embodiments of formula I or formula II, R³ is: C₁₋₆alkyl; halo-C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl; heterocyclyl; heterocyclyl-C₁₋₆alkyl; or -C(O)-R^b wherein R^b is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.
- [0129]** In certain embodiments of formula I or formula II, R³ is: C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl; heterocyclyl; heterocyclyl-C₁₋₆alkyl; or -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.
- [0130]** In certain embodiments of formula I or formula II, R³ is: C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷; heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷; or -C(O)-R^d.
- [0131]** In certain embodiments of formula I or formula II, R³ is: C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; heterocyclyl; heterocyclyl-C₁₋₆alkyl; or -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.
- [0132]** In certain embodiments of formula I or formula II, R³ is: C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; heterocyclyl; or heterocyclyl-C₁₋₆alkyl.
- [0133]** In certain embodiments of formula I or formula II, R³ is: C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; or C₁₋₆alkoxy-C₁₋₆alkyl.
- [0134]** In embodiments of formula I or formula II wherein R³ is heterocyclyl or heterocyclyl-C₁₋₆alkyl, such heterocyclyl may be piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, pyrrolidinyl, tetrahydrofuranyl or oxetanyl.
- [0135]** In embodiments of formula I or formula II wherein R³ is heterocyclyl or heterocyclyl-C₁₋₆alkyl, such heterocyclyl may be piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, pyrrolidinyl, azetidyl, tetrahydrofuranyl or oxetanyl, each optionally substituted one or more times, or one or two times, with R⁷ as defined herein.
- [0136]** In embodiments of formula I or formula II wherein R³ is heterocyclyl or heterocyclyl-C₁₋₆alkyl, such heterocyclyl may be piperidinyl, morpholinyl, tetrahydropyranyl, tetrahydrofuranyl or oxetanyl.
- [0137]** In embodiments of formula I or formula II wherein R³ is heterocyclyl or heterocyclyl-C₁₋₆alkyl, such heterocyclyl may be piperidinyl, pyrrolidinyl, azetidyl, morpholinyl, tetrahydropyranyl, tetrahydrofuranyl or oxetanyl, each optionally substituted one or more times, or one or two times, with R⁷ as defined herein.
- [0138]** In certain embodiments of formula I or formula II, R³ 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.
- [0139]** In certain embodiments of formula I, R³ 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.
- [0140]** In certain embodiments of formula I or formula II, R³ is hydrogen.
- [0141]** In certain embodiments of formula I or formula II, R³ is C₁₋₆alkyl.
- [0142]** In certain embodiments of formula I or formula II, R³ is halo-C₁₋₆alkyl.
- [0143]** In certain embodiments of formula I or formula II, R³ is C₂₋₆alkenyl.
- [0144]** In certain embodiments of formula I or formula II, R³ is C₂₋₆alkynyl.
- [0145]** In certain embodiments of formula I or formula II, R³ is hydroxy-C₁₋₆alkyl.
- [0146]** In certain embodiments of formula I or formula II, R³ is C₁₋₆alkoxy-C₁₋₆alkyl.
- [0147]** In certain embodiments of formula I or formula II, R³ is C₃₋₆cycloalkyl optionally substituted one or more times with R⁶.
- [0148]** In certain embodiments of formula I or formula II, R³ is C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl.
- [0149]** In certain embodiments of formula I or formula II, R³ is C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.
- [0150]** In certain embodiments of formula I or formula II, R³ is C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl.
- [0151]** In certain embodiments of formula I or formula II, R³ is heterocyclyl optionally substituted one or more times with R⁷.
- [0152]** In certain embodiments of formula I or formula II, R³ is heterocyclyl.
- [0153]** In certain embodiments of formula I or formula II, R³ is heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷.
- [0154]** In certain embodiments of formula I or formula II, R³ is heterocyclyl-C₁₋₆alkyl.
- [0155]** In certain embodiments of formula I or formula II, R³ is -C(O)-R^c.
- [0156]** In certain embodiments of formula I or formula II, R³ is cyano-C₁₋₆alkyl.
- [0157]** In certain embodiments of formula I or formula II, R³ is C₁₋₆alkylsulfonyl.

[0158] In certain embodiments of formula I or formula II, R³ is C₁₋₆alkylsulfonyl-C₁₋₆alkyl.

[0159] In certain embodiments of formula I or formula II, R³ is amino-C₁₋₆alkyl.

[0160] In certain embodiments of formula I or formula II, R³ is aryl optionally substituted one or more times with R⁸.

[0161] In certain embodiments of formula I or formula II, R³ is aryl.

5 **[0162]** In certain embodiments of formula I or formula II, R³ is phenyl optionally substituted one or more times, or one or two times, with R⁸.

[0163] In certain embodiments of formula I or formula II, R³ is heteroaryl optionally substituted one or more times, or one or two times, with R⁸.

[0164] In certain embodiments of formula I or formula II, R³ is heteroaryl.

10 **[0165]** In certain embodiments of formula I or formula II, R³ is C₃₋₆cycloalkyl-sulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.

[0166] In certain embodiments of formula I or formula II, R³ 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; 15 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)azetididin-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)azetididin-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)azetididin-3-yl); 1-(oxetan-3-yl)pyrrolidin-3-yl; 1-isopropylazetididin-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-trifluoroethylamino-carbonyl)-1-methylethyl; 1-(ethylamino-carbonyl)-1-methyl-ethyl; 1-(cyclopropylmethylamino-carbonyl)-1-methylethyl; 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; pyrimidin-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-hydroxycyclopentyl; 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.

[0167] In certain embodiments of formula I or formula II, R³ 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)azetididin-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)azetididin-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)azetididin-3-yl); 1-(oxetan-3-yl)pyrrolidin-3-yl; 1-isopropylazetididin-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-trifluoroethylamino-carbonyl)-1-methylethyl; 1-(ethylamino-carbonyl)-1-methyl-ethyl; 1-(cyclopropylmethylamino-carbonyl)-1-methylethyl; 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; pyrimidin-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-hydroxycyclopentyl; 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.

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- clohexyl; 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-trifluoroethylamino-carbonyl)-1-methylethyl; 1-(ethylamino-carbonyl)-1-methyl-ethyl; 1-(cyclopropylmethylamino-carbonyl)-1-methylethyl; 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; pyrimidin-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-hydroxycyclopentyl; 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.
- [0168]** In certain embodiments of formula I or formula II, R³ 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.
- [0169]** In certain embodiments of formula I or formula II, R³ is: methyl; ethyl; n-propyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; 2-hydroxy-2-methyl-propan-1-yl; or tetrahydropyran-4-yl.
- [0170]** In certain embodiments of formula I or formula II, R³ is: methyl; ethyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; or 2-hydroxy-2-methyl-propan-1-yl.
- [0171]** In certain embodiments of formula I or formula II, R³ is: methyl; ethyl; isopropyl; 2-methoxy-ethyl; oxetan-3-yl; or 2-hydroxy-2-methyl-propan-1-yl.
- [0172]** In certain embodiments of formula I or formula II, R³ is: methyl; ethyl; or isopropyl.
- [0173]** In certain embodiments of formula I or formula II, R³ is hydrogen.
- [0174]** In certain embodiments of formula I or formula II, R³ is methyl.
- [0175]** In certain embodiments of formula I or formula II, R³ is ethyl.
- [0176]** In certain embodiments of formula I or formula II, R³ is n-propyl.
- [0177]** In certain embodiments of formula I or formula II, R³ is isopropyl.
- [0178]** In certain embodiments of formula I or formula II, R³ is 2-methoxy-ethyl.
- [0179]** In certain embodiments of formula I or formula II, R³ is oxetan-3-yl.
- [0180]** In certain embodiments of formula I or formula II, R³ is 2-hydroxy-2-methyl-propan-1-yl.
- [0181]** In certain embodiments of formula I or formula II, R³ is tetrahydropyran-4-yl.
- [0182]** In certain embodiments of formula I or formula II, R³ is morpholin-4-yl-carbonyl.
- [0183]** In certain embodiments of formula I or formula II, R³ is butyl.
- [0184]** In certain embodiments of formula I or formula II, R³ is cyclopropyl.
- [0185]** In certain embodiments of formula I or formula II, R³ is cyclopropylmethyl.
- [0186]** In certain embodiments of formula I or formula II, R³ is cyclobutyl.
- [0187]** In certain embodiments of formula I or formula II, R³ is methanesulfonyl.
- [0188]** In certain embodiments of formula I or formula II, R³ is ethylsulfonyl.
- [0189]** In certain embodiments of formula I or formula II, R³ is cyclopropylsulfonyl.
- [0190]** In certain embodiments of formula I or formula II, R³ is sec-butylsulfonyl.
- [0191]** In certain embodiments of formula I or formula II, R³ is morpholin-4-yl-ethyl.
- [0192]** In certain embodiments of formula I or formula II, R³ is 2-hydroxy-2-methyl-propyl.
- [0193]** In certain embodiments of formula I or formula II, R³ is 3-hydroxy-2-methyl-propan-2-yl.
- [0194]** In certain embodiments of formula I or formula II, R³ is 2-methoxy-propyl.
- [0195]** In certain embodiments of formula I or formula II, R³ is tetrahydro-2H-pyran-4-yl.
- [0196]** In certain embodiments of formula I or formula II, R³ is tetrahydrofuran-3-yl.
- [0197]** In certain embodiments of formula I or formula II, R³ is 2,6-dimethyltetrahydro-2H-pyran-4-yl.
- [0198]** In certain embodiments of formula I or formula II, R³ is tetrahydro-2H-pyran-3-yl).
- [0199]** In certain embodiments of formula I or formula II, R³ is phenyl.
- [0200]** In certain embodiments of formula I or formula II, R³ is 4-(methylsulfonyl)phenyl).
- [0201]** In certain embodiments of formula I or formula II, R³ is 4-cyano-phenyl.
- [0202]** In certain embodiments of formula I or formula II, R³ is 4-fluoro-phenyl.
- [0203]** In certain embodiments of formula I or formula II, R³ is 4-chloro-phenyl.
- [0204]** In certain embodiments of formula I or formula II, R³ is 3,5-difluorophenyl.
- [0205]** In certain embodiments of formula I or formula II, R³ is 4-(dimethylamino-carbonyl)-phenyl).
- [0206]** In certain embodiments of formula I or formula II, R³ is 4-(cyclopropylsulfonyl)phenyl).

- [0207] In certain embodiments of formula I or formula II, R³ is 2,2,2-trifluoroethyl.
- [0208] In certain embodiments of formula I or formula II, R³ is 2-fluoroethyl.
- [0209] In certain embodiments of formula I or formula II, R³ is difluoromethyl.
- 5 [0210] In certain embodiments of formula I or formula II, R³ is 2-dimethyl-1,3-dioxan-5-yl.
- [0211] In certain embodiments of formula I or formula II, R³ is 1-methyl-cyclopropyl-carbonyl.
- [0212] In certain embodiments of formula I or formula II, R³ is 3-methylpyridin-4-yl.
- [0213] In certain embodiments of formula I or formula II, R³ is 2-methylpyridin-4-yl.
- [0214] In certain embodiments of formula I or formula II, R³ is pyridin-2-yl.
- 10 [0215] In certain embodiments of formula I or formula II, R³ is pyrimidin-2-yl.
- [0216] In certain embodiments of formula I or formula II, R³ is pyrimidin-5-yl.
- [0217] In certain embodiments of formula I or formula II, R³ is pyridin-2-ylmethyl.
- [0218] In certain embodiments of formula I or formula II, R³ is 1-(pyridin-2-yl)ethyl.
- [0219] In certain embodiments of formula I or formula II, R³ is cyclopropylsulfonyl.
- 15 [0220] In certain embodiments of formula I or formula II, R³ is 1-cyano-1-methyl-ethyl (also called 2-cyano-propan-2-yl).
- [0221] In certain embodiments of formula I or formula II, R³ is 2-cyano-ethyl.
- [0222] In certain embodiments of formula I or formula II, R³ is 1-cyano-ethyl.
- [0223] In certain embodiments of formula I or formula II, R³ is 2-cyano-2-methyl-propyl.
- [0224] In certain embodiments of formula I or formula II, R³ is 1-(2,2,2-trifluoroethyl)piperidin-4-yl.
- 20 [0225] In certain embodiments of formula I or formula II, R³ is 1-(methylsulfonyl)azetid-3-yl.
- [0226] In certain embodiments of formula I or formula II, R³ is (3-methyloxetan-3-yl)methyl.
- [0227] In certain embodiments of formula I or formula II, R³ is (1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl.
- [0228] In certain embodiments of formula I or formula II, R³ is 1-(oxetan-3-yl)piperidin-4-yl.
- [0229] In certain embodiments of formula I or formula II, R³ is 1-acetyl-piperidin-4-yl.
- 25 [0230] In certain embodiments of formula I or formula II, R³ is 1-(cyclopropyl-carbonyl)-piperidin-4-yl.
- [0231] In certain embodiments of formula I or formula II, R³ is 1-methyl-piperidin-4-yl.
- [0232] In certain embodiments of formula I or formula II, R³ is 1-methyl-2-oxo-piperidin-5-yl.
- [0233] In certain embodiments of formula I or formula II, R³ is 2-oxo-piperidin-5-yl.
- [0234] In certain embodiments of formula I or formula II, R³ is 1-(isopropyl-carbonyl)-piperidin-4-yl.
- 30 [0235] In certain embodiments of formula I or formula II, R³ is 1-(oxetan-3-yl)azetid-3-yl.
- [0236] In certain embodiments of formula I or formula II, R³ is 1-(cyclopropyl-carbonyl)-piperidin-4-yl.
- [0237] In certain embodiments of formula I or formula II, R³ is 2-methoxycyclopentyl.
- [0238] In certain embodiments of formula I or formula II, R³ is 3-methoxycyclopentyl.
- [0239] In certain embodiments of formula I or formula II, R³ is 1-methoxy-2-methylpropan-2-yl.
- 35 [0240] In certain embodiments of formula I or formula II, R³ is tetrahydro-2H-1,1-dioxo-thiopyran-4-yl.
- [0241] In certain embodiments of formula I or formula II, R³ is 3-fluoro-1-(oxetan-3-yl)piperidin-4-yl.
- [0242] In certain embodiments of formula I or formula II, R³ is 1-methoxypropan-2-yl.
- [0243] In certain embodiments of formula I or formula II, R³ is 1-(2,2,2-trifluoroethyl)azetid-3-yl.
- [0244] In certain embodiments of formula I or formula II, R³ is 1-(oxetan-3-yl)pyrrolidin-3-yl.
- 40 [0245] In certain embodiments of formula I or formula II, R³ is 1-isopropylazetid-3-yl.
- [0246] In certain embodiments of formula I or formula II, R³ is 3-fluoro-1-methylpiperidin-4-yl.
- [0247] In certain embodiments of formula I or formula II, R³ is 1-ethyl-3-fluoropiperidin-4-yl.
- [0248] In certain embodiments of formula I or formula II, R³ is 1-methylpyrrolidin-3-yl.
- [0249] In certain embodiments of formula I or formula II, R³ is 2-methoxyethyl)piperidin-4-yl).
- 45 [0250] In certain embodiments of formula I or formula II, R³ is 1-methyl-1-(methylamino-carbonyl)ethyl.
- [0251] In certain embodiments of formula I or formula II, R³ is 2-methyl-2-morpholino-propyl.
- [0252] In certain embodiments of formula I or formula II, R³ is 4,4-difluorocyclohexyl.
- [0253] In certain embodiments of formula I or formula II, R³ is dimethylamino-carbonyl-methyl.
- [0254] In certain embodiments of formula I or formula II, R³ is methylamino-carbonyl-methyl.
- 50 [0255] In certain embodiments of formula I or formula II, R³ is 1-methyl-1-(dimethylamino-carbonyl)-ethyl.
- [0256] In certain embodiments of formula I or formula II, R³ is pyrrolidin-1-yl-carbonyl.
- [0257] In certain embodiments of formula I or formula II, R³ is 1-cyano-cyclopropyl.
- [0258] In certain embodiments of formula I or formula II, R³ is 1-(pyrrolidin-1-yl-carbonyl)-ethyl.
- [0259] In certain embodiments of formula I or formula II, R³ is 1-(dimethylamino-carbonyl)-ethyl.
- 55 [0260] In certain embodiments of formula I or formula II, R³ is 1-(methoxy-carbonyl)-ethyl.
- [0261] In certain embodiments of formula I or formula II, R³ is 1-(tert-butylamino-carbonyl)-1-methyl-ethyl.
- [0262] In certain embodiments of formula I or formula II, R³ is 1-(2,2,2-trifluoroethylamino-carbonyl)-1-methyl-ethyl.
- [0263] In certain embodiments of formula I or formula II, R³ is 1-(ethylamino-carbonyl)-1-methyl-ethyl.
- [0264] In certain embodiments of formula I or formula II, R³ is 1-(cyclopropylmethylamino-carbonyl)-1-methyl-ethyl.

- [0265] In certain embodiments of formula I or formula II, R³ is 1-(ethylamino-carbonyl)-cyclobutyl.
- [0266] In certain embodiments of formula I or formula II, R³ is 1-(isopropylamino-carbonyl)-1-methyl-ethyl.
- [0267] In certain embodiments of formula I or formula II, R³ is 1-cyano-cyclobutyl.
- 5 [0268] In certain embodiments of formula I or formula II, R³ is dimethyl-[1,3]dioxan-5-yl.
- [0269] In certain embodiments of formula I or formula II, R³ is 2-methoxy-2-methyl-propan-1-yl.
- [0270] In certain embodiments of formula I or formula II, R³ is 2-methoxy-1-methyl-ethyl.
- [0271] In certain embodiments of formula I or formula II, R³ is 1-methyl-1-(methoxy-carbonyl)-ethyl.
- [0272] In certain embodiments of formula I or formula II, R³ is 1-oxetan-3-yl-pyrrolidin-3-yl.
- 10 [0273] In certain embodiments of formula I or formula II, R³ is isopropylsulfonyl.
- [0274] In certain embodiments of formula I or formula II, R³ is butane-2-sulfonyl.
- [0275] In certain embodiments of formula I or formula II, R³ is 1-(2-fluoroethyl)-piperidin-4-yl.
- [0276] In certain embodiments of formula I or formula II, R³ is 3-fluoro-1-methyl-piperidin-4-yl.
- [0277] In certain embodiments of formula I or formula II, R³ is 1-ethyl-3-fluoro-piperidin-4-yl. In certain embodiments of formula I or formula II, R³ is pyridin-3-ylmethyl.
- 15 [0278] In certain embodiments of formula I or formula II, R³ is 6-methyl-pyridin-2-ylmethyl.
- [0279] In certain embodiments of formula I or formula II, R³ is 2-(morpholin-1-yl)-1,1-dimethylethyl.
- [0280] In certain embodiments of formula I or formula II, R³ is pyrimidin-2-yl-methyl.
- [0281] In certain embodiments of formula I or formula II, R³ is 3-fluoro-1-(oxetan-3-yl)-piperidin-4-yl.
- [0282] In certain embodiments of formula I or formula II, R³ is 1-(oxetan-3-yl)-piperidin-3-yl.
- 20 [0283] In certain embodiments of formula I or formula II, R³ is 1-([1,3]Dioxolan-2-ylmethyl)-piperidin-4-yl.
- [0284] In certain embodiments of formula I or formula II, R³ is pyridazin-3-ylmethyl.
- [0285] In certain embodiments of formula I or formula II, R³ is piperidin-3-yl.
- [0286] In certain embodiments of formula I or formula II, R³ is pyrazin-2-ylmethyl.
- [0287] In certain embodiments of formula I or formula II, R³ is 2-hydroxy-3-methyl-butan-1-yl.
- 25 [0288] In certain embodiments of formula I or formula II, R³ is 1-([1,3]dioxolan-2-ylmethyl)-pyrrolidin-3-yl.
- [0289] In certain embodiments of formula I or formula II, R³ is pyrimidin-4-ylmethyl.
- [0290] In certain embodiments of formula I or formula II, R³ is 1-methyl-1H-pyrazol-3-ylmethyl.
- [0291] In certain embodiments of formula I or formula II, R³ is 1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl.
- [0292] In certain embodiments of formula I or formula II, R³ is 1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl.
- 30 [0293] In certain embodiments of formula I or formula II, R³ is 3-fluoro-piperidin-4-yl; 2-hydroxy-cyclopentyl.
- [0294] In certain embodiments of formula I or formula II, R³ is 2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl.
- [0295] In certain embodiments of formula I or formula II, R³ is 2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl.
- [0296] In certain embodiments of formula I or formula II, R³ is 2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl.
- [0297] In certain embodiments of formula I or formula II, R³ is 2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl.
- 35 [0298] In certain embodiments of formula I or formula II, R³ is 2-(1-methyl-1H-pyrazol-5-yl).
- [0299] In certain embodiments of formula I or formula II, R³ is 2-(4H-1,2,4-triazol-3-yl)propan-2-yl.
- [0300] In certain embodiments of formula I or formula II, R³ is 1-methyl-1H-pyrazole-4-yl.
- [0301] In embodiments of formula I or formula II wherein R³ is aryl, such aryl may be unsubstituted phenyl or phenyl substituted one or more times with R⁸, or in certain embodiments, once, twice or three times with a group or groups independently selected from C₁₋₆alkyl, halo, halo-C₁₋₆alkyl, C₁₋₆alkoxy, hydroxy or cyano.
- 40 [0302] In embodiments of formula I or formula II wherein R³ is heteroaryl or heteroaryl-C₁₋₆alkyl, such heteroaryl moiety may be pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, isoxazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl or tetrazolyl, each being unsubstituted or substituted once or twice with R⁸, or in certain embodiments, substituted once or twice with C₁₋₆alkyl.
- 45 [0303] In embodiments of formula I or formula II wherein R³ is heteroaryl or heteroaryl-C₁₋₆alkyl, such heteroaryl moiety may be pyrazolyl, pyridinyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazolyl or oxadiazolyl each being unsubstituted or substituted once or twice with R⁸, or in certain embodiments, substituted once or twice with C₁₋₆alkyl.
- [0304] In embodiments of formula I or formula II wherein R³ is heteroaryl or heteroaryl-C₁₋₆alkyl, 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 R⁸.
- 50 [0305] In embodiments of formula I or formula II wherein R³ is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidiny, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R⁷.
- 55 [0306] In embodiments of formula I or formula II wherein R³ is heterocyclyl-C₁₋₆alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidiny, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R⁷.
- [0307] In certain embodiments of formula I or formula II, R³ is -Y-C(O)-R^d.

- [0308]** In certain embodiments of formula I or formula II, Y is a bond.
- [0309]** In certain embodiments of formula I or formula II, Y is C₂₋₆alkylene.
- [0310]** In certain embodiments of formula I or formula II, Y is isopropylidene.
- [0311]** In certain embodiments of formula I or formula II, Y is methylene.
- 5 **[0312]** In certain embodiments of formula I or formula II, Y is ethylene.
- [0313]** In certain embodiments of formula I or formula II, Y is -C(CH₃)₂-.
- [0314]** In certain embodiments of formula I or formula II, Y is -CH₂-.
- [0315]** In certain embodiments of formula I or formula II, Y is -CH(CH₃)-.
- [0316]** In certain embodiments of formula I or formula II, Y is -CH₂-C(CH₃)₂-.
- 10 **[0317]** In certain embodiments of formula I or formula II, Y is -C(CH₃)₂-CH₂-.
- [0318]** In certain embodiments of formula I or formula II, R^d is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.
- [0319]** In certain embodiments of formula I or formula II, R^d is C₁₋₆alkyl.
- [0320]** In certain embodiments of formula I or formula II, R^d is C₁₋₆alkoxy.
- [0321]** In certain embodiments of formula I or formula II, R^d is amino.
- 15 **[0322]** In certain embodiments of formula I or formula II, R^d is halo-C₁₋₆alkyl.
- [0323]** In certain embodiments of formula I or formula II, R^d is hydroxy-C₁₋₆alkyl.
- [0324]** In certain embodiments of formula I or formula II, R^d is C₁₋₆alkoxy-C₁₋₆alkyl.
- [0325]** In certain embodiments of formula I or formula II, R^d is cyano-C₁₋₆alkyl.
- [0326]** In certain embodiments of formula I or formula II, R^d is C₁₋₆alkylsulfonylC₁₋₆alkyl.
- 20 **[0327]** In certain embodiments of formula I or formula II, R^d is amino-C₁₋₆alkyl.
- [0328]** In certain embodiments of formula I or formula II, R^d is C₃₋₆cycloalkyl optionally substituted one or more times with R⁶.
- [0329]** In certain embodiments of formula I or formula II, R^d is C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.
- 25 **[0330]** In certain embodiments of formula I or formula II, R^d is heterocyclyl optionally substituted one or more times with R⁷.
- [0331]** In certain embodiments of formula I or formula II, R^d is heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷.
- [0332]** 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.
- 30 **[0333]** In certain embodiments of formula I or formula II, R^d is 1-methyl-cyclopropyl.
- [0334]** In certain embodiments of formula I or formula II, R^d is methylamino.
- [0335]** In certain embodiments of formula I or formula II, R^d is dimethylamino.
- [0336]** In certain embodiments of formula I or formula II, R^d is pyrrolidin-1-yl.
- 35 **[0337]** In certain embodiments of formula I or formula II, R^d is methoxy.
- [0338]** In certain embodiments of formula I or formula II, R^d is cyclopropyl-methyl.
- [0339]** In certain embodiments of formula I or formula II, R^d is ethyl.
- [0340]** In certain embodiments of formula I or formula II, R^d is 2,2,2-trifluoro-ethyl.
- [0341]** In certain embodiments of formula I or formula II, R^d is tert-butyl.
- 40 **[0342]** In certain embodiments of formula I or formula II, R^d is isopropyl.
- [0343]** In embodiments of formula I or formula II wherein R^d is heterocyclyl or heterocyclyl-C₁₋₆alkyl, such heterocyclyl may be piperidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, pyrrolidinyl, azetidyl, tetrahydrofuranyl or oxetanyl, each optionally substituted one or more times, or one or two times, with R⁷ as defined herein.
- [0344]** In embodiments of formula I or formula II wherein R^d is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidyl, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R⁷.
- 45 **[0345]** In embodiments of formula I or formula II wherein R^d is heterocyclyl-C₁₋₆alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidyl, [1,3]dioxolanyl or tetrahydrothiopyranyl, each being unsubstituted or substituted one or more times with R⁷.
- 50 **[0346]** In certain embodiments of formula I or formula II, R⁴ is: hydrogen; C₁₋₆alkyl; halo; halo-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl; or -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.
- [0347]** In certain embodiments of formula I or formula II, R⁴ is: C₁₋₆alkyl; halo; halo-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl; or -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.
- 55 **[0348]** In certain embodiments of formula I or formula II, R⁴ is: hydrogen; C₁₋₆alkyl; halo; C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with

C₁₋₆alkyl; or -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.

[0349] In certain embodiments of formula I or formula II, R⁴ is: hydrogen; C₁₋₆alkyl; halo; or C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl.

[0350] In certain embodiments of formula I or formula II, R⁴ is hydrogen or C₁₋₆alkyl.

[0351] In certain embodiments of formula I or formula II, R⁴ is hydrogen.

[0352] In certain embodiments of formula I or formula II, R⁴ is C₁₋₆alkyl.

[0353] In certain embodiments of formula I or formula II, R⁴ is halo.

[0354] In certain embodiments of formula I or formula II, R⁴ is cyano.

[0355] In certain embodiments of formula I or formula II, R⁴ is halo-C₁₋₆alkyl.

[0356] In certain embodiments of formula I or formula II, R⁴ is C₁₋₆alkoxy-C₁₋₆alkyl.

[0357] In certain embodiments of formula I or formula II, R⁴ is hydroxy-C₁₋₆alkyl.

[0358] In certain embodiments of formula I or formula II, R⁴ is C₃₋₆cycloalkyl optionally substituted with C₁₋₆alkyl.

[0359] In certain embodiments of formula I or formula II, R⁴ is hydrogen or methyl.

[0360] In certain embodiments of formula I or formula II, R⁴ is C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted with C₁₋₆alkyl.

[0361] In certain embodiments of formula I or formula II, R⁴ is -C(O)-R^c wherein R^c is C₁₋₆alkyl, C₁₋₆alkoxy, amino, or heterocyclyl.

[0362] In certain embodiments of formula I or formula II, R⁴ is -C(O)-R^c wherein R^c is heterocyclyl.

[0363] In embodiments of formula I or formula II wherein R^c is heterocyclyl, such heterocyclyl may be pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl.

[0364] In embodiments of formula I or formula II wherein R^c is heterocyclyl, such heterocyclyl may be piperidinyl, piperazinyl or morpholinyl.

[0365] In certain embodiments of formula I or formula II, R⁴ is: hydrogen; methyl; isopropyl; cyclopropyl; chloro; or morpholin-4-yl-carbonyl.

[0366] In certain embodiments of formula I or formula II, R⁴ is: hydrogen; methyl; isopropyl; cyclopropyl; or chloro.

[0367] In certain embodiments of formula I or formula II, R⁴ is hydrogen.

[0368] In certain embodiments of formula I or formula II, R⁴ is methyl.

[0369] In certain embodiments of formula I or formula II, R⁴ is isopropyl.

[0370] In certain embodiments of formula I or formula II, R⁴ is cyclopropyl.

[0371] In certain embodiments of formula I or formula II, R⁴ is chloro.

[0372] In certain embodiments of formula I or formula II, R⁴ is morpholin-4-yl-carbonyl.

[0373] In certain embodiments of formula I or formula II, R⁴ is 2-fluoro-ethyl.

[0374] In certain embodiments of formula I or formula II, R⁴ is C₃₋₆cycloalkyl optionally substituted one or more times, or one or two times, with R⁶.

[0375] In certain embodiments of formula I or formula II, R⁴ is C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times, or one or two times, with R⁶.

[0376] In certain embodiments of formula I or formula II, R⁴ is -Y-C(O)-R^d.

[0377] In certain embodiments of formula I or formula II, or R³ and R⁴ 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.

[0378] In certain embodiments of formula I or formula II, R⁵ is hydrogen.

[0379] In certain embodiments of formula I or formula II, R⁵ is C₁₋₆alkyl.

[0380] In certain embodiments of formula I or formula II, R⁵ is methyl.

[0381] In certain embodiments of formula I or formula II, each R⁶ is independently C₁₋₆alkyl; halo-C₁₋₆alkyl; C₁₋₆alkoxy; cyano; or halo.

[0382] In certain embodiments of formula I or formula II, R⁶ is C₁₋₆alkyl; halo-C₁₋₆alkyl; C₁₋₆alkoxy; or halo.

[0383] In certain embodiments of formula I or formula II, R⁶ is C₁₋₆alkyl; halo-C₁₋₆alkyl; or halo.

[0384] In certain embodiments of formula I or formula II, R⁶ is C₁₋₆alkyl.

[0385] In certain embodiments of formula I or formula II, R⁶ is halo-C₁₋₆alkyl. In certain embodiments of formula I or formula II, R⁶ is C₁₋₆alkoxy.

[0386] In certain embodiments of formula I or formula II, R⁶ is cyano.

[0387] In certain embodiments of formula I or formula II, R⁶ is halo.

[0388] In certain embodiments of formula I or formula II, R⁶ is Y-C(O)-R^d.

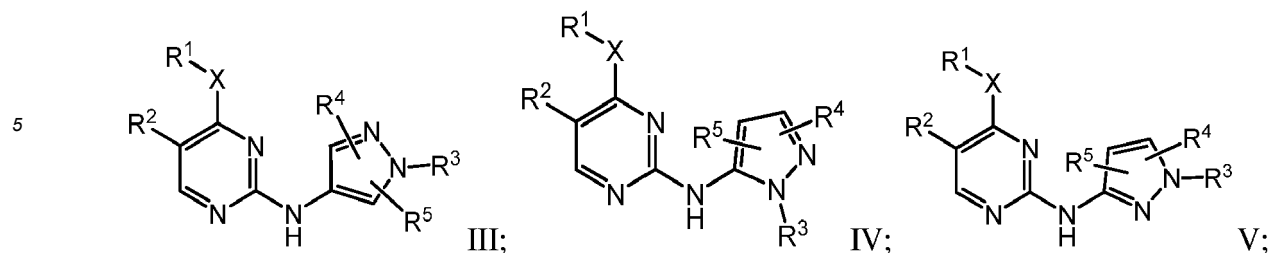
[0389] In certain embodiments of formula I or formula II, R⁶ is oxo.

[0390] In certain embodiments of formula I or formula II, each R⁷ is independently C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; C₁₋₆alkylsulfonyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; heterocyclyl; or C₃₋₆cycloalkylsulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.

[0391] In certain embodiments of formula I or formula II, R⁷ is C₁₋₆alkyl.

[0392] In certain embodiments of formula I or formula II, R⁷ is halo-C₁₋₆alkyl.

- [0393]** In certain embodiments of formula I or formula II, R⁷ is halo.
- [0394]** In certain embodiments of formula I or formula II, R⁷ is C₁₋₆alkylsulfonyl.
- [0395]** In certain embodiments of formula I or formula II, R⁷ is C₁₋₆alkoxy-C₁₋₆alkyl.
- 5 **[0396]** In certain embodiments of formula I or formula II, R⁷ is cyano.
- [0397]** In certain embodiments of formula I or formula II, R⁷ is -Y-C(O)-R^d.
- [0398]** In certain embodiments of formula I or formula II, R⁷ is heterocyclyl.
- [0399]** In certain embodiments of formula I or formula II, R⁷ is C₃₋₆cycloalkylsulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.
- 10 **[0400]** In certain embodiments of formula I or formula II, R⁷ is oxo.
- [0401]** In certain embodiments of formula I or formula II, R⁷ is C₁₋₆alkoxy.
- [0402]** In certain embodiments of formula I or formula II, R⁷ is heterocyclyl-C₁₋₆alkyl.
- [0403]** In certain embodiments of formula I or formula II, R⁷ is C₃₋₆cycloalkyl.
- [0404]** In certain embodiments of formula I or formula II, R⁷ is C₃₋₆cycloalkyl-C₁₋₆alkyl.
- 15 **[0405]** In embodiments of formula I or formula II wherein R⁷ is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidiny, [1,3]dioxolanyl or tetrahydrothiopyranyl.
- [0406]** In embodiments of formula I or formula II wherein R⁷ is heterocyclyl-C₁₋₆alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidiny, [1,3]dioxolanyl or tetrahydrothiopyranyl.
- 20 **[0407]** In certain embodiments of formula I or formula II, each R⁸ is independently oxo; C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; C₁₋₆alkoxy; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶, C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶, or C₃₋₆cycloalkyl-sulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.
- [0408]** In certain embodiments of formula I or formula II, R⁸ is oxo. In certain embodiments of formula I or formula II, R⁷ is C₁₋₆alkyl.
- 25 **[0409]** In certain embodiments of formula I or formula II, R⁷ is halo-C₁₋₆alkyl
- [0410]** In certain embodiments of formula I or formula II, R⁷ is halo.
- [0411]** In certain embodiments of formula I or formula II, R⁷ is C₁₋₆alkoxy.
- [0412]** In certain embodiments of formula I or formula II, R⁷ is C₁₋₆alkoxy-C₁₋₆alkyl.
- 30 **[0413]** In certain embodiments of formula I or formula II, R⁷ is cyano.
- [0414]** In certain embodiments of formula I or formula II, R⁷ is heterocyclyl.
- [0415]** In certain embodiments of formula I or formula II, R⁷ is -Y-C(O)-R^d.
- [0416]** In certain embodiments of formula I or formula II, R⁷ is C₃₋₆cycloalkyl optionally substituted one or more times with R⁶.
- 35 **[0417]** In certain embodiments of formula I or formula II, R⁷ is C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.
- [0418]** In certain embodiments of formula I or formula II, R⁷ is C₃₋₆cycloalkyl-sulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶.
- [0419]** In certain embodiments of formula I or formula II, R⁸ is oxo.
- 40 **[0420]** In certain embodiments of formula I or formula II, R⁸ is C₁₋₆alkyl.
- [0421]** In certain embodiments of formula I or formula II, R⁸ is halo-C₁₋₆alkyl.
- [0422]** In certain embodiments of formula I or formula II, R⁸ is halo.
- [0423]** In certain embodiments of formula I or formula II, R⁸ is C₁₋₆alkyl-sulfonyl.
- [0424]** In certain embodiments of formula I or formula II, R⁸ is C₁₋₆alkoxy.
- 45 **[0425]** In certain embodiments of formula I or formula II, R⁸ is C₁₋₆alkoxy-C₁₋₆alkyl.
- [0426]** In certain embodiments of formula I or formula II, R⁸ is cyano; heterocyclyl.
- [0427]** In certain embodiments of formula I or formula II, R⁸ is heterocyclyl-C₁₋₆alkyl.
- [0428]** In certain embodiments of formula I or formula II, R⁸ is -Y-C(O)-R^d.
- [0429]** In certain embodiments of formula I or formula II, R⁸ is C₃₋₆cycloalkyl.
- 50 **[0430]** In certain embodiments of formula I or formula II, R⁸ is C₃₋₆cycloalkyl-C₁₋₆alkyl, C₃₋₆cycloalkyl-sulfonyl.
- [0431]** In embodiments of formula I or formula II wherein R⁸ is heterocyclyl, such heterocyclyl moiety may be piperidinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidiny, [1,3]dioxolanyl or tetrahydrothiopyranyl.
- [0432]** In embodiments of formula I or formula II wherein R⁸ is heterocyclyl-C₁₋₆alkyl, such heterocyclyl moiety may be piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, pyrrolidinyl, oxetanyl, tetrahydropyranyl, tetrahydrofuranyl, azetidiny, [1,3]dioxolanyl or tetrahydrothiopyranyl.
- 55 **[0433]** In certain embodiments of the invention, compounds of formulas III, IV and V are provided:



wherein X, R¹, R, R², R³, R⁴ and R⁵ are as defined herein.

[0434] In certain embodiments of the invention, the subject compounds are of formula III.

[0435] In certain embodiments of the invention, the subject compounds are of formula IV.

[0436] In certain embodiments of the invention, the subject compounds are of formula V.

15 **[0437]** Where any of R¹, R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, R^a, R^b, R^c and R^d is alkyl or contains an alkyl moiety, such alkyl can be lower alkyl, i.e. C₁-C₆alkyl, and in many embodiments may be C₁-C₄alkyl.

[0438] In a certain embodiment, the invention relates to the compound as described herein, which is selected from the group consisting of

- 20 N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N⁴-methyl-N²-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 25 N⁴-methyl-N²-(1-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 5-chloro-N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
 N⁴-methyl-N²-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 30 N⁴-methyl-N²-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N²-(1,3-dimethyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 35 N⁴-methyl-5-(trifluoromethyl)-N²-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
 40 N²-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 5-Chloro-N-(1,3-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
 N⁴-methyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 45 N²-(5-chloro-1-methyl-1H-pyrazol-4-yl)-N⁴-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,
 50 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,
 55 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,

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N²-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
N²-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
5 5-Chloro-N-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
5-Chloro-N⁴-methyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
N²-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
10 5-Chloro-N-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
5-Chloro-N²-(1,3-dimethyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
15 5-Chloro-N²-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
N⁴-methyl-N²-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
N⁴-methyl-N²-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
20 N²-(2-Ethyl-2H-pyrazol-3-yl)-5-fluoro-N⁴-methyl-pyrimidine-2,4-diamine,
5-Fluoro-N⁴-methyl-N²-(2-methyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,
25 5-Fluoro-N⁴-methyl-N⁴-(2-propyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,
N²-(2,5-Dimethyl-2H-pyrazol-3-yl)-5-fluoro-N⁴-methyl-pyrimidine-2,4-diamine,
N²-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
30 5-Chloro-N-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,
N²-(3-Cyclopropyl-1-methyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
35 5-Chloro-N-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,
5-Chloro-N²-(5-isopropyl-2-methyl-2H-pyrazol-3-yl)-N⁴-methyl-pyrimidine-2,4-diamine,
5-Chloro-4-methoxy-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine,
40 5-Chloro-N⁴-methyl-N²-(1,3,5-trimethyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine,
5-Chloro-N²-(5-cyclopropyl-2-methyl-2H-pyrazol-3-yl)-N⁴-methyl-pyrimidine-2,4-diamine,
45 N⁴-Methyl-N²-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine,
N²-(1-isopropyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
5-Chloro-N-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
50 5-Chloro-N²-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
N²-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
55 5-Chloro-N²-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
5-chloro-N²-(1-isopropyl-1H-pyrazol-5-yl)-N⁴-methylpyrimidine-2,4-diamine,

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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,
5 N²-(1-ethyl-1H-pyrazol-3-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
5-chloro-4-methoxy-N-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine,
10 N²-(1-isopropyl-1H-pyrazol-3-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
N⁴-methyl-N²-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
N²-(1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-di-
15 amine,
5-chloro-4-methoxy-N-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
N⁴-ethyl-N²-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
20 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)meth-
anone,
25 (4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)meth-
anone,
4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)benzotrile,
30 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,
35 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,
40 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,
45 (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,
50 (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,
55 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]-benzotrile,

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- N²-(5-Methoxy-1-methyl-1H-pyrazol-4-yl)-N⁴-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 (5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoro-ethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-amine,
N²-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-trifluoromethyl-pyrimidine-
2,4-diamine,
10 N²-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-trifluoromethyl-pyrimidine-
2,4-diamine,
5-Bromo-N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
15 N²-(1,3-Dimethyl-1H-pyrazol-4-yl)-5-iodo-N⁴-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,
20 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,
25 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,
30 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,
35 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,
40 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,
45 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,
50 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,
55 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,

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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
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,
10
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,
15
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,
20
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,
25
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,
30
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,
35
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,
40
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,
45
N4-methyl-N2-(5-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
50
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,
55
cyclopropyl(4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanone,

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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,
5 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,
10 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,
15 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,
20 4-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzotrile,
4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzotrile,
25 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,
30 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,
35 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,
40 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,
45 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-di-
50 amine,
4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)benzotrile,
N4-ethyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
55 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,

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- N2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
- 5 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,
- 10 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,
- 15 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,
- 20 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,
- 25 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,
- 30 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,
- 35 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,
- 40 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,
- 45 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,
- 50 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,
- 55 N2-(1-(2,6-dimethyltetrahydro-2H-pyran-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,

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(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,
5 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,
10 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,
15 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,
20 (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,
25 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-di-
amine,
30 (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,
35 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,
40 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,
45 (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,
50 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,
55 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,

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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,

5 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,

10 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,

15 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,

20 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,

25 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,

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

35 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,

40 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,

45 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,

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

55 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,

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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-di-
amine,
5
N2-(1-(1-ethyl-3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-di-
amine,
N2-(5-(dimethylamino)-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
10
2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-1-ol,
N2-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
15
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,
20
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,
25
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,
30
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,
35
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,
40
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-di-
amine,
45
4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-benzotrile,
N4-Ethyl-N2-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,
50
1-{14-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-piperidin-1-yl}-2-methyl-pro-
pan-1-one,
1-[4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-1-yl]-2-methyl-pro-
pan-1-one,
55
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,

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N2-[1-(2,6-Dimethyl-tetrahydro-pyran-4-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine,

5 N2-[1-(1,1-Dioxo-hexahydro-1 β -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,

10 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,

15 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,

20 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,

25 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,

30 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,

35 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,

40 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,

45 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,

50 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,

55 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,

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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,
5 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,
10 N2-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-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,
15 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-
20 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,
25 N4-Ethyl-N2-[5-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-di-
amine,
N4-Ethyl-N2-[3-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-di-
30 amine,
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,
35 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,
40 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,
45 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,
50 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,
55 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,

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

10 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,

15 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,

20 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,

25 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,

30 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,

35 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,

40 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,

45 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,

50 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,

55 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,

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- 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,
- 5 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,
- 10 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,
- 15 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,
- 20 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,
- 25 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,
- 30 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,
- 35 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,
- 40 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,
- 45 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,
- 50 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,
- 55 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,

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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,
5 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,
10 2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile,
2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) pyrimidine-5-carbonitrile,
15 2-(1-(4,4-difluorocyclohexyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino) 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,
20 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,
25 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,
30 2-[1-(3,5-Difluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,
2-[1-(4,4-Difluoro-cyclohexyl)-3-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,
35 (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,
40 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,
45 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,
50 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,
55 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,

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

5

(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,

10

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,

15

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,

20

(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,

25

(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,

30

(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,

35

2-(4-(5-chloro-4-(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,

40

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,

45

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,

50

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,

55

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

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- N-(cyclopropylmethyl)-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
- 5 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,
- 10 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,
- 15 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,
- 20 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,
- 25 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-methylpropionitrile,
- 30 (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,
- 35 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,
- 40 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,
- 45 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,
- 50 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,
- 55 2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methylpropionitrile,
- 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.

[0439] In a certain embodiment, the invention relates to the compound as described herein for use as medicament.

[0440] 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.

[0441] 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.

[0442] In a certain embodiment, the invention relates to a composition comprising:

(a) a pharmaceutically acceptable carrier; and

(b) a compound as described herein.

[0443] In a certain embodiment, the invention relates to a compound as described herein for use for treating Parkinson's disease, comprising administering to a subject in need thereof an effective amount of a compound as described herein.

[0444] The invention also provides a compound as described herein for use for treating a disease or condition mediated by or otherwise associated with the LRRK2 receptor, comprising administering to a subject in need thereof an effective amount of a compound of the invention.

[0445] The disease may be a neurodegenerative disease such as Parkinson's disease, Huntington's disease or Lewie body dementia.

[0446] The disease may be a CNS disorder such as Alzheimer's disease or L-Dopa induced dyskinesia.

[0447] 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.

[0448] The disease may be an inflammatory disease such as leprosy, Crohn's disease, amyotrophic lateral sclerosis, rheumatoid arthritis, or ankylosing spondylitis.

[0449] The invention also provides a compound as described herein for use for enhancing cognitive memory, comprising administering to a subject in need thereof an effective amount of a compound of the invention.

[0450] Representative compounds in accordance with the methods of the invention are shown in the experimental examples below.

Synthesis

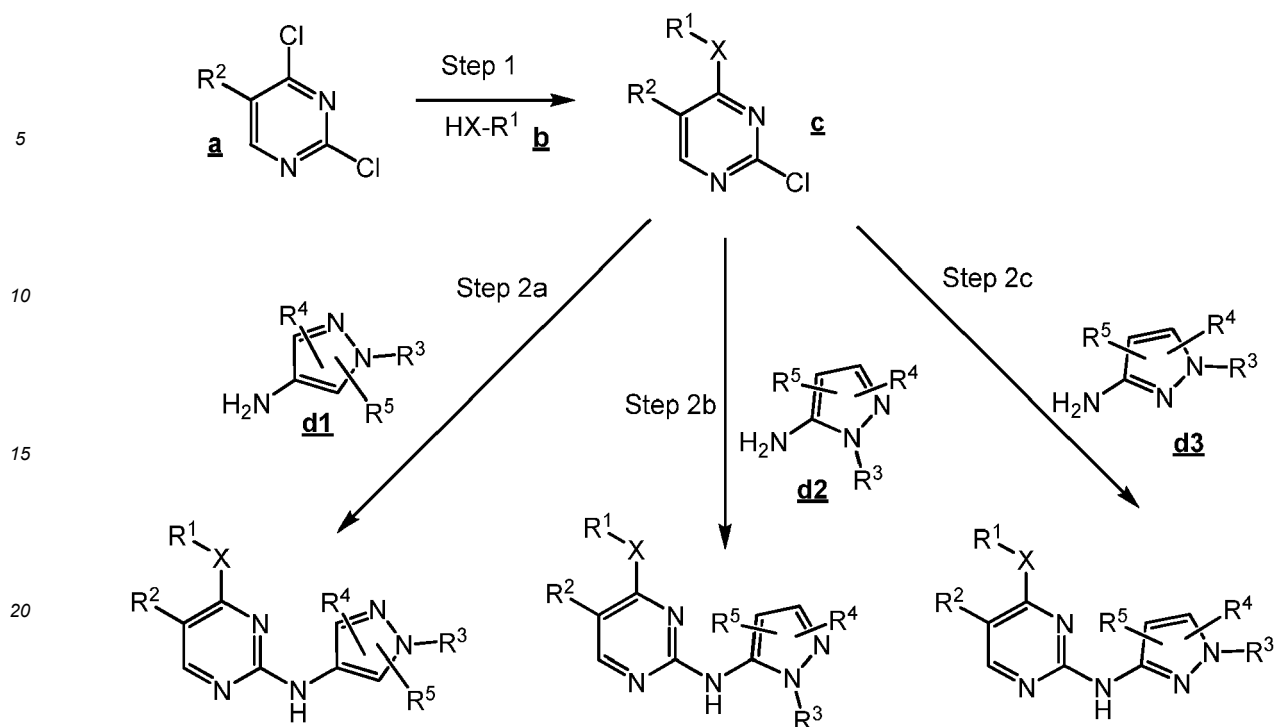
[0451] Compounds of the present invention can be made by a variety of methods depicted in the illustrative synthetic reaction schemes shown and described below.

[0452] 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.

[0453] 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.

[0454] 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.

[0455] Scheme A below illustrates one synthetic procedure usable to prepare specific compounds of formula I, wherein X, R¹, R², R³, R⁴ and R⁵ are as defined herein.



SCHEME A

[0456] 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.

[0457] 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.

[0458] 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

[0459] 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.

[0460] 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.

[0461] 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.

[0462] 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.

[0463] 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.

[0464] 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.

[0465] 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.

[0466] 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 contain 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.

[0467] 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.

[0468] 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.

[0469] 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.

[0470] 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 polyvinylpyrrolidone (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.

[0471] 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.

[0472] 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.

[0473] 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

[0474] 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 enhancement of cognitive memory generally in subjects in need thereof.

Examples

[0475] 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.

[0476] 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

[0477]

AcOH Acetic acid

AIBN 2,2'-Azobis(2-methylpropionitrile)

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	Atm.	Atmosphere
	(BOC) ₂ O	di- <i>tert</i> -Butyl dicarbonate
5	dba	tris(dibenzylideneacetone)
	DCM	Dichloromethane/Methylene chloride
	DIAD	Diisopropyl azodicarboxylate
10	DIPEA	Diisopropylethylamine
	DMAP	4-Dimethylaminopyridine
15	DME	1,2-Dimethoxyethane
	DMF	<i>N,N</i> -Dimethylformamide
	DMSO	Dimethyl sulfoxide
20	DPPF	1,1'-Bis(diphenylphosphino)ferrocene
	Et ₂ O	Diethyl ether
25	EtOH	Ethanol/Ethyl alcohol
	EtOAc	Ethyl acetate
	HATU	2-(1H-7-Azabenzotriazol-1-yl)-1,1,3,3-tetramethyl uronium hexafluorophosphate Methanaminium
30	HBTU	O-Benzotriazol-1-yl- <i>N,N,N',N'</i> -tetramethyluronium hexafluorophosphate
	HOBT	1-Hydroxybenzotriazole
35	HPLC	High pressure liquid chromatography
	RP HPLC	Reverse phase high pressure liquid chromatography
	i-PrOH	Isopropanol/isopropyl alcohol
40	LCMS	Liquid Chromatograph/Mass Spectroscopy
	MeOH	Methanol/Methyl alcohol
45	MW	Microwaves
	NBS	<i>N</i> -Bromosuccinimide
	NMP	1-Methyl-2-pyrrolidinone
50	PSI	Pound per square inch
	RT	Room temperature
55	SFC	Supercritical fluid chromatography
	TBDMS	<i>tert</i> -Butyldimethylsilyl

TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
5 TLC	Thin layer chromatography
Xphos	2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl

Liquid Chromatography-Mass Spectrometry Method A

[0478] 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 μ m, 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

[0479] LC-MS was performed on a Waters 2795 Alliance HT HPLC with Waters 2996 Diode Array Detector coupled to a Micromass ZQ, single quadrupole mass spectrometer using a Phenomenex Luna C18 (2) column (5 μ m, 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

[0480] LC-MS was performed on a Waters 2795 Alliance HT HPLC with Waters 2996 Diode Array Detector coupled to a Micromass ZQ, single quadrupole mass spectrometer using a Waters Xterra MS C18 column (5 μ m, 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

[0481] ^1H 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 60A 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

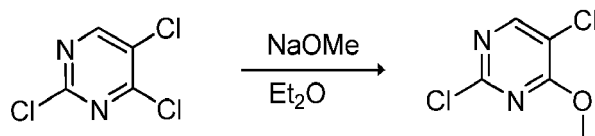
[0482] Where the preparation of starting materials is not described, these are commercially available, known in the literature, or readily obtainable by those skilled in the art using standard procedures. Where it is stated that compounds were prepared analogously to earlier examples or intermediates, 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.

[0483] Compounds made in the following examples are summarized in the Tables below, which shows affinity values for LRRK2 (K_i , 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

[0484]

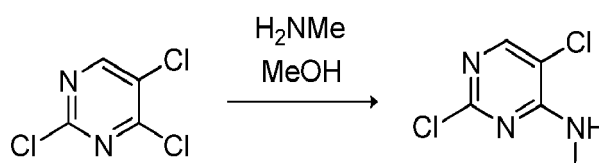
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[0485] To a 250 mL round bottom flask equipped with a stir bar was added 2,4,5-trichloropyrimidine (1 g), and diethyl ether (15 mL). The mixture was cooled to 0°C in an ice bath and then 1 equivalent of sodium methoxide in methanol (prepared from reacting 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. ¹H-NMR (DMSO): δ 8.61 (s, 1H), 4.05 (s, 3H).

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Intermediate 2 2,5-Dichloro-N-methylpyrimidin-4-amine

[0486]

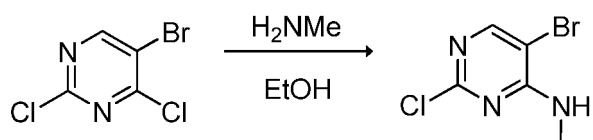


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[0487] To a cooled (0 °C) solution of 2,4,5-trichloropyrimidine (2.0 g, 11 mmol) in methanol (30 mL) was added dropwise a 2 M solution of methylamine in methanol (6.3 mL). The reaction was allowed to warm to room temperature and stirred overnight. The reaction was then concentrated and redissolved in DCM. The solution was washed with sat. NaHCO₃, brine, dried over Na₂SO₄, 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%). ¹H-NMR (DMSO): δ 8.13 (s, 1H), 7.89 (s, 1H), 2.86 (d, J= 4.5, 3H).

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Intermediate 3 5-Bromo-2-chloro-N-methylpyrimidin-4-amine

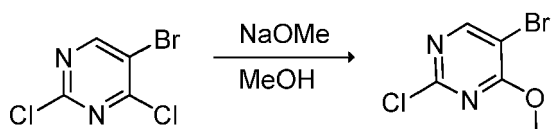
35
[0488]



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[0489] 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%). ¹H-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

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[0490]



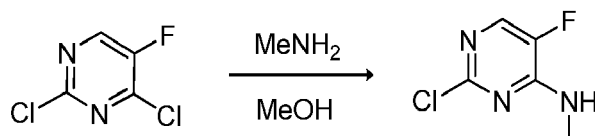
[0491] To a cooled (-78 °C) solution of 5-bromo-2,4-dichloropyrimidine (1.7 g, 7.3 mmol) in THF (30mL) was added

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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 Na₂SO₄, filtered and concentrated to give 5-bromo-2-chloro-4-methoxypyrimidine (1.25 g, 76%). ¹H-NMR (CDCl₃): δ 8.43 (s, 1H), 4.10 (s, 3H).

Intermediate 5 2-chloro-5-fluoro-N-methylpyrimidin-4-amine

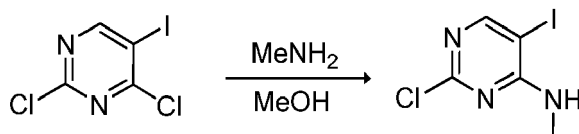
[0492]



[0493] 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

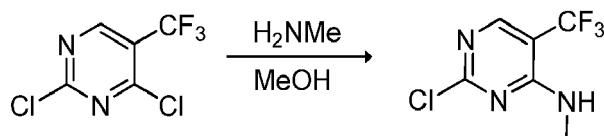
[0494]



[0495] 2-chloro-5-iodo-N-methylpyrimidin-4-amine was prepared following the procedure of Intermediate 5 but using 2,4-dichloro-5-iodopyrimidine. ¹H-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

[0496]

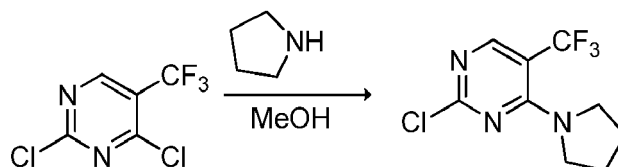


[0497] To a cooled (-10 °C) solution of 2,4-dichloro-5-trifluoromethylpyrimidine (20 g, 0.089 mol) in methanol (100 mL) was added triethylamine (12.5 mL, 0.089 mol) and a 2 M solution of methylamine in methanol (45 mL). The reaction was allowed to warm to room temperature and stirred overnight. The reaction was then concentrated and re-dissolved in ethyl acetate. The solution was washed with sat. NaHCO₃, brine, dried over MgSO₄, 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%). ¹H-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

[0498]

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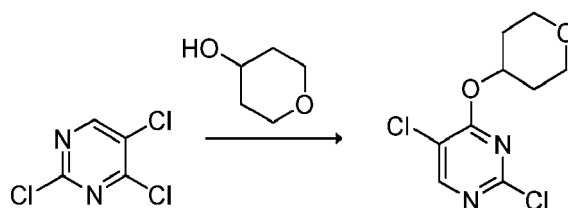
[0499] 2-Chloro-4-(pyrrolidin-1-yl)-5-(trifluoromethyl)pyrimidine was prepared according to the procedure described for intermediate 7 using pyrrolidine.

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Intermediate 9 2,5-Dichloro-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidine

[0500]

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[0501] 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 Na₂SO₄, filtered and concentrated. The crude product was purified by column chromatography (0-30% EtOAc in heptane) to give 2,5-dichloro-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidine. ¹H-NMR (CDCl₃): 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).

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[0502] Additional intermediates prepared using similar methods as described above are listed in Table 1 below:

Table 1

35	10	2-chloro-N-ethyl-5-(trifluoromethyl)pyrimidin-4-amine	
40	11	2-chloro-N-(2,2-difluoroethyl)-5-(trifluoromethyl)pyrimidin-4-amine	
45	12	2-chloro-N-((tetrahydro-2H-pyran-4-yl)methyl)-5-(trifluoromethyl)pyrimidin-4-amine	

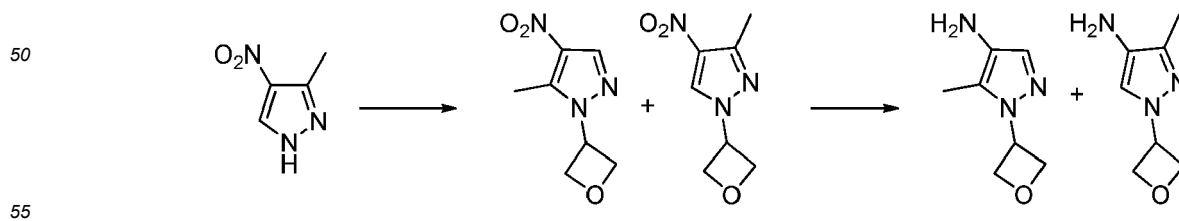
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(continued)

5	13	2,5-dichloro-4-ethoxypyrimidine	
10	14	2-chloro-4-(2,2,2-trifluoroethoxy)-5-(trifluoromethyl)pyrimidine	
15	15	2-chloro-4-(2,2-difluoroethoxy)-5-(trifluoromethyl)pyrimidine	
20	16	2,5-dichloro-4-(2,2-difluoroethoxy)pyrimidine	
25	17	2,5-dichloro-4-(oxetan-3-yloxy)pyrimidine	
30	18	2-chloro-N-cyclopropyl-5-(trifluoromethyl)pyrimidin-4-amine	

45 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

[0503]



Step 1 5-Methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole and 3-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole

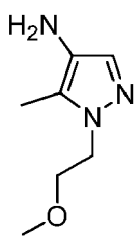
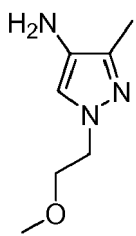
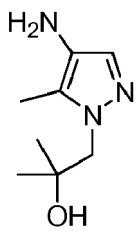
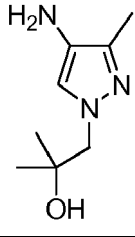
[0504] To a mixture of 3-methyl-4-nitro-pyrazole (0.80 g, 6.3 mmol), cesium carbonate (4.1 g, 12 mmol) in DMF (10 mL) was added 3-iodo-oxetane (3.47 g, 19 mmol). The mixture was stirred at 100 °C for 3 h. The reaction was diluted with water and extracted with ethyl acetate (3x). The combined extracts were washed with brine, dried over Na₂SO₄, filtered and concentrated. The crude product was purified by column chromatography (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

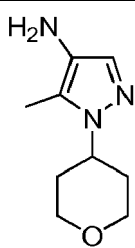
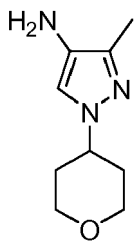
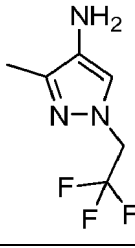
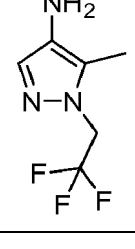
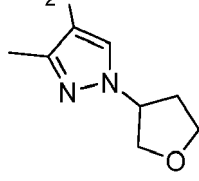
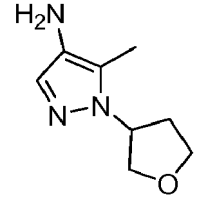
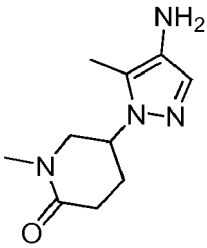
[0505] To a solution of 5-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole and 3-methyl-4-nitro-1-(oxetan-3-yl)-1H-pyrazole (0.137 g, 0.75 mmol) in ethanol (2 mL) was added Pd-C (10 wt%, 0.10 g). The mixture was stirred under a hydrogen atmosphere for 24 hours. The reaction was filtered through Celite® and 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.

[0506] Additional intermediates made using the above procedure are shown in Table 2 below.

Table 2

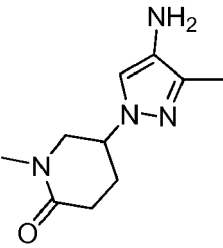
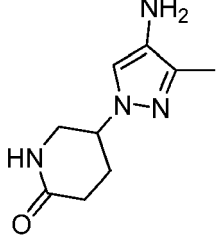
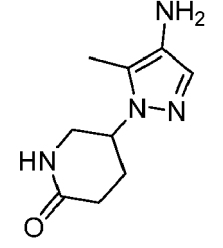
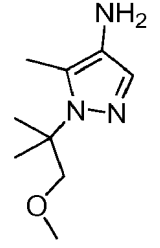
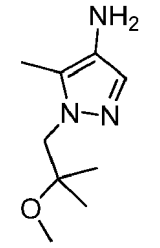
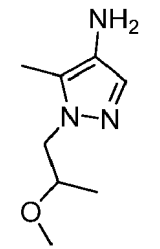
21	1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-amine	
22	1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-amine	
23	1-(4-Amino-5-methyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol	
24	1-(4-amino-3-methyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol	

(continued)

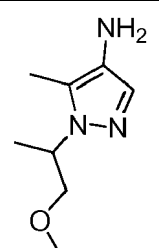
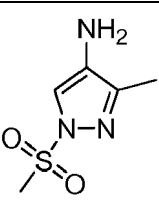
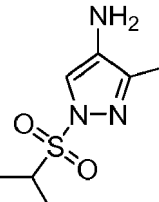
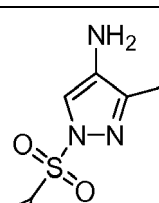
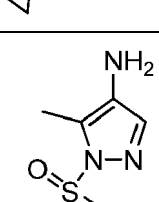
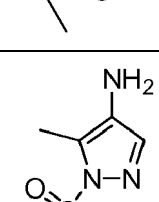
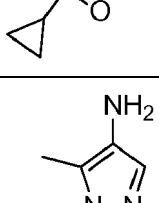
5	25	5-Methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-amine	
10			
15	26	3-Methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-amine	
20			
25	27	3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-amine	
30			
35	28	5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-amine	
40			
45	29	3-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-amine	
50			
55	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	

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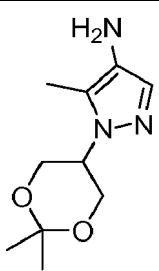
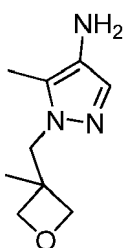
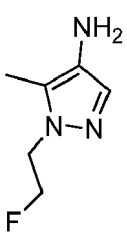
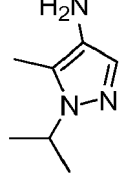
(continued)

5 32	5-(4-amino-3-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one	
10 33	5-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-2-one	
15 20 34	5-(4-amino-5-methyl-1H-pyrazol-1-yl)piperidin-2-one	
25 30 35 35	1-(1-methoxy-2-methylpropan-2-yl)-5-methyl-1H-pyrazol-4-amine	
35 40 45 36	1-(2-methoxy-2-methylpropyl)-5-methyl-1H-pyrazol-4-amine	
45 50 55 37	1-(2-methoxypropyl)-5-methyl-1H-pyrazol-4-amine	

(continued)

5			
10	38	1-(1-methoxypropan-2-yl)-5-methyl-1H-pyrazol-4-amine	
15	39	3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-amine	
20	40	1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-amine	
25	41	1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-amine	
30	42	1-(isopropylsulfonyl)-5-methyl-1H-pyrazol-4-amine	
35	43	1-(cyclopropylsulfonyl)-5-methyl-1H-pyrazol-4-amine	
40	44	1-(sec-butylsulfonyl)-5-methyl-1H-pyrazol-4-amine	
45			
50			
55			

(continued)

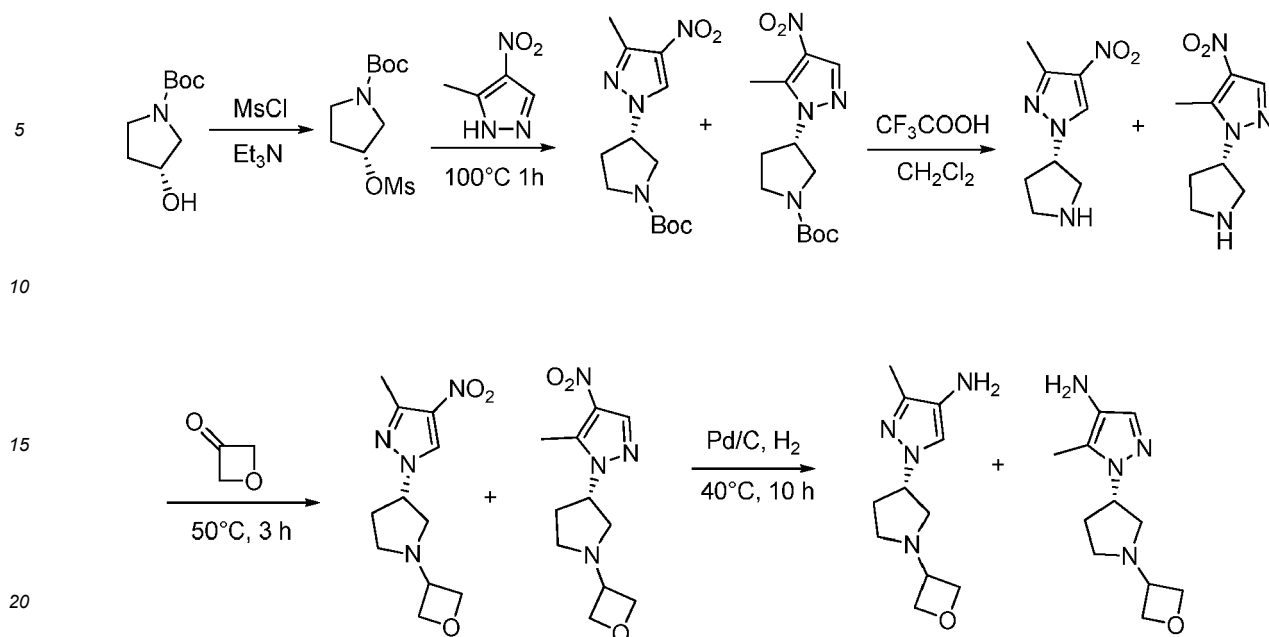
5	45	1-(2,2-dimethyl-1,3-dioxan-5-yl)-5-methyl-1H-pyrazol-4-amine	
10			
15	46	5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-amine	
20			
25	47	1-(2-fluoroethyl)-5-methyl-1H-pyrazol-4-amine	
30			
35	48	1-isopropyl-5-methyl-1H-pyrazol-4-amine	

Intermediate 49 5-Chloro-1-methyl-1H-pyrazol-4-amine**[0507]**

50 **[0508]** 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 Na₂SO₄, 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. ¹H-NMR (CDCl₃): δ 7.90 (s, 1H), 3.88 (s, 2H), 1.55 (s, 3H).

55 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

[0509]



Step 1: (R)-tert-butyl 3-(methylsulfonyloxy)pyrrolidine-1-carboxylate

[0510] (R)-tert-butyl 3-hydroxypyrrolidine-1-carboxylate (5.0 g, 26.7 mmol) and Et₃N (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 NaHCO₃ (30 mL) and H₂O (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

[0511] 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), K₂CO₃ (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 K₂CO₃ 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.

[0512] 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

[0513] 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). CF₃COOH (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

[0514] 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-amine and (S)-5-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-amine

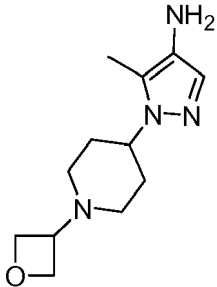
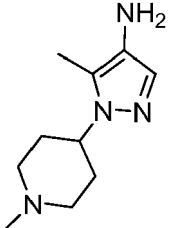
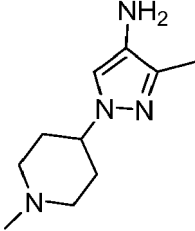
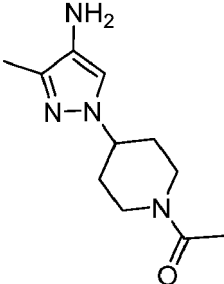
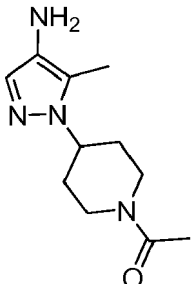
[0515] To the mixture of (S)-3-methyl-4-nitro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazole and (S)-5-methyl-4-nitro-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazole (500 mg, 1.98 mmol), and Zn (506 mg, 7.94 mmol) in methanol (20 mL) was added THF (20 mL) and NH_4Cl (841 mg, 15.9 mmol). The mixture was 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.

[0516] Additional intermediates made using the above procedure are shown in Table 3 below.

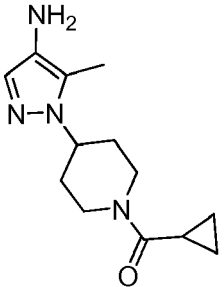
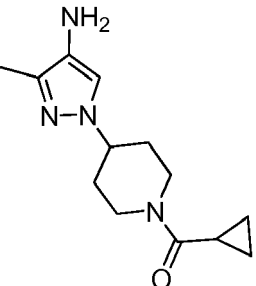
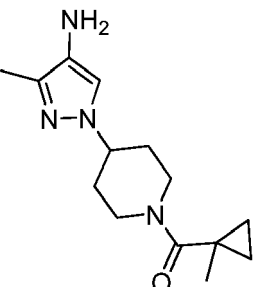
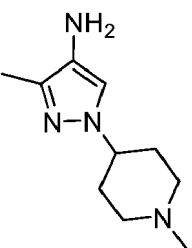
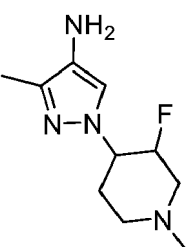
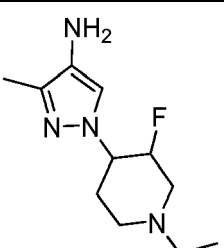
Table 3

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	

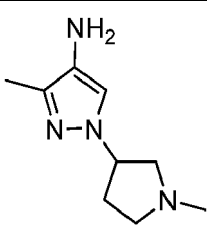
(continued)

5			
10	55	5-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-amine	
15	56	5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
20	57	3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
25	58	1-(4-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone	
30	59	1-(4-(4-amino-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanone	
35			
40			
45			
50			
55			

(continued)

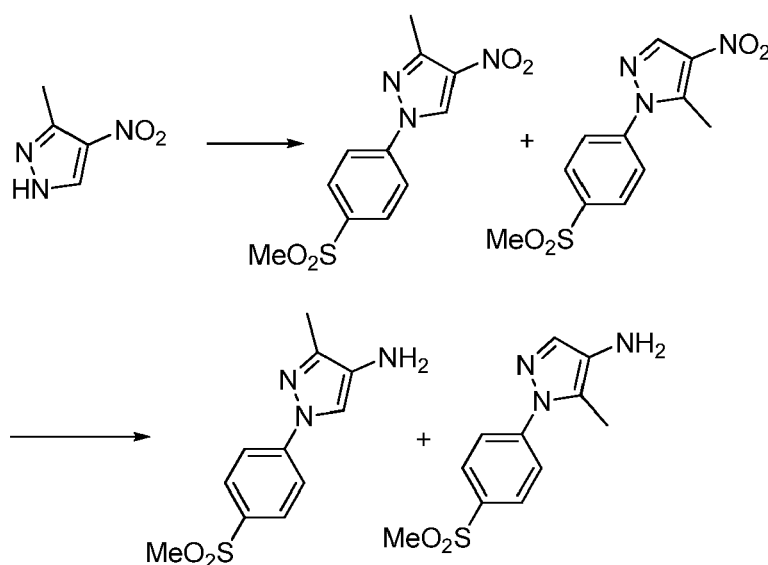
5 60	(4-(4-amino-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(cyclopropyl)methanone	
15 61	(4-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(cyclopropyl)methanone	
25 62	(4-(4-amino-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopropyl)methanone	
35 63	3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
45 64	1-(3-fluoro-1-methylpiperidin-4-yl)-3-methyl-1H-pyrazol-4-amine	
50 55 65	1-(1-ethyl-3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-amine	

(continued)

5 66	3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-amine	
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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

[0517]



Step 1: 3-Methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole compound and 5-ethyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole

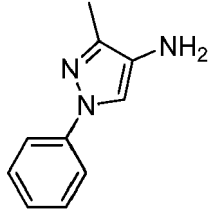
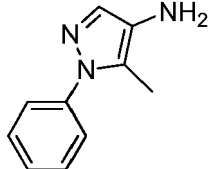
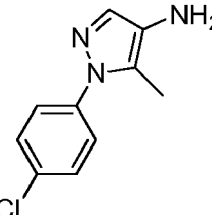
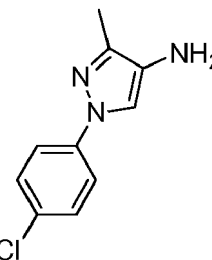
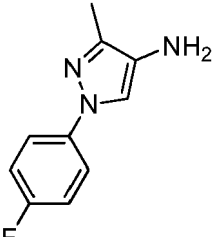
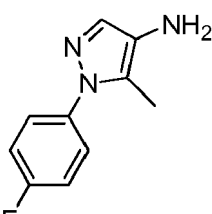
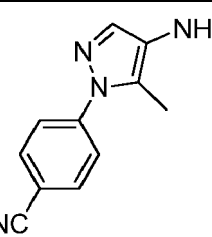
[0518] A mixture of 3-methyl-4-nitro-1H-pyrazole (2.1 g, 17 mmol) and 4-methylsulfonylphenylboronic acid (5.0 g, 25 mmol), copper (II) acetate monohydrate (0.91 g, 5.0 mmol) and pyridine (0.5 g, 6.6 mmol) in DMF was stirred at 95 °C under an oxygen atmosphere for 7 hours. The reaction was diluted with 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

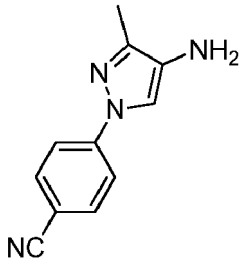
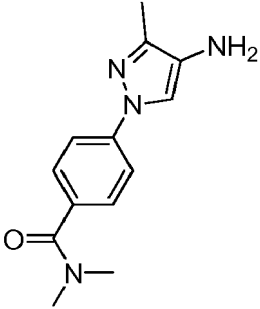
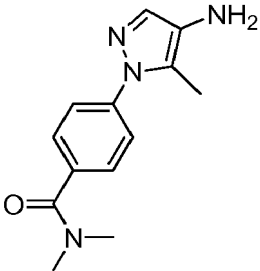
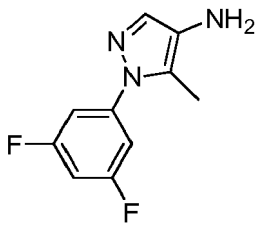
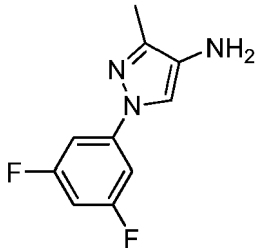
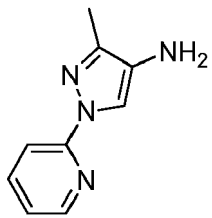
[0519] A suspension of 3-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole compound and 5-methyl-1-(4-(methylsulfonyl)phenyl)-4-nitro-1H-pyrazole (0.57 g, 2.0 mmol) and palladium on carbon (10 wt%, 0.2 g) in ethanol was stirred under a hydrogen atmosphere at 55 °C for 18 hours. The reaction mixture was filtered through celite and concentrated to give the title compounds as a mixture of regioisomers (446 mg, 87%).

[0520] Additional intermediates made using the above procedure are shown in Table 4 below

Table 4

5	69	3-methyl-1-phenyl-1H-pyrazol-4-amine	
10	70	5-methyl-1-phenyl-1H-pyrazol-4-amine	
15	71	1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-amine	
20	72	1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-amine	
25	73	1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-amine	
30	74	1-(4-fluorophenyl)-5-methyl-1H-pyrazol-4-amine	
35	75	4-(4-amino-5-methyl-1H-pyrazol-1-yl)benzonitrile	
40			
45			
50			
55			

(continued)

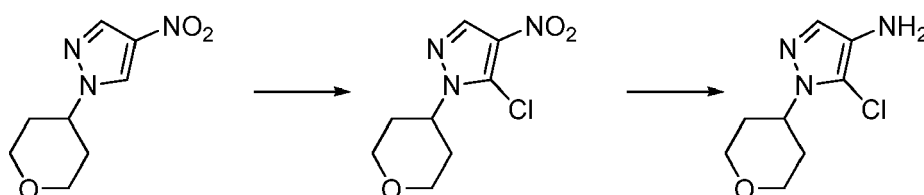
5			
10	76	4-(4-amino-3-methyl-1H-pyrazol-1-yl)benzotrile	
15	77	4-(4-amino-3-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamide	
20			
25	78	4-(4-amino-5-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamide	
30			
35	79	1-(3,5-difluorophenyl)-5-methyl-1H-pyrazol-4-amine	
40			
45	80	1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-amine	
50			
55	81	3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-amine	

(continued)

5	82	3-methyl-1-(pyrimidin-5-yl)-1H-pyrazol-4-amine	
10			
15	83	3-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-amine	
20			
25	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

[0521]



Step 1: 5-Chloro-4-nitro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazole

[0522] To a solution of 4-nitro-1-(tetrahydro-2H-pyran-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%).

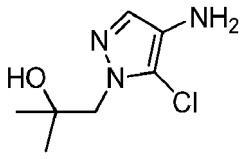
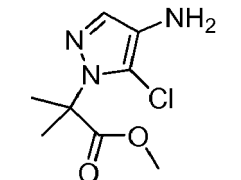
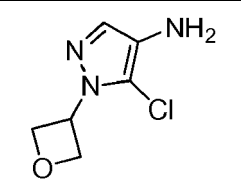
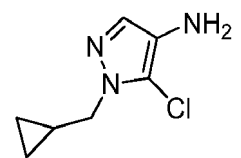
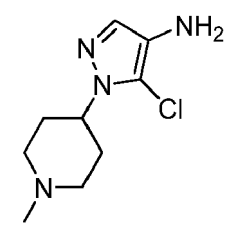
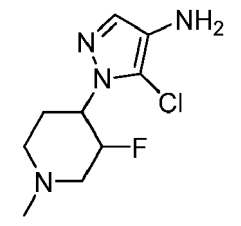
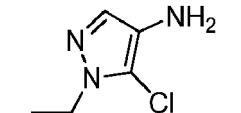
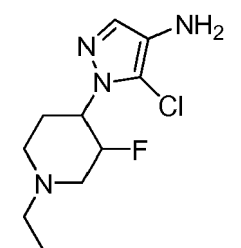
Step 2: 5-Chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-amine

[0523] 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 titrated in EtOAc and filtered. The filtrate was concentrated to give the title compound (0.34 g, quant.)

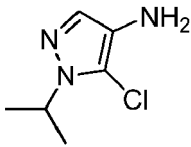
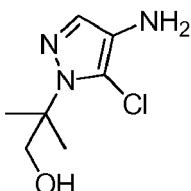
[0524] Additional intermediates made using the above procedure are shown in Table 5 below.

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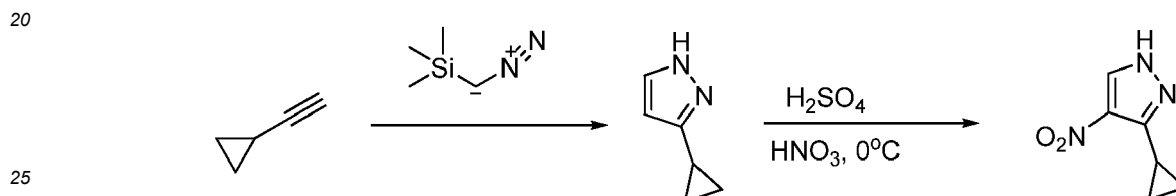
Table 5

5	86	1-(4-amino-5-chloro-1H-pyrazol-1-yl)-2-methylpropan-2-ol	
10	87	methyl 2-(4-amino-5-chloro-1H-pyrazol-1-yl)-2-methylpropanoate	
15	88	5-chloro-1-(oxetan-3-yl)-1H-pyrazol-4-amine	
20	89	5-chloro-1-(cyclopropylmethyl)-1H-pyrazol-4-amine	
25	90	5-chloro-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
30	91	5-chloro-1-(3-fluoro-1-methylpiperidin-4-yl)-1H-pyrazol-4-amine	
35	92	5-chloro-1-ethyl-1H-pyrazol-4-amine	
40	93	5-chloro-1-(1-ethyl-3-fluoropiperidin-4-yl)-1H-pyrazol-4-amine	
45			
50			
55			

(continued)

5	94	5-chloro-1-isopropyl-1H-pyrazol-4-amine	
10	95	2-(4-amino-5-chloro-1H-pyrazol-1-yl)-2-methylpropan-1-ol	

Intermediates 96: 3-Cyclopropyl-4-nitro-1H-pyrazole

[0525]

Step 1: 3-cyclopropyl-1H-pyrazole

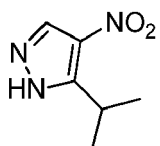
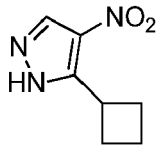
30 **[0526]** Ethynylcyclopropane (660 mg, 10 mmol) mixed with (diazomethyl)trimethylsilane (5 mL, 2M in hexane) in a 30 mL microwave tube was microwaved at 135 °C for 1 h. Then this reaction was concentrated in vacuo to give a light yellow oil product (1.02 g, 94%). This product was pure enough to be used to the next step reaction without further purification. MS: [M+H]⁺ 109.

Step 2: 3-Cyclopropyl-4-nitro-1H-pyrazole

35 **[0527]** To a cooling (0 °C) solution of 3-cyclopropyl-1H-pyrazole (1.5 g, 13.89mmol) in concentrated H₂SO₄ (20 mL, 98%) was added concentrated HNO₃ (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 Na₂SO₄ 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, CDC13) δ 0.97 (m, 2H), 1.22(m, 2H), 2.66 (m, 1H), 8.20(s, 1H), 8.38 (s, 1H).

40 **[0528]** Intermediates made using the above procedure are shown in Table 6 below

Table 6

45	97	5-isopropyl-4-nitro-1H-pyrazole	
50	98	5-cyclobutyl-4-nitro-1H-pyrazole	

(continued)

5

99	5-tert-butyl-4-nitro-1H-pyrazole	
100	4-nitro-5-(trifluoromethyl)-1H-pyrazole	

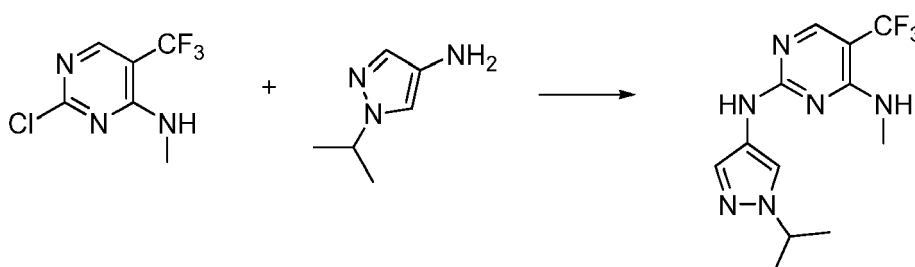
10

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

15

[0529]

20



25

[0530] 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), Pd₂(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 N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine (22 mg, 16%). LCMS (Method A): [MH⁺] = 301.1 at 3.2 min. ¹H-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).

30

35

[0531] 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

40

	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	

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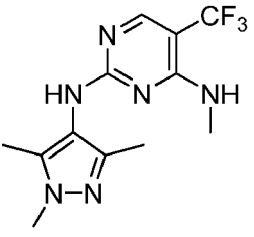
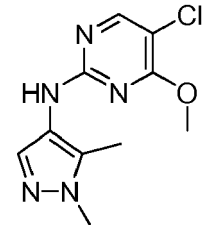
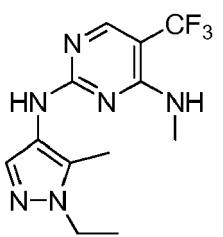
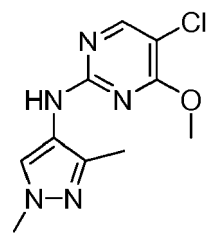
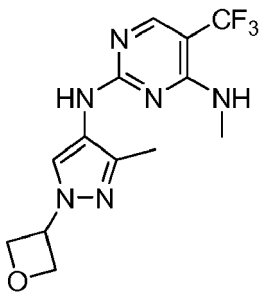
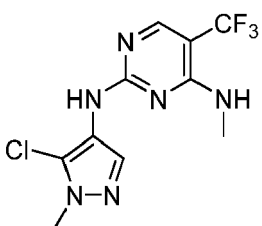
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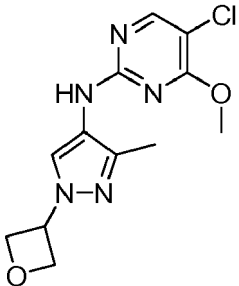
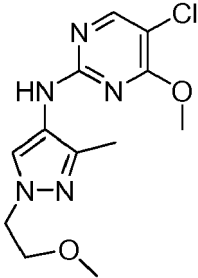
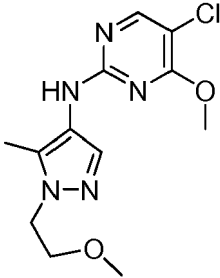
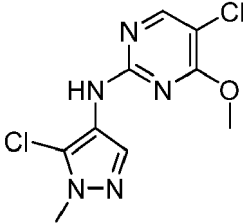
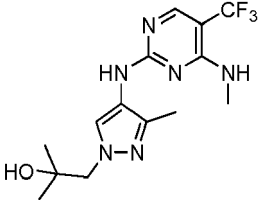
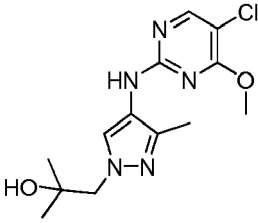
	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	3 N ⁴ -methyl-N ² -(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H-NMR (DMSO): δ 9.53 (s, 1H), 8.08 (s, 1H), 7.88 (s, 1H), 7.55 (s, 1H), 7.04 (s, 1H), 4.17 (t, J = 6.0, 2H), 3.61-3.49 (m, 4H), 2.96 (s, 3H), 2.67 (t, J = 6.4, 2H), 2.39 (s, 3H).	372.1	0.015
15 20	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
25 30	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	
35 40	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
45	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
50 55	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	

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 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
15 20	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
25 30	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
35 40	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
45 50	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	
55	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	

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	20 5-chloro-4-methoxy-N-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)pyrimidin-2-amine		¹ H-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
35 40	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
45	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	
50 55	23 2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-chloropyrimidin-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

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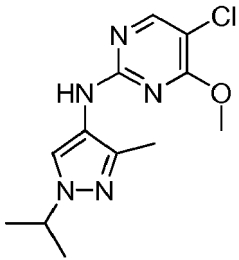
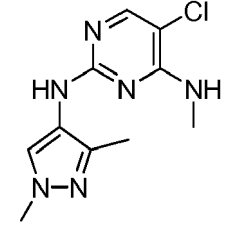
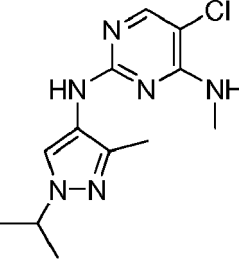
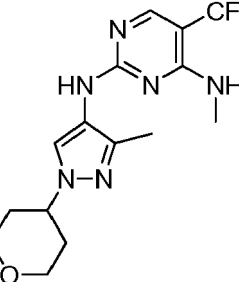
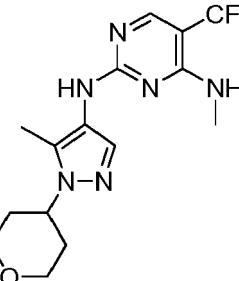
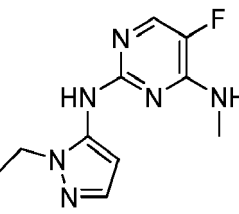
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	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 24 10	N ² -(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)-N ⁴ -methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H-NMR (DMSO): δ 8.82 (s, 1H), 8.04 (s, 1H), 7.64 (s, 1H), 6.88 (s, 1H), 4.13 (t, J = 5.4, 2H), 3.63 (t, J = 5.4, 2H), 3.21 (s, 3H), 2.83 (s, 3H), 2.17 (s, 3H)	331.1	0.019
15 25 20	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	
25 26 30	5-Chloro-N-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidine-2-amine		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, 3H), 1.32 (t, J = 7.3, 3H).	268.0	0.013
35 27 40	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
45 28 50	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	

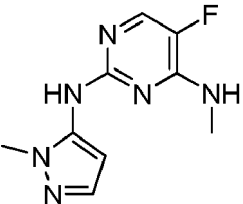
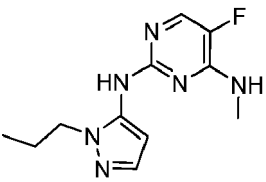
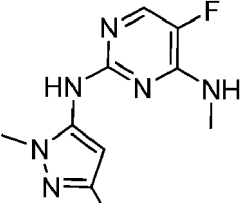
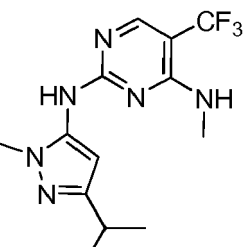
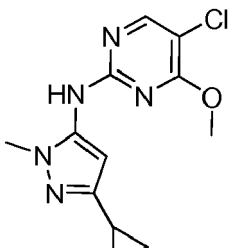
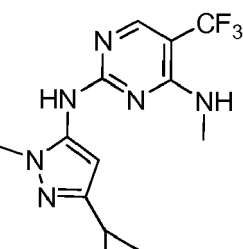
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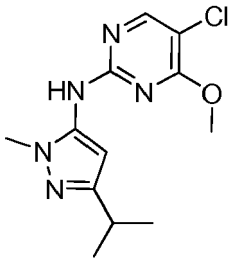
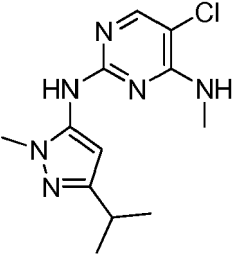
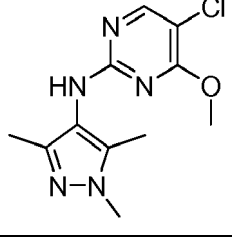
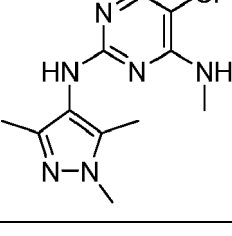
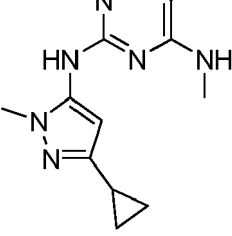
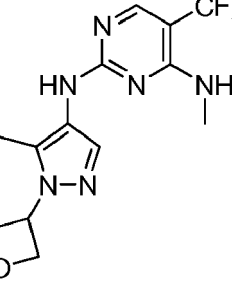
	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	29 5-Chloro-N ² -(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine		¹ H-NMR (DMSO): δ 8.87 (s, 1H), 8.17 (s, 1H), 7.84 (s, 1H), 4.36 (m, 1H), 3.95 (s, 3H), 2.11 (s, 3H), 1.37 (d, J = 6.7, 6H).	282.1	0.022
15 20	30 5-Chloro-N ² -(1,3-dimethyl-1H-pyrazol-4-yl)-N ⁴ -methylpyrimidin-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	
25 30	31 5-Chloro-N ² -(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N ⁴ -methylpyrimidin-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
35 40	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
45 50	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	
55	34 N ² -(2-Ethyl-2H-pyrazol-3-yl)-5-fluoro-N ⁴ -methylpyrimidine-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	

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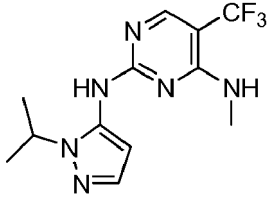
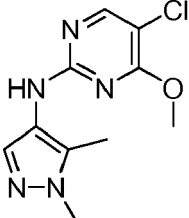
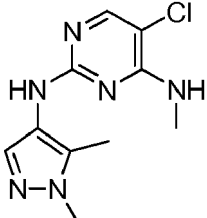
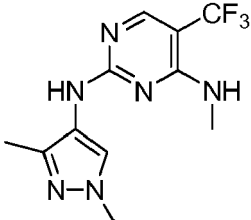
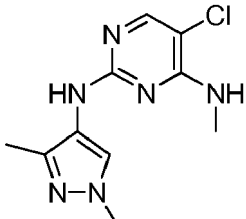
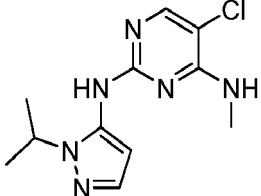
	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	35 5-Fluoro-N ⁴ -methyl-N ² -(2-methyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine		¹ H-NMR (DMSO): δ 8.77 (s, 1H), 7.78 (s, 1H), 7.37 (s, 1H), 7.26 (s, 1H), 6.17 (s, 1H), 3.64 (s, 3H), 2.82 (d, 3H).	223.1	0.267
15	36 5-Fluoro-N ⁴ -methyl-N ⁴ -(2-propyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine		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	
20 25	37 N ² -(2,5-Dimethyl-2H-pyrazol-3-yl)-5-fluoro-N ⁴ -methyl-pyrimidine-2,4-diamine			237.0	
30 35	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
40 45	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
50 55	40 N ² -(3-Cyclopropyl-1-methyl-1H-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	

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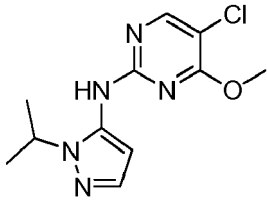
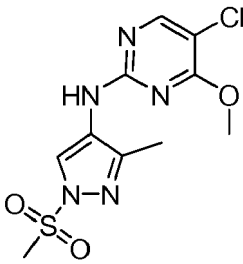
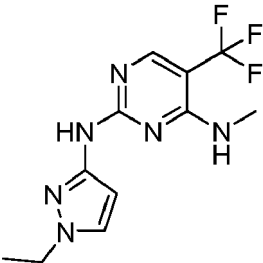
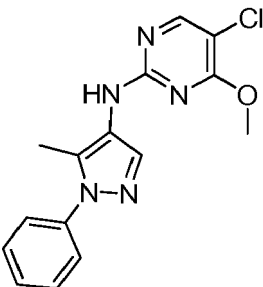
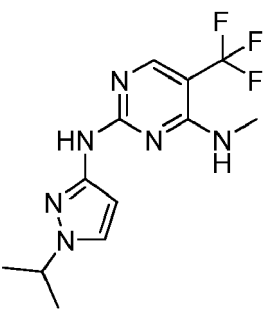
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	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	41 5-Chloro-N-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine		¹ H-NMR (CDCl ₃): δ 8.12 (s, 1 H), 6.65 (s, 1 H), 6.11 (s, 1 H), 3.98 (s, 3 H), 3.72 (s, 3 H), 2.98-2.88 (m, 1 H), 1.27 (d, J = 6.9, 6 H).	282	0.070
15 20	42 5-Chloro-N ² -(5-isopropyl-2-methyl-2H-pyrazol-3-yl)-N ⁴ -methylpyrimidine-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
25 30	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	
35 40	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 50	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, 3 H), 1.92-1.85 (m, 1 H), 0.91-0.85 (m, 2 H), 0.73-0.68 (m, 2 H).	279	0.0134
55	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	

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	47 N ² -(1-isopropyl-1H-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
15 20	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	
25 30	49 5-Chloro-N ² -(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N ⁴ -methylpyrimidin-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	
35 40	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	
45 50	51 5-Chloro-N ² -(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N ⁴ -methylpyrimidin-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	
55	52 5-chloro-N ² -(1-isopropyl-1H-pyrazol-5-yl)-N ⁴ -methylpyrimidin-2,4-diamine				

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5	53	5-chloro-N-(1-isopropyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine			
10					
15	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
20					
25	55	N ² -(1-ethyl-1H-pyrazol-3-yl)-N ⁴ -methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			
30					
35	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
40					
45	57	N ² -(1-isopropyl-1H-pyrazol-3-yl)-N ⁴ -methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			0.0025
50					

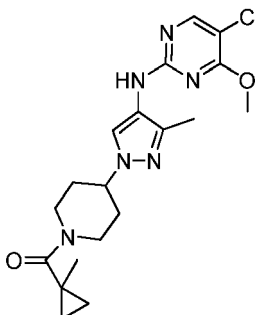
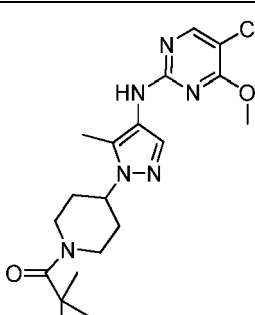
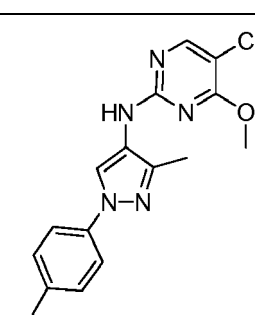
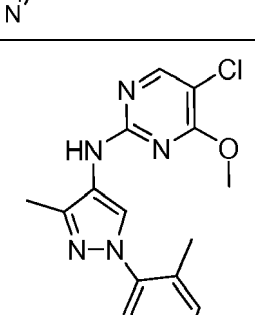
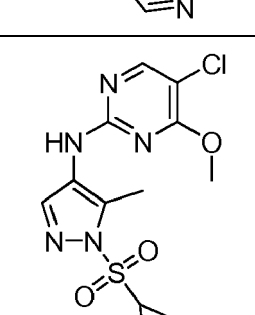
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	59 N ² -(1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-methyl-1H-pyrazol-4-yl)-N ⁴ -methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			387	
30 35	60 5-chloro-4-methoxy-N-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine				0.015
40 45	61 N ⁴ -ethyl-N ² -(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.0046
50 55	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	68 4-(4-(5-chloro-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)benzotrile		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
35 40	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
45 50	70 5-chloro-N-(1-(cyclopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine			334.0	0.015

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	74 5-chloro-4-ethoxy-N-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine		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), 1.98 - 1.77 (m, 4H), 1.34 (t, J = 7.1, 3H).	338.1	
45 50	75 (5-Chloro-4-methoxypyrimidin-2-yl)-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-amine				0.0022

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 76 10	(5-Chloro-4-methoxy-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine				0.0023
15 77 20	(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)-amine				0.0016
25 78 30	(4-Methoxy-5-trifluoromethyl-pyrimidin-2-yl)-(5-methyl-1-phenyl-1H-pyrazol-4-yl)-amine				0.0381
35 79 40	(5-Chloro-4-methoxy-pyrimidin-2-yl)-(1-methanesulfonyl-3-methyl-1H-pyrazol-4-yl)-amine				0.0078
45 80 50	(5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-methyl-1-(tetrahydropyran-4-yl)-1H-pyrazol-4-yl]-amine				0.0663

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	81 4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide				0.0022
15 20	82 4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamide				0.63
25 30	83 4-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-benzotrile				0.0090
35 40	84 N ² -(5-Methoxy-1-methyl-1H-pyrazol-4-yl)-N ⁴ -methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0742
45 50	85 (5-Chloro-4-methoxy-pyrimidin-2-yl)-[5-chloro-1-(tetrahydropyran-4-yl)-1H-pyrazol-4-yl]-amine				0.0066
55					

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	86 (5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoroethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-amine				0.183
15 20	87 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				0.0008
25 30	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

[0532] 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). K_i = 0.017 μM.

[0533] Compounds made using the above procedure are shown in Table 8 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 8

	Name	Structure	¹ H NMR	M+H ⁺	K _i
50 55	90 N ² -(1,3-Dimethyl-1H-pyrazol-4-yl)-5-iodo-N ⁴ -methylpyrimidine-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	

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20 25	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
30 35 40	93 5-bromo-N4-methyl-N2-(5-methyl-1-(1-(2,2,2-trifluoroethyl) piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		¹ H 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
45 50	94 5-bromo-N4-methyl-N2-(3-methyl-1-(1-(2,2,2-trifluoroethyl) piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine		¹ H 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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	103 N4-methyl-N2-(3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		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), 2.86 (s, 3H), 2.15 (s, 3H).		0.0090
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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
45 50	109 5-bromo-N4-methyl-N2-(3-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine			360	0.0084

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	110 5-bromo-N4-methyl-N2-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine			360	
15 20	111 5-bromo-N4-methyl-N2-(1-methyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine				
25 30	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 ₃ OD) 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)		
35 40	113 5-bromo-N4-methyl-N2-(3-methyl-1-propyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		¹ H 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 = 4.3, 3H), 2.15 (s, 3H), 1.70 (h, J = 7.2, 2H), 0.83 (t, J = 7.4, 3H).		0.012
45 50	114 5-chloro-N4-methyl-N2-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine		¹ H 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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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).		
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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		1H NMR (300 MHz, CD ₃ OD) 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
25 30	127 N2-(1-butyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			329.2	0.0003
35 40	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
45 50	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

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	131 N4-methyl-N2-(3-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 8.90 (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 - 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).		0.0374
25 30	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).		
35 40	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
45 50 55	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

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20 25	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
30 35 40	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
45 50	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
55	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 (brs, 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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	143 N4-methyl-N2-(3-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		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
45	pyrimidine-2,4-diamine		= 4.3, 3H), 2.29 (s, 3H).		

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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 (brs, 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
25 30	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 (brs, 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
35 40	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
45 50 55	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	151 5-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-one		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, 6H), 1.99 (m, 1H), 1.08 (m, 3H).		0.0011
35 40	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
45 50	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
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	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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
45 50	158 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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20 25	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
30 35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20	176 N4-ethyl-N2-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.011
25 30	177 N2-(3-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.0067
35 40	178 N2-(5-cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine				0.012
45 50	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

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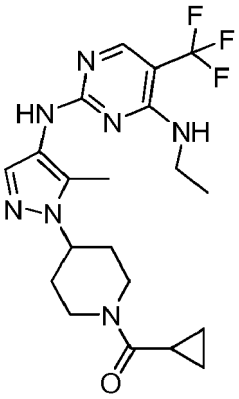
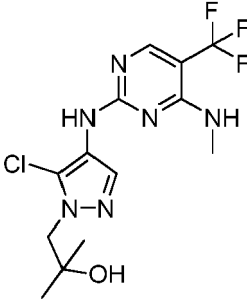
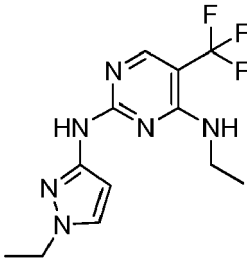
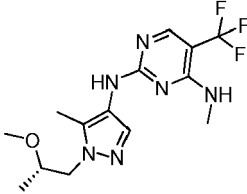
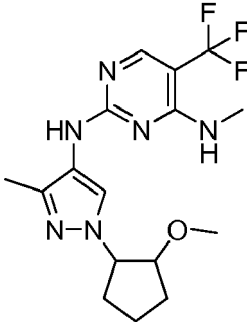
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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 (brs, 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
20 25	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).		0.0008 2
30 35	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
40 45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20 25	185 1-(5-chloro- 4-(4-(methylamino)- 5-(trifluoromethyl) pyrimidin-2-ylamino)-1H- pyrazol-1-yl)-2- methylpropan-2-ol		¹ H NMR (400 MHz, CDCl ₃) δ 8.16 (s, 1H), 8.13 (s, 1H), 6.81 (brs, 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
30 35	186 N4-ethyl-N2-(1-ethyl-1H- pyrazol-3-yl)- 5-(trifluoromethyl) pyrimidine-2,4-diamine		¹ H 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
40	187 (S)-N2-(1-(2- methoxypropyl)-5-methyl- 1H-pyrazol-4-yl)-N4- methyl-5-(trifluoromethyl) pyrimidine-2,4-diamine			345	0.0188
45 50 55	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), 1.64-1.92 (m, 6H).		0.012

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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, CDCl ₃) 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
35 40	192 (R)-N2-(1-(2-methoxypropyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			345	0.0063
45 50	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
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20 25	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
30 35	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
40 45	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 203 10	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
15 204 20	(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
25 205 30	(R)-N2-(1-(1-methoxyprop an-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H-NMR (Bruker, 500MHz, 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
35 206 40	N4-methyl-N2-(4-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H 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
45 207 50	N4-ethyl-N2-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H 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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	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		1H 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
45 50	212 N4-methyl-N2-(5-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H 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, 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).		0.0029

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 213 10	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
15 214 20	N2-(1-(1-isopropylazetidin-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H 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
25 215 30	1-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazole-5-carbonitrile		¹ H NMR (400 MHz, CDCl ₃) δ 8.18 (s, 1H), 8.14 (s, 1H), 7.20 (brs, 1H), 5.29 (s, 1H), 4.01 (s, 3H), 3.09 (d, J = 4.7, 3H).	298	0.0032
35 216 40	N4-ethyl-N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H 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
45 217 50	N2-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		¹ H 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

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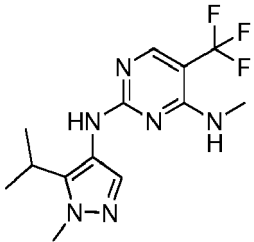
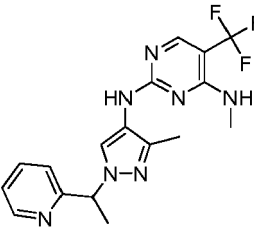
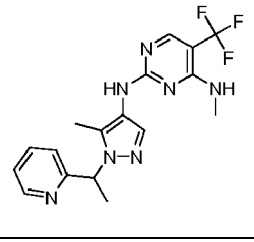
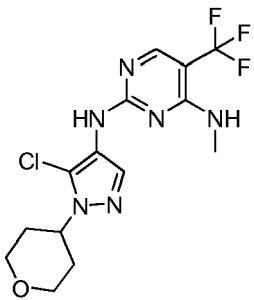
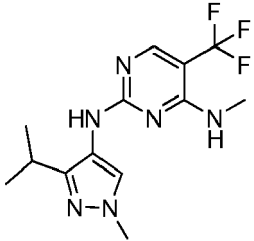
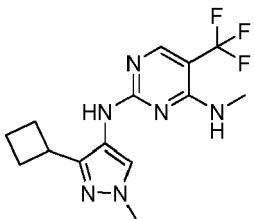
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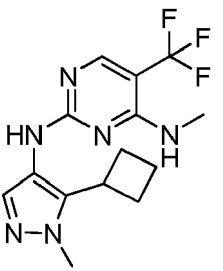
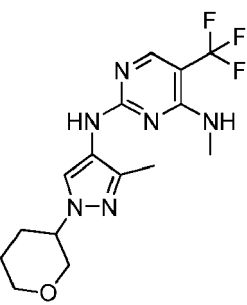
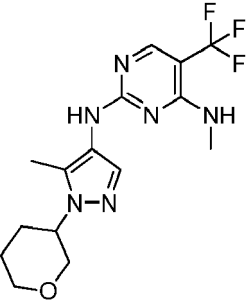
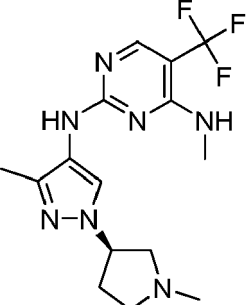
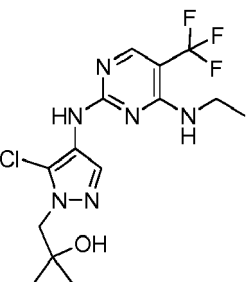
	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	218 N2-(1-(isopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H NMR (400 MHz, DMSO) δ 9.08 (s, 1H), 8.14 (d, J = 21.1, 2H), 7.06 (s, 1H), 3.85 - 3.74 (m, 1H), 2.82 (s, 3H), 2.39 (s, 3H), 1.20 (d, J = 6.8, 6H).		0.0081
15 20	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
25 30	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
35 40	221 1-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-3-isopropyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol				0.0061
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	223 N2-(5-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			315.1	0.014
15 20	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, CDCl ₃) δ 8.54 (d, <i>J</i> = 4.0, 1H), 7.97-8.12 (m, 2H), 7.78-7.81 (m, 1H), 7.32-7.35 (m, 1H), 7.12 (d, <i>J</i> = 7.5, 1H), 5.53-5.57 (m, 1H), 5.90-5.91 (m, 3H), 2.23 (s, 3H), 1.91 (d, <i>J</i> = 7.0, 3H).		0.0024
25 30	225 N4-methyl-N2-(5-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H-NMR (500 MHz, CDCl ₃) δ 8.53 (t, <i>J</i> = 4.0, 1H), 7.98 (s, 1H), 7.72-7.78 (m, 2H), 7.31-7.34 (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, <i>J</i> = 7.5, 3H).		0.0038
35 40	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, <i>J</i> = 11.4, 4.3, 1H), 3.97 (dd, <i>J</i> = 11.3, 4.0, 2H), 3.49 (t, <i>J</i> = 11.4, 2H), 2.83 (s, 3H), 2.01 (qd, <i>J</i> = 12.4, 4.6, 2H), 1.81 (dd, <i>J</i> = 12.8, 2.4, 2H).		0.0007
45	227 N2-(3-isopropyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			315.1	0.069
50 55	228 N2-(3-cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine			327.1	0.0034

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15			2.16 - 1.99 (m, 1H), 1.97 - 1.81 (m, 1H)		
20 25	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
30 35	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
40 45	233 (R)-N4-methyl-N2-(3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine		1H 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
50 55	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	235 1-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol		1HNMR (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
15 20	236 1-(3-cyclopropyl-4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol		1HNMR (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
25 30	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
35 40 45	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20 25	240 (R)-N4-methyl-N2-(5-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimidine-2,4-diamine				
30 35	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
40 45	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
50 55	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 244 10	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
15 245 20	N4-methyl-N2-(3-methyl-1-(2-methyl-2-morpholinopropyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine			414.2	
25 246 30 35	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	
40 247	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
45 248 50	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	

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 249 10	N ² -(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N ⁴ -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
15 250 20	2-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propan-2-ol				0.0122
25 251 30	N ² -[1-(2-Methoxy-ethyl)-3-methyl-1H-pyrazol-4-yl]-N ⁴ -methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0026
35 252 40 45	N ² -[1-(2-Methoxy-ethyl)-5-methyl-1H-pyrazol-4-yl]-N ⁴ -methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0061
50 253 55	5-Bromo-N ² -(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N ⁴ -methylpyrimidine-2,4-diamine				0.0022

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	254 N4-Methyl-N2-[3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0077
15 20	255 5-Bromo-N2-(1-difluoromethyl-5-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine				0.0007
25 30	256 5-Bromo-N2-(1-difluoromethyl-3-methyl-1H-pyrazol-4-yl)-N4-methylpyrimidine-2,4-diamine				0.0022
35 40	257 5-Bromo-N2-(1,5-dimethyl-1H-pyrazol-4-yl)-N4-ethyl-pyrimidine-2,4-diamine				0.0015
45 50	258 5-Bromo-N2-[1-(4-fluorophenyl)-5-methyl-1H-pyrazol-4-yl]-N4-methylpyrimidine-2,4-diamine				

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	259 5-Bromo-N4-methyl-N2-(5-methyl-1-propyl-1H-pyrazol-4-yl)-pyrimidine-2,4-diamine				0.0057
15 20	260 5-Bromo-N2-[1-(4-chlorophenyl)-3-methyl-1H-pyrazol-4-yl]-N4-methylpyrimidine-2,4-diamine				0.0003
25 30	261 N2-(1,5-Dimethyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0013
35 40	262 5-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-2-one				0.0013
45 50	263 4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N,N-dimethylbenzamide				0.0018
55	264 N2-[1-(4-Cyclopropanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0032

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	265 4-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-benzonitrile				0.0048
15 20	266 N4-Ethyl-N2-[1-(4-methanesulfonylphenyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0021
25 30	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
35 40	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	269 N4-Methyl-N2-[3-methyl-1-(3-methyl-pyridin-4-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0091
15 20	270 N2-[1-((R)-2-Methoxypropyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.017
25 30	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
35 40	273 N2-[1-(1,1-Dioxo-hexahydro-1,4-thiopyran-4-yl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.037
45 50	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
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 275	N2-[1-((S)-2-Methoxy-1-methyl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0089
15 276	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
25 277	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
35 278	N2-[1-(1-Isopropyl-azetidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0012
45 279	N4-Ethyl-N2-[5-methyl-1-(propane-2-sulfonyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0047

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5	280	N2-(5-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine			0.0036
10	281	N2-(3-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N4-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine			0.0013
15	282	N4-Ethyl-N2-{1-[1-(2-methoxyethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine			0.0054
20	283	N4-Ethyl-N2-{1-[1-(2-methoxyethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-5-trifluoromethyl-pyrimidine-2,4-diamine			0.002
25	284	N2-{1-[1-(2-Fluoroethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine			0.0042
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	285 N2-{1-[1-(2-Fluoroethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0283
15 20 25	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
30 35	287 N2-(1-Ethanesulfonyl-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0072
40 45	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
50 55	289 N4-Methyl-N2-(3-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.025

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	290 N2-(1-Cyclopropanesulfonyl-3-cyclopropyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				
15 20	291 N4-Methyl-N2-(5-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				
25 30	292 (5-Chloro-4-methoxy-pyrimidin-2-yl)-{1-[1-(2-fluoroethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl]-amine				0.0042
35 40	293 N4-Methyl-N2-[3-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0006
45 50	294 N4-Ethyl-N2-[1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0011

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	295 N4-Ethyl-N2-[1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0004
15 20	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
25 30	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
35 40	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
45 50	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
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	302 1-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2-methyl-propan-2-ol				0.016
15 20	303 2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl-isobutyramide				0.0013
25 30	304 N4-Methyl-N2-(3-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0051
35 40 45	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10 15	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
20 25	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
30 35 40	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
45	309 N4-Methyl-N2-(5-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0028
50 55	310 N4-Methyl-N2-(3-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0093

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	313 3-[5-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile		¹ H 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
35 40	314 N4-Methyl-N2-[5-methyl-1-(6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0015
45 50	315 N4-Methyl-N2-(5-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0014

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	316 N4-Methyl-N2-(5-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0026
15 20	317 N4-Methyl-N2-(3-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0012
25 30	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
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 321	3-Methyl-1-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-butan-2-ol				0.0108
15 322	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				0.0049
25 323	N4-Methyl-N2-(5-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0022
30 324	N4-Methyl-N2-[5-methyl,-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0006
40 325	N4-Methyl-N2-[3-methyl,-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0038
50 326	3-[3-Chloro-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethyl-propionitrile				0.0082

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	329 N4-Methyl-N2-(3-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0052
35 40	330 N2-(5-Fluoromethyl-1-methyl-1H-pyrazol-4-yl)-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0245
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	333 N4-Ethyl-N2-[1-(3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine				0.0007
25 30	334 2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol				0.0063
35 40	335 2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol				0.0033
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	338 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				0.0003
25 30	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
35 40	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
45 50	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
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	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
15 20	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
25 30	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
35 40	345 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				0.115
45	pyrimidine-2,4-diamine				

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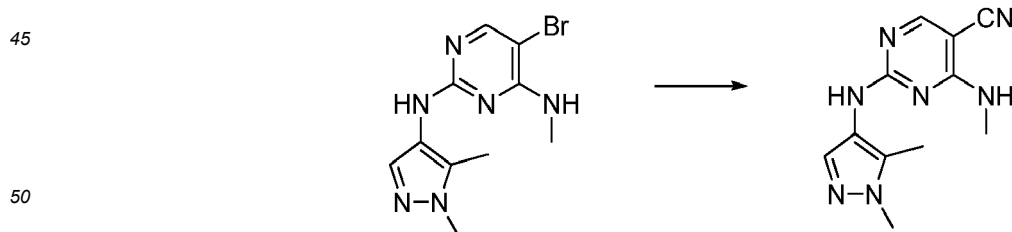
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _I
5 10	346 N2-(1',5-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine				
20 25	347 N2-(1',3-dimethyl-1'H-1,4'-bipyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine				
30 35	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				

40 Example 349 2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile

[0534]



55 [0535] To a mixture of 5-bromo-N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine (95 mg, 0.32 mmol), zinc cyanide (70 mg, 0.60 mmol), Pd₂(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. ¹H-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 = 0.025 μM.

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[0536] 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
5 10 15	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
20 25	351 2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		¹ H 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
30 35	352 2-(1-isopropyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		¹ H 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
40 45	353 2-(1-ethyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		¹ H 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 (t, J = 7.2, 1H).		0.036
50 55	354 2-(3-methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		¹ H 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

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10 15	355 2-(3-methyl-1-(1-(2,2,2-trifluoroethyl)pip eridin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)py rimidine-5-carbonitrile				0.299
20 25	356 2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)pip eridin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)py rimidine-5-carbonitrile				0.0225
30 35	357 2-(1-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)py rimidine-5-carbonitrile				
40 45	358 2-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)py rimidine-5-carbonitrile		¹ H 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

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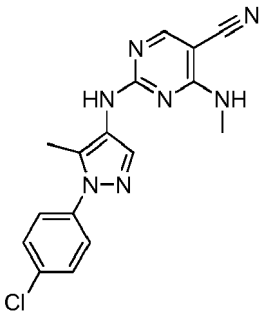
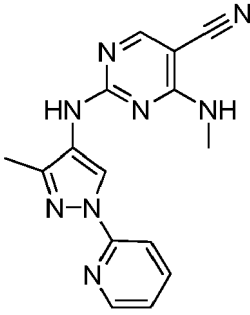
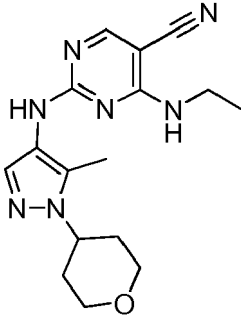
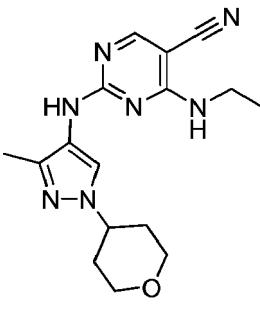
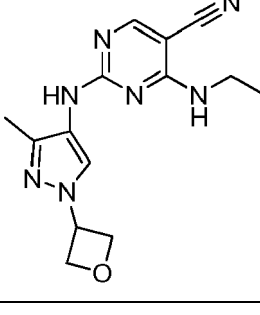
	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	359 2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.28 (s, 1H), 8.26 (s, 1H), 8.06 (s, 1H), 7.59 (s, 1H), 5.00 (q, J = 9.0, 2H), 2.86 (d, J = 4.0, 3H), 2.17 (s, 3H).		0.053
15 20	360 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
25 30	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
35 40	362 2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			314.1	0.086
45 50	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

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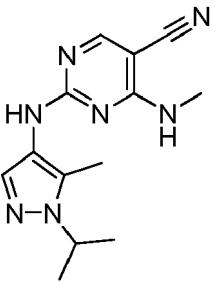
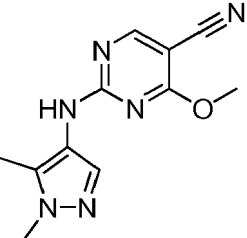
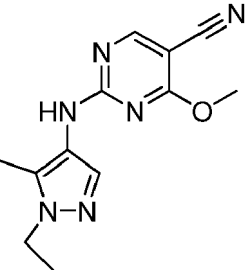
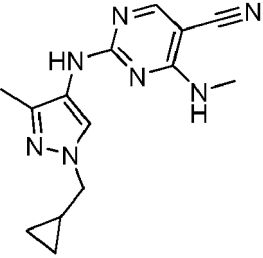
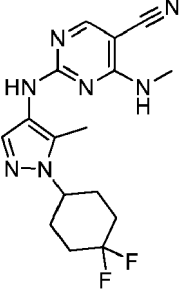
	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	364 2-(1-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		1H NMR (400 MHz, DMSO) δ 9.17 (d, J = 125.4, 1H), 8.12 (d, J = 107.0, 2H), 7.55 (s, 3H), 7.35 (t, J = 8.7, 2H), 2.86 (s, 3H), 2.26 (s, 3H).		0.0019
15 20	365 2-(1-(difluoromethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			280.1	0.035
25 30	366 2-(5-methyl-1-propyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			272.2	0.0054
35 40	367 2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			342.2	0.0018
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	369 2-(1-(4-chlorophenyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile			340.1	0.0025
15 20	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
25 30	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
35 40	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
45 50	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

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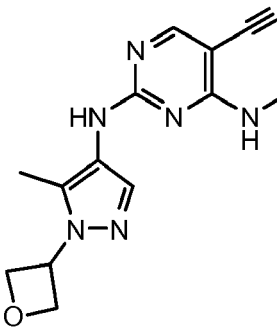
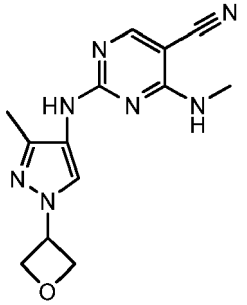
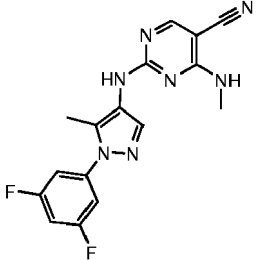
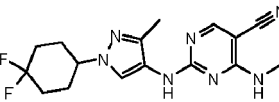
	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	374 2-(1-isopropyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		¹ H NMR (500 MHz, DMSO) δ 8.68 (s, 1H), 8.15 (s, 1H), 7.54 (s, 1H), 7.17-7.19 (m, 1H), 4.40-4.47 (m, 1H), 2.84 (d, J = 7.5, 3H), 2.16 (s, 3H), 1.29-1.36 (m, 6H).		0.0158
15 20	375 2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile				0.145
25 30	377 2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile			259	0.075
35 40	380 2-(1-(cyclopropylmethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		¹ 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
45 50	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

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	383 2-(5-chloro-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile		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
15	pyrimidine-5-carbonitrile		(m, 2H), 1.81 (m, 2H).		
20	384 2-(1-Difluoromethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidine-5-carbonitrile				0.0191
25	385 2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-ethylamino-pyrimidine-5-carbonitrile				0.0127
30	386 2-[1-(4-Fluoro-phenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile				0.0959
35	387 4-Methylamino-2-(3-methyl-1-propyl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile				0.0054

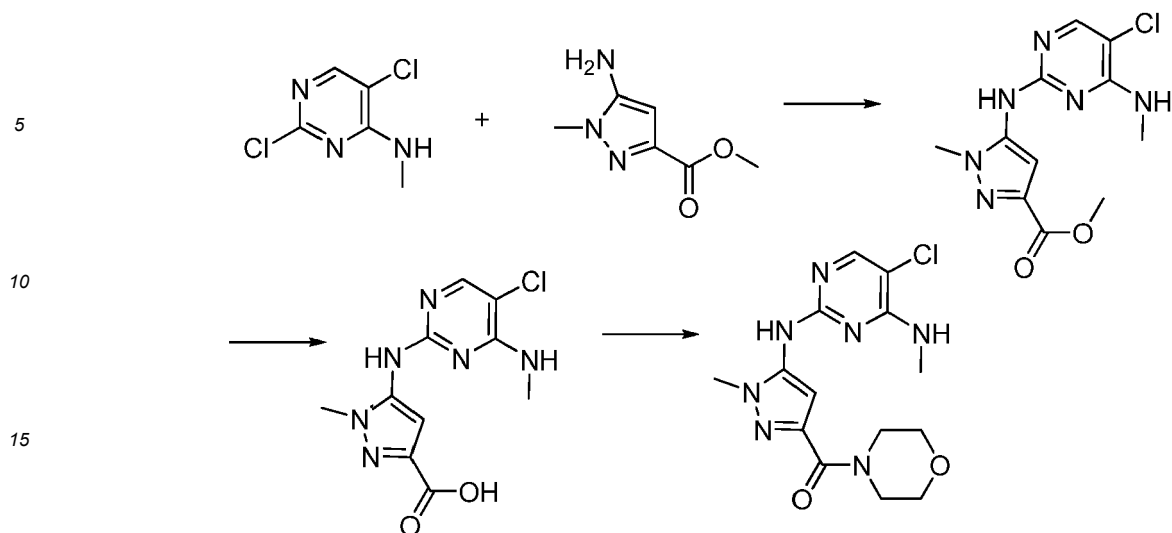
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	388 4-Methylamino-2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile				0.0322
15 20	389 4-Methylamino-2-(3-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidine-5-carbonitrile				0.0372
25 30	390 2-[1-(3,5-Difluorophenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile				0.241
35 40	392 2-[1-(4,4-Difluorocyclohexyl)-3-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile				0.266

Example 393 (5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)(morpholino)methanone

[0537]



20 Step 1 Methyl 5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylate

25 **[0538]** 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.

30 Step 2 5-(5-Chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylic acid

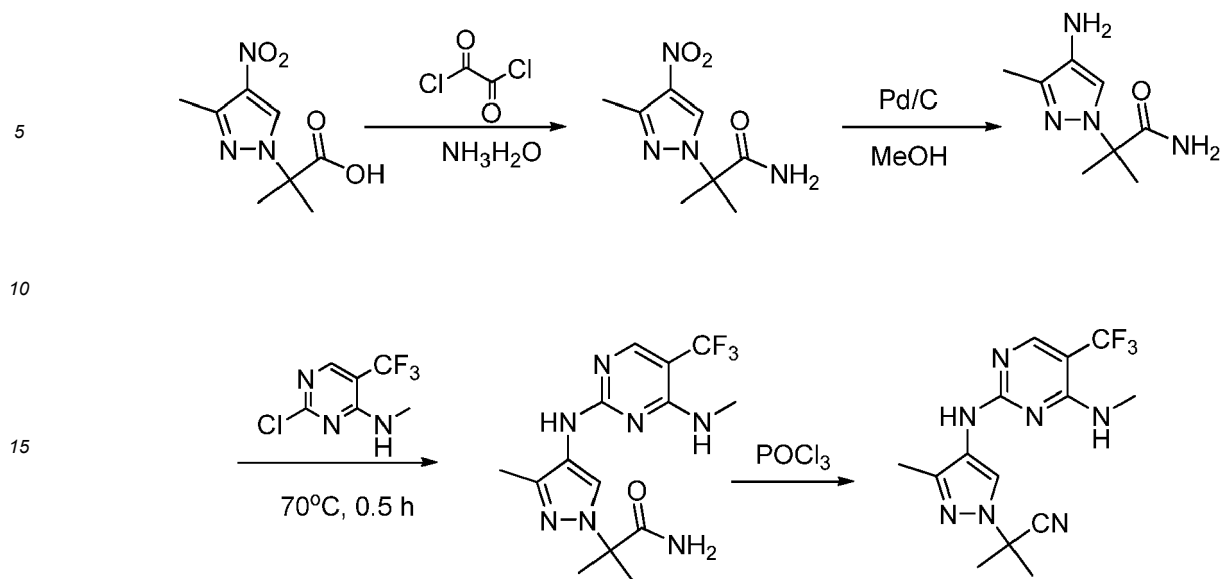
35 **[0539]** To a 100 mL round bottom flask equipped with a stir bar was added 0.964 g of methyl 5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazole-3-carboxylate, 0.28 g of LiOH, 15 mL of tetrahydrofuran and 10 mL of water. The reaction was stirred at room temperature for 18 hours. 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 MgSO₄, 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.

40 Step 3 (5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)(morpholino)methanone

45 **[0540]** 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. ¹H-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 = 0.16 μM.

50 Example 394 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile

55 **[0541]**



Step 1: 2-methyl-2-(3-methyl-4-nitro-1H-pyrazol-1-yl)propanamide.

[0542] To a solution of 2-methyl-2-(3-methyl-4-nitro-1H-pyrazol-1-yl)propanoic acid (2.5 g, 11.7 mmol) in CH₂Cl₂ (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 NH₄OH (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. NH₄Cl (50 mL), dried over anhydrous Na₂SO₄, filtered 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.

[0543] 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

[0544] 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 trifluoroacetic acid (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. Na₂CO₃. 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 (CH₂Cl₂: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

[0545] 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 POCl₃ (5 mL) was stirred at 90 °C for 1 hour. POCl₃ was removed by evaporation, the mixture was added into ice/H₂O (10 ml) and the pH of the solution was adjusted to 8 with sat. Na₂CO₃, the aqueous phase was extracted with ethyl acetate (5 mL x 3). The 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)-

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1H-pyrazol-1-yl)propanenitrile (100 mg, 42%) as a white solid. ¹H-NMR (300 MHz, DMSO-d₆) 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 = 0.0005 μM.

[0546] 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
10					
15	395		¹ H NMR (300 MHz, CD ₃ OD) 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, 3H)		0.015
20					
25	396		¹ H NMR (300 MHz, CD ₃ OD) δ ppm 8.11 (s, 1H), 7.96 (s, 1H), 5.23 (br s, 1H), 4.90 (s, 2H), 3.08 (s, 3H), 3.07 (s, 3H), 2.99 (s, 3H), 2.27 (s, 3H)		0.004
30					
35	397		¹ H NMR (300 MHz, CD ₃ OD) δ ppm 8.14 (s, 1H), 7.94 (s, 1H), 6.19 (br s, 1H), 5.26 (br s, 1H), 4.73 (s, 2H), 3.07 (d, J = 4.8 Hz, 3H), 2.81 (d, J = 4.8 Hz, 3H), 2.32 (s, 3H)		0.0095
40					
45	398		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
50					
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10 15	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
20 25	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
30 35 40	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
45 50	402 1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) cyclopropanecarbonitrile		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				

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	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
15 20	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
25 30	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
35 40	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
45 50	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	408 methyl 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) propanoate		¹ H 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
15 20	409 methyl 2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) propanoate		¹ H 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
25 30	410 2-(3-ethyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile		¹ H 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
35 40	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
45 50	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
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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	413 (S)-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, 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), 1.74-1.79 (m, 3H).		0.040
15 20	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
25 30	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
35 40	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
45 50	417 2-(4-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropanenitrile		¹ H 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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	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
15 20	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
25 30	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
35 40	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
45 50	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

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	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
15 20	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
25 30	425 2-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-ethyl-2-methyl propanamide		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
35 40	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10 15	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
20 25	428 N-ethyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) cyclobutanecarboxamide			398.2	0.024
30 35 40	429 N-isopropyl-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) propanamide				
45 50	430 1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) cyclobutanecarbonitrile			352.1	

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(continued)

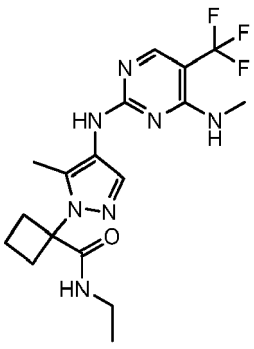
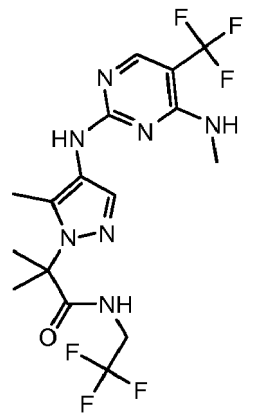
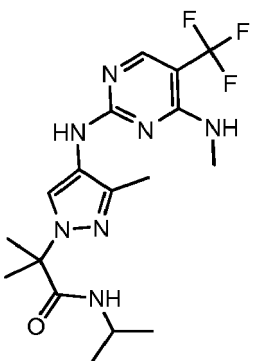
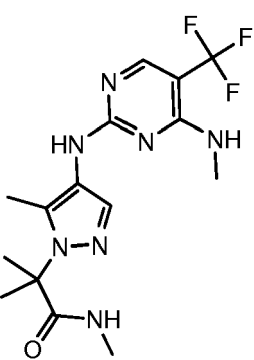
	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	432 N,2-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) propanamide		1H NMR (400 MHz, DMSO) δ 9.04 (s, 1H), 8.13 (s, 1H), 8.10 (s, 1H), 7.17 (s, 1H), 7.01 (s, 1H), 2.93 (d, 3H), 2.55 (d, 3H), 2.17 (s, 3H), 1.64 (s, 6H).	372.1	0.0184
15 20	433 1-(5-chloro-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl) cyclopropanecarbonitrile			358.1	
25 30	434 2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester				0.0122
35 40	435 2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methyl-propionic acid methyl ester				0.0355
45 50	436 (S)-N,N-Dimethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionamide				0.0303

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 437	R)-2-[3-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile				0.0065
15 438	2-[4-(5-Chloro-4-methoxy-pyrimidin-2-ylamino)-3-cyclopropyl-pyrazol-1-yl]-2-methylpropionitrile				0.0058
25 439	(R)-2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitrile				0.0016
35 440	N-Ethyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0095
45 441	N-Ethyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0237

(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10 15	442 1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarboxylic acid ethylamide				0.0156
20 25	443 2-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-N-(2,2,2-trifluoroethyl)-isobutyramide				0.0666
30 35 40	444 N-Isopropyl-2-[3-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0246
45 50	445 N-Methyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.0926

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	446 1-[5-Methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutanecarbonitrile				0.0024
15 20	447 N-tert-Butyl-2-[5-methyl-4-(4-methylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramide				0.067
25 30	448 2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N-methyl-isobutyramide				0.0153
35 40 45	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

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(continued)

	Name	Structure	¹ H NMR	M+H ⁺	K _i
5 10	451 2-[4-(4-Ethylamino-5-trifluoromethyl-pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-2-methylpropionitrile		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
15 20	452 2-(3-chloro-4-(4-(methylamino)-5-(trifluoromethyl) pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile				
25 30 35	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

40 **[0547]** This assay was used to determine a compound's potency in inhibiting activity of LRRK2 by determining, K_i_{app}, IC₅₀, or percent inhibition values. In 384 well proximity plates F black, shallow well plates LRRK2, Eu-anti-GST-antibody, Alexa Fluor® Kinase tracer 236 and test compound were incubated together.

[0548] 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.

45 **[0549]** Assay conditions and materials used were as follows:

Final Assay Conditions:

50	GST-LRRK2 G2019S	10 nM
	Eu-anti-GST-antibody	2nM
	Kinase tracer 236	8.5 nM
	Kinase reaction time:	1 hour
	Temperature:	ambient
55	Total volume:	15 μl
	DMSO	1%

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Materials:

[0550] 384 well proxiplates F black shallow well Perkin Elmer cat# 6008260

5 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
10 EGTA Sigma cat # E3889
Brij-35: Sigma cat # B4184(30% w/v)
DMSO: Sigma cat # D8418
MgCl₂ Sigma cat # M9272

15 **[0551]** Reaction Buffer:H₂O/50 mM Tris, pH 7.4/10mM MgCl₂/1 mM EGTA/0.01% Brij 35

Compound Plate Preparation:

20 **[0552]** 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:

25 **[0553]** 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:

30 **[0554]** 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:

35 **[0555]** Calculate ratio : (665/620)*10000. Subtract mean background values from all data points. Calculate % of control for each test value. Plot % of control vs Compound concentration. Calculate K_i Value (xlfif curve fitting- Morrison equation). Results expressed as a K_i in μM. Equation for K_i:

$$40 \quad Y=V0*(1-((x+Ki*(1+S/Km)+Et)/(2*Et)-(((x+Ki*(1+S/Km)+Et)^2-(4*Et*x))^0.5)/(2*Et)))$$

Where Et = 4nM

45 kd (Tracer) = 8.5nM

Tracer concentration (S) = 8.5nM

Example 455: In Vitro LRRK2 Assay

50 **[0556]** This assay was used to determine a compound's potency in inhibiting activity of LRRK2 by determining, K_{i,app}, IC₅₀, 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 K_i was determined according to the equation:

$$55 \quad Y=V0*(1-((x+Ki*(1+S/Km)+Et)/(2*Et)-(((x+Ki*(1+S/Km)+Et)^2-(4*Et*x))^0.5)/(2*Et))).$$

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Ki values in Table 4 and elsewhere herein are shown in μM .

[0557] Assay conditions and materials used were as follows:

Final Assay Conditions:

5	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)
10	Substrate:	1 μM
	ATP:	130 μM
	Kinase reaction time:	2 hours
	Temperature:	ambient
15	Total volume:	20 μl

ATP^{app} K_{ms}:

20	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:

25	Solid Support:	Black 50 μL volume polypropylene 384 well plate (MatriCal cat # MP 101-1-PP)
	Kinase:	LRRK2 G2019S (Invitrogen cat # PV4882). LRRK2 Wild type (Invitrogen cat # PV4874).
30	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).
35	Coating Reagent #3:	Coating Reagent #3 (Caliper).
	DMSO:	DMSO (Sigma cat # 34869-100ML).
	Complete Reaction Buffer:	H ₂ O/25 mM Tris, pH 8.0/5 mM MgCl_2 /2 mM DTT/0.01% Triton X-100.
	Stop Solution: H ₂ O/100	mM HEPES, pH 7.2/0.015% Brij-35/0.2% Coating Reagent #3/20 mM EDTA.
40	Separation Buffer:	H ₂ O/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:

45 **[0558]** 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 compd + 798 μl DMSO) was added to empty columns 1 and 2. A Precision instrument was used
50 to perform 1:3.16 serial dilutions ("PLK_BM_serial_halflog").

ATP Preparation:

55 **[0559]** ATP was diluted to 282.1 μM in Complete Kinase Buffer (final concentration was 130 μM).

Total and Blank Preparation:

[0560] In Complete Reaction Buffer, substrate was diluted to 4 μ M. Equal volumes of Complete Reaction Buffer and 4 μ M substrate were combined to obtain the blank. Equal volumes of Complete Reaction Buffer and 4 μ M substrate were combined and to the combined solution was added 2X final LRRK2 concentration.

Assay Procedure:

[0561] To a 50 μ l polypropylene plate, 5 μ l/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 μ l compound + 23 μ l ATP;

5 μ l/well compound/ATP in Assay Plate;

5 μ l/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 μ l/well Stop solution was added to the Assay Plate. Results were read on the LabChip 3000.

Lab Chip 3000 Protocol:

[0562] 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

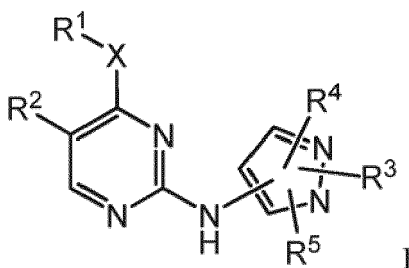
[0563] Parkinson's disease can be replicated in mice and in primates by administration of 1-methyl-4-phenyl tetrahydropyridine (MPTP), a selective nigrostriatal dopaminergic neurotoxin that produces a loss of striatal dopamine (DA) nerve terminal markers. Compounds of the invention may be evaluated for 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.

[0564] 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.

[0565] 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 CO₂ 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.

Claims

1. A compound of the formula I:



or a pharmaceutically acceptable salt thereof,
wherein:

X is: -NR^a; or -O- wherein R^a is hydrogen;

R¹ is: C₁₋₆alkyl;

R² is: halo; cyano; or halo-C₁₋₆alkyl;

R³ is: hydrogen; C₁₋₆alkyl; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano-C₁₋₆alkyl; C₁₋₆alkylsulfonyl; C₁₋₆alkylsulfonyl-C₁₋₆alkyl; amino-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-sulfonyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷; heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷; aryl optionally substituted one or more times with R⁸; aryl-C₁₋₆alkyl wherein the aryl portion is optionally substituted one or more times with R⁸; heteroaryl optionally substituted one or more times with R⁸; heteroaryl-C₁₋₆alkyl wherein the heteroaryl portion is optionally substituted one or more times with R⁸; or -Y-C(O)-R^d;

Y is C₂₋₆alkylene or a bond;

R^d is C₁₋₆alkyl, C₁₋₆alkoxy, amino, C₁₋₆alkyl-amino, di-C₁₋₆alkyl-amino, halo-C₁₋₆alkyl-amino, di-halo-C₁₋₆alkyl-amino, halo-C₁₋₆alkyl, hydroxy-C₁₋₆alkyl, hydroxy, C₁₋₆alkoxy-C₁₋₆alkyl, cyano-C₁₋₆alkyl, C₁₋₆alkylsulfonyl-C₁₋₆alkyl, amino-C₁₋₆alkyl, C₃₋₆cycloalkyl optionally substituted one or more times with R⁶, C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶, heterocyclyl optionally substituted one or more times with R⁷, or heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷;

R⁴ is: hydrogen; C₁₋₆alkyl; halo; cyano; halo-C₁₋₆alkyl; C₂₋₆alkenyl; C₂₋₆alkynyl; C₁₋₆alkoxy; C₁₋₆alkoxy-C₁₋₆alkyl; hydroxy-C₁₋₄alkyl; C₃₋₆cycloalkyl optionally substituted one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; or -Y-C(O)-R^d;

R⁵ is: hydrogen; or C₁₋₆alkyl;

each R⁶ is independently: C₁₋₆alkyl; halo-C₁₋₆alkyl; C₁₋₆alkoxy; oxo; cyano; halo; or Y-C(O)-R^d;

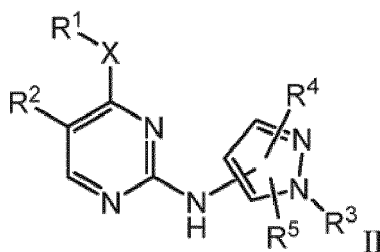
each R⁷ is independently: C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; oxo; C₁₋₆alkoxy; C₁₋₆alkylsulfonyl; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; -Y-C(O)-R^d; heterocyclyl; heterocyclyl-C₁₋₆alkyl; C₃₋₆cycloalkyl; C₃₋₆cycloalkyl-C₁₋₆alkyl; or C₃₋₆cycloalkylsulfonyl; and

each R⁸ is independently: oxo; C₁₋₆alkyl; halo-C₁₋₆alkyl; halo; C₁₋₆alkyl-sulfonyl; C₁₋₆alkoxy; C₁₋₆alkoxy-C₁₋₆alkyl; cyano; heterocyclyl; heterocyclyl-C₁₋₆alkyl; -Y-C(O)-R^d; C₃₋₆cycloalkyl, C₃₋₆Cycloalkyl-C₁₋₆alkyl, or C₃₋₆Cycloalkyl-sulfonyl.

2. The compound of claim 1, wherein R² is: fluoro; bromo; chloro; iodo; trifluoromethyl; or cyano.
3. The compound of any of claims 1-2, wherein R³ is: C₁₋₆alkyl; halo-C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; C₃₋₆cycloalkyl optionally one or more times with R⁶; C₃₋₆cycloalkyl-C₁₋₆alkyl wherein the C₃₋₆cycloalkyl portion is optionally substituted one or more times with R⁶; heterocyclyl optionally substituted one or more times with R⁷; heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷; or -C(O)-R^d.
4. The compound of any of claims 1-3, wherein R³ is: C₁₋₆alkyl; hydroxy-C₁₋₆alkyl; C₁₋₆alkoxy-C₁₋₆alkyl; heterocyclyl optionally substituted one or more times with R⁷; or heterocyclyl-C₁₋₆alkyl wherein the heterocyclyl portion is optionally substituted one or more times with R⁷.
5. The compound of any of claims 1-2, wherein R³ is: methyl; ethyl; propyl; isopropyl; butyl; cyclopropyl; cyclopropyl-methyl; 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; tetrahy-

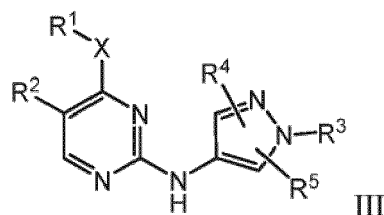
dro-2H-pyran-4-yl; tetrahydrofuran-3-yl; 2,6-dimethyltetrahydro-2H-pyran-4-yl; tetrahydro-2H-pyran-3-yl); phenyl; 4-(methylsulfonyl)phenyl); 4-cyano-phenyl; 4-fluoro-phenyl; 4-chlorophenyl; 3,5-difluorophenyl; 4-(dimethylamino-carbonyl)-phenyl); 4-(cyclopropylsulfonyl)phenyl; 2,2,2-trifluoroethyl; 2-fluoroethyl; 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)azetid-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)azetid-3-yl; 1-(cyclopropyl-carboayl)-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)piperidia-4-yl; 1-methoxypropan-2-yl; 1-(2,2,2-trifluoroethyl)azetid-3-yl); 1-(oxetaa-3-yl)pyrrolidin-3-yl; 1-isopropylazetid-3-yl; 3-fluaro-1-methylpiperidin-4-yl; 1-ethyl-3-fluoropiperidin-4-yl; 1-methyl-pyrrolidin-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; dimethylaminocarbonyl-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-trifluoroethylamino-carbonyl)-1-methyl-ethyl; 1-(ethylaminocarbonyl)-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; pyrimidin-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-([13]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-niazol-3-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl; 2-(1-methyl-1H-pyrazol-3-yl)propaa-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.

6. The compound of any of claims 1-5, wherein R^4 is hydrogen; C_{1-6} alkyl; halo; or C_{3-6} cycloalkyl optionally substituted with C_{1-6} alkyl.
7. The compound of any of claims 1-6, wherein R^4 is hydrogen or C_{1-6} alkyl.
8. The compound of any of claims 1-6, wherein R^4 is chloro or methyl.
9. The compound of any of claims 1-8, wherein R^5 is C_{1-6} alkyl.
10. The compound of any of claims 1-8, wherein R^5 is hydrogen or methyl.
11. The compound of any of claims 1-10, wherein said compounds are of formula II



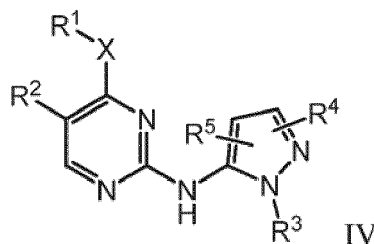
and wherein X, R^1 , R^2 , R^3 , R^4 and R^5 are as recited in any of claims 1-10.

12. The compound of any of claims 1-10, wherein said compound is of formula III



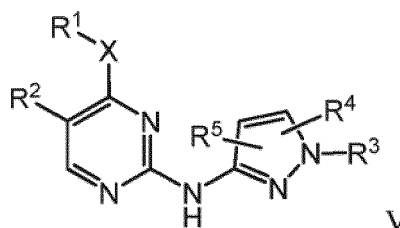
10 and wherein X, R¹, R², R³, R⁴ and R⁵ are as recited in any of claims 1-10.

13. The compound of any of claims 1-10, wherein said compound is of formula IV



25 and wherein X, R¹, R², R³, R⁴ and R⁵ are as recited in any of claims 1-10.

14. The compound of any of claims 1-10, wherein said compound is of formula V



and wherein X, R¹, R², R³, R⁴ and R⁵ are as recited in any of claims 1-10.

15. The compound of claim 1, which is selected from the group consisting of

40 N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidino-2,4-diamine,
 N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N⁴-methyl-N²-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N⁴-methyl-N²-(1-methyl-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 5-chloro-N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
 N⁴-methyl-N²-(1-methyl-1H-pyrazol-5-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 45 N⁴-methyl-N²-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N²-(1,3-dimethyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N⁴-methyl-5-(trifluoromethyl)-N²-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-Chloro-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
 N²-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 5-Chloro-N-(1,3-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
 N⁴-methyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N²-(5-chloro-1-methyl-1H-pyrazol-4-yl)-N⁴-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,

N²-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N²-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 5-Chloro-N-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
 5-Chloro-N⁴-methyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5 N²-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 5-Chloro-N-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
 5-Chloro-N²-(1,3-dimethyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
 5-Chloro-N²-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
 10 N⁴-methyl-N²-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N⁴-methyl-N²-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N²-(2-Ethyl-2H-pyrazol-3-yl)-5-fluoro-N⁴-methylpyrimidine-2,4-diamine,
 5-Fluoro-N⁴-methyl-N²-(2-methyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,
 15 5-Fluoro-N⁴-methyl-N⁴-(2-propyl-2H-pyrazol-3-yl)-pyrimidine-2,4-diamine,
 N²-(2,5-Dimethyl-2H-pyrazol-3-yl)-5-fluoro-N⁴-methylpyrimidine-2,4-diamine,
 N²-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 5-Chloro-N-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,
 N²-(3-Cyclopropyl-1-methyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 20 5-Chloro-N-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amine,
 5-Chloro-N²-(5-isopropyl-2-methyl-2H-pyrazol-3-yl)-N⁴-methylpyrimidine-2,4-diamine,
 5-Chloro-4-methoxy-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2-amine,
 5-Chloro-N⁴-methyl-N²-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-Chloro-N²-(5-cyclopropyl-2-methyl-2H-pyrazol-3-yl)-N⁴-methylpyrimidine-2,4-diamine,
 25 N⁴-Methyl-N²-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-yl)-5-trifluoromethylpyrimidine-2,4-diamine,
 N²-(1-isopropyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidin-2,4-diamine,
 5-Chloro-N-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amine,
 5-Chloro-N²-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
 N²-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 30 5-Chloro-N²-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
 5-Chloro-N²-(1-isopropyl-1H-pyrazol-5-yl)-N⁴-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,
 N²-(1-ethyl-1H-pyrazol-3-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 35 5-chloro-4-methoxy-N-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amine,
 N²-(1-isopropyl-1H-pyrazol-3-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N⁴-methyl-N²-(5-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 N²-(1-(2,2-dimethyl-1,3-dioxan-5-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluoromethyl)pyrimidin-
 2,4-diamine,
 40 5-chloro-4-methoxy-N-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
 N⁴-ethyl-N²-(1-methyl-1H-pyrazol-3-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 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,
 45 (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)benzotrile,
 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,
 50 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,
 55 (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]-benzotrile,
 5 N²-(5-Methoxy-1-methyl-1H-pyrazol-4-yl)-N⁴-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,
 N²-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,
 10 N²-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-trifluoromethyl-pyrimidine-2,4-diamine,
 5-Bromo-N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidine-2,4-diamine,
 N²-(1,3-Dimethyl-1H-pyrazol-4-yl)-5-iodo-N⁴-methyl-pyrimidino-2,4-diamine,
 N⁴-methyl-N²-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidino-2,4-diamine,
 15 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,
 20 5-bromo-N⁴-methyl-N²-(3-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidino-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,
 25 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,
 30 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,
 35 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)azetidia-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-diamine,
 40 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,
 45 N⁴-methyl-N²-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidino-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,
 50 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,
 55 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,
 5 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,
 10 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,
 15 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,
 20 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,
 25 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)benzotrile,
 4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzotrile,
 30 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,
 35 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,
 40 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,
 45 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,
 50 4-(4-(4-(ethylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)benzotrile,
 N4-ethyl-N2-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-3-(trifluoromethyl)pyrimidine-2,4-diamine,
 N,N-dimethyl-4-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide,
 55 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,
 5 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,
 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,
 10 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,
 15 N2-(5-chloro-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidino-2,4-diamine,
 1-(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,
 20 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,
 25 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,
 30 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,
 35 N2-(1-(3-methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidino-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,
 40 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,
 45 (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,
 50 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,
 55 (R)-N2-(1-(1-methoxypropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidino-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-isopropylazetid-3-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimidine-2,4-di-
 amine,
 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-di-
 amine,
 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-di-
 amine,
 N4-methyl-N2-(5-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-di-
 amine,
 (R)-N4-methyl-N2-(3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl)pyrimidine-2,4-di-
 amine,
 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-dimethylpropana-
 mide,
 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-di-
 amine,
 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-di-
 amine,
 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,
 N2-(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,
 5 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,
 10 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,
 15 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]-benzotrile,
 N4-Ethyl-N2-[1-(4-methanesulfonyl-phenyl)-3-methyl-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-di-
 amine,
 20 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,
 25 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-dioxothian-4-yl)-3-methyl-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-
 30 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,
 35 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-di-
 amine,
 N4-Ethyl-N2-[5-methyl-1-(propane-2-sulfonyl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-diamine,
 40 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,
 45 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,
 50 N2-[5-Chloro-1-(3-fluoro-1-methyl-piperidin-4-yl)-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethyl-pyrimidine-2,4-
 diamine,
 N2-(14-Ethnesulfonyl-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,
 55 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-di-
 amine,
 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,
 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-di-
 amine,
 N4-Ethyl-N2-[3-methyl-1-((S)-1-methyl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-trifluoromethyl-pyrimidine-2,4-di-
 amine,
 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-di-
 amine,
 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-[13]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-Pyrimi-
 dine-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-pyrimi-
 dine-2,4-diamine,
 N2-[1-(1-[13]Dioxolan-2-ylmethyl-pyrrolidin-3-yl)-3-methyl-1H-pyrazol-4-yl]-N4-ethyl-5-trifluoromethyl-pyrimi-
 dine-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-trifluorome-
 thyl-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-Pyrimi-
 dine-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)
 5 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)
 10 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) pyri-
 midine-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) pyri-
 midine-2,4-diamine,
 15 N4-ethyl-N2-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromethyl) pyrimi-
 dine-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) primi-
 dine-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) pyri-
 20 midine-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) pyri-
 midine-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,
 25 N2-(1-(2-(4H-1,2,4-triazol-3-yl)propan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N4-methyl-5-(trifluoromethyl)pyrimi-
 dine-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,
 30 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-car-
 bonitrile,
 35 2-(5-methyl-1-(1-(2,2,2-trifluoroethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-car-
 bonitrile,
 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)pyrimidino-5-carbonitrile,
 2-(3-methyl-1-(2,2,2-trifluoroethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,
 40 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-(14-(4-fluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidine-5-carbonitrile,
 45 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,
 50 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,
 55 2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-5-carbonitrile,
 2-(1-ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methoxypyrimidine-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-(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,
 5 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-ylaminol-4-methylamino-pyrimidine-5-carbonitrile,
 2-[1-(4,4-Difluoro-cyclohexyl)-3-methyl-1H-pyrazol-4-ylamino]-4-methylamino-pyrimidine-5-carbonitrile,
 10 (5-(5-chloro-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-gyrazol-3-yl)(morpholino)methanone,
 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propaneni-
 trile,
 N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)aceta-
 mide,
 15 N,N-dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)aceta-
 mide,
 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)pro-
 20 panamide,
 2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolid-
 in-1-yl)propan-1-one,
 2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propaneni-
 trile,
 25 1-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarboni-
 trile,
 (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)pro-
 30 panamide,
 (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,
 35 methyl 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pro-
 panoate,
 methyl 2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pro-
 panoate,
 2-(3-ethyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropanenitrile,
 40 (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)pro-
 panamide,
 (S)-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-
 45 yl)propan-1-one,
 (S)-N,N-dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pro-
 panamide,
 (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,
 50 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-methylpropaneni-
 trile,
 2-(3-cyclopropyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpro-
 panenitrile,
 55 2,2-dimethyl-3-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pro-
 panenitrile,
 2,2-dimethyl-3-(5-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pro-
 panenitrile,

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)-3-(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,
 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-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.

16. The compound of claim 1, which is N2-[5-Chloro-1-(3-fluoro-1-oxetan-3-yl)piperidin-4-yl]-1H-pyrazol-4-yl]-N4-methyl-5-trifluoromethylpyrimidine-2,4-diamine or a pharmaceutically acceptable salt thereof.
17. The compound of claim 1, which is 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile or a pharmaceutically acceptable salt thereof.
18. The compound of any of claims 1-17, or a pharmaceutically acceptable salt thereof for use as a medicament.
19. The compound of any of claims 1-17, or a pharmaceutically acceptable salt thereof for use in the therapeutic and/or

prophylactic treatment of Parkinson's disease.

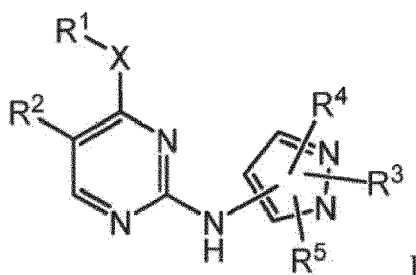
20. The use of a compound of any of claims 1-17, or a pharmaceutically acceptable salt thereof for the preparation of medicaments for the therapeutic and/or prophylactic treatment of Parkinson's disease.

21. A composition comprising:

- (a) a pharmaceutically acceptable carrier; and
 (b) a compound of any of claims 1-17 or a pharmaceutically acceptable salt thereof.

Patentansprüche

1. Verbindung der Formel I:



oder ein pharmazeutisch annehmbares Salz davon,
 worin:

X -NR^a- oder -O- ist, worin R^a Wasserstoff ist;

R¹ C₁₋₆-Alkyl ist;

R² Halogen, Cyano oder Halogen-C₁₋₆-alkyl ist;

R³ Wasserstoff, C₁₋₆-Alkyl, Halogen-C₁₋₆-alkyl, C₂₋₆-Alkenyl, C₂₋₆-Alkynyl, Hydroxy-C₁₋₆-alkyl, C₁₋₆-Alkoxy-C₁₋₆-alkyl, Cyano-C₁₋₆-alkyl, C₁₋₆-Alkylsulfonyl, C₁₋₆-Alkylsulfonyl-C₁₋₆-alkyl, Amino-C₁₋₆-alkyl, C₃₋₆-Cycloalkyl, das gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, C₃₋₆-Cycloalkyl-C₁₋₆-alkyl, worin der C₃₋₆-Cycloalkylrest gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, Heterocyclyl, das gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, Heterocyclyl-C₁₋₆-alkyl, worin der Heterocyclyl-Rest gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, Aryl, das gegebenenfalls ein- oder mehrfach mit R⁸ substituiert ist, Aryl-C₁₋₆-alkyl, worin der Aryl-Rest gegebenenfalls ein- oder mehrfach mit R⁸ substituiert ist, Heteroaryl, das gegebenenfalls ein- oder mehrfach mit R⁸ substituiert ist, Heteroaryl-C₁₋₆-alkyl, worin der Heteroaryl-Rest gegebenenfalls ein- oder mehrfach mit R⁸ substituiert ist, oder-Y-C(O)-R^d ist;

Y C₂₋₆-Alkylen oder eine Bindung ist;

R^d C₁₋₆-Alkyl, C₁₋₆-Alkoxy, Amino, C₁₋₆-Alkylamino, Di-C₁₋₆-alkylamino, Halogen-C₁₋₆-alkylamino, Dihalogen-C₁₋₆-alkylamino, Halogen-C₁₋₆-alkyl, Hydroxy-C₁₋₆-alkyl, Hydroxy, C₁₋₆-Alkoxy-C₁₋₆-alkyl, Cyano-C₁₋₆-alkyl, C₁₋₆-Alkylsulfonyl-C₁₋₆-alkyl, Amino-C₁₋₆-alkyl, C₃₋₆-Cycloalkyl, das gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, C₃₋₆-Cycloalkyl-C₁₋₆-alkyl, worin der C₃₋₆-Cycloalkylrest gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, Heterocyclyl, das gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, oder Heterocyclyl-C₁₋₆-alkyl, worin der Heterocyclylrest gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, ist;

R⁴ Wasserstoff, C₁₋₆-Alkyl, Halogen, Cyano, Halogen-C₁₋₆-alkyl, C₂₋₆-Alkenyl, C₂₋₆-Alkynyl, C₁₋₆-Alkoxy, C₁₋₆-Alkoxy-C₁₋₆-alkyl, Hydroxy-C₁₋₆-alkyl, C₃₋₆-Cycloalkyl, das gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, C₃₋₆-Cycloalkyl-C₁₋₆-alkyl, worin der C₃₋₆-Cycloalkylrest gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, oder-Y-C(O)-R^d ist;

R⁵ Wasserstoff oder C₁₋₆-Alkyl ist;

die R⁶ jeweils unabhängig C₁₋₆-Alkyl, Halogen-C₁₋₆-alkyl, C₁₋₆-Alkoxy, Oxo, Cyano, Halogen oder Y-C(O)-R^d sind;

die R⁷ jeweils unabhängig C₁₋₆-Alkyl, Halogen-C₁₋₆-alkyl, Halogen, Oxo, C₁₋₆-Alkoxy, C₁₋₆-Alkylsulfonyl, C₁₋₆-Alkoxy-C₁₋₆-alkyl, Cyano, -Y-C(O)-R^d; Heterocyclyl, Heterocyclyl-C₁₋₆-alkyl, C₃₋₆-Cycloalkyl, C₃₋₆-Cycloalkyl-C₁₋₆-alkyl oder C₃₋₆-Cycloalkyl-sulfonyl sind; und

die R⁸ jeweils unabhängig Oxo, C₁₋₆-Alkyl, Halogen-C₁₋₆-alkyl, Halogen, C₁₋₆-Alkylsulfonyl, C₁₋₆-Alkoxy,

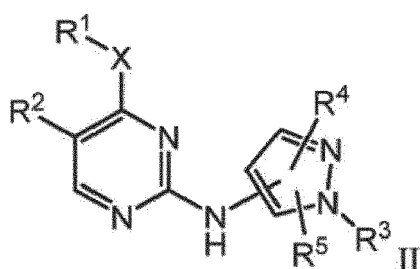
C₁₋₆-Alkoxy-C₁₋₆-alkyl, Cyano, Heterocyclyl, Heterocyclyl-C₁₋₆-alkyl, -Y-C(O)-R^d, C₃₋₆-Cycloalkyl, C₃₋₆-Cycloalkyl-C₁₋₆-alkyl oder C₃₋₆-Cycloalkyl-sulfonyl sind.

2. Verbindung nach Anspruch 1, worin R² Folgendes ist: Fluor, Brom, Chlor, Iod, Trifluormethyl oder Cyano.
3. Verbindung nach einem der Ansprüche 1 bis 2, worin R³ C₁₋₆-Alkyl, Halogen-C₁₋₆-alkyl, Hydroxy-C₁₋₆-alkyl, C₁₋₆-Alkoxy-C₁₋₆-alkyl, C₃₋₆-Cycloalkyl, das gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, C₃₋₆-Cycloalkyl-C₁₋₆-alkyl, worin der C₃₋₆-Cycloalkylrest gegebenenfalls ein- oder mehrfach mit R⁶ substituiert ist, Heterocyclyl, das gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, Heterocyclyl-C₁₋₆-alkyl, worin der Heterocyclylrest gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, oder -C(O)-R^d ist.
4. Verbindung nach einem der Ansprüche 1 bis 3, worin R³ C₁₋₆-Alkyl, Hydroxy-C₁₋₆-alkyl, C₁₋₆-Alkoxy-C₁₋₆-alkyl, Heterocyclyl, das gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, oder Heterocyclyl-C₁₋₆-alkyl, worin der Heterocyclylrest gegebenenfalls ein- oder mehrfach mit R⁷ substituiert ist, ist.
5. Verbindung nach einem der Ansprüche 1 bis 2, worin R³ Methyl, Ethyl, Propyl, Isopropyl, Butyl, Cyclopropyl, Cyclopropylmethyl, Cyclobutyl, Methansulfonyl, Ethylsulfonyl, Cyclopropylsulfonyl, sec-Butylsulfonyl, Morpholin-4-ylethyl, Oxetan-3-yl, 2-Methoxyethyl, 2-Hydroxy-2-methylpropyl, 3-Hydroxy-2-methylpropan-2-yl, 2-Methoxypropyl, Tetrahydro-2H-pyran-4-yl, 2,6-Dimethyltetrahydro-2H-pyran-4-yl, Tetrahydro-2H-pyran-3-yl, Phenyl, 4-(Methylsulfonyl)phenyl, 4-Cyanophenyl, 4-Fluorphenyl, 4-Chlorphenyl, 3,5-Difluorphenyl; 4-(Dimethylaminocarbonyl)phenyl); 4-(Cyclopropylsulfonyl)phenyl; 2,2,2-Trifluorethyl; 2-Fluorethyl; Difluormethyl; 2-Dimethyl-1,3-dioxan-5-yl; 1-Methylcyclopropylsulfonyl; 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-methylethyl; 2-Cyanoethyl; 1-Cyanoethyl; 2-Cyano-2-methylpropyl; 1-(2,2,2-Trifluorethyl)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-Acetylpiperidin-4-yl; 1-(Cyclopropylsulfonyl)-piperidin-4-yl; 1-Methylpiperidin-4-yl; 1-Methyl-2-oxopiperidin-5-yl; 2-Oxopiperidin-5-yl; 1-(Isopropylsulfonyl)piperidin-4-yl; 1-(Oxetan-3-yl)azetidin-3-yl; 1-(Cyclopropylsulfonyl)piperidin-4-yl; 2-Methoxycyclopentyl; 3-Methoxycyclopentyl; 1-Methoxy-2-methylpropan-2-yl; Tetrahydro-2H-1,1-dioxothiopyran-4-yl; 3-Fluor-1-(oxetan-3-yl)piperidin-4-yl; 1-Methoxypropan-2-yl; 1-(2,2,2-Trifluorethyl)azetidin-3-yl; 1-(Oxetan-3-yl)pyrrolidin-3-yl; 1-Isopropylazetidin-3-yl; 3-Fluor-1-methylpiperidin-4-yl; 1-Ethyl-3-fluoropiperidin-4-yl; 1-Methylpyrrolidin-3-yl; 2-(Methoxyethyl)piperidin-4-yl; 1-Methyl-1-(methylaminocarbonyl)ethyl; 2-Methyl-2-morpholinopropyl; 4,4-Difluorcyclohexyl; Morpholin-4-yl-carbonyl; Dimethylaminocarbonylmethyl; Methylaminocarbonylmethyl; 1-Methyl-1-(dimethylaminocarbonyl)ethyl; Pyrrolidin-1-yl-carbonyl; 1-Cyanocyclopropyl; 1-(Pyrrolidin-1-ylcarbonyl)ethyl; 1-(Dimethylaminocarbonyl)ethyl; 1-(Methoxycarbonyl)ethyl; 1-(tert-Butylaminocarbonyl)-1-methylethyl; 1-(2,2,2-Trifluorethylamino-carbonyl)-1-methylethyl; 1-(Ethylaminocarbonyl)-1-methylethyl; 1-(Cyclopropylmethylaminocarbonyl)-1-methylethyl; 1-(Ethylaminocarbonyl)cyclobutyl; 1-(Isopropylamino-carbonyl)-1-methylethyl; 1-Cyanocyclobutyl; 2-Methoxy-1-methylethyl; 1-Methyl-1-(methoxycarbonyl)ethyl; 2-Methoxy-2-methylpropan-1-yl; 1-(Oxetan-3-yl)pyrrolidin-3-yl; Isopropylsulfonyl; Butan-2-sulfonyl; 1-(2-Fluorethyl)piperidin-4-yl; 3-Fluor-1-methylpiperidin-4-yl; 1-Ethyl-3-fluoropiperidin-4-yl; Pyridin-3-ylmethyl; 6-Methylpyridin-2-ylmethyl; 2-(Morpholin-1-yl)-1,1-dimethylethyl; Pyrimidin-2-ylmethyl; 3-Fluor-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-methylbutan-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-Fluoropiperidin-4-yl; 2-Hydroxycyclopentyl; 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; oder 1-Methyl-1H-pyrazol-4-yl.
6. Verbindung nach einem der Ansprüche 1 bis 5, worin R⁴ Wasserstoff, C₁₋₆-Alkyl, Halogen oder C₃₋₆-Cycloalkyl ist, das gegebenenfalls mit C₁₋₆-Alkyl substituiert ist.
7. Verbindung nach einem der Ansprüche 1 bis 6, worin R⁴ Wasserstoff oder C₁₋₆-Alkyl ist.
8. Verbindung nach einem der Ansprüche 1 bis 6, worin R⁴ Chlor oder Methyl ist.
9. Verbindung nach einem der Ansprüche 1 bis 8, worin R⁵ C₁₋₆-Alkyl ist.
10. Verbindung nach einem der Ansprüche 1 bis 8, worin R⁵ Wasserstoff oder Methyl ist.

11. Verbindung nach einem der Ansprüche 1 bis 10, worin die Verbindungen Verbindungen der Formel II sind:

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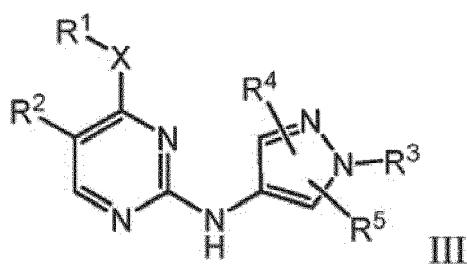
worin X, R¹, R², R³, R⁴ und R⁵ wie in einem der Ansprüche 1 bis 10 definiert sind.

15

12. Verbindung nach einem der Ansprüche 1 bis 10, worin die Verbindung eine Verbindung der Formel III ist:

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25



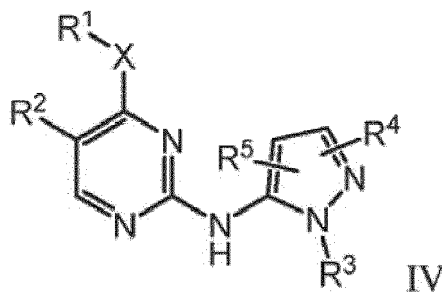
worin X, R¹, R², R³, R⁴ und R⁵ wie in einem der Ansprüche 1 bis 10 definiert sind.

30

13. Verbindung nach einem der Ansprüche 1 bis 10, worin die Verbindung eine Verbindung der Formel IV ist:

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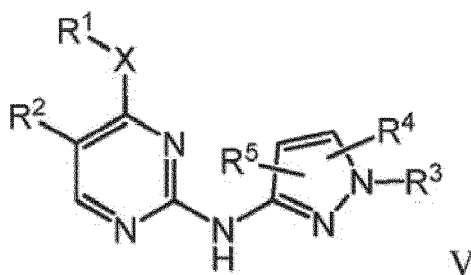
worin X, R¹, R², R³, R⁴ und R⁵ wie in einem der Ansprüche 1 bis 10 definiert sind.

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14. Verbindung nach einem der Ansprüche 1 bis 10, worin die Verbindung eine Verbindung der Formel V ist:

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worin X, R¹, R², R³, R⁴ und R⁵ wie in einem der Ansprüche 1 bis 10 definiert sind.

15. Verbindung nach Anspruch 1, die aus der aus Folgendem bestehenden Gruppe ausgewählt ist:

N²-(1-Isopropyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1,5-Dimethyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(1-methyl-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(1-methyl-1H-pyrazol-5-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(1-methyl-1H-pyrazol-3-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1,3-Dimethyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amin,
 N⁴-Methyl-5-(trifluormethyl)-N²-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Chlor-N-(1-isopropyl-1H-pyrazol-4-yl)-4-(tetrahydro-2H-pyran-4-yloxy)pyrimidin-2-amin,
 5-Chlor-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 N-(1,5-Dimethyl-1H-pyrazol-4-yl)-4-(pyrrolidin-1-yl)-5-(trifluormethyl)pyrimidin-2-amin,
 N²-(1-Ethyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(1,3-dimethyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 N⁴-Methyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(5-Chlor-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-4-methoxy-N-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2-amin,
 5-Chlor-4-methoxy-N-(1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl)pyrimidin-2-amin,
 5-Chlor-4-methoxy-N-(1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl)pyrimidin-2-amin,
 5-Chlor-N-(5-chlor-1-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,
 2-Methyl-1-(3-methyl-4-(4-(methylamino)-5-chlorpyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,
 N²-(1-(2-Methoxyethyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1-(2-Methoxyethyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 5-Chlor-N⁴-methyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 N²-(1-Isopropyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 5-Chlor-N²-(1,3-dimethyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Chlor-N²-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N²-(2-Ethyl-2H-pyrazol-3-yl)-5-fluor-N⁴-methylpyrimidin-2,4-diamin,
 5-Fluor-N⁴-methyl-N²-(2-methyl-2H-pyrazol-3-yl)pyrimidin-2,4-diamin,
 5-Fluor-N⁴-Methyl-N⁴-(2-propyl-2H-pyrazol-3-yl)pyrimidin-2,4-diamin,
 N²-(2,5-Dimethyl-2H-pyrazol-3-yl)-5-fluor-N⁴-methylpyrimidin-2,4-diamin,
 N²-(3-Isopropyl-1-methyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(3-cyclopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amin,
 N²-(3-Cyclopropyl-1-methyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(3-isopropyl-1-methyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amin,
 5-Chlor-N²-(5-isopropyl-2-methyl-2H-pyrazol-3-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Chlor-4-methoxy-N-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2-amin,
 5-Chlor-N⁴-methyl-N²-(1,3,5-trimethyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Chlor-N²-(5-cyclopropyl-2-methyl-2H-pyrazol-3-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1-Isopropyl-1H-pyrazol-5-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 5-Chlor-N²-(1-ethyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N²-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N²-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Chlor-N²-(1-isopropyl-1H-pyrazol-5-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Chlor-N-(1-isopropyl-1H-pyrazol-5-yl)-4-methoxypyrimidin-2-amin,
 5-Chlor-4-methoxy-N-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidin-2-amin,
 N²-(1-Ethyl-1H-pyrazol-3-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-4-methoxy-N-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2-amin,
 N²-(1-Isopropyl-1H-pyrazol-3-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(2,2,2-trifluorethyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,

N²-(1-(2,2-Dimethyl-1,3-dioxan-5-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-dia-
 min,
 5-Chlor-4-methoxy-N-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-pyrimidin-2-amin,
 N⁴-Ethyl-N²-(1-methyl-1H-pyrazol-3-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N-(1,5-dimethyl-1H-pyrazol-4-yl)-4-(oxetan-3-yloxy)pyrimidin-2-amin,
 5-Chlor-4-(2,2-difluorethoxy)-N-(1,5-dimethyl-1H-pyrazol-4-yl)pyrimidin-2-amin, 5-Chlor-N-(1,5-dimethyl-1H-
 pyrazol-4-yl)-4-(2,2,2-trifluorethoxy)pyrimidin-2-amin,
 5-Chlor-4-methoxy-N-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-pyrimidin-2-amin,
 (4-(4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopro-
 pyl)methanon,
 (4-(4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)(1-methylcyclopro-
 pyl)methanon,
 4-(4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)benzonnitril,
 5-Chlor-4-methoxy-N-(3-methyl-1-(3-methylpyridin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amin,
 5-Chlor-N-(1-(cyclopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 5-Chlor-N-(1-(cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-4-methoxypyrimidin-2-amin,
 2-(4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-2-methyl-propannitril,
 2-(4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methyl-propannitril,
 5-Chlor-4-ethoxy-N-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amin,
 (5-Chlor-4-methoxypyrimidin-2-yl)-[1-(4-methansulfonylphenyl)-3-methyl-1H-pyrazol-4-yl]amin,
 (5-Chlor-4-methoxypyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)amin,
 (4-Methoxy-5-(trifluormethyl)pyrimidin-2-yl)-(3-methyl-1-phenyl-1H-pyrazol-4-yl)amin,
 (4-Methoxy-5-(trifluormethyl)pyrimidin-2-yl)-(5-methyl-1-phenyl-1H-pyrazol-4-yl)amin,
 (5-Chlor-4-methoxypyrimidin-2-yl)-(1-methansulfonyl-3-methyl-1H-pyrazol-4-yl)amin,
 (5-Chlor-4-methoxypyrimidin-2-yl)-[5-methyl-1-(tetrahydropyran-4-yl)-1H-pyrazol-4-yl]amin,
 4-[4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-N,N-dimethyl-benzamid,
 4-[4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-N,N-dimethyl-benzamid,
 4-[4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]benzonnitril,
 N²-(5-Methoxy-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 (5-Chlor-4-methoxypyrimidin-2-yl)-[5-chlor-1-(tetrahydropyran-4-yl)-1H-pyrazol-4-yl]-amin,
 (5-Chlor-4-methoxypyrimidin-2-yl)-[1-[1-(2-fluorethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl]amin,
 N²-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-trifluormethylpyrimidin-
 2,4-diamin,
 N²-[1-(1-[1,3]Dioxolan-2-ylmethyl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-(trifluormethyl)pyrimi-
 din-2,4-diamin,
 5-Brom-N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N²-(1,3-dimethyl-1H-pyrazol-4-yl)-5-iod-N⁴-methylpyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(1-(2,2,2-trifluorethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-
 diamin,
 N⁴-Methyl-N²-(3-methyl-1-(1-(2,2,2-trifluorethyl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-
 diamin,
 5-Brom-N⁴-methyl-N²-(5-methyl-1-(1-(2,2,2-trifluorethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(3-methyl-1-(1-(2,2,2-trifluorethyl)piperidin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(3-methyl-1-(2,2,2-trifluorethyl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(5-methyl-1-(2,2,2-trifluorethyl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Chlor-N⁴-ethyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(1-methyl-1H-pyrazol-5-yl)pyrimidin-2,4-diamin,
 2-Methyl-1-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,
 5-Chlor-N⁴-methyl-N²-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-ethyl-N²-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 N²-(1-(Difluormethyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1-(Difluormethyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-ethyl-N²-(1-ethyl-5-methyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Brom-N²-(1-(4-fluorphenyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(3-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,

5-Brom-N⁴-methyl-N²-(5-methyl-1-phenyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(1-methyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(1-(methylsulfonyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(3-methyl-1-propyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Chlor-N⁴-methyl-N²-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-pyrimidin-2,4-diamin,
 5-Brom-N²-(1-(3,5-difluorphenyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Brom-N²-(1-(3,5-difluorphenyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(pyridin-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-Brom-N²-(1-isopropyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Brom-N²-(1-(4-chlorphenyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N²-(1-(4-Chlorphenyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N²-(1-((1S,5S)-8-Oxabicyclo[3.2.1]octan-3-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1-Butyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(pyrimidin-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1-(4-Chlorphenyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-(2-Fluorethyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(1-(oxetan-3-yl)piperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N²-(1-(2-Fluorethyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 1-(4-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanon,
 Cyclopropyl(4-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanon,
 Cyclopropyl(4-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-1-yl)methanon,
 1-(4-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)ethanon,
 N²-(5-Chlor-1-isopropyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(5-Chlor-1-ethyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(pyrimidin-5-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(4-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-3-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(2-methylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(3-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(5-Chlor-1-cyclopropyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(5-Chlor-1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 4-(5-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitril,
 4-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonitril,
 N⁴-Methyl-N²-(3-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(5-methyl-1-(tetrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 5-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-on,
 5-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-1-methylpiperidin-2-on,
 5-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-on,
 5-(5-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-2-on,
 N²-(1-Isopropyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N,N-Dimethyl-4-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamid,
 4-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-N,N-dimethylbenzamid,
 N⁴-Ethyl-N²-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,

N⁴-Ethyl-N²-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(3-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1-(4-(Cyclopropylsulfonyl)phenyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-dia-
 min,
 5 4-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)-benzonnitril,
 N⁴-Ethyl-N²-(5-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N,N-Dimethyl-4-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benza-
 mid,
 N²-(1-(Cyclopropylmethyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 10 N²-(1-(Cyclopropylmethyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-(4-(Cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-dia-
 min,
 N²-(5-Chlor-1-(oxetan-3-yl)-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 15 N²-(1-(Cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-(Cyclopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-ethyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 5-Chlor-N⁴-(2,2-difluorethyl)-N²-(1,5-dimethyl-1H-pyrazol-4-yl)pyrimidin-2,4-diamin,
 5-Chlor-4-methyl-N-(3-methyl-1-(4-(methylsulfonyl)phenyl)-1H-pyrazol-4-yl)pyrimidin-2-amin,
 N²-(1-(4-(Cyclopropylsulfonyl)phenyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-ethyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 20 2-Methyl-1-(4-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)piperidin-
 1-yl)propan-1-on,
 N⁴-Ethyl-N²-(1-methyl-1H-pyrazol-5-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(3-Cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(5-Cyclopropyl-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 25 N⁴-Methyl-N²-(5-methyl-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N²-(5-Chlor-1-((3-methyloxetan-3-yl)methyl)-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 1-(4-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methyl-1H-pyrazol-1-yl)piperidin-1-yl)-2-me-
 thylpropan-1-on,
 N⁴-Ethyl-N²-(3-methyl-1-(1-(oxetan-3-yl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 30 Cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methyl-1H-yl)piperidin-1-yl)metha-
 non,
 Cyclopropyl(4-(4-(4-(ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methyl-1H-yl)piperidin-1-yl)metha-
 non,
 1-(5-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,
 35 N⁴-Ethyl-N²-(1-ethyl-1H-pyrazol-3-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 (S)-N²-(1-(2-Methoxypropyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-(2-Methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 (S)-N²-(1-(2-Methoxypropyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-(1-Methoxy-2-methylpropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-
 40 diamin,
 N²-(1-(2,6-Dimethyltetrahydro-2H-pyran-4-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-
 2,4-diamin,
 (R)-N²-(1-(2-Methoxypropyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-(3-Methoxycyclopentyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 45 N⁴-Methyl-N²-(1-methyl-5-(methylamino)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(methylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(tetrahydro-2H-1,1-dioxo-thiopyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimi-
 din-2,4-diamin,
 2-Methyl-1-(4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-5-(trifluormethyl)-1H-pyrazol-1-yl)pro-
 50 pan-2-ol,
 2-Methyl-1-(4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-3-(trifluormethyl)-1H-pyrazol-1-yl)pro-
 pan-2-ol,
 N²-(1-(3-Fluor-1-(oxetan-3-yl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-
 2,4-diamin,
 55 (R)-N²-(1-(1-Methoxypropan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 1-(3-tert-Butyl-4-(4-(ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,
 N⁴-Methyl-N²-(3-methyl-1-(1-(2,2,2-trifluorethyl)azetidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-
 diamin,

N²-(1-(1-Methoxy-2-methylpropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 (R)-N⁴-Methyl-N²-(3-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5 (R)-N²-(1-(1-Methoxypropan-2-yl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(4-methyl-1H-pyrazol-5-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 10 N⁴-Methyl-N²-(3-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 (R)-N⁴-Methyl-N²-(5-methyl-1-(1-(oxetan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(pyridin-2-ylmethyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 15 N²-(1-(1-(1-Isopropylazetidin-3-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 1-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-5-carbonitril,
 N⁴-Ethyl-N²-(1-(isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-(Isopropylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin 2,4-diamin,
 N²-(1-(Isopropylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin 2,4-diamin,
 20 N²-(1-(sec-Butylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin 2,4-diamin,
 N²-(1-(sec-Butylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin 2,4-diamin,
 1-(4-(4-(Ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-3-isopropyl-1H-pyrazol-1-yl)-2-methylpropan-2-ol,
 N²-(1-(3-Fluor-1-methylpiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 25 N²-(5-Isopropyl-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(1-(pyridin-2-yl)ethyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(5-Chlor-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N²-(3-Isopropyl-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 30 N²-(3-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(5-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-(tetrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N²-(1,5-Dimethyl-1H-pyrazol-4-yl)-N⁴-((tetrahydro-2H-pyran-4-yl)methyl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 35 (R)-N⁴-Methyl-N²-(3-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 1-(5-Chlor-4-(4-(ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,
 1-(3-Cyclopropyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,
 40 1-(3-Cyclopropyl-4-(4-(ethylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-2-ol,
 2-(5-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N,2-dimethylpropanamid,
 N²-(1-(1-(2-Methoxyethyl)piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 45 N²-(1-(1-(2-Methoxyethyl)piperidin-4-yl)-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 (R)-N⁴-Methyl-N²-(5-methyl-1-(1-methylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N²-(5-Chlor-1-(3-fluor-1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 50 N²-(5-Chlor-1-(1-ethyl-3-fluoropiperidin-4-yl)-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(1-(ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(1-(ethylsulfonyl)-5-methyl-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(2-methyl-2-morpholinopropyl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 55 N²-(1-(1-Ethyl-3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(5-(Dimethylamino)-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 2-(5-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-1-ol,

N²-(1-(Ethylsulfonyl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 2-Methyl-1-[3-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-propan-2-ol,
 N²-[1-(2-Methoxyethyl)-3-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-[1-(2-Methoxyethyl)-5-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 5-Brom-N²-(1-ethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 N⁴-Methyl-N²-[3-methyl-1-(2,2,2-trifluorethyl)-1H-pyrazol-4-yl]-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 5-Brom-N²-(1-difluormethyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Brom-N²-(1-difluormethyl-3-methyl-1H-pyrazol-4-yl)-N⁴-methylpyrimidin-2,4-diamin,
 5-Brom-N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-ethylpyrimidin-2,4-diamin,
 5-Brom-N²-[1-(4-fluorphenyl)-5-methyl-1H-pyrazol-4-yl]-N⁴-methylpyrimidin-2,4-diamin,
 5-Brom-N⁴-methyl-N²-(5-methyl-1-propyl-1H-pyrazol-4-yl)-pyrimidin-2,4-diamin,
 5-Brom-N²-[1-(4-chlorphenyl)-3-methyl-1H-pyrazol-4-yl]-N⁴-methylpyrimidin-2,4-diamin,
 N²-(1,5-dimethyl-1H-pyrazol-4-yl)-N⁴-ethyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-piperidin-2-on,
 4-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-N,N-dimethylbenzamid,
 N²-[1-(4-Cyclopropansulfonylphenyl)-3-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-(trifluormethyl)pyrimidin-2,4-dia-
 min,
 4-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-benzonnitril,
 N⁴-Ethyl-N²-[1-(4-methansulfonylphenyl)-3-methyl-1H-pyrazol-4-yl]-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 1-[4-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methyl-pyrazol-1-yl]-piperidin-1-yl]-2-methyl-
 propan-1-on,
 1-[4-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-piperidin-1-yl]-2-methylpro-
 pan-1-on,
 N⁴-Methyl-N²-[3-methyl-1-(3-methylpyridin-4-yl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-[1-((R)-2-Methoxypropyl)-3-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-[1-(2,6-Dimethyltetrahydropyran-4-yl)-5-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-
 diamin,
 N²-[1-(1,1-Dioxothian-4-yl)-3-methylpyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-[1-((R)-2-Methoxy-1-methylethyl)-5-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-dia-
 min,
 N²-[1-((S)-2-Methoxy-1-methylethyl)-3-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-dia-
 min,
 N⁴-Methyl-N²-[3-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-di-
 amin,
 N⁴-Methyl-N²-[5-methyl-1-((S)-1-oxetan-3-yl-pyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-di-
 amin,
 N²-[1-(1-Isopropylazetid-3-yl)-5-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-[5-methyl-1-(propan-2-sulfonyl)-1H-pyrazol-4-yl]-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(5-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N⁴-ethyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(3-Cyclobutyl-1-methyl-1H-pyrazol-4-yl)-N⁴-ethyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-{1-[1-(2-methoxyethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl}-5-(trifluormethyl)pyrimidin-2,4-di-
 amin,
 N⁴-Ethyl-N²-{1-[1-(2-methoxyethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}-5-(trifluormethyl)pyrimidin-2,4-di-
 amin,
 N²-[1-[1-(2-Fluorethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-dia-
 min,
 N²-[1-[1-(2-Fluorethyl)-piperidin-4-yl]-3-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-dia-
 min,
 N²-[5-Chlor-1-(3-fluor-1-methylpiperidin-4-yl)-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-dia-
 min,
 N²-(1-Ethansulfonyl-5-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-[5-methyl-1-(2-methyl-2-morpholin-4-yl-propyl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-
 diamin,
 N⁴-Methyl-N²-(3-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(1-Cyclopropansulfonyl-3-cyclopropyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluorethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-pyridin-3-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 (5-Chlor-4-methoxypyrimidin-2-yl)-{1-[1-(2-fluorethyl)-piperidin-4-yl]-5-methyl-1H-pyrazol-4-yl}amin,
 N⁴-Methyl-N²-[3-methyl-1-(6-methylpyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,

N⁴-Ethyl-N²-[1-(2-methoxyethyl)-3-methyl-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-[1-(2-methoxyethyl)-5-methyl-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 1-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methylpyrazol-1-yl]-2-methylpropan-2-ol,
 1-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-2-methylpropan-2-ol,
 5 N²-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-[1-(1,1-Dimethyl-2-morpholin-4-yl-ethyl)-3-methyl-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Cyclopropyl-N²-(1-methansulfonyl-3-methyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 10 N⁴-Cyclopropyl-N²-(1-methansulfonyl-5-methyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 1-[3-Chlor-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-2-methylpropan-2-ol,
 2-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl isobutyramid,
 N⁴-Methyl-N²-(3-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-trifluormethyl-pyrimidin-2,4-diamin,
 15 N²-[5-Chlor-1-(3-fluor-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-[5-Chlor-1-(3-fluor-1-oxetan-3-yl-piperidin-4-yl)-1H-pyrazol-4-yl]-N⁴-ethyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-[5-methyl-1-((8)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 20 N⁴-Ethyl-N²-[3-methyl-1-((S)-1-oxetan-3-yl-piperidin-3-yl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-pyridazin-3-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 25 N⁴-Ethyl-N²-[5-methyl-1-((S)-1-methylpiperidin-3-yl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-[3-methyl-1-((S)-1-methylpiperidin-3-yl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 3-[5-Chlor-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethylpropionitril,
 N⁴-Methyl-N²-[5-methyl-1-(6-methylpyridin-2-ylmethyl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-pyrimidin-2-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 30 N⁴-Methyl-N²-(5-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-pyrazin-2-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 3-[5-Chlor-4-(4-ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethylpropionitril,
 N⁴-Ethyl-N²-[1-(3-fluor-1-oxetan-3-yl-piperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 3-Methyl-1-[5-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]butan-2-ol,
 35 3-Methyl-1-[3-methyl-4-(4-methylamino-5-(trifluormethyl)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-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(5-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 40 N⁴-Methyl-N²-[5-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-[3-methyl-1-(1-methyl-1H-pyrazol-3-ylmethyl)-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 3-[3-Chlor-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-2,2-dimethylpropionitril,
 45 N⁴-Ethyl-N²-[3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-[1-(1-[1,3]Dioxolan-2-ylmethylpyrrolidin-3-yl)-5-methyl-1H-pyrazol-4-yl]-N⁴-ethyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-pyrimidin-4-ylmethyl-1H-pyrazol-4-yl)-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 N²-(5-Fluormethyl-1-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 50 N⁴-Ethyl-N²-[3-methyl-1-[1-methyl-1-(5-methyl-4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-[3-methyl-1-[1-methyl-1-(4H-[1,2,4]triazol-3-yl)-ethyl]-1H-pyrazol-4-yl]-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-[1-(3-fluoropiperidin-4-yl)-3-methyl-1H-pyrazol-4-yl]-5-(trifluormethyl)-pyrimidin-2,4-diamin,
 55 2-[5-Methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclopentanol,
 2-[3-Methyl-4-(4-methylamino-5-(trifluormethyl)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-(trifluormethyl)pyrimidin-2,4-diamin,

N⁴-Ethyl-N²-(3-methyl-1-(2-(4-methyl-4H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(3-methyl-1-(2-(1-methyl-1H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 5 N⁴-Methyl-N²-(3-methyl-1-(2-(5-methyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 10 N⁴-Methyl-N²-(5-methyl-1-(2-(1-methyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Ethyl-N²-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 15 N⁴-Methyl-N²-(3-methyl-1-(2-(1-methyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N⁴-Methyl-N²-(3-methyl-1-(2-(1-methyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1',5-Dimethyl-1'H-1,4'-bipyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 20 N²-(1',3-Dimethyl-1'H-1,4'-bipyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 N²-(1-(2-(4H-1,2,4-Triazol-3-yl)propan-2-yl)-3-methyl-1H-pyrazol-4-yl)-N⁴-methyl-5-(trifluormethyl)pyrimidin-2,4-diamin,
 2-(1,5-Dimethyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1,3-Dimethyl-1H-pyrazol-4-ylamino)-4-methylamino-pyrimidin-5-carbonitril,
 25 2-(1-Ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1-Isopropyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1-Ethyl-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(3-Methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 30 2-(3-Methyl-1-(1-(2,2,2-trifluorethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methyl-amino)pyrimidin-5-carbonitril,
 2-(5-Methyl-1-(1-(2,2,2-trifluorethyl)piperidin-4-yl)-1H-pyrazol-4-ylamino)-4-(methyl-amino)pyrimidin-5-carbonitril,
 2-(1-Methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 35 2-(5-Methyl-1-(2,2,2-trifluorethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(3-Methyl-1-(2,2,2-trifluorethyl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(5-Methyl-1-phenyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(5-Methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)-pyrimidin-5-carbonitril,
 2-(3-Methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)-pyrimidin-5-carbonitril,
 40 2-(1-Ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-(ethylamino)pyrimidin-5-carbonitril,
 2-(1-(4-Fluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1-(Difluormethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(5-Methyl-1-propyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1-(3,5-difluorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 45 2-(1-(4-Chlorophenyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1-(4-Chlorophenyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(3-Methyl-1-(pyridin-2-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 4-(Ethylamino)-2-(5-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-pyrimidin-5-carbonitril,
 4-(Ethylamino)-2-(3-methyl-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-pyrimidin-5-carbonitril,
 50 4-(Ethylamino)-2-(3-methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)pyrimidin-5-carbonitril,
 2-(1-Isopropyl-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-methoxy-pyrimidin-5-carbonitril,
 2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluorethylamino)pyrimidin-5-carbonitril,
 2-(1-Ethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methoxy-pyrimidin-5-carbonitril,
 55 4-(2,2-difluorethylamino)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)pyrimidin-5-carbonitril,
 2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluorethoxy)pyrimidin-5-carbonitril,
 2-(1-(Cyclopropylmethyl)-3-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)pyrimidin-5-carbonitril,
 2-(1-(4,4-Difluorocyclohexyl)-5-methyl-1H-pyrazol-4-ylamino)-4-(methylamino)-pyrimidin-5-carbonitril,
 2-(3-Methyl-1-(oxetan-3-yl)-1H-pyrazol-4-ylamino)-4-(2,2,2-trifluorethylamino)-pyrimidin-5-carbonitril,

2-(5-Chlor-1-(tetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(methylamino)-pyrimidin-5-carbonitril,
 2-(1-Difluormethyl-5-methyl-1H-pyrazol-4-ylamino)-4-methylaminopyrimidin-5-carbonitril,
 2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-4-ethylaminopyrimidin-5-carbonitril,
 2-[1-(4-Fluorphenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylaminopyrimidin-5-carbonitril,
 5 4-Methylamino-2-(3-methyl-1-propyl-1H-pyrazol-4-ylamino)-pyrimidin-5-carbonitril,
 4-Methylamino-2-(5-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidin-5-carbonitril,
 4-Methylamino-2-(3-methyl-1-oxetan-3-yl-1H-pyrazol-4-ylamino)-pyrimidin-5-carbonitril,
 2-[1-(3,5-difluorphenyl)-5-methyl-1H-pyrazol-4-ylamino]-4-methylaminopyrimidin-5-carbonitril,
 4-(2,2-difluoroethoxy)-2-(1,5-dimethyl-1H-pyrazol-4-ylamino)-pyrimidin-5-carbonitril,
 10 2-[1-(4,4-Difluorocyclohexyl)-3-methyl-1H-pyrazol-4-ylamino]-4-methylaminopyrimidin-5-carbonitril,
 (5-(5-Chlor-4-(methylamino)pyrimidin-2-ylamino)-1-methyl-1H-pyrazol-3-yl)-(morpholino)methanon,
 2-Methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannitril,
 N,N-Dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)aceta-
 mid,
 15 N,N-Dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)aceta-
 mid,
 N-Methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamid,
 N-Methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acetamid,
 N,N,2-Trimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-yl)pro-
 panamid,
 20 2-Methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-
 1-yl)propan-1-on,
 2-Methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannitril,
 1-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropancarbonitril,
 25 (R)-2-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-
 yl)propan-1-on,
 (R)-N,N-Dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-yl)pro-
 panamid,
 (S)-2-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-
 30 yl)propan-1-on,
 3-(5-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannitril,
 3-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannitril,
 Methyl-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-yl)pro-
 panoat,
 35 Methyl-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-yl)pro-
 panoat,
 2-(3-Ethyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropannitril,
 (R)-2-(5-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1-(pyrrolidin-1-yl)propan-1-on,
 (R)-N,N-Dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-yl)pro-
 panamid,
 40 (S)-2-(5-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-(pyrrolidin-1-yl)pro-
 pan-1-on,
 (S)-N,N-Dimethyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-yl)propanamid,
 (S)-2-(5-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannitril,
 45 (S)-2-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannitril,
 2-(4-(5-Chlor-4-(methylamino)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropannitril,
 2-(5-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropannitril,
 2-(3-Cyclopropyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropan-
 nitril,
 50 2,2-dimethyl-3-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannit-
 ril,
 2,2-dimethyl-3-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannit-
 ril,
 1-(5-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-cyclopropancarbonitril,
 55 N-tert-Butyl-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-
 yl)propanamid,
 2-Methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1-yl)-N-(2,2,2-trifluorethyl)pro-
 panamid,

2-(5-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-ethyl-2-methylpropanamid,
 N-(Cyclopropylmethyl)-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)-pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamid,
 5 N-(Cyclopropylmethyl)-2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)-pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamid,
 N-Ethyl-1-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutancarboxamid,
 10 N-Isopropyl-2-methyl-2-(5-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-yl-amino)-1H-pyrazol-1-yl)propanamid,
 1-(3-Methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutancarbonitril,
 2-(4-(4-(Cyclopropylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methyl-1H-pyrazol-1-yl)-2-methylpropannitril,
 N, 2-Dimethyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamid,
 15 1-(5-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-cyclopropancarbonitril,
 2-[4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-5-methylpyrazol-1-yl]-2-methyl-propionsäuremethylester,
 2-[4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-2-methyl-propionsäuremethylester,
 (S)-N,N-Dimethyl-2-[3-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-yl-am ino)-pyrazol-1-yl]-propionamid,
 20 R)-2-[3-Methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitril,
 2-[4-(5-Chlor-4-methoxypyrimidin-2-ylamino)-3-cyclopropylpyrazol-1-yl]-2-methyl-propionitril,
 (R)-2-[5-Methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-propionitril,
 N-Ethyl-2-[3-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramid,
 25 N-Ethyl-2-[5-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramid,
 1-[5-Methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutancarbonsäureethylamid,
 2-[5-Methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-N-(2,2,2-trifluorethyl)isobutyramid,
 30 N-Isopropyl-2-[3-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramid,
 N-Methyl-2-[5-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramid,
 1-[5-Methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-cyclobutancarbonitril,
 N-tert-Butyl-2-[5-methyl-4-(4-methylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-pyrazol-1-yl]-isobutyramid,
 35 2-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-5-methylpyrazol-1-yl]-N-methyl isobutyramid,
 2-[4-(4-Cyclopropylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-N-methylisobutyramid,
 2-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methylpyrazol-1-yl]-2-methylpropionitril,
 2-(3-Chlor-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-methylpropannitril und
 2-[4-(4-Ethylamino-5-(trifluormethyl)pyrimidin-2-ylamino)-3-methyl-pyrazol-1-yl]-N-methyl isobutyramid,

oder ein pharmazeutisch annehmbares Salz davon.

16. Verbindung nach Anspruch 1, die N²-[5-Chlor-1-(3-fluor-1-oxetan-3-yl)piperidin-4-yl]-1H-pyrazol-4-yl]-N⁴-Methyl-5-(trifluormethyl)pyrimidin-2,4-diamin oder ein pharmazeutisch annehmbares Salz davon ist.

17. Verbindung nach Anspruch 1, die 2-Methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluormethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propannitril oder ein pharmazeutisch annehmbares Salz davon ist.

18. Verbindung nach einem der Ansprüche 1 bis 17 oder ein pharmazeutisch annehmbares Salz davon zur Verwendung als Medikament.

19. Verbindung nach einem der Ansprüche 1 bis 17 oder ein pharmazeutisch annehmbares Salz davon zur Verwendung bei der therapeutischen und/oder prophylaktischen Behandlung von Morbus Parkinson.

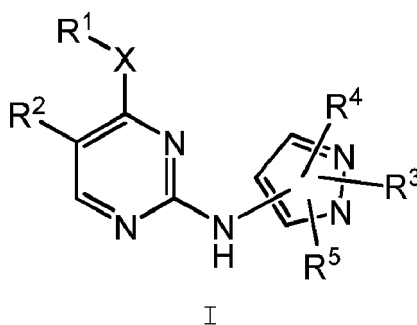
20. Verbindung nach einem der Ansprüche 1 bis 17 oder ein pharmazeutisch annehmbares Salz davon zur Herstellung von Medikamenten für die therapeutische und/oder prophylaktische Behandlung von Morbus Parkinson.

21. Zusammensetzung, die Folgendes umfasst:

- (a) einen pharmazeutisch annehmbaren Träger; und
 (b) eine Verbindung nach einem der Ansprüche 1 bis 17 oder ein pharmazeutisch annehmbares Salz davon.

5 **Revendications**

1. Composé de formule I :



ou un sel pharmaceutiquement acceptable de celui-ci, formule dans laquelle :

X est : -NR^a- ; ou -O-, où R^a est l'hydrogène ;

R¹ est un : alkyle en C₁ à C₆ ;

R² est un : halogéno ; cyano ; ou halogénalkyle en C₁ à C₆ ;

R³ est un : hydrogène ; alkyle en C₁ à C₆ ; halogénalkyle en C₁ à C₆ ; alcényle en C₂ à C₆ ; alcynyle en C₂ à C₆ ; hydroxyalkyle en C₁ à C₆ ; (alkoxy en C₁ à C₆)alkyle en C₁ à C₆ ; cyanoalkyle en C₁ à C₆ ; alkylsulfonyle en C₁ à C₆ ; (alkylsulfonyle en C₁ à C₆) alkyle en C₁ à C₆ ; aminoalkyle en C₁ à C₆ ; cycloalkyle en C₃ à C₆ éventuellement substitué une ou plusieurs fois par R⁶ ; (cycloalkyle en C₃ à C₆) alkyle en C₁ à C₆ dont le fragment cycloalkyle en C₃ à C₆ est éventuellement substitué une ou plusieurs fois par R⁶ ; (cycloalkyle en C₃ à C₆) sulfonyle dont le fragment cycloalkyle en C₃ à C₆ est éventuellement substitué une ou plusieurs fois par R⁶ ; hétérocyclyle éventuellement substitué une ou plusieurs fois par R⁷ ; hétérocyclyl-alkyle en C₁ à C₆ dont le fragment hétérocyclyle est éventuellement substitué une ou plusieurs fois par R⁷ ; aryle éventuellement substitué une ou plusieurs fois par R⁸ ; aryl-alkyle en C₁ à C₆ dont le fragment aryle est éventuellement substitué une ou plusieurs fois par R⁸ ; hétéroaryle éventuellement substitué une ou plusieurs fois par R⁸ ; hétéroaryl-alkyle en C₁ à C₆ dont le fragment hétéroaryle est éventuellement substitué une ou plusieurs fois par R⁸ ; ou -Y-C(O)-R^d ;

Y est un alkylène en C₂ à C₆ ou une liaison ;

R^d est un alkyle en C₁ à C₆, alkoxy en C₁ à C₆, amino, alkylamino en C₁ à C₆, di(alkyle en C₁ à C₆) amino, halogénalkylamino en C₁ à C₆, di(halogénalkyle en C₁ à C₆) amino, halogénalkyle en C₁ à C₆, hydroxyalkyle en C₁ à C₆, hydroxy, (alkoxy en C₁ à C₆)alkyle en C₁ à C₆, cyanoalkyle en C₁ à C₆, (alkylsulfonyle en C₁ à C₆) alkyle en C₁ à C₆, aminoalkyle en C₁ à C₆, cycloalkyle en C₃ à C₆ éventuellement substitué une ou plusieurs fois par R⁶, (cycloalkyle en C₃ à C₆)alkyle en C₁ à C₆ dont le fragment cycloalkyle en C₃ à C₆ est éventuellement substitué une ou plusieurs fois par R⁶, hétérocyclyle éventuellement substitué une ou plusieurs fois par R⁷, ou hétérocyclylalkyle en C₁ à C₆ dont le fragment hétérocyclyle est éventuellement substitué une ou plusieurs fois par R⁷ ;

R⁴ est un : hydrogène ; alkyle en C₁ à C₆ ; halogéno ; cyano ; halogénalkyle en C₁ à C₆ ; alcényle en C₂ à C₆ ; alcynyle en C₂ à C₆ ; alkoxy en C₁ à C₆ ; (alkoxy en C₁ à C₆)alkyle en C₁ à C₆ ; hydroxyalkyle en C₁ à C₆ ; cycloalkyle en C₃ à C₆ éventuellement substitué une ou plusieurs fois par R⁶ ; (cycloalkyle en C₃ à C₆) alkyle en C₁ à C₆ dont le fragment cycloalkyle en C₃ à C₆ est éventuellement substitué une ou plusieurs fois par R⁶ ; ou -Y-C(O)-R^d ;

R⁵ est un : hydrogène ; ou alkyle en C₁ à C₆ ;

chaque R⁶ est indépendamment un : alkyle en C₁ à C₆ ; halogénalkyle en C₁ à C₆ ; alkoxy en C₁ à C₆ ; oxo ; cyano ; halogéno ; ou Y-C(O)-R^d ;

chaque R⁷ est indépendamment un : alkyle en C₁ à C₆ ; halogénalkyle en C₁ à C₆ ; halogéno ; oxo ; alkoxy en C₁ à C₆ ; alkylsulfonyle en C₁ à C₆ ; (alkoxy en C₁ à C₆) alkyle en C₁ à C₆ ; cyano ; -Y-C(O)-R^d ; hétérocyclyle ; hétérocyclyl-alkyle en C₁ à C₆ ; cycloalkyle en C₃ à C₆ ; (cycloalkyle en C₃ à C₆) alkyle en C₁ à C₆ ; ou cycloalkylsulfonyle en C₃ à C₆ ; et

chaque R⁸ est indépendamment un : oxo ; alkyle en C₁ à C₆ ; halogénalkyle en C₁ à C₆ ; halogéno ; alkylsulfonyle en C₁ à C₆ ; alkoxy en C₁ à C₆ ; (alkoxy en C₁ à C₆)alkyle en C₁ à C₆ ; cyano ; hétérocyclyle ; hétérocyclyl-alkyle en C₁ à C₆ ; -Y-C(O)-R^d ; cycloalkyle en C₃ à C₆, (cycloalkyle en C₃ à C₆)alkyle en C₁ à C₆, ou cycloalkylsulfonyle en C₃ à C₆.

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2. Composé selon la revendication 1, dans lequel R² est un : fluoro ; bromo ; chloro ; iodo ; trifluorométhyle ; ou cyano.

3. Composé selon l'une quelconque des revendications 1 et 2, dans lequel R³ est un : alkyle en C₁ à C₆ ; halogénalkyle en C₁ à C₆ ; hydroxyalkyle en C₁ à C₆ ; (alkoxy en C₁ à C₆)alkyle en C₁ à C₆ ; cycloalkyle en C₃ à C₆ éventuellement substitué une ou plusieurs fois par R⁶ ; (cycloalkyle en C₃ à C₆)alkyle en C₁ à C₆ dont le fragment cycloalkyle en C₃ à C₆ est éventuellement substitué une ou plusieurs fois par R⁶ ; hétérocyclyle éventuellement substitué une ou plusieurs fois par R⁷ ; hétérocyclyl-alkyle en C₁ à C₆ dont le fragment hétérocyclyle est éventuellement substitué une ou plusieurs fois par R⁷ ; ou -C(O)-R^d.

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4. Composé selon l'une quelconque des revendications 1 à 3, dans lequel R³ est un : alkyle en C₁ à C₆ ; hydroxyalkyle en C₁ à C₆ ; (alkoxy en C₁ à C₆)alkyle en C₁ à C₆ ; hétérocyclyle éventuellement substitué une ou plusieurs fois par R⁷ ; ou hétérocyclyl-alkyle en C₁ à C₆ dont le fragment hétérocyclyle est éventuellement substitué une ou plusieurs fois par R⁷.

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5. Composé selon l'une quelconque des revendications 1 et 2, dans lequel R³ est un : méthyle ; éthyle ; propyle ; isopropyle ; butyle ; cyclopropyle ; cyclopropylméthyle ; cyclobutyle ; méthanesulfonyle ; éthylsulfonyle ; cyclopropylsulfonyle ; sec-butylsulfonyle ; morpholin-4-yléthyle ; oxétan-3-yle ; 2-méthoxyéthyle ; 2-hydroxy-2-méthylpropyle ; 3-hydroxy-2-méthylpropan-2-yle ; 2-méthoxypropyle ; tétrahydro-2H-pyran-4-yle ; tétrahydrofuran-3-yle ; 2,6-diméthyltétrahydro-2H-pyran-4-yle ; tétrahydro-2H-pyran-3-yle ; phényle ; 4-(méthylsulfonyl)phényle ; 4-cyanophényle ; 4-fluorophényle ; 4-chlorophényle ; 3,5-difluorophényle ; 4-(diméthylaminocarbonyl)phényle ; 4-(cyclopropylsulfonyl)phényle ; 2,2,2-trifluoroéthyle ; 2-fluoroéthyle ; difluorométhyle ; 2-diméthyl-1,3-dioxan-5-yle ; 1-méthylcyclopropylcarbonyl ; 3-méthylpyridin-4-yle ; 2-méthylpyridin-4-yle ; pyridin-2-yle ; pyrimidin-2-yle ; pyrimidin-5-yle ; pyridin-2-ylméthyle ; 1-(pyridin-2-yl)éthyle ; cyclopropylsulfonyle ; 1-cyano-1-méthyléthyle ; 2-cyanoéthyle ; 1-cyanoéthyle ; 2-cyano-2-méthylpropyle ; 1-(2,2,2-trifluoroéthyl)pipéridin-4-yle ; 1-(méthylsulfonyl)azétidin-3-yle ; (3-méthyl-oxétan-3-yl)méthyle ; (1S,5S)-8-oxabicyclo[3.2.1]octan-3-yle ; 1-(oxétan-3-yl)pipéridin-4-yle ; 1-acétylpipéridin-4-yle ; 1-(cyclopropylcarbonyl)pipéridin-4-yle ; 1-méthylpipéridin-4-yle ; 1-méthyl-2-oxopipéridin-5-yle ; 2-oxopipéridin-5-yle ; 1-(isopropylcarbonyl)pipéridin-4-yle ; 1-(oxétan-3-yl)azétidin-3-yle ; 1-(cyclopropylcarbonyl)pipéridin-4-yle ; 2-méthoxycyclopentyle ; 3-méthoxycyclopentyle ; 1-méthoxy-2-méthylpropan-2-yle ; tétrahydro-2H-1,1-dioxothiopyran-4-yle ; 3-fluoro-1-(oxétan-3-yl)pipéridin-4-yle ; 1-méthoxypropan-2-yle ; 1-(2,2,2-trifluoroéthyl)azétidin-3-yle ; 1-(oxétan-3-yl)pyrrolidin-3-yle ; 1-isopropylazétidin-3-yle ; 3-fluoro-1-méthylpipéridin-4-yle ; 1-éthyl-3-fluoropipéridin-4-yle ; 1-méthylpyrrolidin-3-yle ; 2-méthoxyéthyl)pipéridin-4-yle) ; 1-méthyl-1-(méthylaminocarbonyl)éthyle ; 2-méthyl-2-morpholinopropyle ; 4,4-difluorocyclohexyle ; morpholin-4-ylcarbonyl ; diméthylaminocarbonylméthyle ; méthylaminocarbonylméthyle ; 1-méthyl-1-(diméthylaminocarbonyl)éthyle ; pyrrolidin-1-ylcarbonyl ; 1-cyanocyclopropyle ; 1-(pyrrolidin-1-ylcarbonyl)éthyle ; 1-(diméthylaminocarbonyl)éthyle ; 1-(méthoxycarbonyl)éthyle ; 1-(tert-butylaminocarbonyl)-1-méthyléthyle ; 1-(2,2,2-trifluoroéthylaminocarbonyl)-1-méthyléthyle ; 1-(éthylaminocarbonyl)-1-méthyléthyle ; 1-(cyclopropylméthylaminocarbonyl)-1-méthyléthyle ; 1-(éthylaminocarbonyl)cyclobutyle ; 1-(isopropylaminocarbonyl)-1-méthyléthyle ; 1-cyanocyclobutyle ; 2-méthoxy-1-méthyléthyle ; 1-méthyl-1-(méthoxycarbonyl)éthyle ; 2-méthoxy-2-méthylpropan-1-yle ; 1-(oxétan-3-yl)pyrrolidin-3-yle ; isopropylsulfonyle ; butane-2-sulfonyle ; 1-(2-fluoroéthyl)pipéridin-4-yle ; 3-fluoro-1-méthylpipéridin-4-yle ; 1-éthyl-3-fluoropipéridin-4-yle ; pyridin-3-ylméthyle ; 6-méthyl-pyridin-2-ylméthyle ; 2-(morpholin-1-yl)-1,1-diméthyléthyle ; pyrimidin-2-ylméthyle ; 3-fluoro-1-(oxétan-3-yl)pipéridin-4-yle ; 1-(oxétan-3-yl)pipéridin-3-yle ; 1-([1,3]dioxolan-2-ylméthyl)pipéridin-4-yle ; pyridazin-3-ylméthyle ; pipéridin-3-yle ; pyrazin-2-ylméthyle ; 2-hydroxy-3-méthylbutan-1-yle ; 1-([1,3]dioxolan-2-ylméthyl)pyrrolidin-3-yle ; pyrimidin-4-ylméthyle ; 1-méthyl-1H-pyrazol-3-ylméthyle ; 1-méthyl-1-(4H-[1,2,4]triazol-3-yl)éthyle ; 1-méthyl-1-(5-méthyl-4H-[1,2,4]triazol-3-yl)éthyle ; 3-fluoropipéridin-4-yle ; 2-hydroxycyclopentyle ; diméthyl-[1,3]dioxan-5-yle ; 2-(5-méthyl-1,3,4-oxadiazol-2-yl)propan-2-yle ; 2-(4-méthyl-4H-1,2,4-triazol-3-yl)propan-2-yle ; 2-(1-méthyl-1H-1,2,4-triazol-3-yl)propan-2-yle ; 2-(1-méthyl-1H-pyrazol-4-yl)propan-2-yle ; 2-(1-méthyl-1H-pyrazol-3-yl)propan-2-yle ; 2-(1-méthyl-1H-pyrazol-5-yle ; 2-(4H-1,2,4-triazol-3-yl)propan-2-yle ; ou 1-méthyl-1H-pyrazol-4-yle.

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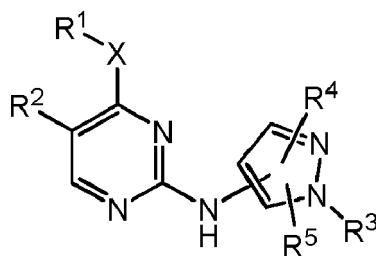
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6. Composé selon l'une quelconque des revendications 1 à 5, dans lequel R⁴ est un hydrogène ; alkyle en C₁ à C₆ ; halogéno ; ou cycloalkyle en C₃ à C₆ éventuellement substitué par alkyle en C₁ à C₆.

7. Composé selon l'une quelconque des revendications 1 à 6, dans lequel R⁴ est un hydrogène ou alkyle en C₁ à C₆.

8. Composé selon l'une quelconque des revendications 1 à 6, dans lequel R⁴ est un chloro ou méthyle.
9. Composé selon l'une quelconque des revendications 1 à 8, dans lequel R⁵ est un alkyle en C₁ à C₆.
- 5 10. Composé selon l'une quelconque des revendications 1 à 8, dans lequel R⁵ est un hydrogène ou méthyle.
11. Composé selon l'une quelconque des revendications 1 à 10, lequel composé est de formule II

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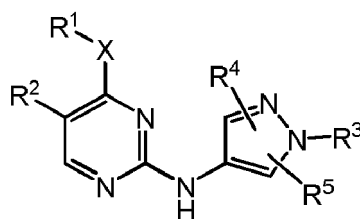
II

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dans laquelle X, R¹, R², R³, R⁴ et R⁵ sont tels que définis dans l'une quelconque des revendications 1 à 10.

12. Composé selon l'une quelconque des revendications 1 à 10, lequel composé est de formule III

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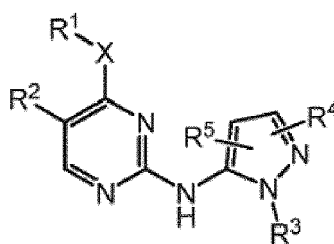
III

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dans laquelle X, R¹, R², R³, R⁴ et R⁵ sont tels que définis dans l'une quelconque des revendications 1 à 10.

13. Composé selon l'une quelconque des revendications 1 à 10, lequel composé est de formule IV

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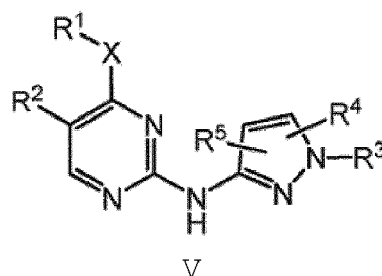
IV

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dans laquelle X, R¹, R², R³, R⁴ et R⁵ sont tels que définis dans l'une quelconque des revendications 1 à 10.

14. Composé selon l'une quelconque des revendications 1 à 10, lequel composé est de formule V

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dans laquelle X, R¹, R², R³, R⁴ et R⁵ sont tels que définis dans l'une quelconque des revendications 1 à 10.

15. Composé selon la revendication 1, qui est choisi dans l'ensemble constitué par les suivantes :

- 15 N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1,5-diméthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(1-(2-morpholinoéthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(1-méthyl-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-N²-(1-isopropyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 20 N⁴-méthyl-N²-(1-méthyl-1H-pyrazol-5-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(1-méthyl-1H-pyrazol-3-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1,3-diméthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-5-(trifluorométhyl)-N²-(1,3,5-triméthyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-chloro-N-(1,5-diméthyl-1H-pyrazol-4-yl)-4-méthoxypyrimidin-2-amine,
 25 N²-(1-éthyl-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-N-(1,3-diméthyl-1H-pyrazol-4-yl)-4-méthoxypyrimidin-2-amine,
 N⁴-méthyl-N²-(3-méthyl-1-(oxétan-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(5-chloro-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-4-méthoxy-N-(3-méthyl-1-(oxétan-3-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
 30 5-chloro-4-méthoxy-N-(1-(2-méthoxyéthyl)-3-méthyl-1H-pyrazol-4-yl)pyrimidin-2-amine,
 5-chloro-4-méthoxy-N-(1-(2-méthoxyéthyl)-5-méthyl-1H-pyrazol-4-yl)pyrimidin-2-amine,
 5-chloro-N-(5-chloro-1-méthyl-1H-pyrazol-4-yl)-4-méthoxypyrimidin-2-amine,
 2-méthyl-1-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,
 2-méthyl-1-(3-méthyl-4-(4-(méthylamino)-5-chloropyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,
 35 N²-(1-(2-méthoxyéthyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(2-méthoxyéthyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-N-(1-éthyl-3-méthyl-1H-pyrazol-4-yl)-4-méthoxypyrimidin-2-amine,
 5-chloro-N⁴-méthyl-N²-(3-méthyl-1-(oxétan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 N²-(1-isopropyl-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 40 5-chloro-N-(1-isopropyl-3-méthyl-1H-pyrazol-4-yl)-4-méthoxypyrimidin-2-amine,
 5-chloro-N²-(1,3-diméthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-chloro-N²-(1-isopropyl-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diami-
 ne,
 45 N⁴-méthyl-N²-(5-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diami-
 ne,
 N²-(2-éthyl-2H-pyrazol-3-yl)-5-fluoro-N⁴-méthylpyrimidine-2,4-diamine,
 5-fluoro-N⁴-méthyl-N²-(2-méthyl-2H-pyrazol-3-yl)pyrimidine-2,4-diamine,
 5-fluoro-N⁴-méthyl-N⁴-(2-propyl-2H-pyrazol-3-yl)pyrimidine-2,4-diamine,
 50 N²-(2,5-diméthyl-2H-pyrazol-3-yl)-5-fluoro-N⁴-méthylpyrimidine-2,4-diamine,
 N²-(3-isopropyl-1-méthyl-1H-pyrazol-5-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-N-(3-cyclopropyl-1-méthyl-1H-pyrazol-5-yl)-4-méthoxypyrimidin-2-amine,
 N²-(3-cyclopropyl-1-méthyl-1H-pyrazol-5-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-N-(3-isopropyl-1-méthyl-1H-pyrazol-5-yl)-4-méthoxypyrimidin-2-amine,
 55 5-chloro-N²-(5-isopropyl-2-méthyl-2H-pyrazol-3-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-chloro-4-méthoxy-N-(1,3,5-triméthyl-1H-pyrazol-4-yl)pyrimidin-2-amine,
 5-chloro-N⁴-méthyl-N²-(1,3,5-triméthyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-chloro-N²-(5-cyclopropyl-2-méthyl-2H-pyrazol-3-yl)-N⁴-méthylpyrimidine-2,4-diamine,

N⁴-méthyl-N²-(5-méthyl-1-oxétan-3-yl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-(1-isopropyl-1H-pyrazol-5-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-N-(1-éthyl-5-méthyl-1H-pyrazol-4-yl)-4-méthoxy-pyrimidin-2-amine,
 5-chloro-N²-(1-éthyl-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5
 N²-(1-éthyl-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-N²-(1-éthyl-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-chloro-N²-(1-isopropyl-1H-pyrazol-5-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-chloro-N-(1-isopropyl-1H-pyrazol-5-yl)-4-méthoxy-pyrimidin-2-amine,
 5-chloro-4-méthoxy-N-(3-méthyl-1-(méthylsulfonyl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
 10
 N²-(1-éthyl-1H-pyrazol-3-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-4-méthoxy-N-(5-méthyl-1-phényl-1H-pyrazol-4-yl)pyrimidin-2-amine,
 N²-(1-isopropyl-1H-pyrazol-3-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-(2,2,2-trifluoroéthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(2,2-diméthyl-1,3-dioxan-5-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-
 15
 diamine,
 5-chloro-4-méthoxy-N-(5-méthyl-1-(4-(méthylsulfonyl)phényl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
 N⁴-éthyl-N²-(1-méthyl-1H-pyrazol-3-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-chloro-4-méthoxy-N-(3-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
 (4-(4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-3-méthyl-1H-pyrazol-1-yl)pipéridin-1-yl) (1-méthylcyclopro-
 20
 pyl)méthanone,
 (4-(4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)pipéridin-1-yl) (1-méthylcyclopro-
 pyl)méthanone,
 4-(4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-3-méthyl-1H-pyrazol-1-yl)benzonitrile,
 5-chloro-4-méthoxy-N-(3-méthyl-1-(3-méthylpyridin-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
 25
 5-chloro-N-(1-(cyclopropylsulfonyl)-5-méthyl-1H-pyrazol-4-yl)-4-méthoxy-pyrimidin-2-amine,
 5-chloro-N-(1-(cyclopropylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-4-méthoxy-pyrimidin-2-amine,
 2-(4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)-2-méthylpropanenitrile,
 2-(4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-3-méthyl-1H-pyrazol-1-yl)-2-méthylpropanenitrile,
 5-chloro-4-éthoxy-N-(5-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)pyrimidin-2-amine,
 30
 (5-chloro-4-méthoxy-pyrimidin-2-yl)-[1-(4-méthanesulfonylphényl)-3-méthyl-1H-pyrazol-4-yl]amine,
 (5-chloro-4-méthoxy-pyrimidin-2-yl)-(3-méthyl-1-phényl-1H-pyrazol-4-yl)amine,
 (4-méthoxy-5-trifluorométhylpyrimidin-2-yl)-(3-méthyl-1-phényl-1H-pyrazol-4-yl)amine,
 (4-méthoxy-5-trifluorométhylpyrimidin-2-yl)-(5-méthyl-1-phényl-1H-pyrazol-4-yl)amine,
 (5-chloro-4-méthoxy-pyrimidin-2-yl)-(1-méthanesulfonyl-3-méthyl-1H-pyrazol-4-yl)amine,
 35
 (5-chloro-4-méthoxy-pyrimidin-2-yl)-[5-méthyl-1-(tétrahydropyran-4-yl)-1H-pyrazol-4-yl]amine,
 4-[4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-N,N-diméthylbenzamide,
 4-[4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-5-méthylpyrazol-1-yl]-N,N-diméthylbenzamide,
 4-[4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-5-méthylpyrazol-1-yl]benzonitrile,
 N²-(5-méthoxy-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 40
 (5-chloro-4-méthoxy-pyrimidin-2-yl)-[5-chloro-1-(tétrahydropyran-4-yl)-1H-pyrazol-4-yl]amine,
 (5-chloro-4-méthoxy-pyrimidin-2-yl)-{1-[1-(2-fluoroéthyl)pipéridin-4-yl]-3-méthyl-1H-pyrazol-4-yl}amine,
 N²[1-(1-[1,3]dioxolan-2-ylméthyl)pipéridin-4-yl]-5-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidi-
 ne-2,4-diamine,
 N²[1-(1-[1,3]dioxolan-2-ylméthyl)pipéridin-4-yl]-3-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidi-
 45
 ne-2,4-diamine,
 5-bromo-N²-(1,5-diméthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 N²-(1,3-diméthyl-1H-pyrazol-4-yl)-5-iodo-N⁴-méthylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-(1-(2,2,2-trifluoroéthyl)pipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidi-
 ne-2,4-diamine,
 50
 N⁴-méthyl-N²-(3-méthyl-1-(1-(2,2,2-trifluoroéthyl)pipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-
 2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(5-méthyl-1-(1-(2,2,2-trifluoroéthyl)pipéridin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-dia-
 mine,
 5-bromo-N⁴-méthyl-N²-(3-méthyl-1-(1-(2,2,2-trifluoroéthyl)pipéridin-4-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-dia-
 55
 mine,
 5-bromo-N⁴-méthyl-N²-(3-méthyl-1-(2,2,2-trifluoroéthyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(5-méthyl-1-(2,2,2-trifluoroéthyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 N⁴-éthyl-N²-(3-méthyl-1-(oxétan-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,

5-chloro-N⁴-éthyl-N²-(3-méthyl-1-(oxétan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(1-méthyl-1H-pyrazol-5-yl)pyrimidine-2,4-diamine,
 2-méthyl-1-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propan-2-ol,
 5-chloro-N⁴-méthyl-N²-(3-méthyl-1-(méthylsulfonyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5 N⁴-méthyl-N²-(3-méthyl-1-(méthylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-bromo-N⁴-éthyl-N²-(3-méthyl-1-(oxétan-3-yl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 N²-(1-(difluorométhyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 10 N²-(1-(difluorométhyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-bromo-N⁴-éthyl-N²-(1-éthyl-5-méthyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-bromo-N²-(1-(4-fluorophényl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(3-méthyl-1-phényl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(5-méthyl-1-phényl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(1-méthyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 15 N⁴-méthyl-N²-(3-méthyl-1-(1-(méthylsulfonyl)azétidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(3-méthyl-1-propyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-chloro-N⁴-méthyl-N²-(3-méthyl-1-((3-méthyl-oxétan-3-yl)méthyl)-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 5-bromo-N²-(1-(3,5-difluorophényl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 20 5-bromo-N²-(1-(3,5-difluorophényl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(pyridin-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-((3-méthyl-oxétan-3-yl)méthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 25 N⁴-méthyl-N²-(3-méthyl-1-propyl-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5-bromo-N²-(1-isopropyl-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-bromo-N²-(1-(4-chlorophényl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 N²-(1-(4-chlorophényl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(4-(méthylsulfonyl)phényl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 30 N⁴-méthyl-N²-(5-méthyl-1-(4-(méthylsulfonyl)phényl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-((1S,5S)-8-oxabicyclo[3.2.1]octan-3-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 35 N²-(1-butyl-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(pyrimidin-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(4-chlorophényl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(2-fluoroéthyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(1-(oxétan-3-yl)pipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 40 N⁴-méthyl-N²-(5-méthyl-1-(1-(oxétan-3-yl)pipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(2-fluoroéthyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 45 1-(4-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-3-méthyl-1H-pyrazol-1-yl)pipéridin-1-yl)éthanone,
 cyclopropyl(4-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pipéridin-1-yl)méthanone,
 cyclopropyl(4-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pipéridin-1-yl)méthanone,
 50 1-(4-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)pipéridin-1-yl)éthanone,
 N²-(5-chloro-1-isopropyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(5-chloro-1-éthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(pyrimidin-5-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 55 N⁴-méthyl-N²-(4-méthyl-1-(1-méthylpipéridin-4-yl)-1H-pyrazol-3-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-(2-méthylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(2-méthylpyridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-éthyl-N²-(3-méthyl-1-((3-méthyl-oxétan-3-yl)méthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine

mine,
N²-(5-chloro-1-cyclopropyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(5-chloro-1-(cyclopropylméthyl)-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
4-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonnitrile,
5 4-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzonnitrile,
N⁴-méthyl-N²-(3-méthyl-1-(tétrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N⁴-méthyl-N²-(5-méthyl-1-(tétrahydrofuran-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
5-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)-1-méthylpipéridin-2-one,
10 5-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-3-méthyl-1H-pyrazol-1-yl)-1-méthylpipéridin-2-one,
5-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pipéridin-2-one,
5-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pipéridin-2-one,
15 N²-(1-isopropyl-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N,N-diméthyl-4-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide,
4-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)-N,N-diméthylbenzamide,
N⁴-éthyl-N²-(5-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
20 N⁴-éthyl-N²-(3-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N⁴-éthyl-N²-(3-méthyl-1-(méthylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(1-(4-(cyclopropylsulfonyl)phényl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
25 4-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)benzonnitrile,
N⁴-éthyl-N²-(5-méthyl-1-(4-(méthylsulfonyl)phényl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N,N-diméthyl-4-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)benzamide,
30 N²-(1-(cyclopropylméthyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(1-(cyclopropylméthyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(1-(4-(cyclopropylsulfonyl)phényl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
35 N²-(5-chloro-1-(oxétan-3-yl)-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N⁴-éthyl-N²-(5-méthyl-1-((3-méthyl-oxétan-3-yl)méthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(1-(cyclopropylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(1-(cyclopropylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-éthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
40 N²-(1-(4-(cyclopropylsulfonyl)phényl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-éthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
2-méthyl-1-(4-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)pipéridin-1-yl)propan-1-one,
N⁴-éthyl-N²-(1-méthyl-1H-pyrazol-5-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
45 N²-(3-cyclopropyl-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(5-cyclopropyl-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N⁴-méthyl-N²-(5-méthyl-1-((3-méthyl-oxétan-3-yl)méthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(5-chloro-1-((3-méthyl-oxétan-3-yl)méthyl)-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
50 1-(4-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)pipéridin-1-yl)-2-méthylpropan-1-one,
N⁴-éthyl-N²-(3-méthyl-1-(1-(oxétan-3-yl)azétidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
55 cyclopropyl(4-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-3-méthyl-1H-pyrazol-1-yl)pipéridin-1-yl)méthanone,
cyclopropyl(4-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-5-méthyl-1H-pyrazol-1-yl)pipéridin-1-yl)méthanone,

1-(5-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropan-2-ol,
 N⁴-éthyl-N²-(1-éthyl-1H-pyrazol-3-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 (S)-N²-(1-(2-méthoxypropyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(2-méthoxycyclopentyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5 (S)-N²-(1-(2-méthoxypropyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(1-méthoxy-2-méthylpropan-2-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-
 2,4-diamine,
 N²-(1-(2,6-diméthyltétrahydro-2H-pyran-4-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidi-
 ne-2,4-diamine,
 10 (R)-N²-(1-(2-méthoxypropyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(3-méthoxycyclopentyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(1-méthyl-5-(méthylamino)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-(méthylsulfonyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-(tétrahydro-2H-1,1-dioxothiopyran-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimi-
 dine-2,4-diamine,
 15 2-méthyl-1-(4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-5-(trifluorométhyl)-1H-pyrazol-1-
 yl)propan-2-ol,
 2-méthyl-1-(4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-3-(trifluorométhyl)-1H-pyrazol-1-
 yl)propan-2-ol,
 20 N²-(1-(3-fluoro-1-(oxétan-3-yl)pipéridin-4-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidi-
 ne-2,4-diamine,
 (R)-N²-(1-(1-méthoxypropan-2-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-dia-
 mine,
 1-(3-tert-butyl-4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropan-2-ol,
 25 N⁴-méthyl-N²-(3-méthyl-1-(1-(2,2,2-trifluoroéthyl)azétidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-
 2,4-diamine,
 N²-(1-(1-méthoxy-2-méthylpropan-2-yl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-
 2,4-diamine,
 (R)-N⁴-méthyl-N²-(3-méthyl-1-(1-(oxétan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-
 2,4-diamine,
 30 (R)-N²-(1-(1-méthoxypropan-2-yl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-dia-
 mine,
 N⁴-méthyl-N²-(4-méthyl-1H-pyrazol-5-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-éthyl-N²-(5-méthyl-1-(1-méthylpipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 35 N⁴-éthyl-N²-(3-méthyl-1-(1-méthylpipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(1-méthylpipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-(1-méthylpipéridin-4-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 (R)-N⁴-méthyl-N²-(5-méthyl-1-(1-(oxétan-3-yl)pyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-
 2,4-diamine,
 40 N⁴-méthyl-N²-(5-méthyl-1-(pyridin-2-ylméthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(pyridin-2-ylméthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(1-isopropylazétidin-3-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diami-
 ne,
 1-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazole-5-carbonitrile,
 45 N⁴-éthyl-N²-(1-(isopropylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(isopropylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(isopropylsulfonyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(sec-butylsulfonyl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(1-(sec-butylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 50 1-(4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-3-isopropyl-1H-pyrazol-1-yl)-2-méthylpropan-2-ol,
 N²-(1-(3-fluoro-1-méthylpipéridin-4-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-
 diamine,
 N²-(5-isopropyl-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(1-(pyridin-2-yl)éthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 55 N⁴-méthyl-N²-(5-méthyl-1-(1-(pyridin-2-yl)éthyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(5-chloro-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diami-
 ne,
 N²-(3-isopropyl-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,

N²-(3-cyclobutyl-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N²-(5-cyclobutyl-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(tétrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diami-
 5 ne,
 N⁴-méthyl-N²-(5-méthyl-1-(tétrahydro-2H-pyran-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diami-
 ne,
 (R)-N⁴-méthyl-N²-(3-méthyl-1-(1-méthylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-dia-
 mine,
 10 1-(5-chloro-4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropan-2-ol,
 1-(3-cyclopropyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropan-
 2-ol,
 1-(3-cyclopropyl-4-(4-(éthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropan-2-
 ol,
 15 2-(5-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N,2-diméthylpropana-
 mide,
 N²-(1-(1-(2-méthoxyéthyl)pipéridin-4-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-
 2,4-diamine,
 N²-(1-(1-(2-méthoxyéthyl)pipéridin-4-yl)-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-
 20 2,4-diamine,
 (R)-N⁴-méthyl-N²-(5-méthyl-1-(1-méthylpyrrolidin-3-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-dia-
 mine,
 N²-(5-chloro-1-(3-fluoro-1-méthylpipéridin-4-yl)-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-
 diamine,
 25 N²-(5-chloro-1-(1-éthyl-3-fluoropipéridin-4-yl)-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-
 diamine,
 N⁴-éthyl-N²-(1-(éthylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-éthyl-N²-(1-(éthylsulfonyl)-5-méthyl-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-(2-méthyl-2-morpholinopropyl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimidine-2,4-
 30 diamine,
 N²-(1-(1-éthyl-3-fluoropipéridin-4-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-
 diamine,
 N²-(5-(diméthylamino)-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 2-(5-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropan-1-ol,
 35 N²-(1-(éthylsulfonyl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 2-méthyl-1-[3-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]propan-2-ol,
 N²-[1-(2-méthoxyéthyl)-3-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[1-(2-méthoxyéthyl)-5-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 5-bromo-N²-(1-éthyl-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-[3-méthyl-1-(2,2,2-trifluoroéthyl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 40 5-bromo-N²-(1-difluorométhyl-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-bromo-N²-(1-difluorométhyl-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthylpyrimidine-2,4-diamine,
 5-bromo-N²-(1,5-diméthyl-1H-pyrazol-4-yl)-N⁴-éthylpyrimidine-2,4-diamine,
 5-bromo-N²-[1-(4-fluorophényl)-5-méthyl-1H-pyrazol-4-yl]-N⁴-méthylpyrimidine-2,4-diamine,
 5-bromo-N⁴-méthyl-N²-(5-méthyl-1-propyl-1H-pyrazol-4-yl)pyrimidine-2,4-diamine,
 45 5-bromo-N²-[1-(4-chlorophényl)-3-méthyl-1H-pyrazol-4-yl]-N⁴-méthylpyrimidine-2,4-diamine,
 N²-(1,5-diméthyl-1H-pyrazol-4-yl)-N⁴-éthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 5-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]pipéridin-2-one,
 4-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-N,N-diméthylbenzamide,
 N²-[1-(4-cyclopropanesulfonylphényl)-3-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidine-2,4-dia-
 50 mine,
 4-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]benzonitrile,
 N⁴-éthyl-N²-[1-(4-méthanesulfonylphényl)-3-méthyl-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 1-[4-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-5-méthylpyrazol-1-yl]pipéridin-1-yl]-2-méthyl-
 propan-1-one,
 55 1-[4-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]pipéridin-1-yl]-2-méthyl-
 propan-1-one,
 N⁴-méthyl-N²-[3-méthyl-1-(3-méthylpyridin-4-yl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[1-(R)-2-méthoxypropyl]-3-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,

N²-[1-(2,6-diméthyltétrahydropyran-4-yl)-5-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[1-(1,1-dioxothian-4-yl)-3-méthylpyrazol-4-yl]-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
 5 N²-[1-(R)-2-méthoxy-1-méthyléthyl]-5-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[1-(S)-2-méthoxy-1-méthyléthyl]-3-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-[3-méthyl-1-((S)-1-oxétan-3-ylpyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 10 N⁴-méthyl-N²-[5-méthyl-1-((S)-1-oxétan-3-ylpyrrolidin-3-yl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[1-(1-isopropylazétidin-3-yl)-5-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-[5-méthyl-1-(propane-2-sulfonyl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[5-cyclobutyl-1-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 15 N²-[3-cyclobutyl-1-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-{1-[1-(2-méthoxyéthyl)pipéridin-4-yl]-3-méthyl-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-{1-[1-(2-méthoxyéthyl)pipéridin-4-yl]-5-méthyl-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 20 N²-[1-[1-(2-fluoroéthyl)pipéridin-4-yl]-5-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-{1-[1-(2-fluoroéthyl)pipéridin-4-yl]-3-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[5-chloro-1-(3-fluoro-1-méthylpipéridin-4-yl)-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 25 N²-(1-éthanesulfonyl-5-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-[5-méthyl-1-(2-méthyl-2-morpholin-4-ylpropyl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-pyridin-3-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
 30 N²-(1-cyclopropanesulfonyl-3-cyclopropyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(5-méthyl-1-pyridin-3-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
 (5-chloro-4-méthoxypyrimidin-2-yl)-{1-[1-(2-fluoroéthyl)pipéridin-4-yl]-5-méthyl-1H-pyrazol-4-yl}amine,
 N⁴-méthyl-N²-[3-méthyl-1-(6-méthylpyridin-2-ylméthyl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 35 N⁴-éthyl-N²-[1-(2-méthoxyéthyl)-3-méthyl-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-[1-(2-méthoxyéthyl)-5-méthyl-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 1-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-5-méthylpyrazol-1-yl]-2-méthylpropan-2-ol,
 1-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-2-méthylpropan-2-ol,
 40 N²-[1-(1,1-diméthyl-2-morpholin-4-yléthyl)-3-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[1-(1,1-diméthyl-2-morpholin-4-yléthyl)-3-méthyl-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 1-[3-chloro-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]-2-méthylpropan-2-ol,
 45 2-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-N-méthylisobutyramide,
 N⁴-méthyl-N²-(3-méthyl-1-pyrimidin-2-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
 N²-[5-chloro-1-(3-fluoro-1-oxétan-3-ylpipéridin-4-yl)-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 50 N²-[5-chloro-1-(3-fluoro-1-oxétan-3-ylpipéridin-4-yl)-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-[5-méthyl-1-((S)-1-oxétan-3-ylpipéridin-3-yl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-[3-méthyl-1-((S)-1-oxétan-3-ylpipéridin-3-yl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 55 N⁴-méthyl-N²-(5-méthyl-1-pyridazin-3-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-méthyl-N²-(3-méthyl-1-pyridazin-3-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-[5-méthyl-1-((S)-1-méthylpipéridin-3-yl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
 N⁴-éthyl-N²-[3-méthyl-1-((S)-1-méthylpipéridin-3-yl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,

3-[5-chloro-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]-2,2-diméthylpropionitrile,
N⁴-méthyl-N²-[5-méthyl-1-(6-méthylpyridin-2-ylméthyl)-1H-pyrazol-4-yl]-5-trifluorométhyl-pyrimidine-2,4-dia-
mine,
5 N⁴-méthyl-N²-(5-méthyl-1-pyrimidin-2-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
N⁴-méthyl-N²-(5-méthyl-1-pyrazin-2-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine 2,4-diamine,
N⁴-méthyl-N²-(3-méthyl-1-pyrazin-2-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine 2,4-diamine,
3-[5-chloro-4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]-2,2-diméthylpropionitrile,
N⁴-éthyl-N²-[1-(3-fluoro-1-oxétan-3-ylpipéridin-4-yl)-3-méthyl-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-
diamine,
10 3-méthyl-1-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]butan-2-ol,
3-méthyl-1-[3-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]butan-2-ol,
N²-[1-(1-[1,3]dioxolan-2-ylméthylpyrrolidin-3-yl)-3-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidi-
ne-2,4-diamine,
N⁴-méthyl-N²-(5-méthyl-1-pyrimidin-4-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
15 N⁴-méthyl-N²-[5-méthyl-1-(1-méthyl-1H-pyrazol-3-ylméthyl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-
diamine,
N⁴-méthyl-N²-[3-méthyl-1-(1-méthyl-1H-pyrazol-3-ylméthyl)-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-
diamine,
20 3-[3-chloro-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]-2,2-diméthylpropionitrile,
N⁴-éthyl-N²-[3-méthyl-1-[1-méthyl-1-(4H-[1,2,4]triazol-3-yl)éthyl]-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-
2,4-diamine,
N²-[1-(1-[1,3]dioxolan-2-ylméthylpyrrolidin-3-yl)-5-méthyl-1H-pyrazol-4-yl]-N⁴-éthyl-5-trifluorométhylpyrimidi-
ne-2,4-diamine,
25 N⁴-méthyl-N²-(3-méthyl-1-pyrimidin-4-ylméthyl-1H-pyrazol-4-yl)-5-trifluorométhylpyrimidine-2,4-diamine,
N²-(5-fluorométhyl-1-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine,
N⁴-éthyl-N²-[3-méthyl-1-[1-méthyl-1-(5-méthyl-4H-[1,2,4]triazol-3-yl)éthyl]-1H-pyrazol-4-yl]-5-trifluorométhyl-
pyrimidine-2,4-diamine,
N⁴-méthyl-N²-[3-méthyl-1-[1-méthyl-1-(4H-[1,2,4]triazol-3-yl)éthyl]-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidi-
ne-2,4-diamine,
30 N⁴-éthyl-N²-[1-(3-fluoropipéridin-4-yl)-3-méthyl-1H-pyrazol-4-yl]-5-trifluorométhylpyrimidine-2,4-diamine,
2-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]cyclopentanol,
2-[3-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]cyclopentanol,
N⁴-éthyl-N²-(3-méthyl-1-(2-(5-méthyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)py-
rimidine-2,4-diamine,
35 N⁴-éthyl-N²-(3-méthyl-1-(2-(4-méthyl-4H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)py-
rimidine-2,4-diamine,
N⁴-éthyl-N²-(3-méthyl-1-(2-(1-méthyl-1H-1,2,4-triazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)py-
rimidine-2,4-diamine,
40 N⁴-méthyl-N²-(3-méthyl-1-(2-(5-méthyl-1,3,4-oxadiazol-2-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluoromé-
thyl)pyrimidine-2,4-diamine,
N⁴-méthyl-N²-(3-méthyl-1-(2-(1-méthyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyri-
midine-2,4-diamine,
N⁴-méthyl-N²-(5-méthyl-1-(2-(1-méthyl-1H-pyrazol-4-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyri-
midine-2,4-diamine,
45 N⁴-éthyl-N²-(3-méthyl-1-(2-(1-méthyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimi-
dine-2,4-diamine,
N⁴-éthyl-N²-(3-méthyl-1-(2-(1-méthyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyrimi-
dine-2,4-diamine,
50 N⁴-méthyl-N²-(3-méthyl-1-(2-(1-méthyl-1H-pyrazol-5-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyri-
midine-2,4-diamine,
N⁴-méthyl-N²-(3-méthyl-1-(2-(1-méthyl-1H-pyrazol-3-yl)propan-2-yl)-1H-pyrazol-4-yl)-5-(trifluorométhyl)pyri-
midine-2,4-diamine,
N²-(1',5-diméthyl-1'H-1,4'-bipyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
55 N²-(1',3-diméthyl-1'H-1,4'-bipyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-2,4-diamine,
N²-(1-(2-(4H-1,2,4-triazol-3-yl)propan-2-yl)-3-méthyl-1H-pyrazol-4-yl)-N⁴-méthyl-5-(trifluorométhyl)pyrimidine-
2,4-diamine,
2-(1,5-diméthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
2-(1,3-diméthyl-1H-pyrazol-4-ylamino)-4-méthylaminopyrimidine-5-carbonitrile,

2-(1-éthyl-5-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1-isopropyl-3-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1-éthyl-3-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(3-méthyl-1-phényl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 5 2-(3-méthyl-1-(1-(2,2,2-trifluoroéthyl)pipéridin-4-yl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(5-méthyl-1-(1-(2,2,2-trifluoroéthyl)pipéridin-4-yl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 10 2-(5-méthyl-1-(2,2,2-trifluoroéthyl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(3-méthyl-1-(2,2,2-trifluoroéthyl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(5-méthyl-1-phényl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(5-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(3-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 15 2-(1-éthyl-5-méthyl-1H-pyrazol-4-ylamino)-4-(éthylamino)pyrimidine-5-carbonitrile,
 2-(1-(4-fluorophényl)-3-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1-(difluorométhyl)-3-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(5-méthyl-1-propyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1-(3,5-difluorophényl)-3-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 20 2-(1-(4-chlorophényl)-3-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1-(4-chlorophényl)-5-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(3-méthyl-1-(pyridin-2-yl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 4-(éthylamino)-2-(5-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,
 4-(éthylamino)-2-(3-méthyl-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,
 25 4-(éthylamino)-2-(3-méthyl-1-(oxétan-3-yl)-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,
 2-(1-isopropyl-5-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1,5-diméthyl-1H-pyrazol-4-ylamino)-4-méthoxypyrimidine-5-carbonitrile,
 2-(1-éthyl-5-méthyl-1H-pyrazol-4-ylamino)-4-méthoxypyrimidine-5-carbonitrile,
 2-(1-(cyclopropylméthyl)-3-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 30 2-(1-(4,4-difluorocyclohexyl)-5-méthyl-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(5-chloro-1-(tétrahydro-2H-pyran-4-yl)-1H-pyrazol-4-ylamino)-4-(méthylamino)pyrimidine-5-carbonitrile,
 2-(1-difluorométhyl-5-méthyl-1H-pyrazol-4-ylamino)-4-méthylaminopyrimidine-5-carbonitrile,
 2-(1,5-diméthyl-1H-pyrazol-4-ylamino)-4-éthylaminopyrimidine-5-carbonitrile,
 2-[1-(4-fluorophényl)-5-méthyl-1H-pyrazol-4-ylamino]-4-méthylaminopyrimidine-5-carbonitrile,
 35 4-méthylamino-2-(3-méthyl-1-propyl-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,
 4-méthylamino-2-(5-méthyl-1-oxétan-3-yl-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,
 4-méthylamino-2-(3-méthyl-1-oxétan-3-yl-1H-pyrazol-4-ylamino)pyrimidine-5-carbonitrile,
 2-[1-(3,5-difluorophényl)-5-méthyl-1H-pyrazol-4-ylamino]-4-méthylaminopyrimidine-5-carbonitrile,
 2-[1-(4,4-difluorocyclohexyl)-3-méthyl-1H-pyrazol-4-ylamino]-4-méthylaminopyrimidine-5-carbonitrile,
 40 (5-(5-chloro-4-(méthylamino)pyrimidin-2-ylamino)-1-méthyl-1H-pyrazol-3-yl)(morpholino)méthanone,
 2-méthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 N,N-diméthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acétamide,
 45 N,N-diméthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acétamide,
 N-méthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acétamide,
 N-méthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)acétamide,
 N,N,2-triméthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 50 2-méthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,
 2-méthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 1-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,
 55 (R)-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,

- (R)-N,N-diméthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 (S)-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,
 5 3-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 3-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 2-méthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate
 de méthyle,
 2-méthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanoate
 10 de méthyle,
 2-(3-éthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropanenitrile,
 (R)-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,
 (R)-N,N-diméthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 15 (S)-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-1-(pyrrolidin-1-yl)propan-1-one,
 (S)-N,N-diméthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 20 (S)-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 (S)-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 2-(4-(5-chloro-4-(méthylamino)pyrimidin-2-ylamino)-3-méthyl-1H-pyrazol-1-yl)-2-méthylpropanenitrile,
 2-(5-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropanenitri-
 25 le,
 2-(3-cyclopropyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropanenitrile,
 2,2-diméthyl-3-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 2,2-diméthyl-3-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile,
 30 1-(5-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,
 N-tert-butyl-2-méthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 35 2-méthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-(2,2,2-trifluoroéthyl)propanamide,
 2-(5-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-N-éthyl-2-méthylpropanamide,
 N-(cyclopropylméthyl)-2-méthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 40 N-(cyclopropylméthyl)-2-méthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 N-éthyl-1-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarboxamide,
 45 N-isopropyl-2-méthyl-2-(5-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 1-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclobutanecarbonitrile,
 N,2-diméthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanamide,
 50 1-(5-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)cyclopropanecarbonitrile,
 ester méthylique d'acide 2-[4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-5-méthylpyrazol-1-yl]-2-méthylpropionique,
 55 ester méthylique d'acide 2-[4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-2-méthylpropionique,
 (S)-N,N-diméthyl-2-[3-méthyl-4-(4-méthylamino-5-trifluorométhyl)pyrimidin-2-ylamino]pyrazol-1-yl]propionamide,
 de,

(R)-2-[3-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]propionitrile,
 2-[4-(5-chloro-4-méthoxy-pyrimidin-2-ylamino)-3-cyclopropylpyrazol-1-yl]-2-méthylpropionitrile,
 (R)-2-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]propionitrile,
 N-éthyl-2-[3-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]isobutyramide,
 N-éthyl-2-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]isobutyramide,
 éthylamide d'acide 1-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]cyclobuta-
 necarboxylique,
 2-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]-N-(2,2,2-trifluoroéthyl)isobu-
 tyramide,
 N-isopropyl-2-[3-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]isobutyramide,
 N-méthyl-2-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]isobutyramide,
 1-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]cyclobutanecarbonitrile,
 N-tert-butyl-2-[5-méthyl-4-(4-méthylamino-5-trifluorométhylpyrimidin-2-ylamino)pyrazol-1-yl]isobutyramide,
 2-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-5-méthylpyrazol-1-yl]-N-méthylisobutyramide,
 2-[4-(4-cyclopropylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-N-méthylisobutyramide,
 2-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-2-méthylpropionitrile,
 2-(3-chloro-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)-2-méthylpropanenitri-
 le, et
 2-[4-(4-éthylamino-5-trifluorométhylpyrimidin-2-ylamino)-3-méthylpyrazol-1-yl]-N-méthylisobutyramide,

ou un sel pharmaceutiquement acceptable d'un tel composé.

16. Composé selon la revendication 1, qui est la N²-[5-chloro-1-(3-fluoro-1-oxétan-3-yl)pipéridin-4-yl]-1H-pyrazol-4-yl]-N⁴-méthyl-5-trifluorométhylpyrimidine-2,4-diamine ou un sel pharmaceutiquement acceptable de celle-ci.

17. Composé selon la revendication 1, qui est le 2-méthyl-2-(3-méthyl-4-(4-(méthylamino)-5-(trifluorométhyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile ou un sel pharmaceutiquement acceptable de celui-ci.

18. Composé selon l'une quelconque des revendications 1 à 17, ou un sel pharmaceutiquement acceptable de celui-ci, destiné à être utilisé en tant que médicament.

19. Composé selon l'une quelconque des revendications 1 à 17, ou un sel pharmaceutiquement acceptable de celui-ci, destiné à être utilisé dans le traitement thérapeutique et/ou prophylactique de la maladie de Parkinson.

20. Utilisation d'un composé selon l'une quelconque des revendications 1 à 17 ou d'un sel pharmaceutiquement acceptable de celui-ci, pour la préparation de médicaments destinés au traitement thérapeutique et/ou prophylactique de la maladie de Parkinson.

21. Composition comprenant :

- (a) un véhicule pharmaceutiquement acceptable ; et
- (b) un composé selon l'une quelconque des revendications 1 à 17 ou un sel pharmaceutiquement acceptable de celui-ci.

REFERENCES CITED IN THE DESCRIPTION

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