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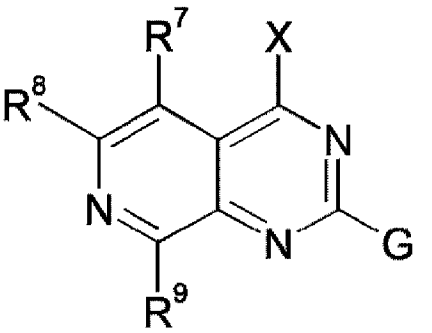

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(57) Abrégé/Abstract:
The present invention provides a compound of formula (I) (see formula I) or a salt thereof. A compound of formula (I) and its salts have aPKC inhibitory activity, and may be used to treat proliferative disorders.

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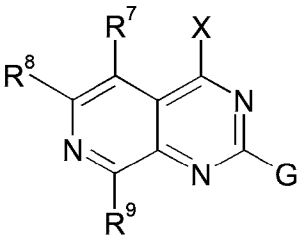
ABSTRACT

The present invention provides a compound of formula (I)



(I)

or a salt thereof. A compound of formula (I) and its salts have aPKC inhibitory activity, and may be used to treat proliferative disorders.

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AZAQUINAZOLINE INHIBITORS OF ATYPICAL PROTEIN KINASE C

BACKGROUND OF THE INVENTION

PKCι and PKCζ (accession numbers NM_002740 and NM_002744 respectively) together define the atypical sub-class of the protein kinase C (PKC) family. The aPKCs are structurally and functionally distinct from the other PKC sub-classes, classic/conventional and novel, as their catalytic activity is not dependent on diacylglycerol and calcium (Ono, Y., Fujii, T., Ogita, K., Kikkawa, U., Igarashi, K., and Nishizuka, Y. (1989). Protein kinase C zeta subspecies from rat brain: its structure, expression, and properties. Proc Natl Acad Sci U S A *86*, 3099-3103). Structurally, PKCι and PKCζ contain a C-terminal serine/threonine kinase domain (AGC class) and an N-terminal regulatory region containing a Phox Bem 1 (PB1) domain involved in mediating protein:protein interactions critical for aPKC function. At the amino acid level the aPKCs share 72% overall homology, however, the kinase domains share 84% identity and differ in the active site by just a single amino acid. This striking homology suggests an ATP-competitive ligand would not be expected to exhibit significant aPKC isoform selectivity.

The aPKCs have been implicated in a diverse number of signalling pathways, demonstrating both redundant and distinct signalling functions. Both isoforms have emerged as central players in the mechanisms that regulate the establishment and maintenance of cellular polarity in multiple cell types (reviewed in Suzuki, A., and Ohno, S. (2006). The PAR-aPKC system: lessons in polarity. J Cell Sci *119*, 979-987). Genetic dissection of their functions using knockout mice have also revealed preferential roles for PKCζ in the regulation of NF-kB signalling (Leitges, M., Sanz, L., Martin, P., Duran, A., Braun, U., Garcia, J.F., Camacho, F., Diaz-Meco, M.T., Rennert, P.D., and Moscat, J. (2001). Targeted disruption of the zetaPKC gene results in the impairment of the NF-kappaB pathway. Mol Cell *8*, 771-780), and PKCι in insulin secretion and action (Farese, R.V., Sajan, M.P., Yang, H., Li, P., Mastorides, S., Gower, W.R., Jr., Nimal, S., Choi, C.S., Kim, S., Shulman, G.I., *et al.* (2007). Muscle-specific knockout of PKC-lambda impairs glucose transport and induces metabolic and diabetic syndromes. J Clin Invest *117*, 2289-2301). In addition, both isoforms have been implicated in the pathogenesis of cancer making a strong case for the inhibition of the aPKCs as a novel therapeutic avenue.

PKCι is a known oncogene in non-small cell lung cancer (NSCLC). In one study it was shown to be overexpressed in 69% of NSCLC cases at the protein level. Consistent with this, the PKCι gene (*PRKCI* residing on chromosome 3q26) was shown to be amplified in 36.5% of NSCLC tumours examined, including 96% of the squamous cell carcinoma sub-type (Regala, R.P., Weems, C., Jamieson, L., Khoor, A., Edell, E.S., Lohse, C.M., and Fields, A.P. (2005b). Atypical protein kinase C iota is an oncogene in human non-small cell lung cancer. Cancer Res *65*, 8905-8911). Amplification of 3q26 has also been reported in 44% of ovarian cancers, including >70% of serous epithelial ovarian cancers where 3q26 amplification is translated into increased PKCι protein expression. Moreover, increased PKCι expression is associated with poor prognosis in NSCLC and ovarian cancer where it may serve as a diagnostic biomarker of aggressive disease (Eder, A.M., Sui, X., Rosen, D.G., Nolden, L.K., Cheng, K.W., Lahad, J.P., Kango-Singh, M., Lu, K.H., Warneke, C.L., Atkinson, E.N., *et al.* (2005). Atypical PKCiota contributes to poor prognosis through loss of apical-basal polarity and cyclin E overexpression in ovarian cancer. Proc Natl Acad Sci U S A *102*, 12519-12524; Zhang, L., Huang, J., Yang, N., Liang, S., Barchetti, A., Giannakakis, A., Cadungog, M.G., O'Brien-Jenkins, A., Massobrio, M., Roby, K.F., *et al.* (2006). Integrative genomic analysis of protein kinase C (PKC) family identifies PKCiota as a biomarker and potential oncogene in ovarian carcinoma. Cancer Res *66*, 4627-4635). 3q26 amplifications have been observed in many other cancers including oesophageal squamous cell carcinoma (Yang, Y.L., Chu, J.Y., Luo, M.L., Wu, Y.P., Zhang, Y., Feng, Y.B., Shi, Z.Z., Xu, X., Han, Y.L., Cai, Y., *et al.* (2008). Amplification of PRKCI, located in 3q26, is associated with lymph node metastasis in esophageal squamous cell carcinoma. Genes Chromosomes Cancer *47*, 127-136) and breast cancer (Kojima, Y., Akimoto, K., Nagashima, Y., Ishiguro, H., Shirai, S., Chishima, T., Ichikawa, Y., Ishikawa, T., Sasaki, T., Kubota, Y., *et al.* (2008). The overexpression and altered localization of the atypical protein kinase C lambda/iota in breast cancer correlates with the pathologic type of these tumors. Hum Pathol *39*, 824-831) suggesting that PKCι may also participate in the pathogenesis of these diseases.

In NSCLC the primary function of PKCι is to drive transformed growth via a Rac1 / PAK / MEK / ERK signalling axis. However, PKCι also functions in NSCLC survival, resistance to chemotherapy, and invasion via distinct pathways (reviewed in Fields, A.P., and Regala, R.P. (2007). Protein kinase C iota: human oncogene, prognostic marker and therapeutic target. Pharmacol Res *55*, 487-497). In ovarian cancer transformed growth is

correlated with deregulated epithelial cell polarity and increased cycle E expression (Eder et al., *Proc Natl Acad Sci USA 102*, 12519-125242005) suggesting that PKCι can influence the cancer phenotype through multiple mechanisms. Compelling evidence has emerged to suggest that inhibition of PKCι may be a useful therapeutic approach to combat tumours characterised by increased PKCι expression. In transgenic models, mice with elevated PKCι activity in the colon are more susceptible to carcinogen-induced colon carcinogenesis, and expression of a kinase-dead mutant of PKCι blocks the transformation of intestinal cells by oncogenic Ras (Murray, N.R., Jamieson, L., Yu, W., Zhang, J., Gokmen-Polar, Y., Sier, D., Anastasiadis, P., Gatalica, Z., Thompson, E.A., and Fields, A.P. (2004). Protein kinase Ciota is required for Ras transformation and colon carcinogenesis in vivo. J Cell Biol *164*, 797-802). Finally, genetic or pharmacological inhibition of PKCι by a gold derivative – aurothiomalate (ATM) – blocks the growth of NSCLC cells in soft agar and significantly decreases tumour volume in xenograft models of NSCLC(Regala, R.P., Thompson, E.A., and Fields, A.P. (2008). Atypical protein kinase C iota expression and aurothiomalate sensitivity in human lung cancer cells. Cancer Res *68*, 5888-5895; Regala, R.P., Weems, C., Jamieson, L., Copland, J.A., Thompson, E.A., and Fields, A.P. (2005a). Atypical protein kinase Ciota plays a critical role in human lung cancer cell growth and tumorigenicity. J Biol Chem *280*, 31109-31115).

Despite the high degree of similarity between aPKC isoforms, the role of PKCζ in cancer is distinct from that of PKCι. PKCζ plays a role in NSCLC cell survival by phosphorylating and antagonising the pro-apoptotic effects of Bax in response to nicotine (Xin, M., Gao, F., May, W.S., Flagg, T., and Deng, X. (2007). Protein kinase Czeta abrogates the proapoptotic function of Bax through phosphorylation. J Biol Chem *282*, 21268-21277). PKCζ activity has also been linked to resistance against a wide range of cytotoxic and genotoxic agents. For instance, in human leukaemia cells, overexpression of PKCζ confers resistance against 1-β-D-arabinofuranosylcytosine (ara-C), daunorubicin, etoposide, and mitoxantrone-induced apoptosis (Filomenko, R., Poirson-Bichat, F., Billerey, C., Belon, J.P., Garrido, C., Solary, E., and Bettaieb, A. (2002). Atypical protein kinase C zeta as a target for chemosensitization of tumor cells. Cancer Res *62*, 1815-1821; Plo, I., Hernandez, H., Kohlhagen, G., Lautier, D., Pommier, Y., and Laurent, G. (2002). Overexpression of the atypical protein kinase C zeta reduces topoisomerase II catalytic activity, cleavable complexes formation, and drug-induced cytotoxicity in monocytic U937 leukemia cells. J Biol Chem *277*, 31407-31415). Furthermore, inhibition of PKCζ activity through expression

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of a kinase-dead mutant sensitises leukaemia cells to the cytotoxic effects of etoposide both *in vitro* and *in vivo* (Filomenko et al., 2002). Atypical protein kinase C regulates dual pathways for degradation of the oncogenic coactivator SRC-3/AIB1. Mol Cell *29*, 465-476), and both of these proteins have been postulated to play a role in tamoxifen resistance in breast cancer (Iorns, E., Lord, C.J., and Ashworth, A. (2009). Parallel RNAi and compound screens identify the PDK1 pathway as a target for tamoxifen sensitization. Biochem J *417*, 361-370; Osborne, C.K., Bardou, V., Hopp, T.A., Chamness, G.C., Hilsenbeck, S.G., Fuqua, S.A., Wong, J., Allred, D.C., Clark, G.M., and Schiff, R. (2003). Role of the estrogen receptor coactivator AIB1 (SRC-3) and HER-2/neu in tamoxifen resistance in breast cancer. J Natl Cancer Inst *95*, 353-361). Together these studies suggest that inhibition of PKCζ activity may have beneficial therapeutic effects by acting as a chemosensitiser to a wide array of commonly used chemotoxic agents in the clinic.

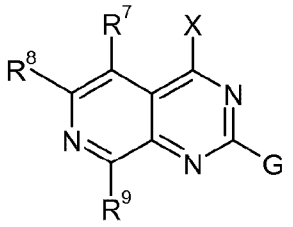
Further evidence that small molecule inhibition of PKCζ could have important therapeutic benefits has recently emerged from tumour models that link PKCζ signalling to the mTOR pathway. PKCζ is constitutively activated in follicular lymphoma and has been identified as a novel target for the anti-CD20 therapeutic antibody rituximab (Leseux, L., Laurent, G., Laurent, C., Rigo, M., Blanc, A., Olive, D., and Bezombes, C. (2008). PKC zeta mTOR pathway: a new target for rituximab therapy in follicular lymphoma. Blood *111*, 285-291). Rituximab inhibits follicular lymphoma proliferation by targeting a PKCζ-MAPK-mTOR pathway, suggesting that PKCζ is both a target of Rituximab, and a key regulator of its' anti-leukaemic effect. Regulation of the mTOR/p70S6K pathway by PKCζ has also been implicated in the transition of prostate cancer cells to an androgen-independent state (Inoue, T., Yoshida, T., Shimizu, Y., Kobayashi, T., Yamasaki, T., Toda, Y., Segawa, T., Kamoto, T., Nakamura, E., and Ogawa, O. (2006). Requirement of androgen-dependent activation of protein kinase Czeta for androgen-dependent cell proliferation in LNCaP Cells and its roles in transition to androgen-independent cells. Mol Endocrinol *20*, 3053-3069). Finally, mice containing a homozygous deletion of Par4, a negative regulator of PKCζ, exhibit greatly enhanced PKCζ activity. These mice spontaneously develop tumours of the prostate and endometrium, and potentiate Ras-induced lung carcinogenesis consistent with a role for PKCζ in lung cancer (Garcia-Cao, I., Duran, A., Collado, M., Carrascosa, M.J., Martin-Caballero, J., Flores, J.M., Diaz-Meco, M.T., Moscat, J., and Serrano, M. (2005). Tumour-suppression activity of the proapoptotic regulator Par4. EMBO Rep *6*, 577-583; Joshi, J.,

Fernandez-Marcos, P.J., Galvez, A., Amanchy, R., Linares, J.F., Duran, A., Pathrose, P., Leitges, M., Canamero, M., Collado, M., *et al.* (2008). Par-4 inhibits Akt and suppresses Ras-induced lung tumorigenesis. EMBO J *27*, 2181-2193).

A need exists for aPKC inhibitors for use as pharmaceutical agents.

SUMMARY OF THE INVENTION

The invention provides a compound of formula (I)



(I)

or a salt thereof, wherein R^7, R^8, R^9, G, and X are as defined herein.

A compound of formula (I) and its salts have aPKC inhibitory activity, and may be used to treat aPKC-dependent disorders or conditions.

The present invention further provides a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof together with at least one pharmaceutically acceptable carrier, diluent, or excipient therefor.

In another aspect, the present invention provides a method of treating a subject suffering from an aPKC-dependent disorder or condition comprising: administering to the subject a compound of formula (I) or a pharmaceutically acceptable salt thereof.

The present invention further provides a method of treating a proliferative disorder in a subject, comprising administering to the subject a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof.

DETAILED DESCRIPTION OF THE INVENTION

I. Definitions

"About" as used herein when referring to a measurable value such as an amount, a temporal duration, and the like, is meant to encompass reasonable variations of the value, such as, for example, ±10% from the specified value. For example, the phrase "about 50" encompasses reasonable variations of 50, such as ±10% of the numerical value 50, or from 45 to 55.

"Alkyl" or "alkyl group" refers to a monoradical of a branched or unbranched saturated hydrocarbon chain. Examples include, but are not limited to, methyl, ethyl, n-propyl, n-butyl, n-pentyl, n-hexyl, n-heptyl, n-octyl, n-nonyl, n-decyl, isopropyl, tert-butyl, isobutyl, etc. Alkyl groups typically contain 1-10 carbon atoms, such as 1-6 carbon atoms or 1-4 carbon atoms, and can be substituted or unsubstituted.

"Alkylene" or "alkylene group" refers to a diradical of a branched or unbranched saturated hydrocarbon chain. Examples include, but are not limited to, methylene ($–CH_2–$), the ethylene isomers ($–CH(CH_3)–$ and $–CH_2CH_2–$), the propylene isomers ($–CH(CH_3)CH_2–$, $–CH(CH_2CH_3)–$, $–C(CH_3)_2–$, and $–CH_2CH_2CH_2–$), etc. Alkylene groups typically contain 1-10 carbon atoms, such as 1-6 carbon atoms, and can be substituted or unsubstituted.

"Alkenyl" or "alkenyl group" refers to a monoradical of a branched or unbranched hydrocarbon chain containing at least one double bond. Examples include, but are not limited to, ethenyl, 3-buten-1-yl, 2-ethenylbutyl, and 3-hexen-1-yl. Alkenyl groups typically contain 2-10 carbon atoms, such as 2-6 carbon atoms or 2-4 carbon atoms, and can be substituted or unsubstituted.

"Alkynyl" or "alkynyl group" refers to a monoradical of a branched or unbranched hydrocarbon chain containing at least one triple bond. Examples include, but are not limited to, ethynyl, 3-butyn-1-yl, propynyl, 2-butyn-1-yl, and 3-pentyn-1-yl. Alkynyl groups typically contain 2-10 carbon atoms, such as 2-6 carbon atoms or 2-4 carbon atoms, and can be substituted or unsubstituted.

"Aryl" or "aryl group" refers to phenyl and 7-15 membered monoradical bicyclic or tricyclic hydrocarbon ring systems, including bridged, spiro, and/or fused ring systems, in which at least one of the rings is aromatic. Aryl groups can be substituted or unsubstituted. Examples include, but are not limited to, naphthyl, indanyl, 1,2,3,4-tetrahydronaphthalenyl, 6,7,8,9-tetrahydro-5H-benzocycloheptenyl, and 6,7,8,9-tetrahydro-5H-benzocycloheptenyl. An aryl group may contain 6 (i.e., phenyl) or 9 to 15 ring atoms, such as 6 (i.e., phenyl) or 9-11 ring atoms, e.g., 6 (i.e., phenyl), 9 or 10 ring atoms.

"Arylene" or "arylene group" refers to a phenylene ($–C_6H_4–$) or a 7-15 membered diradical bicyclic or tricyclic hydrocarbon ring systems, including bridged, spiro, and/or fused ring systems, in which at least one of the rings is aromatic. Arylene groups can be

substituted or unsubstituted. For example, an arylene group may contain 6 (i.e., phenylene) or 9 to 15 ring atoms; such as 6 (i.e., phenylene) or 9-11 ring atoms; e.g., 6 (i.e., phenylene), 9 or 10 ring atoms. An arylene group can also include ring systems substituted on ring carbons with one or more –OH functional groups (which may further tautomerize to give a ring C=O group).

"Arylalkyl" or "arylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by an aryl group, wherein alkyl group and aryl group are as previously defined (i.e., arylalkyl–). Arylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, benzyl ($C_6H_5CH_2$–).

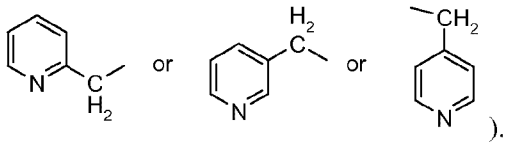
"Cycloalkyl" or "cycloalkyl group" refers to a monoradical non-aromatic carbocyclic ring system, which may be saturated or unsaturated, substituted or unsubstituted, and may be monocyclic, bicyclic, or tricyclic, and may be bridged, spiro, and/or fused. Examples include, but are not limited to, cyclopropyl, cyclopropenyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, norbornyl, norbornenyl, bicyclo[2.2.1]hexane, bicyclo[2.2.1]heptane, bicyclo[2.2.1]heptene, bicyclo[3.1.1]heptane, bicyclo[3.2.1]octane, bicyclo[2.2.2]octane, bicyclo[3.2.2]nonane, bicyclo[3.3.1]nonane, and bicyclo[3.3.2]decane. The cycloalkyl group may contain from 3 to 10 ring atoms, such as 3 to 7 ring atoms (e.g., 3 ring atoms, 5 ring atoms, 6 ring atoms, or 7 ring atoms).

"Cycloalkylalkyl" or "cycloalkylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by a cycloalkyl group, wherein alkyl group and cycloalkyl group are as previously defined (i.e., cycloalkylalkyl–). Cycloalkylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, cyclohexylmethyl ($C_6H_{11}CH_2$–).

"Haloalkyl" or "haloalkyl group" refers to alkyl groups in which one or more hydrogen atoms are replaced by halogen atoms. Haloalkyl includes both saturated alkyl groups and unsaturated alkenyl and alkynyl groups, such as for example –CF_3, –CHF_2, –CH_2F, –CF_2CF_3, –$CHFCF_3$, –CH_2CF_3, –CF_2CH_3, –$CHFCH_3$, –$CF_2CF_2CF_3$, –$CF_2CH_2CH_3$, –$CF{=}CF_2$, –$CCl{=}CH_2$, –$CBr{=}CH_2$, –$CI{=}CH_2$, –C≡C-CF_3, –$CHFCH_2CH_3$ and –$CHFCH_2CF_3$.

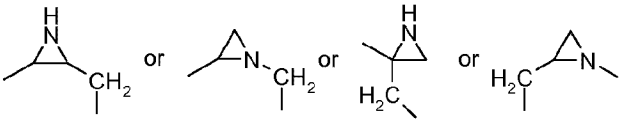
"Halogen" includes fluorine, chlorine, bromine and iodine atoms.

"Heteroaryl" or "heteroaryl group" refers to (a) 5 and 6 membered monocyclic aromatic rings, which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen or sulfur, and (b) 7-15 membered bicyclic and tricyclic rings, which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen or sulfur, and in which at least one of the rings is aromatic. Heteroaryl groups can be substituted or unsubstituted, and may be bridged, spiro, and/or fused. Examples include, but are not limited to, 2,3-dihydrobenzofuranyl, 1,2-dihydroquinolinyl, 3,4-dihydroisoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydroquinolinyl, benzoxazinyl, benzthiazinyl, chromanyl, furanyl, 2-furanyl, 3-furanyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, oxazolyl, pyridinyl, 2-, 3-, or 4-pyridinyl, pyrimidinyl, 2-, 4-, or 5-pyrimidinyl, pyrazolyl, pyrrolyl, 2- or 3-pyrrolyl, pyrazinyl, pyridazinyl, 3- or 4-pyridazinyl, 2-pyrazinyl, thienyl, 2-thienyl, 3-thienyl, tetrazolyl, thiazolyl, thiadiazolyl, triazinyl, triazolyl, pyridin-2-yl, pyridin-4-yl, pyrimidin-2-yl, pyridazin-4-yl, pyrazin-2-yl, naphthyridinyl, pteridinyl, phthalazinyl, purinyl, alloxazinyl, benzimidazolyl, benzofuranyl, benzofurazanyl, 2H-1-benzopyranyl, benzothiadiazine, benzothiazinyl, benzothiazolyl, benzothiophenyl, benzoxazolyl, cinnolinyl, furopyridinyl, indolinyl, indolizinyl, indolyl, or 2-, 3-, 4-, 5-, 6-, or 7-indolyl, 3H-indolyl, quinazolinyl, quinoxalinyl, isoindolyl, isoquinolinyl, 10-aza-tricyclo[6.3.1.$0^{2,7}$]dodeca-2(7),3,5-trienyl, 12-oxa-10-aza-tricyclo[6.3.1.$0^{2,7}$]dodeca-2(7),3,5-trienyl, 12-aza-tricyclo[7.2.1.$0^{2,7}$]dodeca-2(7),3,5-trienyl, 10-aza-tricyclo[6.3.2.$0^{2,7}$]trideca-2(7),3,5-trienyl, 2,3,4,5-tetrahydro-1H-benzo[d]azepinyl, 1,3,4,5-tetrahydro-benzo[d]azepin-2-onyl, 1,3,4,5-tetrahydro-benzo[b]azepin-2-onyl, 2,3,4,5-tetrahydro-benzo[c]azepin-1-onyl, 1,2,3,4-tetrahydro-benzo[e][1,4]diazepin-5-onyl, 2,3,4,5-tetrahydro-1H-benzo[e][1,4]diazepinyl, 5,6,8,9-tetrahydro-7-oxa-benzocycloheptenyl, 2,3,4,5-tetrahydro-1H-benzo[b]azepinyl, 1,2,4,5-tetrahydro-benzo[e][1,3]diazepin-3-onyl, 3,4-dihydro-2H-benzo[b][1,4]dioxepinyl, 3,4-dihydro-2H-benzo[f][1,4]oxazepin-5-onyl, 6,7,8,9-tetrahydro-5-thia-8-aza-benzocycloheptenyl, 5,5-dioxo-6,7,8,9-tetrahydro-5-thia-8-aza-benzocycloheptenyl, and 2,3,4,5-tetrahydro-benzo[f][1,4]oxazepinyl. For example, a heteroaryl group may contain 5, 6, or 8-15 ring atoms. As another example, a heteroaryl group may contain 5 to 10 ring atoms, such as 5, 6, 9, or 10 ring atoms.

"Heteroarylalkyl" or "heteroarylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by a heteroaryl group, wherein alkyl group and heteroaryl group are as previously defined (i.e., heteroarylalkyl–). Heteroarylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, the pyridinylmethyl isomers ().

"Heterocycloalkyl" or "heterocycloalkyl group" refers to 3-15 membered monocyclic, bicyclic, and tricyclic non-aromatic rings, which may be saturated or unsaturated, can be substituted or unsubstituted, may be bridged, spiro, and/or fused, and which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen, sulfur or phosphorus. Examples include, but are not limited to, tetrahydrofuranyl, pyrrolidinyl, pyrrolinyl, imidazolidinyl, imidazolinyl, pyrazolidinyl, pyrazolinyl, piperidyl, piperazinyl, indolinyl, isoindolinyl, morpholinyl, thiomorpholinyl, homomorpholinyl, homopiperidyl, homopiperazinyl, thiomorpholinyl-5-oxide, thiomorpholinyl-S,S-dioxide, pyrrolidinyl, tetrahydropyranyl, piperidinyl, tetrahydrothienyl, homopiperidinyl, homothiomorpholinyl-S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl-5-oxide, tetrahydrothienyl-S,S-dioxide, homothiomorpholinyl-5-oxide, quinuclidinyl, 2-oxa-5-azabicyclo[2.2.1]heptanyl, 8-oxa-3-aza-bicyclo[3.2.1]octanyl, 3,8-diaza-bicyclo[3.2.1]octanyl, 2,5-diaza-bicyclo[2.2.1]heptanyl, 3,8-diaza-bicyclo[3.2.1]octanyl, 3,9-diaza-bicyclo[4.2.1]nonanyl, 2,6-diaza-bicyclo[3.2.2]nonanyl, [1,4]oxaphosphinanyl- 4-oxide, [1,4]azaphosphinanyl- 4-oxide, [1,2]oxaphospholanyl- 2-oxide, phosphinanyl-1-oxide, [1,3]azaphospholidinynl- 3-oxide, [1,3]oxaphospholanyl- 3-oxide and 7-oxabicyclo[2.2.1]heptanyl. A heterocycloalkyl group may contain, in addition to carbon atom(s), at least one nitrogen, oxygen, or sulfur. For example, a heterocycloalkyl group may contain, in addition to carbon atom(s), at least one nitrogen or oxygen. A heterocycloalkyl group may contain, in addition to carbon atom(s), at least one nitrogen. A heterocycloalkyl group may contain carbon atoms

and 1 or 2 nitrogen atoms. A heterocycloalkyl group may contain carbon atoms and an oxygen atom. A heterocycloalkyl group may contain carbon atoms, a nitrogen atom, and an oxygen atom. A heterocycloalkyl group may contain carbon atoms, a nitrogen atom, and a sulfur atom. A heterocycloalkyl group may contain carbon atoms and a sulfur atom. A heterocycloalkyl group may contain from 3 to 10 ring atoms. A heterocycloalkyl group may contain from 3 to 7 ring atoms. A heterocycloalkyl group may contain from 5 to 7 ring atoms, such as 5 ring atoms, 6 ring atoms, or 7 ring atoms. Unless otherwise indicated, the foregoing heterocycloalkyl groups can be C- attached or N-attached where such is possible and results in the creation of a stable structure. For example, piperidinyl can be piperidin-1-yl (N-attached) or piperidin-4-yl (C-attached).

"Heterocycloalkylene" or "heterocycloalkylene group" refers to diradical, 3-15 membered monocyclic, bicyclic, or tricyclic non-aromatic ring systems, which may be saturated or unsaturated, can be substituted or unsubstituted, may be bridged, spiro, and/or fused, and which contain, in addition to carbon atom(s), at least one heteroatom, such as nitrogen, oxygen, sulfur or phosphorus. Examples include, but are not limited to, the azridinylene isomers ().

The heterocycloalkylene group may contain, in addition to carbon atom(s), at least one nitrogen, oxygen, or sulfur. The heterocycloalkylene group may contain, in addition to carbon atom(s), at least one nitrogen or oxygen. The heterocycloalkylene group may contain, in addition to carbon atom(s), at least one nitrogen. For example, a heterocycloalkylene group may contain from 3 to 10 ring atoms; such as from 3 to 7 ring atoms. A heterocycloalkylene group may contain from 5 to 7 ring atoms, such as 5 ring atoms, 6 ring atoms, or 7 ring atoms. Unless otherwise indicated, the foregoing heterocycloalkylene groups can be C- attached and/or N-attached where such is possible and results in the creation of a stable structure. A heterocycloalkylene group can also include ring systems substituted on ring carbons with one or more –OH functional groups (which may further tautomerize to give a ring C=O group) and/or substituted on a ring sulfur atom by one (1) or two (2) oxygen atoms to give S=O or

SO_2 groups, respectively, and/or substituted on a ring phosphorus by an oxygen atom to give P=O.

"Heterocycloalkylalkyl" or "heterocycloalkylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by a heterocycloalkyl group, wherein alkyl group and heterocycloalkyl group are as previously defined (i.e., heterocycloalkylalkyl–). Heteroycloalkylalkyl groups can be substituted or unsubstituted. Examples include, but are not limited to, pyrrolidinylmethyl ($C_4H_8NCH_2$–).

"Pharmaceutically acceptable" refers to physiologically tolerable materials, which do not typically produce an allergic or other untoward reaction, such as gastric upset, dizziness and the like, when administered to a human.

"Pharmaceutical composition" refers to a composition that can be used to treat a disease, condition, or disorder in a human.

"Pseudohalogen" refers to –OCN, –SCN, $–CF_3$, and –CN.

"Stable" or "chemically stable" refers to a compound that is sufficiently robust to be isolated to a useful degree of purity from a reaction mixture. The present invention is directed solely to the preparation of stable compounds. When lists of alternative substituents include members which, owing to valency requirements, chemical stability, or other reasons, cannot be used to substitute a particular group, the list is intended to be read in context to include those members of the list that are suitable for substituting the particular group. For example, R^1 can be $C_{1\text{-}6}$alkyl optionally substituted by 1-13 R^{19}; when R^1 is methyl, the methyl group is optionally substituted by 1-3 R^{19}.

"Therapeutically effective amount" refers to an amount of a compound sufficient to inhibit, halt, or cause an improvement in a disorder or condition being treated in a particular subject or subject population. For example in a human or other mammal, a therapeutically effective amount can be determined experimentally in a laboratory or clinical setting, or may be the amount required by the guidelines of the United States Food and Drug Administration, or equivalent foreign agency, for the particular disease and subject being treated. It should be appreciated that determination of proper dosage forms, dosage amounts, and routes of administration is within the level of ordinary skill in the pharmaceutical and medical arts.

"Treatment" refers to the acute or prophylactic diminishment or alleviation of at least one symptom or characteristic associated or caused by a disorder being treated. For

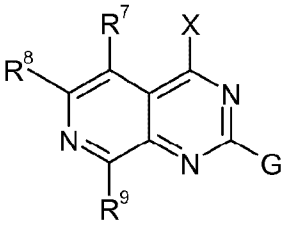
example, treatment can include diminishment of several symptoms of a disorder or complete eradication of a disorder.

II. Compounds

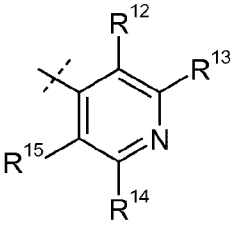
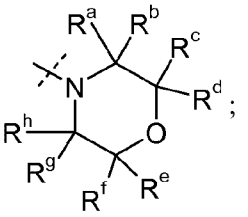
The compounds of the present invention are defined by the following numbered Embodiments. When a higher numbered Embodiment refers back to multiple previous lower numbered Embodiments in the alternative and contains a new limitation not present in the lower numbered Embodiments, the higher numbered Embodiment is intended to be an express description of each and every one of the alternatives. For example, if Embodiment 2 refers back to Embodiment 1 and contains a limitation not present in Embodiment 1, Embodiment 3 refers back Embodiments 1 or 2 and contains a limitation(s) not present in Embodiments 1 or 2, and Embodiment 4 refers back to any of Embodiments 1-3 and contains a limitation(s) not present in Embodiments 1, 2, or 3, then Embodiment 4 is intended to be an explicit description of a genus having the limitations of Embodiments 1 and 4, an explicit description of a genus having the limitations of Embodiments 2 and 4 (i.e., 1, 2, and 4), and an explicit description of a genus having the limitations of Embodiments 3 and 4 (i.e., 1, 3, and 4, and 1, 2, 3 and 4). By way of example, if Embodiment 1 is a compound of formula (I) defining R^7, R^8 and R^9 independently as alkyl or aryl, Embodiment 2 is a compound of Embodiment 1 defining R^7 as alkyl, Embodiment 3 is a compound of Embodiments 1 or 2 defining R^8 as alkyl, and Embodiment 4 is a compound of any of Embodiments 1-3 defininining R^9 as alkyl, then Embodiment 4 is an explicit description of a genus having the limitations of Embodiments 1 and 4 (i.e., a compound of formula (I) in which R^7 and R^8 are alkyl or aryl, and R^9 is alkyl), an explicit description of a genus having the limitations of Embodiments 2 and 4 (i.e., a compound of formula (I) in which R^8 is alkyl or aryl, and R^7 and R^9 are alkyl), an explicit description of a genus having the limitations of Embodiments 3 and 4 (i.e., a compound of formula (I) in which R^7 is alkyl or aryl, and R^8 and R^9 are alkyl; and a compound of formula (I) in which R^7, R^8 and R^9 are all alkyl). It should be noted in this regard that when a higher numbered Embodiment refers to a lower numbered Embodiment and contains limitations for a group(s) not present in the lower numbered Embodiment, the higher numbered Embodiment should be interpreted in context to ignore the missing group(s). For example, if Embodiment 1 recites a compound of formula (I) in which X is H, C_{1-10}alkyl, or $-C(=O)R^{28}$, Embodiment 2 recites a compound of Embodiment 1 in

which X is H or C_{1-10}alkyl, and Embodiment 3 recites a compound of Embodiments 1 or 2 in which R^{28} is alkyl, then Embodiment 3 defines a genus having the limitations of Embodiments 1 and 3 and a genus having the limitation of Embodiments 2 and 3 (i.e., 1, 2, and 3). In the genus defined by the limitations of Embodiments 2 and 3, X cannot be –C(=O)R^{28}; therefore this genus should be interpreted to ignore the Embodiment 3 definition of R^{28} = alkyl (i.e., the genus of Embodiments 2 and 3 has the same scope as the genus of Embodiment 2).

The compounds of the present invention are defined herein using structural formulas that do not specifically recite the mass numbers or the isotope ratios of the constituent atoms. It is intended that the present invention includes compounds in which the constituent atoms are present in any ratio of isotope forms. For example, carbon atoms may be present in any ratio of ^{12}C, ^{13}C, and ^{14}C; hydrogen atoms may be present in any ratio of ^{1}H, ^{2}H, and ^{3}H; etc. Preferably, the constituent atoms in the compounds of the present invention are present in their naturally occurring ratios of isotope forms.

Embodiment 1. A compound of formula (I)  (I) or a salt form thereof,

wherein

G is a group of formula  or  ;

X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered

heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{28}$, $–C(=O)OR^{28}$, $–C(=O)NR^{24}R^{28}$, $–C(=O)C(=O)R^{28}$, $–NR^{24}R^{28}$, $–NR^{24}NR^{24}R^{28}$, $–N=NR^{28}$, $–NR^{24}OR^{28}$, $–NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)C(=O)R^{28}$, $–NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)OR^{28}$, $–NR^{24}C(=O)NR^{24}R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $–NR^{24}S(=O)_2R^{28}$, $–NR^{24}S(=O)_2NR^{24}R^{28}$, $–OR^{28}$, $–OC(=O)R^{28}$, $–OC(=O)NR^{24}R^{28}$, $–OC(=O)OR^{28}$, $–OS(=O)R^{28}$, $–OS(=O)_2R^{28}$, $–OS(=O)_2OR^{28}$, $–OS(=O)_2NR^{24}R^{28}$, $–S(=O)_nR^{28}$, $–S(=O)_2NR^{24}R^{28}$, and $–S(=O)NR^{24}R^{28}$;

R^7, R^8, R^9, R^{12}, R^{13}, R^{14}, R^{15}, R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, $–C(=NR^{25})R^{20}$, $–C(=NR^{25})NR^{22}R^{23}$, $–C(=NOH)NR^{22}R^{23}$, $–C(=NOR^{26})R^{20}$, $–C(=NNR^{22}R^{23})R^{20}$, $–C(=NNR^{24}C(=O)R^{21})R^{20}$, $–C(=NNR^{24}C(=O)OR^{21})R^{20}$, $–C(=S)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –

$OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$;

or any of R^7 and R^8, R^{12} and R^{13}, R^{14} and R^{15}, R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19};

R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-C(=NR^{35})R^{30}$, $-C(=NR^{35})NR^{32}R^{33}$, $-C(=NOH)NR^{32}R^{33}$, $-C(=NOR^{36})R^{30}$, $-C(=NNR^{32}R^{33})R^{30}$, $-C(=NNR^{34}C(=O)R^{31})R^{30}$, $-C(=NNR^{34}C(=O)OR^{31})R^{30}$, $-C(=S)NR^{32}R^{33}$, $-NC$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}C(=S)R^{30}$, $-NR^{34}C(=S)OR^{30}$, $-NR^{34}C(=S)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-NR^{34}P(=O)R^{78}R^{78}$, $-NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-NR^{34}P(=O)(OR^{30})(OR^{30})$, $-NR^{34}P(=O)(SR^{30})(SR^{30})$, $-OR^{30}$, $=O$, $-OCN$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-$

$OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-OS(=O)R^{30}$, $-OS(=O)_2R^{30}$, $-OS(=O)_2OR^{30}$, $-OS(=O)_2NR^{32}R^{33}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-OP(=O)(OR^{30})(OR^{30})$, $-OP(=O)(SR^{30})(SR^{30})$, $-Si(R^{34})_3$, $-SCN$, $=S$, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-SP(=O)(OR^{30})(OR^{30})$, $-SP(=O)(SR^{30})(SR^{30})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$;

R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{2-6}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{28} at each occurrence is independently chosen from C_{1-10}alkyl optionally substituted by 1-13 R^{49}, C_{2-10}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-

21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59};

or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69};

R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-C(=NR^{75})R^{70}$, $-C(=NR^{75})NR^{72}R^{73}$, $-C(=NOH)NR^{72}R^{73}$, $-C(=NOR^{76})R^{70}$, $-C(=NNR^{72}R^{73})R^{70}$, $-C(=NNR^{74}C(=O)R^{71})R^{70}$, $-C(=NNR^{74}C(=O)OR^{71})R^{70}$, $-C(=S)NR^{72}R^{73}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $=NR^{70}$, $=NOR^{70}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)R^{70}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, $=O$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, $-SCN$, $=S$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, –

$P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, and $-P(=O)(SR^{70})(SR^{70})$;

R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89};

R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{99}, C_{2-6}alkenyl optionally substituted by 1-11 R^{99}, C_{2-6}alkynyl optionally substituted by 1-9 R^{99}, C_{6-11}aryl optionally substituted by 1-11 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{99};

or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{109};

R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89};

or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89};

R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{119}, C_{2-6}alkenyl optionally substituted by 1-11 R^{119}, C_{2-6}alkynyl optionally substituted by 1-9 R^{119}, C_{6-11}aryl optionally substituted by 1-11 R^{119}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{119}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{119}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{119}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{119}, halogen, –CN, –$C(=O)R^{110}$, –$C(=O)OR^{110}$, –$C(=O)NR^{112}R^{113}$, –$C(=O)C(=O)R^{110}$, –$C(=NR^{115})R^{110}$, –$C(=NR^{115})NR^{112}R^{113}$, –$C(=NOH)NR^{112}R^{113}$, –$C(=NOR^{116})R^{110}$, –$C(=NNR^{112}R^{113})R^{110}$, –$C(=NNR^{114}C(=O)R^{111})R^{110}$, –$C(=NNR^{114}C(=O)OR^{111})R^{110}$, –$C(=S)NR^{112}R^{113}$, –NC, –$NO_2$, –$NR^{112}R^{113}$, –$NR^{114}NR^{112}R^{113}$, –$N=NR^{114}$, $=NR^{110}$, $=NOR^{110}$, –$NR^{114}OR^{116}$, –$NR^{114}C(=O)R^{110}$, –$NR^{114}C(=O)C(=O)R^{110}$, –$NR^{114}C(=O)OR^{111}$, –$NR^{114}C(=O)C(=O)OR^{111}$, –$NR^{114}C(=O)NR^{112}R^{113}$, –$NR^{114}C(=O)NR^{114}C(=O)R^{110}$, –$NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, –$NR^{114}C(=NR^{115})NR^{112}R^{113}$, –$NR^{114}C(=O)C(=O)NR^{112}R^{113}$, –$NR^{114}C(=S)R^{110}$, –$NR^{114}C(=S)OR^{110}$, –$NR^{114}C(=S)NR^{112}R^{113}$, –$NR^{114}S(=O)_2R^{111}$, –$NR^{114}S(=O)_2NR^{112}R^{113}$, –$NR^{114}P(=O)R^{118}R^{118}$, –$NR^{114}P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, –$NR^{114}P(=O)(OR^{110})(OR^{110})$, –$NR^{114}P(=O)(SR^{110})(SR^{110})$, –$OR^{110}$, =O, –OCN, –$OC(=O)R^{110}$, –$OC(=O)NR^{112}R^{113}$, –$OC(=O)OR^{110}$, –$OC(=NR^{115})NR^{112}R^{113}$, –$OS(=O)R^{110}$, –$OS(=O)_2R^{110}$, –$OS(=O)_2OR^{110}$, –$OS(=O)_2NR^{112}R^{113}$, –$OP(=O)R^{118}R^{118}$, –$OP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, –$OP(=O)(OR^{110})(OR^{110})$, –$OP(=O)(SR^{110})(SR^{110})$, –$Si(R^{114})_3$, –SCN, =S, –$S(=O)_nR^{110}$, –$S(=O)_2OR^{110}$, –$SO_3R^{1111}$, –$S(=O)_2NR^{112}R^{113}$, –$S(=O)NR^{112}R^{113}$, –$SP(=O)R^{118}R^{118}$, –$SP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, –$SP(=O)(OR^{110})(OR^{110})$, –$SP(=O)(SR^{110})(SR^{110})$, –$P(=O)R^{118}R^{118}$, –$P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, –$P(=O)(OR^{110})(OR^{110})$, and –$P(=O)(SR^{110})(SR^{110})$;

R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{139}, C_{2-6}alkenyl optionally substituted by 1-11 R^{139}, C_{2-6}alkynyl optionally substituted by 1-9 R^{139}, C_{6-11}aryl optionally substituted by 1-11 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{139};
or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{149};

R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{159}, C_{2-6}alkenyl optionally substituted by 1-11

R^{159}, C_{2-6}alkynyl optionally substituted by 1-9 R^{159}, C_{6-11}aryl optionally substituted by 1-11 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{159}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{159}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{159}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{159}, halogen, –CN, –$C(=O)R^{150}$, –$C(=O)OR^{150}$, –$C(=O)NR^{152}R^{153}$, –$C(=O)C(=O)R^{150}$, –$C(=NR^{155})R^{150}$, –$C(=NR^{155})NR^{152}R^{153}$, –$C(=NOH)NR^{152}R^{153}$, –$C(=NOR^{156})R^{150}$, –$C(=NNR^{152}R^{153})R^{150}$, –$C(=NNR^{154}C(=O)R^{151})R^{150}$, –$C(=NNR^{154}C(=O)OR^{151})R^{150}$, –$C(=S)NR^{152}R^{153}$, –NC, –$NO_2$, –$NR^{152}R^{153}$, –$NR^{154}NR^{152}R^{153}$, –$N=NR^{154}$, $=NR^{150}$, $=NOR^{150}$, –$NR^{154}OR^{156}$, –$NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)C(=O)R^{150}$, –$NR^{154}C(=O)OR^{151}$, –$NR^{154}C(=O)C(=O)OR^{151}$, –$NR^{154}C(=O)NR^{152}R^{153}$, –$NR^{154}C(=O)NR^{154}C(=O)R^{150}$, –$NR^{154}C(=O)NR^{154}C(=O)OR^{150}$, –$NR^{154}C(=NR^{155})NR^{152}R^{153}$, –$NR^{154}C(=O)C(=O)NR^{152}R^{153}$, –$NR^{154}C(=S)R^{150}$, –$NR^{154}C(=S)OR^{150}$, –$NR^{154}C(=S)NR^{152}R^{153}$, –$NR^{154}S(=O)_2R^{151}$, –$NR^{154}S(=O)_2NR^{152}R^{153}$, –$NR^{154}P(=O)R^{158}R^{158}$, –$NR^{154}P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$NR^{154}P(=O)(OR^{150})(OR^{150})$, –$NR^{154}P(=O)(SR^{150})(SR^{150})$, –$OR^{150}$, =O, –OCN, –$OC(=O)R^{150}$, –$OC(=O)NR^{152}R^{153}$, –$OC(=O)OR^{150}$, –$OC(=NR^{155})NR^{152}R^{153}$, –$OS(=O)R^{150}$, –$OS(=O)_2R^{150}$, –$OS(=O)_2OR^{150}$, –$OS(=O)_2NR^{152}R^{153}$, –$OP(=O)R^{158}R^{158}$, –$OP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$OP(=O)(OR^{150})(OR^{150})$, –$OP(=O)(SR^{150})(SR^{150})$, –$Si(R^{154})_3$, –SCN, =S, –$S(=O)_nR^{150}$, –$S(=O)_2OR^{150}$, –$SO_3R^{1515}$, –$S(=O)_2NR^{152}R^{153}$, –$S(=O)NR^{152}R^{153}$, –$SP(=O)R^{158}R^{158}$, –$SP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$SP(=O)(OR^{150})(OR^{150})$, –$SP(=O)(SR^{150})(SR^{150})$, –$P(=O)R^{158}R^{158}$, –$P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, –$P(=O)(OR^{150})(OR^{150})$, and –$P(=O)(SR^{150})(SR^{150})$;

R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally

substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{179}, C_{2-6}alkenyl optionally substituted by 1-11 R^{179}, C_{2-6}alkynyl optionally substituted by 1-9 R^{179}, C_{6-11}aryl optionally substituted by 1-11 R^{179}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{179}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{179};
or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{189};

R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{199}, C_{2-6}alkenyl optionally substituted by 1-11 R^{199}, C_{2-6}alkynyl optionally substituted by 1-9 R^{199}, C_{6-11}aryl optionally substituted by 1-11 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{199}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{199}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-

40 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{199}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{199}, halogen, –CN, –$C(=O)R^{190}$, –$C(=O)OR^{190}$, –$C(=O)NR^{192}R^{193}$, –$C(=O)C(=O)R^{190}$, –$C(=NR^{195})R^{190}$, –$C(=NR^{195})NR^{192}R^{193}$, –$C(=NOH)NR^{192}R^{193}$, –$C(=NOR^{196})R^{190}$, –$C(=NNR^{192}R^{193})R^{190}$, –$C(=NNR^{194}C(=O)R^{191})R^{190}$, –$C(=NNR^{194}C(=O)OR^{191})R^{190}$, –$C(=S)NR^{192}R^{193}$, –NC, –$NO_2$, –$NR^{192}R^{193}$, –$NR^{194}NR^{192}R^{193}$, –$N=NR^{194}$, $=NR^{190}$, $=NOR^{190}$, –$NR^{194}OR^{196}$, –$NR^{194}C(=O)R^{190}$, –$NR^{194}C(=O)C(=O)R^{190}$, –$NR^{194}C(=O)OR^{191}$, –$NR^{194}C(=O)C(=O)OR^{191}$, –$NR^{194}C(=O)NR^{192}R^{193}$, –$NR^{194}C(=O)NR^{194}C(=O)R^{190}$, –$NR^{194}C(=O)NR^{194}C(=O)OR^{190}$, –$NR^{194}C(=NR^{195})NR^{192}R^{193}$, –$NR^{194}C(=O)C(=O)NR^{192}R^{193}$, –$NR^{194}C(=S)R^{190}$, –$NR^{194}C(=S)OR^{190}$, –$NR^{194}C(=S)NR^{192}R^{193}$, –$NR^{194}S(=O)_2R^{191}$, –$NR^{194}S(=O)_2NR^{192}R^{193}$, –$NR^{194}P(=O)R^{198}R^{198}$, –$NR^{194}P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$NR^{194}P(=O)(OR^{190})(OR^{190})$, –$NR^{194}P(=O)(SR^{190})(SR^{190})$, –$OR^{190}$, =O, –OCN, –$OC(=O)R^{190}$, –$OC(=O)NR^{192}R^{193}$, –$OC(=O)OR^{190}$, –$OC(=NR^{195})NR^{192}R^{193}$, –$OS(=O)R^{190}$, –$OS(=O)_2R^{190}$, –$OS(=O)_2OR^{190}$, –$OS(=O)_2NR^{192}R^{193}$, –$OP(=O)R^{198}R^{198}$, –$OP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$OP(=O)(OR^{190})(OR^{190})$, –$OP(=O)(SR^{190})(SR^{190})$, –$Si(R^{194})_3$, –SCN, =S, –$S(=O)_nR^{190}$, –$S(=O)_2OR^{190}$, –$SO_3R^{1919}$, –$S(=O)_2NR^{192}R^{193}$, –$S(=O)NR^{192}R^{193}$, –$SP(=O)R^{198}R^{198}$, –$SP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$SP(=O)(OR^{190})(OR^{190})$, –$SP(=O)(SR^{190})(SR^{190})$, –$P(=O)R^{198}R^{198}$, –$P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –$P(=O)(OR^{190})(OR^{190})$, and –$P(=O)(SR^{190})(SR^{190})$;

R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{219}, C_{2-6}alkenyl optionally substituted by 1-11 R^{219}, C_{2-6}alkynyl optionally substituted by 1-9 R^{219}, C_{6-11}aryl optionally substituted by 1-11 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{219};

or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{229};

R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-21 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(=O)C(=O)R^{230}$, $–C(=NR^{230})R^{230}$, $–C(=NR^{230})NR^{230}R^{230}$, $–C(=NOH)NR^{230}R^{230}$, $–C(=NOR^{230})R^{230}$, $–C(=NNR^{230}R^{230})R^{230}$, $–C(=NNR^{230}C(=O)R^{230})R^{230}$, $–C(=NNR^{230}C(=O)OR^{230})R^{230}$, $–C(=S)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–N=NR^{230}$, $=NR^{230}$, $=NOR^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, –

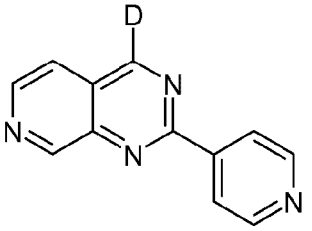
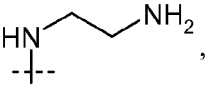
$NR^{230}C(=O)NR^{230}R^{230}$, $-NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $-NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $-NR^{230}C(=NR^{230})NR^{230}R^{230}$, $-NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $-NR^{230}C(=S)R^{230}$, $-NR^{230}C(=S)OR^{230}$, $-NR^{230}C(=S)NR^{230}R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-NR^{230}S(=O)_2NR^{230}R^{230}$, $-NR^{230}P(=O)R^{231}R^{231}$, $-NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-NR^{230}P(=O)(OR^{230})(OR^{230})$, $-NR^{230}P(=O)(SR^{230})(SR^{230})$, $-OR^{230}$, =O, –OCN, $-OC(=O)R^{230}$, $-OC(=O)NR^{230}R^{230}$, $-OC(=O)OR^{230}$, $-OC(=NR^{230})NR^{230}R^{230}$, $-OS(=O)R^{230}$, $-OS(=O)_2R^{230}$, $-OS(=O)_2OR^{230}$, $-OS(=O)_2NR^{230}R^{230}$, $-OP(=O)R^{231}R^{231}$, $-OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-OP(=O)(OR^{230})(OR^{230})$, $-OP(=O)(SR^{230})(SR^{230})$, $-Si(R^{230})_3$, –SCN, =S, $-S(=O)_nR^{230}$, $-S(=O)_2OR^{230}$, $-SO_3R^{230}$, $-S(=O)_2NR^{230}R^{230}$, $-S(=O)NR^{230}R^{230}$, $-SP(=O)R^{231}R^{231}$, $-SP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-SP(=O)(OR^{230})(OR^{230})$, $-SP(=O)(SR^{230})(SR^{230})$, $-P(=O)R^{231}R^{231}$, $-P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-P(=O)(OR^{230})(OR^{230})$, and $-P(=O)(SR^{230})(SR^{230})$;

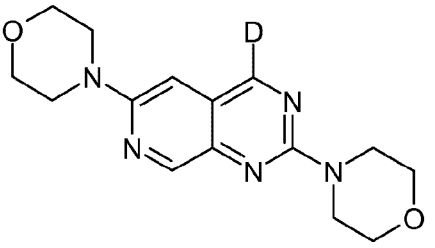
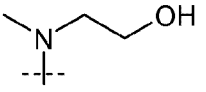
R^{230} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl;

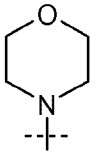
R^{231} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl; and

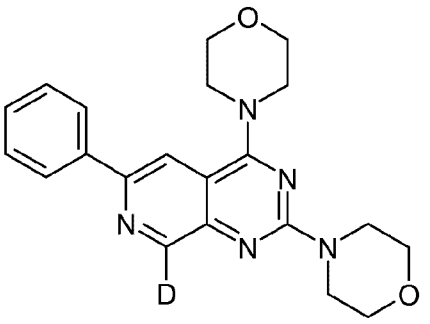
n at each occurrence is independently chosen from 0, 1, and 2;

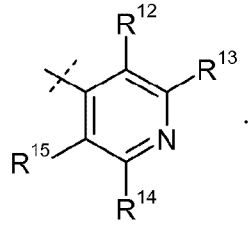
with the proviso that the compound is not

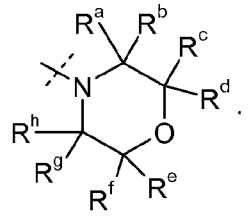
(a)  in which D is H or  , or a salt form thereof;

(b)  in which D is  or

 , or a salt form thereof; or

(c)  in which D is H or $-CH_3$, or a salt form thereof.

Embodiment 2. The compound of Embodiment 1, wherein G is a group of formula  .

Embodiment 3. The compound of Embodiment 1, wherein G is a group of formula  .

Embodiment 4. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally

substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-C(=O)C(=O)R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}NR^{24}R^{28}$, $-N=NR^{28}$, $-NR^{24}OR^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OC(=O)OR^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2OR^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 5. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 6. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-10}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6

R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, –C(=O)R^{28}, –C(=O)OR^{28}, –C(=O)N$R^{24}R^{28}$, –N$R^{24}R^{28}$, –NR^{24}C(=O)R^{28}, –NR^{24}C(=O)OR^{28}, –NR^{24}C(=O)N$R^{24}R^{28}$, –NR^{24}S(=O)$_2R^{28}$, –NR^{24}S(=O)$_2$N$R^{24}R^{28}$, –OR^{28}, –OC(=O)R^{28}, –OC(=O)N$R^{24}R^{28}$, –OS(=O)R^{28}, –OS(=O)$_2R^{28}$, –OS(=O)$_2$N$R^{24}R^{28}$, –S(=O)$_n R^{28}$, –S(=O)$_2$N$R^{24}R^{28}$, and –S(=O)N$R^{24}R^{28}$.

Embodiment 7. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, –C(=O)R^{28}, –C(=O)OR^{28}, –C(=O)N$R^{24}R^{28}$, –N$R^{24}R^{28}$, –NR^{24}C(=O)R^{28}, –NR^{24}C(=O)OR^{28}, –NR^{24}C(=O)N$R^{24}R^{28}$, –NR^{24}S(=O)$_2R^{28}$, –NR^{24}S(=O)$_2$N$R^{24}R^{28}$, –OR^{28}, –OC(=O)R^{28}, –OC(=O)N$R^{24}R^{28}$, –OS(=O)R^{28}, –OS(=O)$_2R^{28}$, –OS(=O)$_2$N$R^{24}R^{28}$, –S(=O)$_n R^{28}$, –S(=O)$_2$N$R^{24}R^{28}$, and –S(=O)N$R^{24}R^{28}$.

Embodiment 8. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, –C(=O)R^{28}, –C(=O)OR^{28}, –C(=O)N$R^{24}R^{28}$, –N$R^{24}R^{28}$, –NR^{24}C(=O)R^{28}, –NR^{24}C(=O)N$R^{24}R^{28}$, –NR^{24}S(=O)$_2R^{28}$, –OR^{28}, –OC(=O)R^{28}, –S(=O)$_n R^{28}$, and –S(=O)$_2$N$R^{24}R^{28}$.

Embodiment 9. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered

heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)OR^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-NR^{24}S(=O)_2NR^{24}R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-OC(=O)NR^{24}R^{28}$, $-OS(=O)R^{28}$, $-OS(=O)_2R^{28}$, $-OS(=O)_2NR^{24}R^{28}$, $-S(=O)_nR^{28}$, $-S(=O)_2NR^{24}R^{28}$, and $-S(=O)NR^{24}R^{28}$.

Embodiment 10. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 11. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 12. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 13. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 14. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 15. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-7 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-11 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 16. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 17. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)OR^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-$

$NR^{24}C(=O)NR^{24}R^{28}$, $-NR^{24}S(=O)_2R^{28}$, $-OR^{28}$, $-OC(=O)R^{28}$, $-S(=O)_nR^{28}$, and $-S(=O)_2NR^{24}R^{28}$.

Embodiment 18. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 19. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-C(=O)R^{28}$, $-C(=O)NR^{24}R^{28}$, $-NR^{24}R^{28}$, $-NR^{24}C(=O)R^{28}$, $-NR^{24}S(=O)_2R^{28}$, and $-OR^{28}$.

Embodiment 20. The compound of any of Embodiments 1-3, wherein X is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 21. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 22. The compound of any of Embodiments 1-3, wherein X is chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 23. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, and $-OR^{28}$.

Embodiment 24. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 25. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 26. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, $-NR^{24}R^{28}$, $-OR^{28}$, and $-SR^{28}$.

Embodiment 27. The compound of any of Embodiments 1-3, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 28. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-9 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 29. The compound of any of Embodiments 1-3, wherein X is chosen from 3-9 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 30. The compound of any of Embodiments 1-3, wherein X is chosen from H, 3-7 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 31. The compound of any of Embodiments 1-3, wherein X is chosen from 3-7 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and $-NR^{24}R^{28}$.

Embodiment 32. The compound of any of Embodiments 1-3, wherein X is 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 33. The compound of any of Embodiments 1-3, wherein X is 3-9 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 34. The compound of any of Embodiments 1-3, wherein X is 3-7 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 35. The compound of any of Embodiments 1-3, wherein X is 5-6 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 36. The compound of any of Embodiments 1-3, wherein X is 6 membered heterocycloalkyl optionally substituted by 1-6 R^{19}.

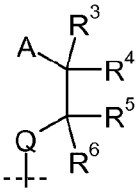
Embodiment 37. The compound of any of Embodiments 1-3, wherein X is morpholinyl, piperidinyl, or piperazinyl optionally substituted by 1-6 R^{19}.

Embodiment 38. The compound of any of Embodiments 1-3, wherein X is piperidinyl or piperazinyl optionally substituted by 1-6 R^{19}.

Embodiment 39. The compound of any of Embodiments 1-3, wherein X is piperidinyl optionally substituted by 1-6 R^{19}.

Embodiment 40. The compound of any of Embodiments 1-3, wherein X is piperazinyl optionally substituted by 1-6 R^{19}.

Embodiment 41. The compound of any of Embodiments 1-3, wherein X is $-NR^{24}R^{28}$.

Embodiment 42. The compound of any of Embodiments 1-3, wherein X is chosen from H and  , wherein

A is $-NR^1R^2$, $-CR^iR^jR^k$, $-OR^{18a}$, or $-SR^{18b}$;

Q is $-NR^{11}-$, $-CR^mR^n-$, $-O-$, or $-S-$;

R^k is H, halogen, $-CN$, $-NO_2$, $-NR^{16}R^{17}$, $-OR^{18c}$, $-SR^{18d}$, or $-CR^oR^pR^q$;

R^q is H, halogen, $-CN$, $-NO_2$, $-NR^{16a}R^{17a}$ or $-OR^{18e}$;

R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, and $-OR^{70}$;

R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79},

C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-C(=NR^{75})R^{70}$, $-C(=NR^{75})NR^{72}R^{73}$, $-C(=NOH)NR^{72}R^{73}$, $-C(=NOR^{76})R^{70}$, $-C(=NNR^{72}R^{73})R^{70}$, $-C(=NNR^{74}C(=O)R^{71})R^{70}$, $-C(=NNR^{74}C(=O)OR^{71})R^{70}$, $-C(=S)NR^{72}R^{73}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)R^{70}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, $-SCN$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, and $-P(=O)(SR^{70})(SR^{70})$;

or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking

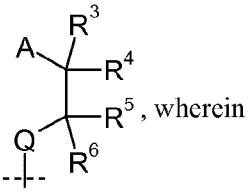
them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or R^4 and R^5 or R^n and R^5 can together form a double bond;

or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O, =NR^{70}, =NOR^{70}, or =S.

Embodiment 43. The compound of any of Embodiments 1-3, wherein X is



, wherein

A is $-NR^1R^2$, $-CR^iR^jR^k$, $-OR^{18a}$, or $-SR^{18b}$;

Q is $-NR^{11}-$, $-CR^mR^n-$, $-O-$, or $-S-$;

R^k is H, halogen, $-CN$, $-NO_2$, $-NR^{16}R^{17}$, $-OR^{18c}$, $-SR^{18d}$, or $-CR^oR^pR^q$;

R^q is H, halogen, $-CN$, $-NO_2$, $-NR^{16a}R^{17a}$ or $-OR^{18e}$;

R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, and $-OR^{70}$;

R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally

substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$C(=O)C(=O)R^{70}$, –$C(=NR^{75})R^{70}$, –$C(=NR^{75})NR^{72}R^{73}$, –$C(=NOH)NR^{72}R^{73}$, –$C(=NOR^{76})R^{70}$, –$C(=NNR^{72}R^{73})R^{70}$, –$C(=NNR^{74}C(=O)R^{71})R^{70}$, –$C(=NNR^{74}C(=O)OR^{71})R^{70}$, –$C(=S)NR^{72}R^{73}$, –NC, –$NO_2$, –$NR^{72}R^{73}$, –$NR^{74}NR^{72}R^{73}$, –$N=NR^{74}$, –$NR^{74}OR^{76}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}C(=O)C(=O)R^{70}$, –$NR^{74}C(=O)OR^{71}$, –$NR^{74}C(=O)C(=O)OR^{71}$, –$NR^{74}C(=O)NR^{72}R^{73}$, –$NR^{74}C(=O)NR^{74}C(=O)R^{70}$, –$NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, –$NR^{74}C(=NR^{75})NR^{72}R^{73}$, –$NR^{74}C(=O)C(=O)NR^{72}R^{73}$, –$NR^{74}C(=S)R^{70}$, –$NR^{74}C(=S)OR^{70}$, –$NR^{74}C(=S)NR^{72}R^{73}$, –$NR^{74}S(=O)_2R^{71}$, –$NR^{74}S(=O)_2NR^{72}R^{73}$, –$NR^{74}P(=O)R^{78}R^{78}$, –$NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$NR^{74}P(=O)(OR^{70})(OR^{70})$, –$NR^{74}P(=O)(SR^{70})(SR^{70})$, –$OR^{70}$, –OCN, –$OC(=O)R^{70}$, –$OC(=O)NR^{72}R^{73}$, –$OC(=O)OR^{70}$, –$OC(=NR^{75})NR^{72}R^{73}$, –$OS(=O)R^{70}$, –$OS(=O)_2R^{70}$, –$OS(=O)_2OR^{70}$, –$OS(=O)_2NR^{72}R^{73}$, –$OP(=O)R^{78}R^{78}$, –$OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$OP(=O)(OR^{70})(OR^{70})$, –$OP(=O)(SR^{70})(SR^{70})$, –$Si(R^{74})_3$, –SCN, –$S(=O)_nR^{70}$, –$S(=O)_2OR^{70}$, –SO_3R^{77}, –$S(=O)_2NR^{72}R^{73}$, –$S(=O)NR^{72}R^{73}$, –$SP(=O)R^{78}R^{78}$, –$SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$SP(=O)(OR^{70})(OR^{70})$, –$SP(=O)(SR^{70})(SR^{70})$, –$P(=O)R^{78}R^{78}$, –$P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$P(=O)(OR^{70})(OR^{70})$, and –$P(=O)(SR^{70})(SR^{70})$;

or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and

R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or R^4 and R^5 or R^n and R^5 can together form a double bond;

or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O, $=NR^{70}$, $=NOR^{70}$, or =S.

Embodiment 44. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, and $-OR^{70}$; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, –

$NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-OR^{70}$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-Si(R^{74})_3$, $-SCN$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, and $-P(=O)(OR^{70})(OR^{70})$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O, $=NR^{70}$, $=NOR^{70}$, or =S.

Embodiment 45. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, and $-OR^{70}$; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by

1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-OR^{70}$, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, –SCN, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, and $-P(=O)(OR^{70})(OR^{70})$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-10 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 46. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-}

$_{11}$cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, and 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-11}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, –SCN, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, and $-S(=O)NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 47. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl

optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-11}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, and 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, C_{4-11}cycloalkylalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 4-11 membered heterocycloalkylalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, 6-12 membered heteroarylalkyl optionally substituted by 1-10 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–OR^{70}$, –OCN, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, –SCN, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 48. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl

optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, and 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-10 R^{79}, C_{2-6}alkenyl optionally substituted by 1-10 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-10 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^i and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-10 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-10 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-10 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-10 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 49. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18c} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, and 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkenyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by

1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 50. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the

atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 51. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 52. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1

and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 53. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 54. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 55. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4,

R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, –CN, –C(=O)OR^{70}, –C(=O)$NR^{72}R^{73}$, –$NR^{72}R^{73}$, and –OR^{70}; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 56. The compound of Embodiments 42 or 43, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –C(=O)R^{70}, –C(=O)OR^{70}, –C(=O)$NR^{72}R^{73}$, –NC, –NO_2, –$NR^{72}R^{73}$, –$NR^{74}OR^{76}$, –NR^{74}C(=O)R^{70}, –NR^{74}C(=O)OR^{71}, –NR^{74}C(=O)$NR^{72}R^{73}$, –NR^{74}S(=O)$_2R^{71}$, –NR^{74}S(=O)$_2NR^{72}R^{73}$, –OR^{70}, –OC(=O)R^{70}, –OC(=O)$NR^{72}R^{73}$, –S(=O)$_nR^{70}$, and –S(=O)$_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79} or a 5-11 membered heteroaryl optionally substituted by 1-6 R^{79}; or R^4 and R^5 or R^n and R^5 can together form a double bond; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 57. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl

optionally substituted by 1-6 R^{79}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –NO_2, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 58. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6

R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 59. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, and R^{18c} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 60. The compound of any of Embodiments 42-59, wherein 0-3 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 61. The compound of any of Embodiments 42-59, wherein 0-2 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d}

and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 62. The compound of any of Embodiments 42-59, wherein 1-2 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 63. The compound of any of Embodiments 42-59, wherein none of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 64. The compound of any of Embodiments 42-59, wherein one of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 65. The compound of any of Embodiments 42-59, wherein two of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl or an optionally substituted heteroaryl.

Embodiment 66. The compound of any of Embodiments 42-59, wherein 0-3 of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17},

R^{16} and R^{i}, R^{16} and R^{3}, R^{16} and R^{5}, R^{16} and R^{11}, R^{16} and R^{n}, R^{j} and R^{11}, R^{18a} and R^{3}, R^{18a} and R^{5}, R^{18a} and R^{11}, R^{18a} and R^{n}, R^{18b} and R^{3}, R^{18b} and R^{5}, R^{18b} and R^{11}, R^{18b} and R^{n}, R^{18c} and R^{i}, R^{18c} and R^{3}, R^{18c} and R^{5}, R^{18c} and R^{11}, R^{18c} and R^{n}, R^{18d} and R^{i}, R^{18d} and R^{3}, R^{18d} and R^{5}, R^{18d} and R^{11}, and R^{18d} and R^{n}, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 67. The compound of any of Embodiments 42-59, wherein 0-2 of R^{1} and R^{2}, R^{1} and R^{3}, R^{1} and R^{5}, R^{1} and R^{11}, R^{1} and R^{n}, R^{4} and R^{11}, R^{6} and R^{11}, R^{16} and R^{17}, R^{16} and R^{i}, R^{16} and R^{3}, R^{16} and R^{5}, R^{16} and R^{11}, R^{16} and R^{n}, R^{j} and R^{11}, R^{18a} and R^{3}, R^{18a} and R^{5}, R^{18a} and R^{11}, R^{18a} and R^{n}, R^{18b} and R^{3}, R^{18b} and R^{5}, R^{18b} and R^{11}, R^{18b} and R^{n}, R^{18c} and R^{i}, R^{18c} and R^{3}, R^{18c} and R^{5}, R^{18c} and R^{11}, R^{18c} and R^{n}, R^{18d} and R^{i}, R^{18d} and R^{3}, R^{18d} and R^{5}, R^{18d} and R^{11}, and R^{18d} and R^{n}, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 68. The compound of any of Embodiments 42-59, wherein 1-2 of R^{1} and R^{2}, R^{1} and R^{3}, R^{1} and R^{5}, R^{1} and R^{11}, R^{1} and R^{n}, R^{4} and R^{11}, R^{6} and R^{11}, R^{16} and R^{17}, R^{16} and R^{i}, R^{16} and R^{3}, R^{16} and R^{5}, R^{16} and R^{11}, R^{16} and R^{n}, R^{j} and R^{11}, R^{18a} and R^{3}, R^{18a} and R^{5}, R^{18a} and R^{11}, R^{18a} and R^{n}, R^{18b} and R^{3}, R^{18b} and R^{5}, R^{18b} and R^{11}, R^{18b} and R^{n}, R^{18c} and R^{i}, R^{18c} and R^{3}, R^{18c} and R^{5}, R^{18c} and R^{11}, R^{18c} and R^{n}, R^{18d} and R^{i}, R^{18d} and R^{3}, R^{18d} and R^{5}, R^{18d} and R^{11}, and R^{18d} and R^{n}, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 69. The compound of any of Embodiments 42-59, wherein none of R^{1} and R^{2}, R^{1} and R^{3}, R^{1} and R^{5}, R^{1} and R^{11}, R^{1} and R^{n}, R^{4} and R^{11}, R^{6} and R^{11}, R^{16} and R^{17}, R^{16} and R^{i}, R^{16} and R^{3}, R^{16} and R^{5}, R^{16} and R^{11}, R^{16} and R^{n}, R^{j} and R^{11}, R^{18a} and R^{3}, R^{18a} and R^{5}, R^{18a} and R^{11}, R^{18a} and R^{n}, R^{18b} and R^{3}, R^{18b} and R^{5}, R^{18b} and R^{11}, R^{18b} and R^{n}, R^{18c} and R^{i}, R^{18c} and R^{3}, R^{18c} and R^{5}, R^{18c} and R^{11}, R^{18c} and R^{n}, R^{18d} and R^{i}, R^{18d} and R^{3}, R^{18d} and R^{5}, R^{18d} and R^{11}, and R^{18d} and R^{n}, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 70. The compound of any of Embodiments 42-59, wherein one of R^{1} and R^{2}, R^{1} and R^{3}, R^{1} and R^{5}, R^{1} and R^{11}, R^{1} and R^{n}, R^{4} and R^{11}, R^{6} and R^{11}, R^{16} and R^{17}, R^{16} and R^{i}, R^{16} and R^{3}, R^{16} and R^{5}, R^{16} and R^{11}, R^{16} and R^{n}, R^{j} and R^{11}, R^{18a} and R^{3}, R^{18a} and R^{5}, R^{18a} and R^{11}, R^{18a} and R^{n}, R^{18b} and R^{3}, R^{18b} and R^{5}, R^{18b} and R^{11}, R^{18b} and R^{n}, R^{18c} and R^{i}, R^{18c} and R^{3}, R^{18c} and R^{5}, R^{18c} and R^{11}, R^{18c} and R^{n}, R^{18d} and R^{i}, R^{18d} and R^{3}, R^{18d} and R^{5}, R^{18d}

and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 71. The compound of Embodiment 70, wherein said optionally substituted heterocarbocyclyl is a 3-7 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 72. The compound of Embodiment 70, wherein said optionally substituted heterocarbocyclyl is a 5-6 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 73. The compound of any of Embodiments 42-59, wherein two of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n, together with the atoms linking them, form an optionally substituted heterocycloalkyl.

Embodiment 74. The compound of any of Embodiments 42-73, wherein 0-2 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 75. The compound of any of Embodiments 42-73, wherein 0-1 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 76. The compound of any of Embodiments 42-73, wherein none of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 77. The compound of any of Embodiments 42-73, wherein one of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4

and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted aryl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted heteroaryl.

Embodiment 78. The compound of any of Embodiments 42-73, wherein 0-2 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 79. The compound of any of Embodiments 42-73, wherein 0-1 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 80. The compound of any of Embodiments 42-73, wherein none of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 81. The compound of any of Embodiments 42-73, wherein one of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted cycloalkyl or optionally substituted heterocycloalkyl.

Embodiment 82. The compound of any of Embodiments 42-73, wherein 0-2 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 83. The compound of any of Embodiments 42-73, wherein 0-1 of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 84. The compound of any of Embodiments 42-73, wherein none of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 85. The compound of any of Embodiments 42-73, wherein one of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m, together with the atoms linking them, form an optionally substutituted heterocycloalkyl.

Embodiment 86. The compound of Embodiment 85, wherein said optionally substituted heterocarbocyclyl is a 3-7 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 87. The compound of Embodiment 85, wherein said optionally substituted heterocarbocyclyl is a 5-6 membered heterocarbocycl optionally substituted with 1-4 R^{79}.

Embodiment 88. The compound of any of Embodiments 42-87, wherein neither R^4 and R^5 nor R^n and R^5 together form a double bond.

Embodiment 89. The compound of any of Embodiments 42-88, wherein none of R^3 and R^4, R^5 and R^6, R^i and R^j, or R^m and R^n together form =O, =NR^{70}, =NOR^{70}, or =S.

Embodiment 90. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; R^2 is chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

Embodiment 91. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; R^2 is chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –

$NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 92. The compound of Embodiments 42 or 43, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; R^2 is chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, –CN, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, and $-OR^{70}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

Embodiment 93. The compound of any of Embodiments 42-89, wherein at least five of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least four of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 94. The compound of any of Embodiments 42-89, wherein at least five of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least five of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 95. The compound of any of Embodiments 42-89, wherein at least six of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least five of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 96. The compound of any of Embodiments 42-89, wherein at least six of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least six of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 97. The compound of any of Embodiments 42-89, wherein at least seven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least six of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 98. The compound of any of Embodiments 42-89, wherein at least seven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least seven of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 99. The compound of any of Embodiments 42-89, wherein at least eight of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least seven of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 100. The compound of any of Embodiments 42-89, wherein at least eight of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least eight of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 101. The compound of any of Embodiments 42-89, wherein at least nine of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least eight of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 102. The compound of any of Embodiments 42-89, wherein at least nine of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 103. The compound of any of Embodiments 42-89, wherein at least ten of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 104. The compound of any of Embodiments 42-89, wherein at least eleven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 105. The compound of any of Embodiments 42-89, wherein R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and at least nine of R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 106. The compound of any of Embodiments 42-89, wherein at least eleven of R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; and R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are H.

Embodiment 107. The compound of any of Embodiments 42-106, wherein R^q is H, $-NR^{16a}R^{17a}$ or $-OR^{18c}$.

Embodiment 108. The compound of any of Embodiments 42-106, wherein R^q is $-NR^{16a}R^{17a}$ or $-OR^{18e}$.

Embodiment 109. The compound of any of Embodiments 42-108, wherein R^k is H, halogen, $-CN$, $-NR^{16}R^{17}$, $-OR^{18c}$, $-SR^{18d}$, or $-CR^oR^pR^q$.

Embodiment 110. The compound of any of Embodiments 42-108, wherein R^k is H, $-CN$, $-NR^{16}R^{17}$, $-OR^{18c}$, $-SR^{18d}$, or $-CR^oR^pR^q$.

Embodiment 111. The compound of any of Embodiments 42-108, wherein R^k is H, –CN, $–NR^{16}R^{17}$, $–OR^{18c}$, or $–CR^oR^pR^q$.

Embodiment 112. The compound of any of Embodiments 42-108, wherein R^k is H, $–NR^{16}R^{17}$, $–OR^{18c}$, or $–CR^oR^pR^q$.

Embodiment 113. The compound of any of Embodiments 42-108, wherein R^k is $–NR^{16}R^{17}$, $–OR^{18c}$, or $–CR^oR^pR^q$.

Embodiment 114. The compound of any of Embodiments 42-106, wherein R^k is H.

Embodiment 115. The compound of any of Embodiments 42-106, wherein R^k is $–NR^{16}R^{17}$.

Embodiment 116. The compound of any of Embodiments 42-106, wherein R^k is $–OR^{18c}$.

Embodiment 117. The compound of any of Embodiments 42-108, wherein R^k is $–CR^oR^pR^q$.

Embodiment 118. The compound of any of Embodiments 42-117, wherein A is $–NR^1R^2$, $–CR^iR^jR^k$, or $–OR^{18a}$.

Embodiment 119. The compound of any of Embodiments 42-106, wherein A is $–NR^1R^2$ or $–OR^{18a}$.

Embodiment 120. The compound of any of Embodiments 42-117, wherein A is $–CR^iR^jR^k$.

Embodiment 121. The compound of any of Embodiments 42-106, wherein A is $–NR^1R^2$.

Embodiment 122. The compound of any of Embodiments 42-106, wherein A is $–OR^{18a}$.

Embodiment 123. The compound of any of Embodiments 42-122, wherein Q is $–NR^{11}–$, $–CR^mR^n–$, or –O–.

Embodiment 124. The compound of any of Embodiments 42-122, wherein Q is $–NR^{11}–$.

Embodiment 125. The compound of any of Embodiments 42-122, wherein Q is $–CR^mR^n–$.

Embodiment 126. The compound of any of Embodiments 42-122, wherein Q is –O–.

Embodiment 127. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2, –$CR^iR^jR^k$, or –OR^{18a}; Q is –NR^{11}–, –CR^mR^n–, or –O–; and R^k is –$NR^{16}R^{17}$, or –OR^{18c}.

Embodiment 128. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2, –$CR^iR^jR^k$, or –OR^{18a}; Q is –NR^{11}–; and R^k is –$NR^{16}R^{17}$, or –OR^{18c}.

Embodiment 129. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2, –$CR^iR^jR^k$, or –OR^{18a}; Q is –NR^{11}–; and R^k is –OR^{18c}.

Embodiment 130. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2 or –OR^{18a}; and Q is –NR^{11}–.

Embodiment 131. The compound of any of Embodiments 42-106, wherein A is –NR^1R^2; and Q is –NR^{11}–.

Embodiment 132. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 133. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 134. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-9 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 135. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 136. The compound of any of Embodiments 1-3, wherein X is chosen from –NHR^{28} and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 137. The compound of any of Embodiments 1-3, wherein X is chosen from $-NHR^{28}$ and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, $-CN$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, and $-OR^{30}$.

Embodiment 138. The compound of any of Embodiments 1-3, wherein X is chosen from $-NHR^{28}$ and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, $-CN$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, and $-OR^{30}$.

Embodiment 139. The compound of any of Embodiments 1-3, wherein X is chosen from $-NHR^{28}$ and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, $-CN$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, and $-OR^{30}$.

Embodiment 140. The compound of any of Embodiments 1-3, wherein X is chosen from $-NHR^{28}$ and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, $-CN$, and $-OH$.

Embodiment 141. The compound of any of Embodiments 1-3, wherein X is chosen from $-NH(C_{1-6}$alkyl optionally substituted by 1-6 $R^{49})$, $-NH(C_{7-11}$arylalkyl optionally substituted by 1-6 $R^{49})$, –NH(3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{49}), –NH(4-11 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{49}), and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 142. The compound of any of Embodiments 1-3, wherein X is chosen from $-NH(C_{1-6}$alkyl optionally substituted by 1-6 $R^{49})$, $-NH(C_{7-11}$arylalkyl optionally substituted by 1-6 $R^{49})$, –NH(3-10 membered heterocycloalkyl), –NH(4-11 membered

heterocycloalkylalkyl), and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 143. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 144. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-9 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 145. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

Embodiment 146. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 147. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2

members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, and $-OR^{30}$.

Embodiment 148. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, and $-OR^{30}$.

Embodiment 149. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, and $-OR^{30}$.

Embodiment 150. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, and $-OR^{30}$.

Embodiment 151. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, and –OH.

Embodiment 152. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 153. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(benzyl), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 154. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

Embodiment 155. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, and –OH.

Embodiment 156. The compound of any of Embodiments 1-3, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}) and –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms).

Embodiment 200. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, $–C(=NR^{25})R^{20}$, $–C(=NR^{25})NR^{22}R^{23}$, $–C(=NOH)NR^{22}R^{23}$, $–C(=NOR^{26})R^{20}$, $–C(=NNR^{22}R^{23})R^{20}$, $–C(=NNR^{24}C(=O)R^{21})R^{20}$, $–C(=NNR^{24}C(=O)OR^{21})R^{20}$, $–C(=S)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, $–OP(=O)(SR^{20})(SR^{20})$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–SP(=O)(OR^{20})(OR^{20})$, $–SP(=O)(SR^{20})(SR^{20})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–P(=O)(OR^{20})(OR^{20})$, and $–P(=O)(SR^{20})(SR^{20})$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 201. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 202. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 203. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-4 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-4 R^{19}, C_{2-6}alkynyl optionally substituted by 1-4 R^{19}, C_{6-10}aryl optionally substituted by 1-4 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-4 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-4 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-4 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-4 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-4 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-4 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-4 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-4 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-4 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-4 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-4 R^{19}.

Embodiment 204. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 205. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 206. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$,$–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 207. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-7}cycloalkyl, C_{4-8}cycloalkylalkyl, 3-7 membered heterocycloalkyl, 4-8 membered heterocycloalkylalkyl, 5-6 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$,$–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can,

together with the atoms linking them, form a C_{6-10}aryl, C_{3-7}cycloalkyl, 3-7 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 208. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, C_{4-8}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-8 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 209. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 210. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{3-}

$_7$cycloalkyl optionally substituted by 1-3 R^{19}, or a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 211. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{3-7}cycloalkyl, 3-7 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, –C(=O)R^{20}, –C(=O)$NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and –$S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{3-7}cycloalkyl, or a 3-7 membered heterocycloalkyl.

Embodiment 212. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)OR^{20}, –C(=O)$NR^{22}R^{23}$, $–NO_2$, –$NR^{22}R^{23}$, and $–OR^{20}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 213. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, and $–OR^{20}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl

optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 214. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)$NR^{22}R^{23}$, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 215. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)$NR^{22}R^{23}$, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)$NR^{22}R^{23}$, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 216. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-}

$_6$alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 217. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, and $-S(=O)NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 218. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-10 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, and $–S(=O)NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 219. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–Si(R^{24})_3$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 220. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, –

$C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–Si(R^{24})_3$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 221. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 222. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$,and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 222. The compound of any of Embodiments 1-156, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 223. The compound of any of Embodiments 1-156 or 200-222, wherein R^8 is not phenyl or morpholinyl.

Embodiment 224. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and –

$S(=O)_2NR^{22}R^{23}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 225. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 226. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; R^8 is chosen

from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 227. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 228. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, and $-OC(=O)R^{20}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6

R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 229. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 230. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 231. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 232. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, and $–OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_nR^{20}$.

Embodiment 233. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_nR^{20}$.

Embodiment 234. The compound of any of Embodiments 1-156 or 200-233, wherein R^8 is H.

Embodiment 235. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{1-6}alkyl, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 236. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl, C_{6-10}aryl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 237. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 238. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-OR^{20}$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 239. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-O(C_{1-6}alkyl)$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 240. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-OR^{20}$; R^8 is H; and R^9 is H.

Embodiment 241. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-O(C_{1-6}alkyl)$; R^8 is H; and R^9 is H.

Embodiment 242. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and $-O(C_{1-6}alkyl)$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 243. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and $-OR^{20}$; R^8 is H; and R^9 is H.

Embodiment 244. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and $-O(C_{1-6}alkyl)$; R^8 is H; and R^9 is H.

Embodiment 245. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and $-O(CH_3)$; R^8 is H; and R^9 is H.

Embodiment 246. The compound of any of Embodiments 1-156, wherein R^7 is H; R^8 is H; and R^9 is H.

Embodiment 247. The compound of any of Embodiments 1-156, wherein R^7 is cyclopropyl; R^8 is H; and R^9 is H.

Embodiment 248. The compound of any of Embodiments 1-156, wherein R^7 is $-O(CH_3)$; R^8 is H; and R^9 is H.

Embodiment 249. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, cyclopropyl, and $-O(C_{1-6}alkyl)$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9

membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 250. The compound of any of Embodiments 1-156, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-O(CH_3)$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

Embodiment 300. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them,

form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 301. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 302. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-$

$NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 303. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 304. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-11}aryl optionally substituted by 1-3 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-$

$NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 305. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 306. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them,

form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 307. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 308. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 309. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, –

$NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, and $-S(=O)NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 310. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, and $-S(=O)NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 311. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-}

$_{6}$alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, –SCN, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 312. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 313. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl

optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 314. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, –SCN, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 315. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 316. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, –

$C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 317. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 318. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 319. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-$

$OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 320. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 321. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 322. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 323. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 324. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen

from H, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 325. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 326. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 327. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 328. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 329. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 330. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 331. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 332. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 333. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 334. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 335. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 336. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 337. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 338. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 339. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 340. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 341. The compound of any of Embodiments 300-340, wherein R^{14} is H.

Embodiment 342. The compound of any of Embodiments 300-341, wherein R^{15} is H.

Embodiment 343. The compound of any of Embodiments 300-342, wherein R^{12} is H.

Embodiment 344. The compound of any of Embodiments 300-343, wherein R^{13} is H.

Embodiment 345. The compound of any of Embodiments 300-340, wherein R^{14} and R^{15} are H.

Embodiment 346. The compound of any of Embodiments 300-340, wherein R^{12} are R^{15} are H.

Embodiment 347. The compound of any of Embodiments 300-340, wherein R^{12}, R^{14}, and R^{15} are H.

Embodiment 348. The compound of any of Embodiments 300-340, wherein R^{12} are R^{14} are H.

Embodiment 349. The compound of any of Embodiments 1, 2, 4-156, 200-250, or 300-340, wherein R^{12}, R^{13}, R^{14}, and R^{15} are H.

Embodiment 350. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

Embodiment 351. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1 R^{19}.

Embodiment 352. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

Embodiment 353. The compound of any of Embodiments 300-342, wherein R^{12} and R^{13}, together with the atoms linking them, form a pyrrolyl ring.

Embodiment 354. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 355. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 356. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 357. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 358. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by

1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 359. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 360. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 361. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 362. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 363. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted

by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 364. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 365. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 366. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 367. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 368. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 369. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can,

together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 370. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

Embodiment 371. The compound of any of Embodiments 1, 2, 4-156, or 200-250, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

Embodiment 400. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-$

SO_3R^{27}, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 401. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{78}R^{78}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-

6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 402. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, and $–S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 403. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –

SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 404. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 405. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d

and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 406. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 407. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 408. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–NR^{24}S(=O)_2R^{21}$.

Embodiment 409. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–NR^{24}S(=O)_2R^{21}$.

Embodiment 410. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $–NR^{22}R^{23}$,and $–NR^{24}C(=O)R^{20}$.

Embodiment 411. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}.

Embodiment 412. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and benzyl optionally substituted by 1-3 R^{19}.

Embodiment 413. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 414. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 415. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 416. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 417. The compound of any of Embodiments 400-416, wherein at least three of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 418. The compound of any of Embodiments 400-416, wherein at least four of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 419. The compound of any of Embodiments 400-416, wherein at least five of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 420. The compound of any of Embodiments 400-416, wherein at least six of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 421. The compound of any of Embodiments 400-416, wherein at least seven of R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 422. The compound of any of Embodiments 400-416, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H.

Embodiment 423. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-}

$_{17}$cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, –$C(=O)R^{20}$, –$C(=O)OR^{20}$, –$C(=O)NR^{22}R^{23}$, –$C(=O)C(=O)R^{20}$, –$C(=NR^{25})R^{20}$, –$C(=NR^{25})NR^{22}R^{23}$, –$C(=NOH)NR^{22}R^{23}$, –$C(=NOR^{26})R^{20}$, –$C(=NNR^{22}R^{23})R^{20}$, –$C(=NNR^{24}C(=O)R^{21})R^{20}$, –$C(=NNR^{24}C(=O)OR^{21})R^{20}$, –$C(=S)NR^{22}R^{23}$, –NC, –$NO_2$, –$NR^{22}R^{23}$, –$NR^{24}NR^{22}R^{23}$, –$N=NR^{24}$, –$NR^{24}OR^{26}$, –$NR^{24}C(=O)R^{20}$, –$NR^{24}C(=O)C(=O)R^{20}$, –$NR^{24}C(=O)OR^{21}$, –$NR^{24}C(=O)C(=O)OR^{21}$, –$NR^{24}C(=O)NR^{22}R^{23}$, –$NR^{24}C(=O)NR^{24}C(=O)R^{20}$, –$NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, –$NR^{24}C(=NR^{25})NR^{22}R^{23}$, –$NR^{24}C(=O)C(=O)NR^{22}R^{23}$, –$NR^{24}C(=S)R^{20}$, –$NR^{24}C(=S)OR^{20}$, –$NR^{24}C(=S)NR^{22}R^{23}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$NR^{24}P(=O)R^{78}R^{78}$, –$NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$NR^{24}P(=O)(OR^{20})(OR^{20})$, –$NR^{24}P(=O)(SR^{20})(SR^{20})$, –$OR^{20}$, –OCN, –$OC(=O)R^{20}$, –$OC(=O)NR^{22}R^{23}$, –$OC(=O)OR^{20}$, –$OC(=NR^{25})NR^{22}R^{23}$, –$OS(=O)R^{20}$, –$OS(=O)_2R^{20}$, –$OS(=O)_2OR^{20}$, –$OS(=O)_2NR^{22}R^{23}$, –$OP(=O)R^{78}R^{78}$, –$OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$OP(=O)(OR^{20})(OR^{20})$, –$OP(=O)(SR^{20})(SR^{20})$, –$Si(R^{24})_3$, –SCN, –$S(=O)_nR^{20}$, –$S(=O)_2OR^{20}$, –SO_3R^{27}, –$S(=O)_2NR^{22}R^{23}$, –$S(=O)NR^{22}R^{23}$, –$SP(=O)R^{78}R^{78}$, –$SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$SP(=O)(OR^{20})(OR^{20})$, –$SP(=O)(SR^{20})(SR^{20})$, –$P(=O)R^{78}R^{78}$, –$P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$P(=O)(OR^{20})(OR^{20})$, and –$P(=O)(SR^{20})(SR^{20})$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 424. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, 6-21

membered heteroarylalkyl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, $–OP(=O)(SR^{20})(SR^{20})$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–SP(=O)(OR^{20})(OR^{20})$, $–SP(=O)(SR^{20})(SR^{20})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–P(=O)(OR^{20})(OR^{20})$, and $–P(=O)(SR^{20})(SR^{20})$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 425. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, and $–S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g,

R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 426. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 427. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and

R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 428. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or any of R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 429. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 430. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 431. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, halogen, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-NR^{24}S(=O)_2R^{21}$.

Embodiment 432. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-NR^{24}S(=O)_2R^{21}$.

Embodiment 433. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, $-NR^{22}R^{23}$,and $-NR^{24}C(=O)R^{20}$.

Embodiment 434. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}.

Embodiment 435. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and benzyl optionally substituted by 1-3 R^{19}.

Embodiment 436. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 437. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 438. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl optionally substituted by 1 R^{19}.

Embodiment 439. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, methyl optionally substituted by 1 R^{19}, and benzyl.

Embodiment 440. The compound of any of Embodiments 1, 3-156, 200-250, or 300-371, wherein R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are H.

Embodiment 500. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–C(=O)C(=O)R^{30}$, $–C(=NR^{35})R^{30}$, $–C(=NR^{35})NR^{32}R^{33}$, $–C(=NOH)NR^{32}R^{33}$, $–C(=NOR^{36})R^{30}$, $–C(=NNR^{32}R^{33})R^{30}$, $–C(=NNR^{34}C(=O)R^{31})R^{30}$, $–C(=NNR^{34}C(=O)OR^{31})R^{30}$, $–C(=S)NR^{32}R^{33}$, –NC, $–NO_2$, $–NR^{32}R^{33}$, $–NR^{34}NR^{32}R^{33}$, $–N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $–NR^{34}OR^{36}$, $–NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)C(=O)R^{30}$, $–NR^{34}C(=O)OR^{31}$, $–NR^{34}C(=O)C(=O)OR^{31}$, $–NR^{34}C(=O)NR^{32}R^{33}$, $–NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $–NR^{34}C(=NR^{35})NR^{32}R^{33}$, $–NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $–NR^{34}C(=S)R^{30}$, $–NR^{34}C(=S)OR^{30}$, $–NR^{34}C(=S)NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–NR^{34}S(=O)_2NR^{32}R^{33}$, $–NR^{34}P(=O)R^{78}R^{78}$, $–NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–NR^{34}P(=O)(OR^{30})(OR^{30})$, $–NR^{34}P(=O)(SR^{30})(SR^{30})$, $–OR^{30}$, =O, –OCN, $–OC(=O)R^{30}$, $–OC(=O)NR^{32}R^{33}$, $–OC(=O)OR^{30}$, $–OC(=NR^{35})NR^{32}R^{33}$, $–OS(=O)R^{30}$, $–OS(=O)_2R^{30}$, $–OS(=O)_2OR^{30}$, $–OS(=O)_2NR^{32}R^{33}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–OP(=O)(OR^{30})(OR^{30})$, $–OP(=O)(SR^{30})(SR^{30})$, $–Si(R^{34})_3$, –SCN, =S, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–SP(=O)(OR^{30})(OR^{30})$, $–SP(=O)(SR^{30})(SR^{30})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$.

Embodiment 501. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{39}, C_{2-6}alkenyl optionally substituted by 1-6 R^{39}, C_{2-6}alkynyl optionally substituted by 1-6 R^{39}, C_{6-11}aryl optionally substituted by 1-6 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{39}, 6-21

membered heteroarylalkyl optionally substituted by 1-6 R^{39}, halogen, –CN, –C(=O)R^{30}, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –C(=O)C(=O)R^{30}, –C(=NR^{35})R^{30}, –C(=NR^{35})$NR^{32}R^{33}$, –C(=NOH)$NR^{32}R^{33}$, –C(=NOR^{36})R^{30}, –C(=$NNR^{32}R^{33}$)R^{30}, –C(=NNR^{34}C(=O)R^{31})R^{30}, –C(=NNR^{34}C(=O)OR^{31})R^{30}, –C(=S)$NR^{32}R^{33}$, –NC, –NO_2, –$NR^{32}R^{33}$, –$NR^{34}NR^{32}R^{33}$, –N=NR^{34}, =NR^{30}, =NOR^{30}, –$NR^{34}OR^{36}$, –NR^{34}C(=O)R^{30}, –NR^{34}C(=O)C(=O)R^{30}, –NR^{34}C(=O)OR^{31}, –NR^{34}C(=O)C(=O)OR^{31}, –NR^{34}C(=O)$NR^{32}R^{33}$, –NR^{34}C(=O)NR^{34}C(=O)R^{30}, –NR^{34}C(=O)NR^{34}C(=O)OR^{30}, –NR^{34}C(=NR^{35})$NR^{32}R^{33}$, –NR^{34}C(=O)C(=O)$NR^{32}R^{33}$, –NR^{34}C(=S)R^{30}, –NR^{34}C(=S)OR^{30}, –NR^{34}C(=S)$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, –$NR^{34}S(=O)_2NR^{32}R^{33}$, –$NR^{34}$P(=O)$R^{78}R^{78}$, –$NR^{34}$P(=O)($NR^{32}R^{33}$)($NR^{32}R^{33}$), –$NR^{34}$P(=O)($OR^{30}$)($OR^{30}$), –$NR^{34}$P(=O)($SR^{30}$)($SR^{30}$), –$OR^{30}$, =O, –OCN, –OC(=O)$R^{30}$, –OC(=O)$NR^{32}R^{33}$, –OC(=O)$OR^{30}$, –OC(=$NR^{35}$)$NR^{32}R^{33}$, –$OS(=O)R^{30}$, –$OS(=O)_2R^{30}$, –$OS(=O)_2OR^{30}$, –$OS(=O)_2NR^{32}R^{33}$, –OP(=O)$R^{78}R^{78}$, –OP(=O)($NR^{32}R^{33}$)($NR^{32}R^{33}$), –OP(=O)($OR^{30}$)($OR^{30}$), –OP(=O)($SR^{30}$)($SR^{30}$), –$Si(R^{34})_3$, –SCN, =S, –$S(=O)_nR^{30}$, –$S(=O)_2OR^{30}$, –$SO_3R^{37}$, –$S(=O)_2NR^{32}R^{33}$, –S(=O)$NR^{32}R^{33}$, –SP(=O)$R^{78}R^{78}$, –SP(=O)($NR^{32}R^{33}$)($NR^{32}R^{33}$), –SP(=O)($OR^{30}$)($OR^{30}$), –SP(=O)($SR^{30}$)($SR^{30}$), –P(=O)$R^{78}R^{78}$, –P(=O)($NR^{32}R^{33}$)($NR^{32}R^{33}$), –P(=O)($OR^{30}$)($OR^{30}$), and –P(=O)($SR^{30}$)($SR^{30}$).

Embodiment 502. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{39}, C_{2-6}alkenyl optionally substituted by 1-6 R^{39}, C_{2-6}alkynyl optionally substituted by 1-6 R^{39}, C_{6-11}aryl optionally substituted by 1-6 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{39}, halogen, –CN, –C(=O)R^{30}, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –C(=O)C(=O)R^{30}, –NC, –NO_2, –$NR^{32}R^{33}$, –$NR^{34}NR^{32}R^{33}$, –$NR^{34}OR^{36}$, –NR^{34}C(=O)R^{30}, –NR^{34}C(=O)C(=O)R^{30}, –NR^{34}C(=O)OR^{31}, –NR^{34}C(=O)C(=O)OR^{31}, –NR^{34}C(=O)$NR^{32}R^{33}$, –NR^{34}C(=O)NR^{34}C(=O)R^{30}, –NR^{34}C(=O)NR^{34}C(=O)OR^{30}, –NR^{34}C(=NR^{35})$NR^{32}R^{33}$, –NR^{34}C(=O)C(=O)$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, –$NR^{34}S(=O)_2NR^{32}R^{33}$, –$OR^{30}$, =O, –OCN, –OC(=O)$R^{30}$, –OC(=O)$NR^{32}R^{33}$, –OC(=O)$OR^{30}$, –OC(=$NR^{35}$)$NR^{32}R^{33}$, –$Si(R^{34})_3$, –SCN, =S, –$S(=O)_nR^{30}$, –$S(=O)_2OR^{30}$, –

SO_3R^{37}, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 503. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-NC$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OCN$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-Si(R^{34})_3$, $-SCN$, =S, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 504. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)C(=O)R^{30}$, $-NC$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}NR^{32}R^{33}$, $-NR^{34}OR^{36}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OCN$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-Si(R^{34})_3$, $-SCN$, =S,

$-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 505. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, =S, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 506. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)OR^{31}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, =S, $-S(=O)_nR^{30}$, $-S(=O)_2NR^{32}R^{33}$, and $-S(=O)NR^{32}R^{33}$.

Embodiment 507. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{39}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-$

$NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, =S, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 508. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –CN, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, =S, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 509. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –CN, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}S(=O)_2R^{31}$, $-OR^{30}$, =O, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 510. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –CN, $-C(=O)R^{30}$, $-C(=O)NR^{32}R^{33}$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}S(=O)_2R^{31}$, $-OR^{30}$, =O, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 511. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl

optionally substituted by 1-3 R^{39}, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}C(=O)R^{30}$, $–OR^{30}$, and =O.

Embodiment 512. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}C(=O)R^{30}$, $–OR^{30}$, and =O.

Embodiment 513. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, and $–OR^{30}$.

Embodiment 514. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, –CN, $–C(=O)NR^{32}R^{33}$, $–NO_2$, $–NR^{32}R^{33}$, and $–OR^{30}$.

Embodiment 515. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}.

Embodiment 516. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $–C(=O)OR^{30}$, $–NR^{32}R^{33}$, and $–OR^{30}$.

Embodiment 517. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl

optionally substituted by 1-3 R^{39}, phenyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 518. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 519. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl optionally substituted by 1 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl optionally substituted by 1 R^{39}, 5-6 membered heteroaryl, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 520. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, $-C(=O)OR^{30}$, $-NR^{32}R^{33}$, and $-OR^{30}$.

Embodiment 521. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, $-CN$, $-C(=O)R^{30}$, $-C(=O)OR^{30}$, $-C(=O)NR^{32}R^{33}$, $-NO_2$, $-NR^{32}R^{33}$, $-NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-OR^{30}$, $=O$, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-Si(R^{34})_3$, $=S$, $-S(=O)_nR^{30}$, and $-S(=O)_2NR^{32}R^{33}$.

Embodiment 522. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl

optionally substituted by 1-3 R^{39}, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}C(=O)R^{30}$, –$NR^{34}S(=O)_2R^{31}$, –OR^{30}, =O, –OC(=O)R^{30}, –$S(=O)_nR^{30}$, and –$S(=O)_2NR^{32}R^{33}$.

Embodiment 523. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, –OR^{30}, and =O.

Embodiment 524. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, and –OR^{30}.

Embodiment 525. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, 6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, –OR^{30}, and =O.

Embodiment 526. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, 6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5 membered heteroaryl optionally substituted by 1-3 R^{39}, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, and –OR^{30}.

Embodiment 527. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, morpholinyl optionally substituted by 1-3 R^{39}, pyrazolyl optionally substituted by 1-3 R^{39}, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 528. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl optionally substituted by 1-3 R^{39}, morpholinyl optionally substituted by 1-3 R^{39}, pyrazolyl optionally substituted by 1-3 R^{39}, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, and $–OR^{30}$.

Embodiment 529. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 530. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, –$C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, and $–OR^{30}$.

Embodiment 531. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, benzyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 532. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, benzyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, and $–OR^{30}$.

Embodiment 533. The compound of any of Embodiments 1-156, 200-250, 300-371, or 400-440, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, benzyl optionally substituted by 1-3 R^{39}, cyclopropyl, morpholinyl, pyrazolyl, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

Embodiment 600. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-6 R^{49}, C_{2-6}alkynyl optionally substituted by 1-6 R^{49}, C_{6-11}aryl optionally substituted by 1-6 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{49}.

Embodiment 601. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-6 R^{49}, C_{2-6}alkynyl optionally substituted by 1-6 R^{49}, C_{6-10}aryl optionally substituted by 1-6 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{49}.

Embodiment 602. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{2-6}alkenyl optionally substituted by 1-3 R^{49}, C_{2-6}alkynyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 603. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 604. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 605. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 606. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}.

Embodiment 607. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 608. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 609. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 610. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{49}.

Embodiment 611. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 612. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 613. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 614. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37}

at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 615. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and cyclopropyl optionally substituted by 1-3 R^{49}.

Embodiment 616. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl.

Embodiment 617. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl.

Embodiment 618. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 619. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 620. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 621. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37}

at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 622. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 623. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 624. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 625. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl.

Embodiment 626. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 627. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 628. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 629. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 630. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 631. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 632. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 633. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and cyclopropyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 634. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 635. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 636. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 637. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 638. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 639. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 640. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 641. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 642. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 643. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 644. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H,

C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 645. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 646. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{49}, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 647. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 648. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 649. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 650. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered

heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 651. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 652. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 653. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 654. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 655. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 656. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-}

$_{6}$cycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 657. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 658. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 659. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl optionally substituted by 1-3 R^{49}; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 660. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and cyclopropyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 661. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, benzyl optionally substituted by 1-3 R^{49}, cyclopropyl, thienyl, and pyrazinyl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 662. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 663. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H,

phenyl optionally substituted by 1 R^{49}, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 664. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 665. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, C_{3-6}cycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 666. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 667. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20} at each occurrence is independently chosen from H, phenyl, cyclopropyl, 5 membered heterocycloalkyl, and 5 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 668. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, or 500-533, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

Embodiment 700. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{2-6}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49}.

Embodiment 701. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-3 R^{49}, C_{2-6}alkynyl optionally substituted by 1-3 R^{49}, C_{6-11}aryl optionally substituted by 1-3 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{49}.

Embodiment 702. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{2-6}alkenyl optionally substituted by 1-3 R^{49}, C_{2-6}alkynyl optionally substituted by 1-3 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 703. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, C_{6-10}aryl optionally substituted by 1-3 R^{49}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{49}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 704. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{49}.

Embodiment 705. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 706. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}.

Embodiment 707. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{49}.

Embodiment 708. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5-6 membered heterocycloalkyl.

Embodiment 709. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5 membered heterocycloalkyl optionally substituted by 1-6 R^{49}.

Embodiment 710. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and 5 membered heterocycloalkyl.

Embodiment 711. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{49} and pyrrolidinyl.

Embodiment 712. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{49} and 5 membered heterocycloalkyl.

Embodiment 713. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is C_{1-6}alkyl optionally substituted by 1-6 R^{49}.

Embodiment 714. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, or 600-668, wherein R^{28} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 750. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each

occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 751. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-11}aryl optionally substituted by 1-3 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 752. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 753. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 754. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 755. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 756. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 757. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 4-5 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 758. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 759. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 760. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 761. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, and 6 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 762. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1 R^{59}, and 6 membered heteroaryl optionally substituted by 1 R^{59}.

Embodiment 763. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21

membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 764. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-11}aryl optionally substituted by 1-3 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 765. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, bezyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 766. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally

substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence are independently chosen from H and C_{1-6}alkyl.

Embodiment 767. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, benzyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence are independently chosen from H and C_{1-6}alkyl.

Embodiment 768. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 4-5 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 769. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{23} and R^{33} at each occurrence are independently chosen from H and C_{1-6}alkyl.

Embodiment 770. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{59}.

Embodiment 771. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, benzyl, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-9

membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{59}.

Embodiment 772. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 773. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 774. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} and R^{32} at each occurrence are independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, benzyl, and 6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 775. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{59}, and 6 membered heteroaryl optionally substituted by 1 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 776. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or

R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 777. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-11}aryl optionally substituted by 1-3 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 778. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, C_{2-6}alkenyl optionally substituted by 1-3 R^{59}, C_{2-6}alkynyl optionally substituted by 1-3 R^{59}, C_{6-10}aryl optionally substituted by 1-3 R^{59}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 779. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{59}, 3-6 membered

heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 780. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{69}.

Embodiment 781. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 782. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 783. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl optionally substituted by 1-3 R^{59}, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 784. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, C_{3-10}cycloalkyl, 4-5 membered heterocycloalkyl, and 5-9 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 785. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, C_{6-10}aryl optionally substituted by 1-3 R^{59}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 786. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 787. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1-3 R^{59}, and 6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 788. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22} at each occurrence is independently chosen from H, phenyl optionally substituted by 1 R^{59}, and 6 membered heteroaryl optionally substituted by 1 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 789. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 790. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 791. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69}.

Embodiment 792. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they

are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{69}.

Embodiment 793. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{69} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{69}.

Embodiment 794. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-6 membered heterocycloalkyl optionally substituted by 1-6 R^{69} or a 5-6 membered heteroaryl optionally substituted by 1-6 R^{69}.

Embodiment 795. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, or 700-714, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 800. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkenyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-C(=NR^{75})R^{70}$, $-C(=NR^{75})NR^{72}R^{73}$, $-C(=NOH)NR^{72}R^{73}$, $-C(=NOR^{76})R^{70}$, $-C(=NNR^{72}R^{73})R^{70}$, $-C(=NNR^{74}C(=O)R^{71})R^{70}$, $-C(=NNR^{74}C(=O)OR^{71})R^{70}$, $-C(=S)NR^{72}R^{73}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $=NR^{70}$, $=NOR^{70}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, –

$NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)R^{70}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, =O, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, –SCN, =S, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, and $-P(=O)(SR^{70})(SR^{70})$.

Embodiment 801. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{6-11}aryl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, –NC, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, =O, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-Si(R^{74})_3$, –SCN, =S, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$.

Embodiment 802. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{6-10}aryl optionally substituted by 1-6 R^{79}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, =O, –OCN, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-Si(R^{74})_3$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$.

Embodiment 803. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, C_{6-10}aryl optionally substituted by 1-3 R^{79}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, =O, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-Si(R^{74})_3$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$.

Embodiment 804. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, =O, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-Si(R^{74})_3$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$.

Embodiment 805. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}S(=O)_2R^{71}$, $-OR^{70}$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-S(=O)_nR^{70}$, and $-S(=O)_2NR^{72}R^{73}$.

Embodiment 806. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl

optionally substituted by 1-3 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{79}, halogen, –CN, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –OR^{70}, and –$S(=O)_nR^{70}$.

Embodiment 807. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –OR^{70}, and –$S(=O)_nR^{70}$.

Embodiment 808. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, cyclopropyl, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –OR^{70}, and –$S(=O)_nR^{70}$.

Embodiment 809. The compound of any of Embodiments 800-808, wherein R^{39} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, and 5-6 membered heteroaryl.

Embodiment 810. The compound of any of Embodiments 800-808, wherein R^{39} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, and 6 membered heteroaryl.

Embodiment 811. The compound of any of Embodiments 800-810, wherein R^{49} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –$C(=O)NR^{72}R^{73}$, and –$NR^{72}R^{73}$.

Embodiment 812. The compound of any of Embodiments 800-810, wherein R^{49} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, 5-6 membered heterocycloalkyl, 6 membered heteroaryl, halogen, –$C(=O)NR^{72}R^{73}$, and –$NR^{72}R^{73}$.

Embodiment 813. The compound of any of Embodiments 800-812, wherein R^{59} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79},

phenyl optionally substituted by 1-3 R^{79}, cyclopropyl, 5-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–NR^{72}R^{73}$, $–OR^{70}$, and $–S(=O)_nR^{70}$.

Embodiment 814. The compound of any of Embodiments 800-812, wherein R^{59} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, cyclopropyl, 6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $–NR^{72}R^{73}$, $–OR^{70}$, and $–S(=O)_nR^{70}$.

Embodiment 815. The compound of any of Embodiments 800-814, wherein R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}.

Embodiment 816. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}.

Embodiment 817. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, or 750-795, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently C_{1-6}alkyl.

Embodiment 850. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89}.

Embodiment 851. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{89}, C_{2-6}alkenyl optionally substituted by 1-6 R^{89}, C_{2-6}alkynyl optionally substituted by 1-6 R^{89}, C_{6-10}aryl optionally substituted by 1-6 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{89}.

Embodiment 852. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{2-6}alkenyl optionally substituted by 1-3 R^{89}, C_{2-6}alkynyl optionally substituted by 1-3 R^{89}, C_{6-10}aryl optionally substituted by 1-3 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}.

Embodiment 853. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, benzyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}.

Embodiment 854. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 855. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, benzyl optionally substituted by 1-3 R^{89}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{89}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{89}.

Embodiment 856. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 857. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75},

R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 858. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{89}, and 5-6 membered heteroaryl.

Embodiment 859. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{89}.

Embodiment 860. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 861. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, or 800-817, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is H.

Embodiment 862. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{99}, C_{2-6}alkenyl optionally substituted by 1-11 R^{99}, C_{2-6}alkynyl optionally substituted by 1-9 R^{99}, C_{6-11}aryl optionally substituted by 1-11 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{109}.

Embodiment 863. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-

6 R^{99}, C_{2-6}alkenyl optionally substituted by 1-6 R^{99}, C_{2-6}alkynyl optionally substituted by 1-6 R^{99}, C_{6-11}aryl optionally substituted by 1-6 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{109}.

Embodiment 864. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{99}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{109}.

Embodiment 865. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{99}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{99}.

Embodiment 866. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{99}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-10

membered heterocycloalkyl optionally substituted by 1-3 R^{109} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{109}.

Embodiment 867. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{99}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{99}.

Embodiment 868. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, benzyl optionally substituted by 1-3 R^{99}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{99}.

Embodiment 869. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 870. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 871. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{99}, phenyl optionally substituted by 1-3 R^{99}, and benzyl optionally substituted by 1-3 R^{99}.

Embodiment 872. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{99}.

Embodiment 873. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 874. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 875. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-861, wherein R^{72} and R^{73} at each occurrence is H.

Embodiment 876. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89}.

Embodiment 877. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{2-6}alkenyl optionally substituted by 1-3 R^{89}, C_{2-6}alkynyl optionally substituted by 1-3 R^{89}, C_{6-11}aryl optionally substituted by 1-3 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89}.

Embodiment 878. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{2-6}alkenyl optionally substituted by 1-3 R^{89}, C_{2-6}alkynyl optionally substituted by 1-3 R^{89}, C_{6-10}aryl optionally substituted by 1-3 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 879. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, C_{6-10}aryl optionally substituted by 1-3 R^{89}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{89}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{89}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 880. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, benzyl optionally substituted by 1-3 R^{89}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{89}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 881. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 882. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl, and benzyl.

Embodiment 883. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{89}, phenyl optionally substituted by 1-3 R^{89}, and benzyl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 884. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form an azaphosphinane ring optionally substituted by 1-3 C_{1-6}alkyl.

Embodiment 885. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form an azaphosphinane ring optionally substituted by 1-3 R^{89}.

Embodiment 886. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-875, wherein R^{78} at each occurrence is C_{1-6}alkyl.

Embodiment 900. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{119}, C_{2-6}alkenyl optionally substituted by 1-6 R^{119}, C_{2-6}alkynyl optionally substituted by 1-6 R^{119}, C_{6-11}aryl optionally substituted by 1-6 R^{119}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{119}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{119}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{119}, 6-21 membered heteroarylalkyl optionally

substituted by 1-6 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–C(=O)C(=O)R^{110}$, $–C(=NR^{115})R^{110}$, $–C(=NR^{115})NR^{112}R^{113}$, $–C(=NOH)NR^{112}R^{113}$, $–C(=NOR^{116})R^{110}$, $–C(=NNR^{112}R^{113})R^{110}$, $–C(=NNR^{114}C(=O)R^{111})R^{110}$, $–C(=NNR^{114}C(=O)OR^{111})R^{110}$, $–C(=S)NR^{112}R^{113}$, –NC, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}NR^{112}R^{113}$, $–N=NR^{114}$, $=NR^{110}$, $=NOR^{110}$, $–NR^{114}OR^{116}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}R^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $–NR^{114}C(=NR^{115})NR^{112}R^{113}$, $–NR^{114}C(=O)C(=O)NR^{112}R^{113}$, $–NR^{114}C(=S)R^{110}$, $–NR^{114}C(=S)OR^{110}$, $–NR^{114}C(=S)NR^{112}R^{113}$, $–NR^{114}S(=O)_2R^{111}$, $–NR^{114}S(=O)_2NR^{112}R^{113}$, $–NR^{114}P(=O)R^{118}R^{118}$, $–NR^{114}P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–NR^{114}P(=O)(OR^{110})(OR^{110})$, $–NR^{114}P(=O)(SR^{110})(SR^{110})$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–OC(=NR^{115})NR^{112}R^{113}$, $–OS(=O)R^{110}$, $–OS(=O)_2R^{110}$, $–OS(=O)_2OR^{110}$, $–OS(=O)_2NR^{112}R^{113}$, $–OP(=O)R^{118}R^{118}$, $–OP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–OP(=O)(OR^{110})(OR^{110})$, $–OP(=O)(SR^{110})(SR^{110})$, $–Si(R^{114})_3$, –SCN, =S, $–S(=O)_nR^{110}$, $–S(=O)_2OR^{110}$, $–SO_3R^{1111}$, $–S(=O)_2NR^{112}R^{113}$, $–S(=O)NR^{112}R^{113}$, $–SP(=O)R^{118}R^{118}$, $–SP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–SP(=O)(OR^{110})(OR^{110})$, $–SP(=O)(SR^{110})(SR^{110})$, $–P(=O)R^{118}R^{118}$, $–P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $–P(=O)(OR^{110})(OR^{110})$, and $–P(=O)(SR^{110})(SR^{110})$.

Embodiment 901. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{119}, C_{6-11}aryl optionally substituted by 1-6 R^{119}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, –NC, $–NO_2$, $–NR^{112}R^{113}$, $–NR^{114}NR^{112}R^{113}$, $–NR^{114}OR^{116}$, $–NR^{114}C(=O)R^{110}$, $–NR^{114}C(=O)OR^{111}$, $–NR^{114}C(=O)NR^{112}R^{113}$, $–NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $–NR^{114}S(=O)_2R^{111}$, $–NR^{114}S(=O)_2NR^{112}R^{113}$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–OC(=O)NR^{112}R^{113}$, $–OC(=O)OR^{110}$, $–Si(R^{114})_3$, –SCN, =S, $–S(=O)_nR^{110}$, and $–S(=O)_2NR^{112}R^{113}$.

Embodiment 902. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted

by 1-6 R^{119}, C_{6-10}aryl optionally substituted by 1-6 R^{119}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{119}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{119}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{119}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{119}, halogen, –CN, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-NO_2$, $-NR^{112}R^{113}$, $-NR^{114}C(=O)R^{110}$, $-NR^{114}C(=O)OR^{111}$, $-NR^{114}C(=O)NR^{112}R^{113}$, $-NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $-NR^{114}S(=O)_2R^{111}$, $-NR^{114}S(=O)_2NR^{112}R^{113}$, $-OR^{110}$, =O, $-OC(=O)R^{110}$, $-OC(=O)NR^{112}R^{113}$, $-OC(=O)OR^{110}$, $-Si(R^{114})_3$, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{112}R^{113}$.

Embodiment 903. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, C_{6-10}aryl optionally substituted by 1-3 R^{119}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{119}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{119}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{119}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{119}, halogen, –CN, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-NO_2$, $-NR^{112}R^{113}$, $-NR^{114}C(=O)R^{110}$, $-NR^{114}C(=O)OR^{111}$, $-NR^{114}C(=O)NR^{112}R^{113}$, $-NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $-NR^{114}S(=O)_2R^{111}$, $-NR^{114}S(=O)_2NR^{112}R^{113}$, $-OR^{110}$, =O, $-OC(=O)R^{110}$, $-OC(=O)NR^{112}R^{113}$, $-OC(=O)OR^{110}$, $-Si(R^{114})_3$, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{112}R^{113}$.

Embodiment 904. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, phenyl optionally substituted by 1-3 R^{119}, benzyl optionally substituted by 1-3 R^{119}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{119}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{119}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{119}, halogen, –CN, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-NO_2$, $-NR^{112}R^{113}$, $-NR^{114}C(=O)R^{110}$, $-NR^{114}C(=O)OR^{111}$, $-NR^{114}C(=O)NR^{112}R^{113}$, $-NR^{114}C(=O)NR^{114}C(=O)R^{110}$, $-NR^{114}S(=O)_2R^{111}$, $-NR^{114}S(=O)_2NR^{112}R^{113}$, $-OR^{110}$, =O, $-OC(=O)R^{110}$, $-OC(=O)NR^{112}R^{113}$, $-OC(=O)OR^{110}$, $-Si(R^{114})_3$, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{112}R^{113}$.

Embodiment 905. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89},

R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, phenyl optionally substituted by 1-3 R^{119}, benzyl optionally substituted by 1-3 R^{119}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{119}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{119}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{119}, halogen, –CN, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-NO_2$, $-NR^{112}R^{113}$, $-NR^{114}C(=O)R^{110}$, $-NR^{114}S(=O)_2R^{111}$, $-OR^{110}$, $-OC(=O)R^{110}$, $-OC(=O)NR^{112}R^{113}$, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{112}R^{113}$.

Embodiment 906. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-NO_2$, $-NR^{112}R^{113}$, $-NR^{114}C(=O)R^{110}$, $-NR^{114}S(=O)_2R^{111}$, $-OR^{110}$, $-OC(=O)R^{110}$, $-OC(=O)NR^{112}R^{113}$, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{112}R^{113}$.

Embodiment 907. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, –CN, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-NO_2$, $-NR^{112}R^{113}$, $-OR^{110}$, and $-S(=O)_nR^{110}$.

Embodiment 908. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}, phenyl optionally substituted by 1-3 R^{119}, benzyl optionally substituted by 1-3 R^{119}, halogen, –CN, $-C(=O)OR^{110}$, $-C(=O)NR^{112}R^{113}$, $-NO_2$, $-NR^{112}R^{113}$, $-OR^{110}$, and $-S(=O)_nR^{110}$.

Embodiment 909. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-NR^{112}R^{113}$, and $-OR^{110}$.

Embodiment 910. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89},

R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, $-NR^{112}R^{113}$, and $-OR^{110}$.

Embodiment 911. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119} and halogen.

Embodiment 912. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{119}.

Embodiment 913. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, or 850-886, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently C_{1-6}alkyl.

Embodiment 914. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129}.

Embodiment 915. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{129}, C_{2-6}alkenyl optionally substituted by 1-6 R^{129}, C_{2-6}alkynyl optionally substituted by 1-6 R^{129}, C_{6-10}aryl optionally substituted by 1-6 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{129}.

Embodiment 916. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{129}, C_{2-6}alkenyl optionally substituted by 1-3 R^{129}, C_{2-6}alkynyl optionally substituted by 1-3 R^{129}, C_{6-10}aryl optionally substituted by 1-3 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 917. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, benzyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 918. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 919. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, benzyl optionally substituted by 1-3 R^{129}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{129}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 920. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 921. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 922. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{129}, and 5-6 membered heteroaryl.

Embodiment 923. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{129}.

Embodiment 924. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 925. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-913, wherein R^{110}, R^{111}, R^{114}, R^{115}, R^{116} and R^{117} at each occurrence is H.

Embodiment 926. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{139}, C_{2-6}alkenyl optionally substituted by 1-11 R^{139}, C_{2-6}alkynyl optionally substituted by 1-9 R^{139}, C_{6-11}aryl optionally substituted by 1-11 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered

heterocycloalkyl optionally substituted by 1-28 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{149}.

Embodiment 927. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{139}, C_{2-6}alkenyl optionally substituted by 1-6 R^{139}, C_{2-6}alkynyl optionally substituted by 1-6 R^{139}, C_{6-11}aryl optionally substituted by 1-6 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{139}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{149}.

Embodiment 928. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{139}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{149}.

Embodiment 929. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{139}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{139}.

Embodiment 930. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{139}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{149} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{149}.

Embodiment 931. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{139}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{139}.

Embodiment 932. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, benzyl optionally substituted by 1-3 R^{139}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{139}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{139}.

Embodiment 933. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 934. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 935. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{139}, phenyl optionally substituted by 1-3 R^{139}, and benzyl optionally substituted by 1-3 R^{139}.

Embodiment 936. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{139}.

Embodiment 937. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 938. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 939. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-925, wherein R^{112} and R^{113} at each occurrence is H.

Embodiment 940. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129}.

Embodiment 941. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3

R^{129}, C_{2-6}alkenyl optionally substituted by 1-3 R^{129}, C_{2-6}alkynyl optionally substituted by 1-3 R^{129}, C_{6-11}aryl optionally substituted by 1-3 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{129}.

Embodiment 942. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, C_{2-6}alkenyl optionally substituted by 1-3 R^{129}, C_{2-6}alkynyl optionally substituted by 1-3 R^{129}, C_{6-10}aryl optionally substituted by 1-3 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 943. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, C_{6-10}aryl optionally substituted by 1-3 R^{129}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{129}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{129}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 944. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, benzyl optionally substituted by 1-3 R^{129}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{129}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{129}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{129}.

Embodiment 945. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 946. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl, and benzyl.

Embodiment 947. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{129}, phenyl optionally substituted by 1-3 R^{129}, and benzyl optionally substituted by 1-3 R^{129}.

Embodiment 948. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 949. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{129}.

Embodiment 950. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-939, wherein R^{118} at each occurrence is C_{1-6}alkyl.

Embodiment 951. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{159}, C_{2-6}alkenyl optionally substituted by 1-6 R^{159}, C_{2-6}alkynyl optionally substituted by 1-6 R^{159}, C_{6-11}aryl optionally substituted by 1-6 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{159}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{159}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{159}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{159}, halogen, –CN, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-C(=O)C(=O)R^{150}$, $-C(=NR^{155})R^{150}$, $-C(=NR^{155})NR^{152}R^{153}$, $-C(=NOH)NR^{152}R^{153}$, $-C(=NOR^{156})R^{150}$, $-C(=NNR^{152}R^{153})R^{150}$, $-C(=NNR^{154}C(=O)R^{151})R^{150}$, $-C(=NNR^{154}C(=O)OR^{151})R^{150}$, $-C(=S)NR^{152}R^{153}$, –NC, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}NR^{152}R^{153}$, $-N=NR^{154}$, $=NR^{150}$, $=NOR^{150}$, $-NR^{154}OR^{156}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)C(=O)OR^{151}$, –

$NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)NR^{154}C(=O)OR^{150}$, $-NR^{154}C(=NR^{155})NR^{152}R^{153}$, $-NR^{154}C(=O)C(=O)NR^{152}R^{153}$, $-NR^{154}C(=S)R^{150}$, $-NR^{154}C(=S)OR^{150}$, $-NR^{154}C(=S)NR^{152}R^{153}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-NR^{154}P(=O)R^{158}R^{158}$, $-NR^{154}P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-NR^{154}P(=O)(OR^{150})(OR^{150})$, $-NR^{154}P(=O)(SR^{150})(SR^{150})$, $-OR^{150}$, =O, $-OCN$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-OC(=NR^{155})NR^{152}R^{153}$, $-OS(=O)R^{150}$, $-OS(=O)_2R^{150}$, $-OS(=O)_2OR^{150}$, $-OS(=O)_2NR^{152}R^{153}$, $-OP(=O)R^{158}R^{158}$, $-OP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-OP(=O)(OR^{150})(OR^{150})$, $-OP(=O)(SR^{150})(SR^{150})$, $-Si(R^{154})_3$, $-SCN$, =S, $-S(=O)_nR^{150}$, $-S(=O)_2OR^{150}$, $-SO_3R^{1515}$, $-S(=O)_2NR^{152}R^{153}$, $-S(=O)NR^{152}R^{153}$, $-SP(=O)R^{158}R^{158}$, $-SP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-SP(=O)(OR^{150})(OR^{150})$, $-SP(=O)(SR^{150})(SR^{150})$, $-P(=O)R^{158}R^{158}$, $-P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-P(=O)(OR^{150})(OR^{150})$, and $-P(=O)(SR^{150})(SR^{150})$.

Embodiment 952. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{159}, C_{6-11}aryl optionally substituted by 1-6 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NC$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}NR^{152}R^{153}$, $-NR^{154}OR^{156}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, =O, $-OCN$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, $-SCN$, =S, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 953. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{159}, C_{6-10}aryl optionally substituted by 1-6 R^{159}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{159}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{159}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{159}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, =O, $-$

$OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 954. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, C_{6-10}aryl optionally substituted by 1-3 R^{159}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{159}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{159}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{159}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, $=O$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 955. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, phenyl optionally substituted by 1-3 R^{159}, benzyl optionally substituted by 1-3 R^{159}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{159}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{159}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}C(=O)OR^{151}$, $-NR^{154}C(=O)NR^{152}R^{153}$, $-NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-OR^{150}$, $=O$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-Si(R^{154})_3$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 956. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, phenyl optionally substituted by 1-3 R^{159}, benzyl optionally substituted by 1-3 R^{159}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{159}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{159}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$,

$-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-OR^{150}$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 957. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, $-CN$, $-C(=O)R^{150}$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-NR^{154}C(=O)R^{150}$, $-NR^{154}S(=O)_2R^{151}$, $-OR^{150}$, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-S(=O)_nR^{150}$, and $-S(=O)_2NR^{152}R^{153}$.

Embodiment 958. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-CN$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-OR^{150}$, and $-S(=O)_nR^{150}$.

Embodiment 959. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}, phenyl optionally substituted by 1-3 R^{159}, benzyl optionally substituted by 1-3 R^{159}, halogen, $-CN$, $-C(=O)OR^{150}$, $-C(=O)NR^{152}R^{153}$, $-NO_2$, $-NR^{152}R^{153}$, $-OR^{150}$, and $-S(=O)_nR^{150}$.

Embodiment 960. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-NR^{152}R^{153}$, and $-OR^{150}$.

Embodiment 961. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, $-NR^{152}R^{153}$, and $-OR^{150}$.

Embodiment 962. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159} and halogen.

Embodiment 963. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{159}.

Embodiment 964. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-950, wherein R^{119}, R^{129}, R^{139} and R^{149} at each occurrence is independently C_{1-6}alkyl.

Embodiment 965. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169}.

Embodiment 966. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{169}, C_{2-6}alkenyl optionally substituted by 1-6 R^{169}, C_{2-6}alkynyl optionally substituted by 1-6 R^{169}, C_{6-10}aryl optionally substituted by 1-6 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{169}.

Embodiment 967. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{2-6}alkenyl optionally substituted by 1-3 R^{169}, C_{2-6}alkynyl optionally substituted by 1-3 R^{169}, C_{6-10}aryl optionally substituted by 1-3 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3

R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 968. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, benzyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 969. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 970. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, benzyl optionally substituted by 1-3 R^{169}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{169}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 971. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 972. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 973. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein

R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{169}, and 5-6 membered heteroaryl.

Embodiment 974. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{169}.

Embodiment 975. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 976. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-964, wherein R^{150}, R^{151}, R^{154}, R^{155}, R^{156} and R^{157} at each occurrence is H.

Embodiment 977. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{179}, C_{2-6}alkenyl optionally substituted by 1-11 R^{179}, C_{2-6}alkynyl optionally substituted by 1-9 R^{179}, C_{6-11}aryl optionally substituted by 1-11 R^{179}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{179}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{189}.

Embodiment 978. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{179}, C_{2-6}alkenyl optionally substituted by 1-6 R^{179}, C_{2-6}alkynyl optionally substituted by 1-6 R^{179}, C_{6-11}aryl optionally substituted by 1-6 R^{179}, C_{7-16}arylalkyl optionally

substituted by 1-6 R^{179}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{189}.

Embodiment 979. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{179}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{189}.

Embodiment 980. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{179}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{179}.

Embodiment 981. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{179}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{179}; or any R^{152} and R^{153} may form, together with the nitrogen atom to

which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{189} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{189}.

Embodiment 982. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{179}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{179}.

Embodiment 983. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, benzyl optionally substituted by 1-3 R^{179}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{179}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{179}.

Embodiment 984. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 985. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 986. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{179}, phenyl optionally substituted by 1-3 R^{179}, and benzyl optionally substituted by 1-3 R^{179}.

Embodiment 987. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein

R^{152} and R^{153} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{179}.

Embodiment 988. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 989. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 990. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-976, wherein R^{152} and R^{153} at each occurrence is H.

Embodiment 991. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169}.

Embodiment 992. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{2-6}alkenyl optionally substituted by 1-3 R^{169}, C_{2-6}alkynyl optionally substituted by 1-3 R^{169}, C_{6-11}aryl optionally substituted by 1-3 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{169}.

Embodiment 993. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{2-6}alkenyl optionally substituted by 1-3 R^{169}, C_{2-6}alkynyl optionally substituted by 1-3 R^{169}, C_{6-10}aryl optionally substituted by 1-3 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 994. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, C_{6-10}aryl optionally substituted by 1-3 R^{169}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{169}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{169}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 995. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, benzyl optionally substituted by 1-3 R^{169}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{169}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{169}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{169}.

Embodiment 996. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 997. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl, and benzyl.

Embodiment 998. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein

R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{169}, phenyl optionally substituted by 1-3 R^{169}, and benzyl optionally substituted by 1-3 R^{169}.

Embodiment 999. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 1000. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{169}.

Embodiment 1001. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-990, wherein R^{158} at each occurrence is C_{1-6}alkyl.

Embodiment 1002. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{199}, C_{2-6}alkenyl optionally substituted by 1-6 R^{199}, C_{2-6}alkynyl optionally substituted by 1-6 R^{199}, C_{6-11}aryl optionally substituted by 1-6 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{199}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{199}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{199}, 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{199}, halogen, –CN, $–C(=O)R^{190}$, $–C(=O)OR^{190}$, $–C(=O)NR^{192}R^{193}$, $–C(=O)C(=O)R^{190}$, $–C(=NR^{195})R^{190}$, $–C(=NR^{195})NR^{192}R^{193}$, $–C(=NOH)NR^{192}R^{193}$, $–C(=NOR^{196})R^{190}$, $–C(=NNR^{192}R^{193})R^{190}$, $–C(=NNR^{194}C(=O)R^{191})R^{190}$, $–C(=NNR^{194}C(=O)OR^{191})R^{190}$, $–C(=S)NR^{192}R^{193}$, –NC, $–NO_2$, $–NR^{192}R^{193}$, $–NR^{194}NR^{192}R^{193}$, $–N=NR^{194}$, $=NR^{190}$, $=NOR^{190}$, $–NR^{194}OR^{196}$, $–NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)C(=O)R^{190}$, $–NR^{194}C(=O)OR^{191}$, $–NR^{194}C(=O)C(=O)OR^{191}$, $–NR^{194}C(=O)NR^{192}R^{193}$, $–NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)NR^{194}C(=O)OR^{190}$, $–NR^{194}C(=NR^{195})NR^{192}R^{193}$, $–NR^{194}C(=O)C(=O)NR^{192}R^{193}$, $–NR^{194}C(=S)R^{190}$, $–NR^{194}C(=S)OR^{190}$, $–NR^{194}C(=S)NR^{192}R^{193}$, $–NR^{194}S(=O)_2R^{191}$, $–NR^{194}S(=O)_2NR^{192}R^{193}$, $–NR^{194}P(=O)R^{198}R^{198}$, $–NR^{194}P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $–NR^{194}P(=O)(OR^{190})(OR^{190})$, $–NR^{194}P(=O)(SR^{190})(SR^{190})$, $–OR^{190}$, =O, –OCN, $–OC(=O)R^{190}$, $–OC(=O)NR^{192}R^{193}$, $–OC(=O)OR^{190}$, $–OC(=NR^{195})NR^{192}R^{193}$, $–OS(=O)R^{190}$, $–OS(=O)_2R^{190}$, $–OS(=O)_2OR^{190}$, –

$OS(=O)_2NR^{192}R^{193}$, $-OP(=O)R^{198}R^{198}$, $-OP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-OP(=O)(OR^{190})(OR^{190})$, $-OP(=O)(SR^{190})(SR^{190})$, $-Si(R^{194})_3$, $-SCN$, $=S$, $-S(=O)_nR^{190}$, $-S(=O)_2OR^{190}$, $-SO_3R^{1919}$, $-S(=O)_2NR^{192}R^{193}$, $-S(=O)NR^{192}R^{193}$, $-SP(=O)R^{198}R^{198}$, $-SP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-SP(=O)(OR^{190})(OR^{190})$, $-SP(=O)(SR^{190})(SR^{190})$, $-P(=O)R^{198}R^{198}$, $-P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-P(=O)(OR^{190})(OR^{190})$, and $-P(=O)(SR^{190})(SR^{190})$.

Embodiment 1003. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{199}, C_{6-11}aryl optionally substituted by 1-6 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{199}, halogen, $-CN$, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NC$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}NR^{192}R^{193}$, $-NR^{194}OR^{196}$, $-NR^{194}C(=O)R^{190}$, $-NR^{194}C(=O)OR^{191}$, $-NR^{194}C(=O)NR^{192}R^{193}$, $-NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $-NR^{194}S(=O)_2R^{191}$, $-NR^{194}S(=O)_2NR^{192}R^{193}$, $-OR^{190}$, $=O$, $-OCN$, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-OC(=O)OR^{190}$, $-Si(R^{194})_3$, $-SCN$, $=S$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1004. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-6 R^{199}, C_{6-10}aryl optionally substituted by 1-6 R^{199}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{199}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{199}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{199}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{199}, halogen, $-CN$, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}C(=O)R^{190}$, $-NR^{194}C(=O)OR^{191}$, $-NR^{194}C(=O)NR^{192}R^{193}$, $-NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $-NR^{194}S(=O)_2R^{191}$, $-NR^{194}S(=O)_2NR^{192}R^{193}$, $-OR^{190}$, $=O$, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-OC(=O)OR^{190}$, $-Si(R^{194})_3$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1005. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, C_{6-10}aryl optionally substituted by 1-3 R^{199}, C_{7-11}arylalkyl optionally

substituted by 1-3 R^{199}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{199}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{199}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{199}, halogen, –CN, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}C(=O)R^{190}$, $-NR^{194}C(=O)OR^{191}$, $-NR^{194}C(=O)NR^{192}R^{193}$, $-NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $-NR^{194}S(=O)_2R^{191}$, $-NR^{194}S(=O)_2NR^{192}R^{193}$, $-OR^{190}$, =O, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-OC(=O)OR^{190}$, $-Si(R^{194})_3$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1006. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, phenyl optionally substituted by 1-3 R^{199}, benzyl optionally substituted by 1-3 R^{199}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{199}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{199}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{199}, halogen, –CN, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}C(=O)R^{190}$, $-NR^{194}C(=O)OR^{191}$, $-NR^{194}C(=O)NR^{192}R^{193}$, $-NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $-NR^{194}S(=O)_2R^{191}$, $-NR^{194}S(=O)_2NR^{192}R^{193}$, $-OR^{190}$, =O, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-OC(=O)OR^{190}$, $-Si(R^{194})_3$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1007. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, phenyl optionally substituted by 1-3 R^{199}, benzyl optionally substituted by 1-3 R^{199}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{199}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{199}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{199}, halogen, –CN, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}C(=O)R^{190}$, $-NR^{194}S(=O)_2R^{191}$, $-OR^{190}$, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1008. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{190}$, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-NR^{194}C(=O)R^{190}$, –

$NR^{194}S(=O)_2R^{191}$, $-OR^{190}$, $-OC(=O)R^{190}$, $-OC(=O)NR^{192}R^{193}$, $-S(=O)_nR^{190}$, and $-S(=O)_2NR^{192}R^{193}$.

Embodiment 1009. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, –CN, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-OR^{190}$, and $-S(=O)_nR^{190}$.

Embodiment 1010. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}, phenyl optionally substituted by 1-3 R^{199}, benzyl optionally substituted by 1-3 R^{199}, halogen, –CN, $-C(=O)OR^{190}$, $-C(=O)NR^{192}R^{193}$, $-NO_2$, $-NR^{192}R^{193}$, $-OR^{190}$, and $-S(=O)_nR^{190}$.

Embodiment 1011. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, halogen, $-NR^{192}R^{193}$, and $-OR^{190}$.

Embodiment 1012. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, $-NR^{192}R^{193}$, and $-OR^{190}$.

Embodiment 1013. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199} and halogen.

Embodiment 1014. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{199}.

Embodiment 1015. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1001, wherein R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently C_{1-6}alkyl.

Embodiment 1016. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209}.

Embodiment 1017. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{209}, C_{2-6}alkenyl optionally substituted by 1-6 R^{209}, C_{2-6}alkynyl optionally substituted by 1-6 R^{209}, C_{6-10}aryl optionally substituted by 1-6 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{209}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-6 R^{209}.

Embodiment 1018. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{2-6}alkenyl optionally substituted by 1-3 R^{209}, C_{2-6}alkynyl optionally substituted by 1-3 R^{209}, C_{6-10}aryl optionally substituted by 1-3 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1019. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, benzyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10

membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1020. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 1021. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, benzyl optionally substituted by 1-3 R^{209}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{209}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1022. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1023. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1024. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl optionally substituted by 1 R^{209}, and 5-6 membered heteroaryl.

Embodiment 1025. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{209}.

Embodiment 1026. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 1027. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1015, wherein R^{190}, R^{191}, R^{194}, R^{195}, R^{196} and R^{197} at each occurrence is H.

Embodiment 1028. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{219}, C_{2-6}alkenyl optionally substituted by 1-11 R^{219}, C_{2-6}alkynyl optionally substituted by 1-9 R^{219}, C_{6-11}aryl optionally substituted by 1-11 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{229}.

Embodiment 1029. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{219}, C_{2-6}alkenyl optionally substituted by 1-6 R^{219}, C_{2-6}alkynyl optionally substituted by 1-6 R^{219}, C_{6-11}aryl optionally substituted by 1-6 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-6 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-6 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-6 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered

heterocycloalkyl optionally substituted by 1-6 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{229}.

Embodiment 1030. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{219}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{229}.

Embodiment 1031. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{219}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{219}.

Embodiment 1032. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{219}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{219}; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{229} or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{229}.

Embodiment 1033. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, C_{5-6}cycloalkyl optionally substituted by 1-3 R^{219}, 5-6 membered

heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{219}.

Embodiment 1034. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, benzyl optionally substituted by 1-3 R^{219}, 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{219}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{219}.

Embodiment 1035. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 1036. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, benzyl, C_{5-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1037. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{219}, phenyl optionally substituted by 1-3 R^{219}, and benzyl optionally substituted by 1-3 R^{219}.

Embodiment 1038. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{219}.

Embodiment 1039. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 1040. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 1041. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1027, wherein R^{192} and R^{193} at each occurrence is H.

Embodiment 1042. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209}.

Embodiment 1043. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{2-6}alkenyl optionally substituted by 1-3 R^{209}, C_{2-6}alkynyl optionally substituted by 1-3 R^{209}, C_{6-11}aryl optionally substituted by 1-3 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{209}.

Embodiment 1044. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{2-6}alkenyl optionally substituted by 1-3 R^{209}, C_{2-6}alkynyl optionally substituted by 1-3 R^{209}, C_{6-10}aryl optionally substituted by 1-3 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10 membered heterocycloalkyl

optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1045. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, C_{6-10}aryl optionally substituted by 1-3 R^{209}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{209}, C_{3-10}cycloalkyl optionally substituted by 1-3 R^{209}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1046. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, benzyl optionally substituted by 1-3 R^{209}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{209}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{209}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{209}.

Embodiment 1047. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 1048. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl, and benzyl.

Embodiment 1049. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{209}, phenyl optionally substituted by 1-3 R^{209}, and benzyl optionally substituted by 1-3 R^{209}.

Embodiment 1050. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 1051. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{209}.

Embodiment 1052. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1041, wherein R^{198} at each occurrence is C_{1-6}alkyl.

Embodiment 1053. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-21 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(=O)C(=O)R^{230}$, $–C(=NR^{230})R^{230}$, $–C(=NR^{230})NR^{230}R^{230}$, $–C(=NOH)NR^{230}R^{230}$, $–C(=NOR^{230})R^{230}$, $–C(=NNR^{230}R^{230})R^{230}$, $–C(=NNR^{230}C(=O)R^{230})R^{230}$, $–C(=NNR^{230}C(=O)OR^{230})R^{230}$, $–C(=S)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–N=NR^{230}$, $=NR^{230}$, $=NOR^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=NR^{230})NR^{230}R^{230}$, $–NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $–NR^{230}C(=S)R^{230}$, $–NR^{230}C(=S)OR^{230}$, $–NR^{230}C(=S)NR^{230}R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–NR^{230}P(=O)(SR^{230})(SR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OC(=O)OR^{230}$, $–OC(=NR^{230})NR^{230}R^{230}$, $–OS(=O)R^{230}$, $–OS(=O)_2R^{230}$, $–OS(=O)_2OR^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–OP(=O)(OR^{230})(OR^{230})$, $–OP(=O)(SR^{230})(SR^{230})$, $–Si(R^{230})_3$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2OR^{230}$, $–SO_3R^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–SP(=O)R^{231}R^{231}$, $–SP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–SP(=O)(OR^{230})(OR^{230})$, $–SP(=O)(SR^{230})(SR^{230})$, $–P(=O)R^{231}R^{231}$, $–P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–P(=O)(OR^{230})(OR^{230})$, and $–P(=O)(SR^{230})(SR^{230})$.

Embodiment 1054. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally

substituted by 1-6 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-15 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-15 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(=O)C(=O)R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OC(=O)OR^{230}$, $–OS(=O)R^{230}$, $–OS(=O)_2R^{230}$, $–OS(=O)_2OR^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–OP(=O)(OR^{230})(OR^{230})$, $–Si(R^{230})_3$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2OR^{230}$, $–SO_3R^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–P(=O)R^{231}R^{231}$, $–P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, and $–P(=O)(OR^{230})(OR^{230})$.

Embodiment 1055. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-10 membered heterocycloalkyl, 4-10 membered heterocycloalkylalkyl, 5-10 membered heteroaryl, 6-10 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–P(=O)R^{231}R^{231}$, and $–P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$.

Embodiment 1056. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, halogen, –CN, $–C(=O)R^{230}$, –

$C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NO_2$, $-NR^{230}R^{230}$, $-NR^{230}OR^{230}$, $-NR^{230}C(=O)R^{230}$, $-NR^{230}C(=O)NR^{230}R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-NR^{230}S(=O)_2NR^{230}R^{230}$, $-OR^{230}$, =O, –OCN, $-OC(=O)R^{230}$, $-S(=O)_nR^{230}$, $-S(=O)_2NR^{230}R^{230}$, and $-S(=O)NR^{230}R^{230}$.

Embodiment 1057. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{230}$, $-C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NO_2$, $-NR^{230}R^{230}$, $-NR^{230}C(=O)R^{230}$, $-NR^{230}C(=O)NR^{230}R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-NR^{230}S(=O)_2NR^{230}R^{230}$, $-OR^{230}$, =O, $-S(=O)_nR^{230}$, and $-S(=O)_2NR^{230}R^{230}$.

Embodiment 1058. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{230}$, $-C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NR^{230}R^{230}$, $-NR^{230}C(=O)R^{230}$, $-NR^{230}S(=O)_2R^{230}$, $-OR^{230}$, =O, $-S(=O)_nR^{230}$, and $-S(=O)_2NR^{230}R^{230}$.

Embodiment 1059. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{230}$, $-C(=O)OR^{230}$, $-C(=O)NR^{230}R^{230}$, $-NR^{230}R^{230}$, $-OR^{230}$, =O, $-S(=O)_nR^{230}$, and $-S(=O)_2NR^{230}R^{230}$.

Embodiment 1060. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 halogen, halogen, and $-NR^{230}R^{230}$.

Embodiment 1061. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, and $-NR^{230}R^{230}$.

Embodiment 1062. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{230}R^{230}$.

Embodiment 1063. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is $-NR^{230}R^{230}$.

Embodiment 1064. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is C_{1-6}alkyl.

Embodiment 1065. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{230}R^{230}$; R^{209}, R^{219} and R^{229} at each occurrence is C_{1-6}alkyl.

Embodiment 1066. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{230}R^{230}$; R^{209}, R^{219} and R^{229} at each occurrence is $-NR^{230}R^{230}$.

Embodiment 1067. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1052, wherein R^{199} at each occurrence is $-NR^{230}R^{230}$; R^{209}, R^{219} and R^{229} at each occurrence is C_{1-6}alkyl.

Embodiment 1068. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl.

Embodiment 1069. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 1070. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is C_{1-6}alkyl.

Embodiment 1071. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1067, wherein R^{230} at each occurrence is H.

Embodiment 1072. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1071, wherein R^{231} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl.

Embodiment 1073. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1071, wherein R^{231} at each occurrence is C_{1-6}alkyl.

Embodiment 1074. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1071, wherein R^{231} at each occurrence is C_{1-6}-haloalkyl.

Embodiment 1075. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 0, 1, and 2.

Embodiment 1076. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 0 and 2.

Embodiment 1077. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 1 and 2.

Embodiment 1078. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is independently chosen from 0 and 1.

Embodiment 1079. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is 0.

Embodiment 1080. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is 1.

Embodiment 1081. The compound of any of Embodiments 1-156, 200-250, 300-371, 400-440, 500-533, 600-668, 700-714, 750-795, 800-817, 850-886, or 900-1074, wherein n at each occurrence is 2.

The above Embodiments include salts of acidic and basic compounds of formula (I). Preferably, the salts are pharmaceutically acceptable. Pharmaceutically acceptable acid addition salts of basic compounds of formula (I) include, but are not limited to, salts derived from inorganic acids such as hydrochloric, nitric, phosphoric, sulfuric, hydrobromic, hydriodic, and phosphorus, as well as the salts derived from organic acids, such as aliphatic mono- and dicarboxylic acids, phenyl-substituted alkanoic acids, hydroxy alkanoic acids, alkanedioic acids, aromatic acids, and aliphatic and aromatic sulfonic acids. Such salts thus include, but are not limited to, sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, nitrate, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, chloride, bromide, iodide, acetate, propionate, caprylate, isobutyrate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, mandelate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, phthalate, benzenesulfonate, toluenesulfonate, phenylacetate, citrate, lactate, maleate, tartrate, and methanesulfonate. See, for example, Berge et al., "Pharmaceutical Salts," J. of Pharmaceutical Science, 1977; 66:1-19.

Acid addition salts may be prepared by contacting a compound of formula (I) with a sufficient amount of the desired acid to produce the salt in the conventional manner. The free base form of the compound of formula (I) may be regenerated by contacting the salt form with a base and isolating the free base in the conventional manner.

Pharmaceutically acceptable base salts of acidic compounds of formula (I) are formed with metals or amines, such as alkali and alkaline earth metal hydroxides, or of organic amines. Examples of metals used as cations include, but are not limited to, sodium, potassium, magnesium, and calcium. Examples of suitable amines include, but are not limited to, N,N'- dibenzylethylenediamine, chloroprocaine, choline, diethanolamine, ethylenediamine (ethane-1,2-diamine), N-methylglucamine, and procaine. See, for example, Berge et al., "Pharmaceutical Salts," J. of Pharmaceutical Science, 1977; 66:1-19.

Base salts may be prepared by contacting a compound of formula (I) with a sufficient amount of the desired base to produce the salt in the conventional manner. The acid form of the compound of formula (I) may be regenerated by contacting the salt form with an acid and isolating the acid in a conventional manner.

Some compounds of the present invention may exist as stereoisomers, including enantiomers, diastereomers, and geometric isomers. Geometric isomers include compounds of the present invention that have alkenyl groups, which may exist as entgegen or zusammen conformations, in which case all geometric forms thereof, both entgegen and zusammen, cis and trans, and mixtures thereof, are within the scope of the present invention. Some compounds of the present invention have cycloalkyl groups, which may be substituted at more than one carbon atom, in which case all geometric forms thereof, both cis and trans, and mixtures thereof, are within the scope of the present invention. All of these forms, including (R), (S), epimers, diastereomers, cis, trans, syn, anti, (E), (Z), tautomers, and mixtures thereof, are included in the compounds of the present invention.

The compounds of the present invention may be in any physical form, including amorphous or crystalline solids in any polymorphic form, in any state of purity. Crystalline polymorphic forms include unsolvated forms as well as solvated forms, such as hydrated forms.

III. Pharmaceutical Compositions

The present invention further provides pharmaceutical compositions comprising a compound of any of the above Embodiments (e.g., a compound of formula (I) or a pharmaceutically acceptable salt thereof), together with a pharmaceutically acceptable excipient. For preparing a pharmaceutical composition from a compound of the present invention, pharmaceutically acceptable excipients can be either solid or liquid. An excipient can be one or more substances which may act as, e.g., a carrier, diluent, flavoring agent, binder, preservative, tablet disintegrating agent, or an encapsulating material. The pharmaceutical composition may contain two or more compounds of the present invention (e.g., two different salt forms of a compound of formula (I), may be used together in the same pharmaceutical composition). Preferably, the pharmaceutical composition contains a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt form thereof. In one embodiment, the composition contains an amount of a compound of formula (I) or a pharmaceutically acceptable salt form thereof effective to treat an atypical protein kinase C (aPKC)-dependent disorder or condition. Preferably, a compound of the present invention will cause a decrease in symptoms or disease indicia associated with an aPKC-dependent disorder as measured quantitatively or qualitatively. The

composition may also contain, in addition to a compound of formula (I) or a pharmaceutically acceptable salt form thereof and a pharmaceutically acceptable excipient, another therapeutic compound, such as a compound useful in the treatment of cancer.

A compound of the present invention can be formulated as a pharmaceutical composition in any delivery form, such as a syrup, an elixir, a suspension, a powder, a granule, a tablet, a capsule, a lozenge, a troche, an aqueous solution, a cream, an ointment, a lotion, a gel, an emulsion, etc. Solid form preparations include powders, tablets, pills, capsules, cachets, suppositories, and dispersible granules. Preferably, the pharmaceutical composition is a tablet or capsule. In one embodiment, the pharmaceutical composition is a tablet. In another embodiment, the pharmaceutical composition is a capsule.

In powders, the excipient may be a finely divided solid in a mixture with a finely divided active component (i.e., compound of the present invention). In tablets, the active component may be mixed with an excipient having the necessary binding properties in suitable proportions and compacted in the shape and size desired. Suitable excipients include magnesium carbonate, magnesium stearate, talc, sugar, lactose, pectin, dextrin, starch, gelatin, tragacanth, methylcellulose, sodium carboxymethylcellulose, low melting wax, cocoa butter, and the like.

The pharmaceutical composition preferably contains from 1% to 95% (w/w) of the active compound (i.e., compound of the present invention). More preferably, the pharmaceutical composition contains from 5% to 70% (w/w) of the active compound.

For preparing suppositories, a low melting wax, such as a mixture of fatty acid glycerides or cocoa butter, may be melted and the active component dispersed homogeneously therein, as by stirring. The molten homogeneous mixture may then be poured into convenient sized molds, allowed to cool, and thereby to solidify.

Liquid form preparations include solutions, suspensions, and emulsions. Formulations suitable for parenteral administration, such as, for example, by intravenous, intramuscular, intradermal, and subcutaneous routes, include aqueous and non-aqueous, isotonic sterile injection solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, and aqueous and nonaqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. In the practice of this invention, compositions can be administered, for example, by intravenous infusion, orally, topically,

intraperitoneally, intravesically or intrathecally. The formulations of compounds can be presented in unit-dose or multi-dose sealed containers, such as ampoules and vials. Injection solutions and suspensions can be prepared from sterile powders, granules, and tablets of the kind previously described.

A compound of the present invention, alone or in combination with other suitable components, can be made into aerosol formulations (e.g., they can be "nebulized") to be administered via inhalation. Aerosol formulations can be placed into pressurized acceptable propellants, such as dichlorodifluoromethane, propane, nitrogen, and the like.

Pharmaceutically acceptable excipients are determined in part by the particular composition being administered, as well as by the particular method used to administer the composition. Accordingly, there is a wide variety of suitable formulations of pharmaceutical compositions of the present invention (see, e.g., *Remington: The Science and Practice of Pharmacy*, 20th ed., Gennaro et al. Eds., Lippincott Williams and Wilkins, **2000**).

The quantity of active component in a pharmaceutical composition may be varied or adjusted from, e.g., 1 mg to 1,000 mg, 5 mg to 500 mg, 10 mg to 300 mg, or 25 mg to 250 mg, according to the particular application and the desired size of the dosage form.

The dose administered to a subject is preferably sufficient to induce a beneficial therapeutic response in the subject over time. The beneficial dose can vary from subject to subject depending upon, e.g., the subject's condition, body weight, surface area, and side effect susceptibility. Administration can be accomplished via single or divided doses.

IV. Method of Treatment

In another aspect, the present invention provides a method of treating an aPKC-dependent disorder or condition in a subject comprising: administering to the subject a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in treating an aPKC-dependent disorder or condition in a subject. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in the preparation of a medicament for treating an aPKC-dependent disorder or condition in a subject. Preferably, the compound is administered to the subject as a pharmaceutical

composition comprising a pharmaceutically acceptable excipient. Preferably, the compound is administered to the subject in a pharmaceutically acceptable amount. In one embodiment, the aPKC-dependent condition or disorder is cancer. In another embodiment, the aPKC-dependent condition is selected from non-small cell lung cancer (NSCLC), squamous cell carcinoma (e.g., oesophageal squamous cell carcinoma), leukaemia, prostate cancer, non-Hodgkin's lymphoma (e.g., follicular lymphoma), endometrial cancer, lung cancer and breast cancer.

The aPKC-dependent disorder or condition can be treated prophylactically, acutely, or chronically using compounds of the present invention, depending on the nature of the disorder or condition. Typically, the subject in each of these methods is human, although other mammals can also benefit from the administration of a compound of the present invention.

In another embodiment, the present invention provides a method of treating a proliferative disorder in a subject, comprising administering to the subject a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in treating a proliferative disorder in a subject. In another aspect, the present invention provides a compound of formula (I) as defined in any of the above Embodiments or a pharmaceutically acceptable salt form thereof for use in the preparation of a medicament for treating a proliferative disorder in a subject. Preferably, the compound is administered to the subject in a pharmaceutical composition comprising a pharmaceutically acceptable excipient. Preferably, the compound is administered to the subject in a pharmaceutically acceptable amount. In certain embodiments, the proliferative disorder is aPKC-dependent. In certain embodiments, the proliferative disorder is cancer. In certain embodiments, the proliferative disorder is selected from non-small cell lung cancer (NSCLC), squamous cell carcinoma (e.g., oesophageal squamous cell carcinoma), leukaemia, prostate cancer, non-Hodgkin's lymphoma (e.g., follicular lymphoma), endometrial cancer, lung cancer and breast cancer.

The proliferative disorder can be treated prophylactically, acutely, or chronically using a compound of the present invention, depending on the nature of the disorder or condition. Typically, the subject in each of these methods is human, although other mammals can also benefit from the administration of a compound of the present invention.

In therapeutic applications, the compounds of the present invention can be prepared and administered in a wide variety of oral and parenteral dosage forms. Thus, the compounds of the present invention can be administered by injection, that is, intravenously, intramuscularly, intracutaneously, subcutaneously, intraduodenally, or intraperitoneally. Also, the compounds described herein can be administered by inhalation, for example, intranasally. Additionally, the compounds of the present invention can be administered transdermally. In another embodiment, the compounds of the present invention are delivered orally. The compounds can also be delivered rectally, bucally or by insufflation.

Determination of the proper dosage for a particular situation is within the skill of the practitioner. Generally, treatment is initiated with smaller dosages which are less than the optimum dose of the compound. Thereafter, the dosage is increased by small increments until the optimum effect under the circumstances is reached. For convenience, the total daily dosage may be divided and administered in portions during the day, if desired. A typical dose is about 1 mg to about 1,000 mg per day, such as about 5 mg to about 500 mg per day. In certain embodiments, the dose is about 10 mg to about 300 mg per day, such as about 25 mg to about 250 mg per day.

V. Chemistry

Abbreviations

For convenience, the following common abbreviations are used herein:

LCMS for Liquid Chromatography-Mass Spectrometry.

HPLC for High Pressure Liquid Chromatography.

NMR for Nuclear Magnetic Resonance.

RT for Retention Time.

MI for Molecular Ion

h for hours

min for minutes

$AlCl_3$ for aluminium chloride

BBr_3 for boron tribromide

Boc for *tert*-butoxycarbonyl

cataCXium C for trans-Bis(acetato)bis[o-(di-o-tolylphosphino)benzyl] dipalladium(II).

Cs_2CO_3 for cesium carbonate

CuI for copper(I)iodide

DAST for diethylaminosulfur trifluoride

DBU for 1,8-diazabicyclo(5.4.0)undec-7-ene

DMAP for 4-(dimethylamino) pyridine

DCE for 1,1-dichloroethane or ethylidene chloride

DCM for dichloromethane or methylene chloride

DEA for diethanolamine

DIPEA for *N,N*,-di-isopropyethylamine, Hunig's base

DMA for *N,N*-dimethylacetamide

DMF for *N,N*-dimethylformamide

DMSO for dimethylsulfoxide.

Et_3N for triethylamine

EtOH for ethyl alcohol, ethanol

Ex for example

HCl for hydrochloric acid

H_2SO_4 for sulfuric acid

Int for intermediate

KOH for potassium hydroxide

MW for microwave

mCPBA for meta-Chloroperoxybenzoic acid

MeOH for methyl alcohol, methanol

$Mo(CO)_6$ for Molybdenum hexacarbonyl

MP-BH_4 for macroporous triethylammonium methyl polystyrene borohydride

NaOH for sodium hydroxide

Na_2CO_3 for sodium carbonate

Na_2SO_4 for sodium sulphate

NaOAc for sodium acetate

NaOtBu for sodium t-butoxide

NMP for 1-methyl-2-pyrrolidinone

NMM for N-methylmorpholine

$Pd(dba)_2$ for Bis(dibenzylideneacetone)palladium

$Pd(OAc)_2$ for Palladium diacetate

$Pd(Ph_3)_4$ for tetrakis(triphenylphosphine)palladium

$Pd(PPh_3)_2Cl_2$ for Bis(triphenylphosphine)palladium(II) dichloride

$POCl_3$ for phosphorus oxychloride

PPh_3 for triphenylphosphine

PS-TsCl for polystyrene sulfonyl chloride

PS-PPh_3-Pd for polystyrene triphenylphosphine-Pd(0)

SCX-2 for a silica-based sorbent with a chemically bonded propylsulfonic acid functional group

TBAF for Tetra-n-butylammonium fluoride

TBDMS for tert-butyldimethylsilyl

TCA for trichloroacetic acid

TFA for trifluoroacetic acid

THF for tetrahydrofuran

TMS azide for trimethylsilyl azide

Xantphos for 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene

XPhos for 2-Dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl

LCMS Methods

Samples analysed by High Performance Liquid Chromatography-Mass Spectrometry employed the following conditions. Unless otherwise noted, Method X was utilized.

Method 1

Method 1 employed Gilson 306 pumps, Gilson 811C mixer, Gilson 806 manometric module, and Gilson UV/VIS 152 detector at 254 nm wavelength. The mass spectrometer was a Finnigan AQA and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 4.60 mm. The injection volume was 10 μl. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 1.5 mL/min, using 95% water: 5% acetonitrile, changed linearly to 5% water: 95% acetonitrile over 5.5 minutes and then maintained at this mixture for 2 minutes.

Method 2

Method 2 employed Waters 515 pumps, a Waters 2525 mixer and a Waters 2996 diode array detector. The detection was performed between 210 nm and 650 nm. The mass

spectrometer was a Waters micromass ZQ and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 4.60 mm. The injection volume was 10 μl. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 1.5 mL/min, using 95% water: 5% acetonitrile, changed linearly to 5% water: 95% acetonitrile over 5.5 minutes and then maintained at this mixture for 2 minutes.

Method 3

Method 3 employed Waters 515 pumps, a Waters 2525 mixer and a Waters 2487 UV detector (single wavelength 254 nm). The mass spectrometer was a Waters micromass ZQ and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 4.60 mm. The injection volume was 10 μl. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 1.5 mL/min, using 95% water: 5% acetonitrile, changed linearly to 5% water: 95% acetonitrile over 5.5 minutes and then maintained at this mixture for 2 minutes.

Method 4

Method 4 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2996 diode array detector. The detection was performed between 210 nm and 650 nm. The mass spectrometer used was a Waters 3100 which detected masses between 100 and 700 g/mol. The column used was a XBridge, 5 micron pore size, C18, 50x4.60 mm.The injection volume was 10 μl of a solution (around 1mg/ml). The flow rate was 1.5 mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide) (3 ml/10l) and acetonitrile 0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 95% water: 5% acetonitrile ramping up to 5% water:95% acetonitrile over 5.50 minutes. The eluent level was returned to the starting conditions of 95% water: 5% acetonitrile over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 5

Method 5 employed Waters 515 pumps, a Waters 2525 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254 nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a SunFire, 5 micron pore size, C18 column of dimensions 50x4.60 mm was used. The injection volume was 10μL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water and methanol

contained 0.1% formic acid. The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5 minutes, these conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 6

Method 6 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2996 diode array detector. The detection was done between 210 nm and 650 nm. The mass spectrometer used was a Waters 3100 which detected masses between 100 and 700g/mol. The column used was a XBridge, 5 micron pore size, C18 ,50x4.60 mm. The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide) (3 ml/10l) and methanol0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5 minutes. These conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 7

Method 7 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a SunFire, 5 micron pore size, C18 column of dimensions 50x4.60 mm was used. The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water and methanol contained 0.1% formic acid. The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5minutes., these conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

Method 8

Method 8 employed Waters 515 pumps, a Waters 2525 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a SunFire, 5 micron pore size, C18 column of dimensions 50x4.60 mm was used. The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water and methanol contained 0.1% formic acid. The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 3 minutes., these conditions were held for 2.5 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected.The run lasted 7 minutes in total.

Method 9

Method 9 employed Waters 515 pumps, a Waters 2545 mixer with valves directing to the different columns and a Waters 2487 UV detector. The detection was done between at 254nm. The mass spectrometer used was a Waters micromass ZQ which detected masses between 100 and 700g/mol. The column used was a XBridge, 5 micron pore size, C18 ,50x4.60 mm.The injection volume was 10µL of a solution (around 1mg/mL). The flow rate was 1.5 mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide) (3 ml/10l)and methanol0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 85% water:15% methanol ramping up to 15% water:85% methanol over 4.5 minutes. These conditions were held for 1 minute before the eluent level was returned to the starting conditions of 85% water:15% methanol over 6 seconds. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected.The run lasted 7 minutes in total.

Method 10

LCMS results were obtained on either of two instruments. LCMS analysis was performed on a Waters Aquity Ultra Performance LC with a 2.1 mm x 50 mm Waters Aquity UPLC BEH C18 1.7 µm column. The target column temperature was 45°C, with a run time of two (2) minutes, a flow rate of 0.600 mL/min, and a solvent mixture of 5% (0.1% formic acid/water):95% (acetonitrile/0.1% formic acid). The mass spectrometry data was acquired on a Micromass LC-ZQ 2000 quadrupole mass spectrometer. Alternatively, LCMS analysis was performed on a Bruker Esquire 200 ion trap.

Preparative HPLC Methods

Samples purified by Mass Spectrometry directed High Performance Liquid Chromatography employed the following conditions.

Method A

Method A employed Waters 515 pumps, a Waters 2525 mixer and a Waters 2487 UV detector (single wavelength 254 nm). The mass spectrometer was a Waters micromass ZQ and the column used was a Waters SunFire, 5 μm pore size, C18 of dimensions 50 x 19mm. The injection volume was up to 500 μL of solution at a maximum concentration of 50 mg/mL. The mobile phase consisted of a mixture of water and acetonitrile containing 0.1% formic acid. The eluent flow rate was 25 mL/min using 95% water, 5% acetonitrile, changing linearly over 5.3 minutes to 95% acetonitrile, 5% water, and maintaining for 0.5 minutes.

Method B

Method B employed Waters 515 pumps a Waters 2545 mixer with valves directing to the different columns and a Waters 2996 diode array detector. The detection was performed between 210 nm and 650 nm. The mass spectrometer used was a Waters 3100 which detected masses between 100 and 700 g/mol. The column used was a XBridge, 5 micron pore size, C18, 50x19 mm. The injection volume was chosen by the user and can be up to 500μL of the solution (max 50mg/mL). The flow rate was 25mL/min and the mobile phases of water pH 10 0.03% ammonium hydroxide (3 ml/10l)and acetonitrile 0.03% ammonium hydroxide (3 ml/10l) .The elution was started at 95% water:5% acetonitrile ramping up to 5% water:95% acetonitrile over 5.30 minutes. The eluent level was returned to the starting conditions of 95% water: 5% acetonitrile over 0.6 minutes. These conditions were held for 1.4 minutes to allow equilibration of the column before the next sample was injected. The run lasted 7 minutes in total.

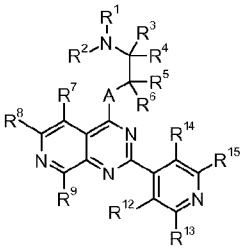
Analytical HPLC Methods

Meihod X

Method X employs gradient elution (0 to 100%) acetonitrile (containing 0.1% trifluoroacetic acid):water (containing 0.1% trifluoroacetic acid) over five minutes on a 4.6 X 75 mm (2.5 micron) Zorbax XDB-C8 column at 2.5 ml/min on an Agilent 1100 series HPLC.

Synthesis

Several methods for the chemical synthesis of 4-substituted-2-(pyridin-4-yl)-azaquinazoline compounds (for convenience, collectively referred to herein as "4PAZ compounds") of the present invention are described herein. These and/or other well known methods may be modified and/or adapted in known ways in order to facilitate the synthesis of additional compounds within the scope of the present invention.



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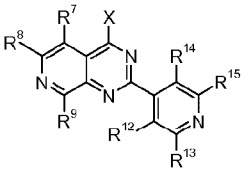
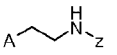


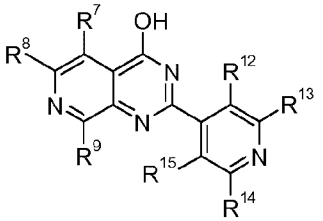
[F-002]



[F-003]

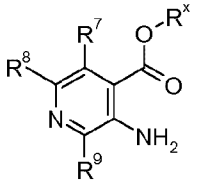
In one approach, 4PAZ compounds of general formula [F-001] (where A = NH or N alkyl) are prepared by reacting a compound of formula [F-002] (where X is a halogen such as chlorine or a sulfonate) with a compound of formula [F-003] (where A is NH or NH2 and Z on the terminal nitrogen is H, alkyl or a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) in a suitable solvent such as DMF in the presence of a suitable base such as triethylamine. The reaction is suitably conducted at an elevated temperature for example 40 °C. Where Z is a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc, compounds of formula [F-001] are prepared by a suitable deprotection reaction. For example: where Z is a Boc protecting group reaction with an acid such as TFA in a suitable solvent such as DCM. The reaction is suitably conducted at ambient temperature. In one approach, compounds of formula [F-001] (where A = O) are prepared by reacting a compound of formula [F-002] (where X is a halogen such as chlorine or sulfonate) with a

compound of formula [F-003] (where A is OH and Z on the terminal nitrogen is H, alkyl or a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) in a suitable solvent such as DMA in the presence of a suitable base such as sodium hydride. The reaction is suitably conducted at ambient temperature. Where Z is a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc, compounds of formula [F-001] are prepared by a suitable deprotection reaction. For example: where Z is a Boc protecting group reaction with an acid such as TFA in a suitable solvent such as DCM. The reaction is suitably conducted at ambient temperature.

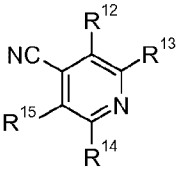


[F-004]

In one approach, compounds of formula [F-002] (where X is a halogen such as chlorine) are prepared by reacting a compound of formula [F-004] with a suitable halogenating agent such as phosphorous oxychloride. The reaction is suitably conducted at elevated temperature such as 125 °C. Compounds of formula [F-002] (where X is a sulfonate) are prepared by reacting a compound of formula [F-004] with a suitably substituted sulfonyl chloride in a suitable solvent such as DMA in the presence of a suitable base such as triethylamine and a catalytic amount of DMAP. The reaction is suitably conducted at ambient temperature.



[F-005]

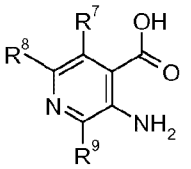


[F-006]

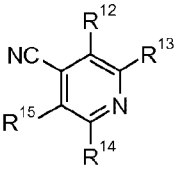
In one approach, compounds of formula [F-004] are prepared by reacting a compound of formula [F-005] (where Rx is an alkyl group such as methyl or ethyl) with a compound of formula [F-006] in a suitable solvent in a dry non-aprotic solvent such as dioxane or THF in

the presence of a hindered alkoxide base such as potassium-tert-pentylate 1.7M in toluene or potassium-tert-butoxide. The reaction is suitably conducted at ambient temperature.

In one approach, compounds of formula [F-004] are prepared by reacting a compound of formula [F-007] with a compound of formula [F-006] in a suitable solvent in a protic solvent such as methanol in the presence of a base such as sodium methoxide. The reaction is suitably conducted first at ambient temperature then at reflux overnight.



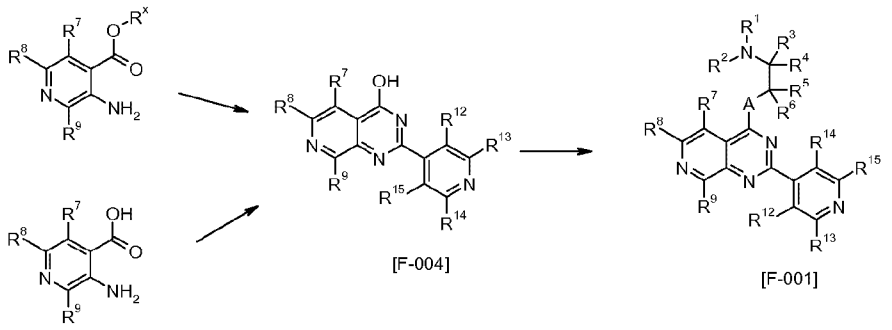
[F-007]



[F-006]

An example of a method as described above is illustrated in the following scheme.

[F-005]



[F-007]

[F-004]

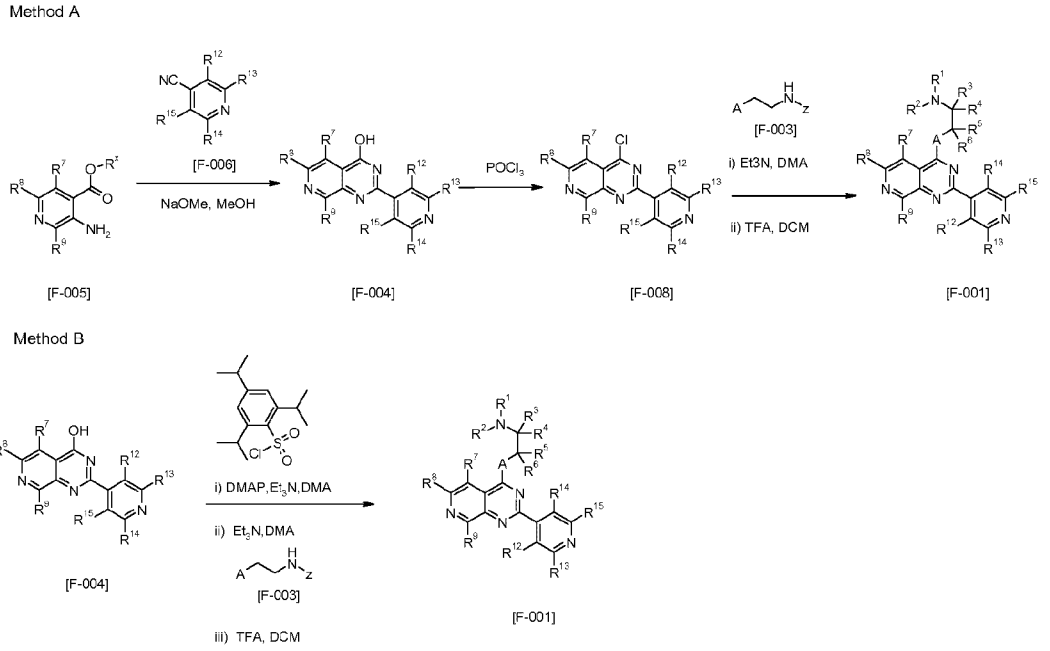
[F-001]

General synthesis of 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A1

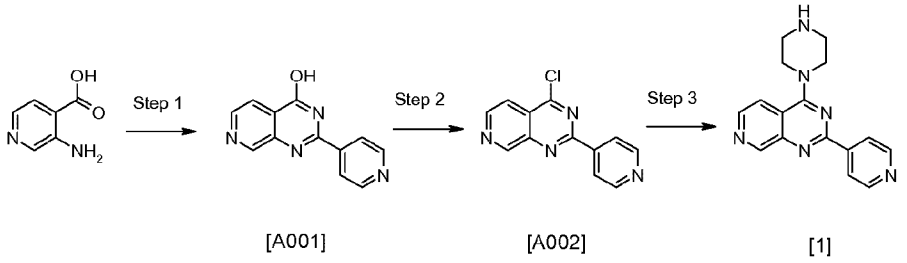
Substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-001] were prepared by the reaction of a 2-amino-pyridyl derivative of general formula [F-005] with a 4-cyanopyridyl derivative of general formula [F-006] in the presence of a base such as sodium methoxide in a polar aprotic solvent such as methanol. The reaction is suitably conducted at elevated temperature to yield the cyclised 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol product of general formula [F-004]. 4-substituted-1-yl-2-pyridin-4-yl-

pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride to yield 4-chloro-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-008] which were reacted with primary or secondary amino derivative of general formula [F-003], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-003], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC

Scheme A1



Synthesis of 4-Piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [1] Method A



Synthesis of 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [A001]

A mixture of 4-Cyanopyridine (8.25 g, 79.2 mmol), sodium methoxide (891 mg, 16.5 mmol) and methanol (400 mL) was stirred at room temperature for 60 minutes. 3-Amino-isonicotinic acid (9.12g, 66.0 mmol) was added and the mixture heated to reflux for 3 days. After cooling to room temperature the solid precipitate was collected by filtration then dried in the vacuum oven to yield the title compound as an off-white solid (6.02 g): (1H, 300MHz, d6-dmso) 13.10 (1H, br s), 9.16 (1H, s), 8.80 (2H, dd), 8.70 (1H, d), 8.10 (2H, dd), 8.00 (1H, dd)

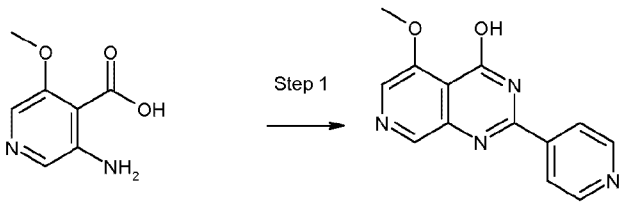
Synthesis of 4-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [A002]

2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol [A001] (4 g, 17.8 mmol) in $POCl_3$ (50 mL, 538 mmol) was heated to 110°C for 3 hours. The reaction mixture was concentrated under vacuum, quenched with saturated $NaHCO_3$ solution, extracted into DCM, washed with water then brine, passed through a phase separator cartridge and evaporated to yield the title compound [A002] (2.6 g) as a yellow / brown solid which was used without further purification: LCMS method: 1, RT:4.09 min, MI 243 [M+H].

Synthesis of 1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [1]

A solution of 4-Chloro-2-pyridin-4-yl-pyrido[3,4- d]pyrimidine [A002] (100 mg, 0.43 mmol), piperazine (172mg, 2 mmol) in anhydrous DMA (5 mL) was stirred at room temperature for 3 days. The reaction mixture was partitioned between NaOH (2M aqueous solution) and ethyl acetate. The organic layer was further washed with water then brine, dried ($MgSO_4$), passed through a phase separator cartridge and evaporated to yield the crude material, which was purified by preparative HPLC (method A) to yield the title compound (1.87mg). LCMS method: 1, RT:3.49 min, MI 293 [M+H]; 1H-NMR (300MHz; DMSO-d6): 9.26 (1H, s), 8.76 (2H, d), 8.58 (1H, d),8.32 (2H, d), 8.24 (1H, s), 7.92 (1H, d), 3.96 (4H, br tr), 2.99 (4H, br tr)

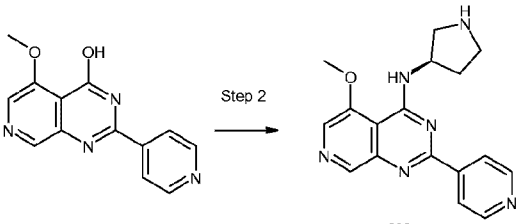
Synthesis of (5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine [2] method B



[A003]

Synthesis of 5-Methoxy-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A003]

To a stirred solution of 2-chloro-4-pyridinecarbonitrile (1g, 9.6 mmol) in MeOH (20 mL) was added 0.5 M NaOMe (2 mmol, 4 mL) followed by 3-Amino-5-methoxy-isonicotinic acid (1.35g, 8 mmol). The RM was heated at 75° C over night. The RM was left to cool and a solid ppt formed which was collected by filtration, washed with cold MeOH and dried in a vac oven to give the title compound as a pale brown solid (610 mg, 30% yield). LCMS method: 1, RT:3.82 min, MI 255.09 [M+H].



[A003] [2]

Synthesis of (5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine [2]

5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4- [A003] (0.157 mmol, 0.04 g), 2,4,6-triisopropylbenzenesulfonyl chloride (0.173 mmol, 0.052 g), were dissolved in anhydrous DMA (2mL), and Et_3N (0.314mmol, 0.045 mL), and DMAP (5mg) were added sequentially. The mixture was stirred at room temperature for 1 hour and (R)-3-amino-pyrrolidine-1-carboxylic acid tert-butyl ester (0.236 mmol, 0.044 g) was added. The mixture was stirred at room temperature overnight. The solvent was then removed under reduced pressure and the residue was stirred in trifluoroacetic acid (1 mL) at room temperature for 3h. The solution was poured on to an SCX-2 cartridge (5 g), washed with methanol (10 mL) and then washed with ammonia (2N in methanol, 2 0mL). The ammonia washes were concentrated in vacuo to a brown residue that was purified by preparative HPLC (method A) to yield the title compound (0.016g). LCMS method: 1, RT:1.47 min, MI 323 [M+H]; 1H-NMR 300 MHz (1H d6-dmso) 8.81 (1H, s), 8.76 (2H, dd), 8.35 (1H, s), 8.32 (2H, dd), 8.23 (1H, d), 6.42 (1H, s), 4.98 (1H, m), 4.14 (3H, s), 3.19-3.07 (2H, m), 2.41-2.29 (2H, m), 2.07-1.95 (2H, m).

Synthesis of 2-(3-Fluoro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [A004]

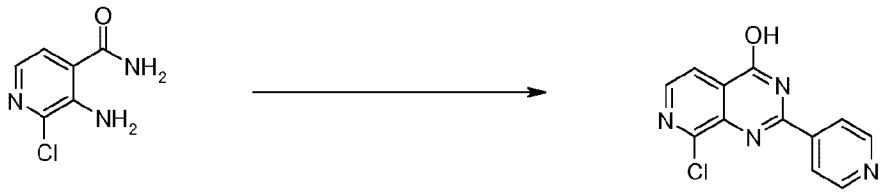
[A004]

2-(3-Fluoro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol [A004]

3-Amino-2-chloro-isonicotinamide (0.5 g, 3.64 mmol), 3-Fluoroisonicotinaldehyde (0.54 g, 4.37 mmol), NaHSO3 (0.75 g, 7.29 mmol) and DMA (5 mL) were added successively to a microwave vial. The vial was sealed then heated at 160°C for 6min. Water (10 mL) was

added and the resulting solid was filtered and used without further purification. LCMS method: 1, RT:3.07 min, MI 243 [M+H]

Synthesis of 8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A005]

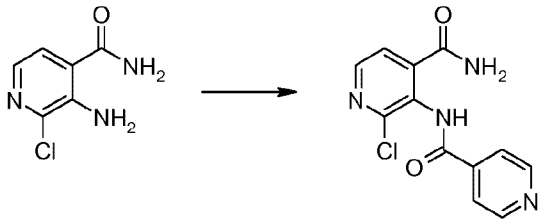


[A005]

8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A005]

A solution of 3-Amino-2-chloro-isonicotinamide (0.5 g, 2.91 mmol) and 4-Pyridinecarboxaldehyde (0.35 g, 3.32 mmol) in DMA (10mL) was heated under microwave (100°C, 2h). Sodium hydrogen sulfite (0.606 g, 5.83 mmol) was then added and the mixture was heated under microwave (150°C, 1h). Water was then added to the mixture and the resulting solid (0.34 g, 45%) was collected, washed with water and then by MeOH. LCMS method: 1, RT:3.89 min, MI 258 [M+H]

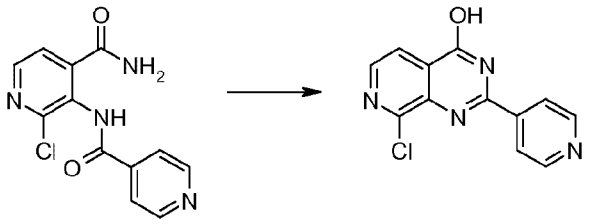
Synthesis of 8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A005]



[A006]

Synthesis of 2-Chloro-3-[(pyridine-4-carbonyl)-amino]-isonicotinamide [A006]

To a suspension of 3-Amino-2-chloro-isonicotinamide (0.5 g, 2.913 mmol) and K_2CO_3 (1g, 7.28mmol) in refluxing Et_2O (25 mL), Isonicotinoyl chloride hydrochloride (0.622 g, 3.5 mmol) was added portionwise. The mixture was stirred under reflux for 4h. The solvent was removed under reduced pressure and water (50 mL) was added. The resulting solid was filtered, washed with H_2O and then collected, dried with an azeotrope with toluene, to yield the title compound (0.78 g, 96 %) which was used without further purification. LCMS method: 1, RT:2.55 min, MI 277 [M+H]

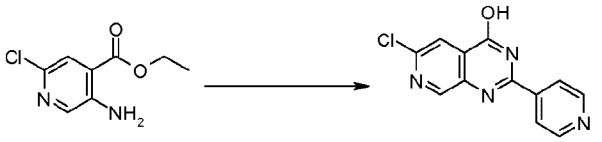


[A006] [A005]

Synthesis of 8-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A004]

To a solution of 2-Chloro-3-[(pyridine-4-carbonyl)-amino]-isonicotinamide [A006] (0.2 g, 0.723 mmol) in MeOH (20 mL) was added a solution of cesium carbonate (0.47 g, 1.44 mmol) in H_2O (2 mL). The mixture was stirred at room temperature overnight. The MeOH was removed under reduced pressure and water (10 mL) was added. Acetic acid was added slowly and the resulting solid was collected, dried with a toluene azeotrope to yield the title compound which was used without further purification. LCMS method: 1, RT:3.43 min, MI 259 [M+H]

Synthesis of 6-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A007]

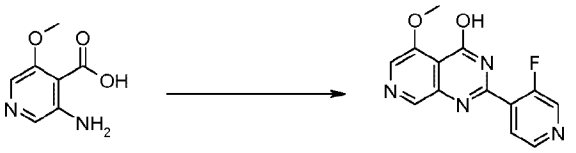


[A007]

6-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A007]

A solution of potassium pentoxide (2.6 mL, 5.1 mmol, 25% soln in Toluene) was added dropwise (~0.5mL/min) to a solution of 5-Amino-2-chloro-isonicotinic acid ethyl ester (0.4 g, 2 mmol) and 4-cyanopyridine (0.25 g, 2.4 mmol) in anhydrous THF (5 mL) cooled in an ice bath. The reaction was allowed to warm to RT and left to stir at room temperature overnight. Water (9 mL) was added and the mixture was stirred at RT for 20 mins. Acetic acid (~1mL) was then added and the mixture was left to stir at RT and the resulting yellow precipitate was filtered and the siolid washed with deionised water (2x 3mL). To give the title compound (0.43g, 83% yield). LCMS method: 1, RT: 2.21 min, MI 259 [M+H]

Synthesis of 2-(3-Fluoro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [A008]

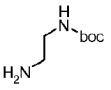
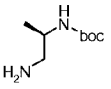
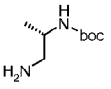
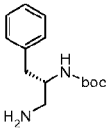


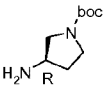
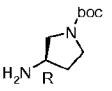
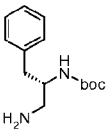
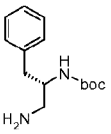
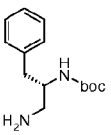
[A008]

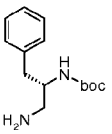
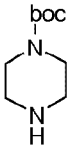
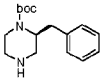
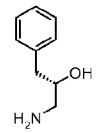
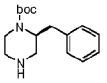
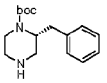
2-(3-Fluoro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [A008]

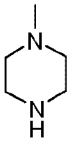
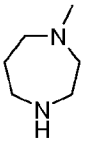
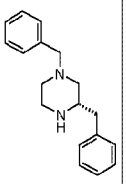
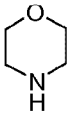
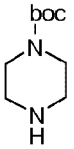
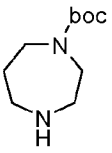
To a stirred solution of 3-Fluoroisonicotinonitrile (0.088 g, 0.71 mmol) in MeOH (5 mL) was added NaOMe (0.008 g, 0.15 mmol). After 1hr 3-amino-5-methoxy-isonicotinic acid (0.1 g, 0.54 mmol) was added and the RM heated to 85 °C for 18hr. The solution became yellow in colour. The reaction mixture was alloed to cool to RT and the white solid was collected by filtration and washed with MeOH to yield the title compound (0.07g, 43% yield). LCMS method: 1, RT:1.19 min, MI 271.24 [M+H]

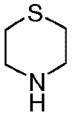
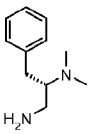
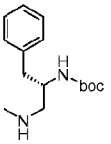
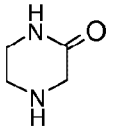
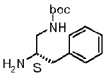
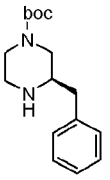
The following compounds were synthesised according to the general synthesis shown in scheme [A1]:

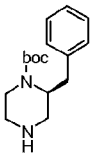
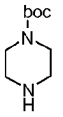
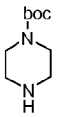
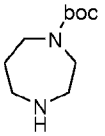
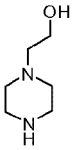
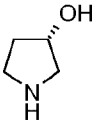
Ex	Pre-cursor	Met-hod	Amine [F-003]	Analysis		Name
				LCMS	NMR	
3	[A001]	A		Method 1: RT: 2.2 min, MI: 267 [M+H]		N-(2-aminoethyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
4	[A001	A		Method 1: RT:2.45 min, MI , 281 [M+H]		N-[(2R)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
5	[A001]	A		Method 1: RT: 2.52 min, MI, 281 [M+H]		N-[(2S)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
6	[A001]	B		Method 1: RT: 2.51 min, MI, 357 [M+H]	(1H, 300MHz, d6-dmso); 9.15ppm (1H, d), 8.70ppm (2H, d), 8.62ppm (2H, d), 8.20ppm (1H, d), 8.12ppm (2H, d), 7.35-7.26ppm	N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-

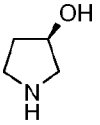
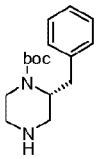
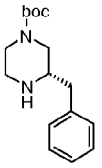
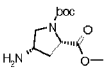
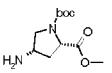
					(5H, m), 3.86ppm, (1H, d), 3.35ppm (2H, m), 2.27ppm (2H, m)	d]pyrimidin-4-amine
7	[A001]	B		Method 1: RT: 0.88 min, MI, 293 [M+H]	(1H, 300MHz, d6-dmso), 9.18 (1H, s), 8.94-8.90 (1H, m), 8.76 (2H, dd), 8.65 (1H, d), 8.35 (2H, dd), 4.94-4.85 (1H, m), 3.87-3.74 (3H, m), 3.19-3.07 (2H, m), 2.30-2.18 (2H, m), 2.02-1.92 (2H, m)	(3R)-N-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
8	[A004]	B		Method 1: RT: 0.5 min, MI, 311 [M+H]	(1H, 300MHz, d6-dmso), 9.47 (1H, brd), 9.15 (1H, s), 8.71 (1H, d), 8.66 (1H, d), 8.57 (1H, d), 8.47 (1H, s), 8.39 (1H, d), 8.08 (1H, dd), 4.92 (1H, br s), 3.46 (1H, dd), 3.34-3.22 (2H, m), 2.30-2.20 (1H, m), 2.18-2.08 (1H, m)	(3R)-N-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
9	[A003]	B		Method 1: RT: 2.92 min, MI, 387 [M+H]	(1H, 300MHz, d6-dmso); 8.72 (1H, s), 8.68 (2H, d), 8.28 (1H, s), 8.00 (2H, d), 7.39-7.30 (5H, m), 4.00 (3H, s), 3.96-3.91 (1H, m), 3.59 (2H, br s), 3.00 (1H, dd), 2.79 (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
10	[A004]	B		Method 1: RT: ,2.95 min MI, 375 [M+H]	(1H, 300MHz, d6-dmso), 9.12 (1H, s), 8.69 (1H, d), 8.53 (1H, d), 8.46 (1H, S), 8.21 (1H, d), 7.83 (1H, dd), 7.28-7.19 (5H, m), 3.81 (1H, dd), 3.66-3.49 (2H, m), 2.90 (1H, dd), 2.80 (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
11	[A005]	B		Method 1: RT: 2.98 min, MI: 392 [M+H]	(1H, 300MHz, d6-dmso), 8.70 (2H, d), 8.40 (1H, d), 8.36 (1H, br s), 7.98 (2H, d), 7.43-7.32 (5H, m), 3.97 (1H, d), 3.69-3.54 (2H, m), 3.06 (1H, dd), 2.84 (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

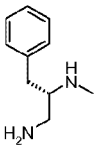
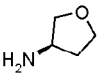
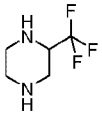
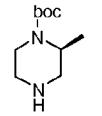
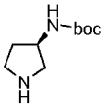
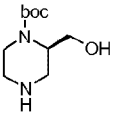
12	[A007]	A		Method 1: RT: 6.51 min , MI: 391 [M+H]	(1H, 300MHz, d6-dmso) 9.06 (1H, s), 8.69 (2H, dd), 7.98 (2H, dd), 7.87 (1H, s), 7.42-7.27 (5H, m), 4.54 (1H, dd), 4.37 (1H, d), 3.58-3.48 (1H, m), 3.04-2.93 (3H, m), 2.85-2.59 (3H, m)	N-[(2S)-2-amino-3-phenylpropyl]-6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
13	[A007]	A		Method 1: RT: 4.35 min , MI: 327 [M+H]	(300MHz, 1H, d6-dmso) 9.20 (1H, s), 8.79 (2H, d), 8.35 (2H, d), 8.13 (1H, s), 6.61 (1H, s), 4.15 (4H, br s), 3.33 (4H, br s)	1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
14	[A007]	A		Method 1: RT: 2.91 min, MI: 443.9 [M+H]	(300MHz, 1H, d6-dmso) 9.06 (1H, s), 8.69 (2H, dd), 7.98 (2H, dd), 7.87 (1H, s), 7.41-7.29 (5H, m), 4.54 (1H, dd), 4.37 (1H, d), 3.53 (1H, dt), 3.03-2.93 (3H, m), 2.85-2.57 (3H, m)	(3S)-3-benzyl-1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
15	[A001]	A		Method 1: RT: 4.30 min , MI: 358 [M+H]	(300MHz, 1H, d4-MeOH) 8.55 (d, 1H), 8.22 (dd, 2H), 8.03 (dd, 1H), 7.76 (m, 5H), 4.28 (m, 1H), 4.09 (1H, dd), 3.58 (1H, dd), 2.96 (1H, dd), 2.88 (1H, dd)	(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-ol
16	[A001]	A		Method 1: RT: 2.44 min , MI: 383 [M+H]	(1H, 300MHz, $CDCl_3$) 9.34 (s, 1H), 8.73 (d, 2H), 8.46 (d, 1H), 8.21 (d, 2H), 7.49 (d, 1H), 7.33 (m, 3H), 7.25 (d, 2H), 4.58 (d, 1H), 4.48 (d, 1H), 3.46 (t, 1H), 3.02 (m, 4H), 2.76 (m, 2H)	(3S)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
17	[A001]	A		Method 1: RT: 2.45 min , MI: 383 [M+H]	(1H, 300MHz, $CDCl_3$) 9.34 (s, 1H), 8.73 (d, 2H), 8.46 (d, 1H), 8.21 (d, 2H), 7.49 (d, 1H), 7.33 (m, 3H), 7.25 (d, 2H), 4.58 (d, 1H), 4.48 (d, 1H), 3.46 (t, 1H), 3.02 (m, 4H), 2.76 (m, 2H)	(3R)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

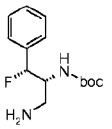
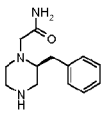
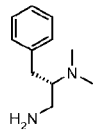
18	[A001]	A		Method 1: RT: 3.99 min , MI: 307 [M+H]	(1H, 300MHz, d6-dmso) 9.26 (1H, s), 8.75 (2H, dd), 8.58 (1H, d), 8.31 (2H, dd), 7.91 (1H, d), 3.98-3.96 (4H, m), 2.55-2.52 (4H, m), 2.25 (3H, s)	1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
19	[A001]	A		Method 1: RT: 4.00 min , MI: 321 [M+H]	(1H, 300MHz, d6-dmso) 9.19 (1H, s), 8.75 (2H, dd), 8.52 (1H, d), 8.29 (2H, dd), 7.98 (1H, d), 4.13-4.06 (4H, m), 2.85-2.83 (2H, m), 2.55-2.51 (2H, m), 2.26 (3H, s), 2.10-2.03 (2H, m)	1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane
20	[A001]	A		Method 1: RT: 4.29 min , MI: 473 [M+H]	(1H, 300MHz, $CDCl_3$) 9.31 (s, 1H), 8.75 (d, 2H), 8.47 (d, 1H), 8.30 (d, 2H), 7.49 (d, 1H), 7.36 (m, 5H), 7.02 (m, 5H), 5.02 (s, 1H), 4.30 (d, 1H), 3.90 (td, 1H), 3.62 (d, 1H), 3.45 (d, 1H), 3.26 (m, 2H), 3.04 (d, 1H), 2.92 (d, 1H), 2.35 (m, 2H)	(2S)-2,4-dibenzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
21	[A001]	A		Method 1: RT: 2.86 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.28 (1H, s), 8.76 (2H, d), 8.59 (1H, d), 8.33 (2H, d), 7.97 (1H, d), 4.02-3.99 (4H, t), 3.83-3.80 (4H, t)	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine
22	[A001]	A		Method 1: RT: 4.76 min , MI: 349 [M+H]	(1H, 300MHz, d6-dmso) 9.28 (1H, s), 8.77 (2H, dd), 8.60 (1H, d), 8.34 (2H, dd), 7.97 (1H, d), 4.03-4.00 (4H, m), 3.61 (4H, br s), 1.43 (9H, s)	tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxylate
23	[A001]	A		Method 1: RT: 4.18 min , MI: 407 [M+H]	(1H, 300MHz, d6-dmso) 9.22 (1H, s), 8.76 (2H, dd), 8.56 (1H, d), 8.30 (2H, dd), 8.08-8.03 (1H, m), 4.28-4.22 (2H, m), 4.15-4.10 (2H, m), 3.72-3.65 (2H, m), 3.42 (2H, br s), 2.09-1.97 (2H, m), 1.11 (4H, s), 0.93 (5H, s)	tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane-1-carboxylate

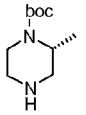
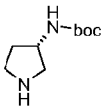
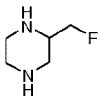
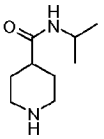
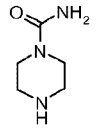
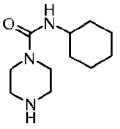
24	[A001]	A		Method 1: RT: 3.8 min , MI: 310 [M+H]	(1H, 300MHz, d6-dmso) 9.29 (1H, s), 8.76 (2H, dd), 8.60 (1H, d), 8.32 (2H, dd), 7.87 (1H, d), 4.23-4.20 (4H, m), 2.93-2.89 (4H, m)	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]thiomorpholine
25	[A001]	A	 [A009]	Method 1: RT: 2.34 min , MI: 385 [M+H]	(1H, 300MHz, d6-dmso) 9.13 (1H, s), 8.67 (2H, dd), 8.61 (1H, d), 8.15 (1H, d), 7.99 (2H, d), 7.37-7.26 (5H, m), 3.76 (2H, br s), 3.33-3.13 (1H, m), 3.07-2.88 (2H, m), 2.35 (6H, br s)	N,N-Dimethyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine
26	[A001]	A	 [A013]	Method 1: RT: 2.44 min , MI: 371 [M+H]	(1H, 300MHz, d6-dmso) 9.15 (1H, s), 8.77 – 8.75 (2H, m), 8.64 (1H, d), 8.30 – 8.28 (2H, m), 8.24 (1H, d), 7.32 – 7.29 (2H, m), 7.20 – 7.15 (2H, m), 7.09 – 7.04 (1H, m), 5.08 – 4.99 (1H, m), 3.11 – 2.87 (4H, m), 2.38 (3H, s).	N-[(2S)-2-amino-3-phenylpropyl]-N-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
27	[A001]	A		Method 1: RT: 2.21 min , MI: 307 [M+H]	1H NMR (d6-DMSO, 300MHz) 9.28 (1H, s), 8.77 (2H, d), 8.61 (1H, d), 8.34 (2H, d), 8.31 (1H, s), 8.03 (1H, d), 4.51 (2H, s), 4.18 (2H, t), 3.53-3.43 (2H, m).	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-one
28	[A001]	A		Method 1: RT: 2.44 min , MI: 357 [M+H]	-	N-[(2S)-1-amino-3-phenylpropan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
29	[A001]	A		Method 1: RT: 2.12 min, MI: 383.18 [M+H]	(1H, 300MHz, $CDCl_3$) 9.27 (s, 1H), 8.75 (d, 2H), 8.47 (d, 1H), 8.29 (d, 2H), 7.45 (d, 1H), 7.11 (m, 5H), 5.05 (m, 1H), 4.28 (d, 1H), 3.83 (dt, 1H), 3.23 (m, 3H), 3.09 (m, 2H), 3.01 (dt, 1H).	(2R)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

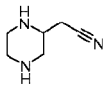
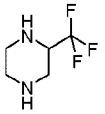
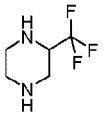
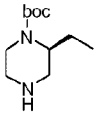
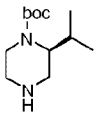
30	[A003]	B		Method 1: RT: 2.71 min, MI: 413.17 [M+H]	(1H, 500MHz, d6-dmso) 8.77 (s, 1H), 8.69 (d, 2H), 8.22 (s, 1H), 8.03 (d, 2H), 7.34 (m, 3H), 7.27 (d, 2H), 4.27 (m, 1H), 4.02 (m, 1H), 3.90 (s, 3H), 3.22 (t, 1H), 2.99 (m, 2H), 2.83 (t, 1H), 2.72 (dd, 1H), 2.63 (t, 1H), 2.62 (dd, 1H).	(3S)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
31	[A003]	B		Method 1: RT: 1.261 min , MI: 323.07 [M+H]	(1H, 300MHz, d6-dmso) 8.86 (1H, t), 8.78 – 8.76 (2H, m), 8.36 (1H, s), 8.32 – 8.30 (2H, m), 4.08 (3H, s), 3.75 (4H, m), 3.03 (4H, m).	1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
32	[A005]	B		Method 1: RT: 1.39 min , MI: 327 [M+H]	(1H, 300MHz, d6-dmso) 8.79 (d, 2H), 8.32-8.37 (m, 3H), 7.92 (d, 1H), 3.94 (brs, 4H), 2.95 (brs, 4H).	1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
33	[A001]	A		Method 1: RT: 3.92 min , MI: 307 [M+H]	(1H, 300MHz, d6-dmso) 9.21 (1H, s), 8.77 – 8.75 (2H, m), 8.54 (1H, d), 8.32 – 8.30 (2H, m), 8.00 (1H, d), 4.14 – 4.07 (4H, m), 3.15 – 3.12 (2H, m), 2.85 – 2.81 (2H, m), 2.04 – 1.97 (2H, m).	1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane
34	[A001]	A		Method 1: RT: 4.04 min , MI: 337 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.78 – 8.76 (2H, m), 8.60 (1H, d), 8.34 – 8.32 (2H, m), 7.94 (1H, d), 4.50 (1H, br m), 4.00 (4H, br m), 3.60 – 3.54 (2H, m), 2.67 (4H, br m), 2.49 – 2.46 (2H, m).	2-{4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}ethan-1-ol
35	[A001]	A		Method 1: RT: 2.35 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.19 (1H, s), 8.77 – 8.74 (2H, m), 8.56 (1H, d), 8.34 – 8.32 (2H, m), 8.17 (1H, br m), 5.18 (1H, d), 4.49 (1H, br m), 4.08 (3H, br m), 3.88 (1H, br d), 2.05 (2H, br m).	(3S)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol

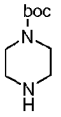
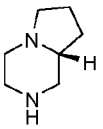
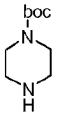
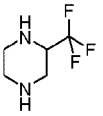
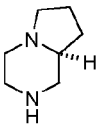
36	[A001]	A		Method 1: RT: 2.39 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.19 (1H, s), 8.77 – 8.74 (2H, m), 8.56 (1H, d), 8.34 – 8.32 (2H, m), 8.17 (1H, br m), 5.18 (1H, d), 4.49 (1H, br m), 4.08 (3H, br m), 3.88 (1H, br d), 2.05 (2H, br m).	(3R)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol
37	[A003]	B		Method 1: RT: 2.74 min, MI: 413.17 [M+H]	(1H, 500MHz, d6-dmso) 8.79 (s, 1H), 8.70 (d, 2H), 8.23 (s, 1H), 8.05 (d, 2H), 7.33 (m, 3H), 7.27 (d, 2H), 3.21 (t, 1H), 3.17 (d, 2H), 3.00 (d, 1H), 2.92 (m, 1H), 2.82 (t, 1H), 2.76 (dd, 1H), 2.68 (d, 1H), 2.61 (dd, 1H).	(3R)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
38	[A001]	A		Method 1: RT: 2.06 min, MI: 383.17 [M+H]	(1H, 500MHz, $CDCl_3$) 9.29 (s, 1H), 8.75 (d, 2H), 8.47 (d, 1H), 8.28 (d, 2H), 7.45 (d, 1H), 7.09 (m, 5H), 5.04 (m, 1H), 4.25 (d, 1H), 3.83 (t, 1H), 3.28 (m, 2H), 3.22 (d, 1H), 3.09 (m, 2H), 3.02 (t, 1H).	(2S)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
39	[A001]	A	 [A015]	Method 1: RT: 1.04 min, MI: 351.25 [M+H]	(1H, 300MHz, d4-MeOH): 9.20 (s, 1H), 8.71 (dd, 2H), 8.59 (d, 1H), 8.48 (dd, 2H), 8.08 (d, 1H), 4.98 (m, 1H), 4.99 (m, 1H), 4.02 (dd, 1H), 3.74 (s, 3H), 3.42 (dd, 1H), 3.25 (dd, 1H), 2.78 (m, 2H), 2.21 (m, 1H).	methyl (2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-carboxylate
40	[A001]	A	 [A015]	Method 1: RT: 0.52 min , MI: 463 [M+H]	(1H, 300MHz, d4-MeOH): 9.21 (s, 1H), 8.71 (ss, 2H), 8.60 (d, 1H), 8.50 (dd, 2H), 8.09 (d, 1H), 4.99 (m, 1H), 4.29 (m, 1H), 3.86 (m, 2H), 3.73 (s, 3H), 3.47 (dd, 1H), 3.14 (m, 2H), 2.89 (dd, 1H), 2.74 (m, 1H), 2.49 (m, 1H), 2.12 (m, 1H), 1.88 (m, 1H).	methyl (2S,4S)-4-[(2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-amido]pyrrolidine-2-carboxylate

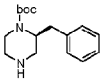
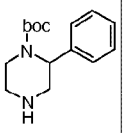
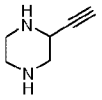
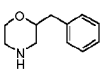
41	[A003]	A		Method 1: RT: 5.14 min , MI: 401 [M+H]	(1H, 300MHz, d6-dmso) 8.77 (s, 1H), 8.72 – 8.70 (2H, m), 8.33 (1H, s), 8.20 (1H, s), 8.12 – 8.10 (2H, m), 7.33 – 7.23 (5H, m), 4.12 (3H, s), 3.86 – 3.78 (1H, m), 3.62 – 3.53 (1H, m), 3.18 – 3.11 (1H, m), 2.98 – 2.92 (1H, m)2.71 – 2.64 (1H, m), 2.45 (3H, s).	[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl](methyl)amine
42	[A001]	A		Method 1: RT: 3.0 min , MI: 294 [M+H]	(1H, 300MHz, d6-dmso) 9.21 (1H, s), 8.81 – 8.77 (3H, m), 8.67 (1H, d), 8.37 – 8.33 (3H, m), 6.57 (2H, s), 5.00 – 4.90 (1H, m), 4.14 – 4.09 (1H, m), 4.01 – 3.94 (1H, m), 3.86 – 3.79 (2H, m), 2.42 – 2.33 (1H, m), 2.20 – 2.09 (1H, m).	N-[(3R)-oxolan-3-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
43	[A003]	B		Method 1: RT: 3.41 min, MI: 391.13 [M+H]	(1H, 300MHz, $CDCl_3$) 9.01 (s, 1H), 8.76 (d, 2H), 8.31 (d, 2H), 8.22 (s, 1H), 4.42 (d, 1H), 4.15 – 4.04 (m, 1H), 4.07 (s, 3H), 3.62 (br m, 1H), 3.33 – 3.12 (m, 3H), 3.00 (t, 1H).	1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
44	[A003]	B		3jdf138qc, 96%, 337.23, 1.37min, + [M+H] LC-MS17QC	(1H, 300MHz, $CDCl_3$) 8.95 (s, 1H), 8.74 (d, 2H), 8.31 (d, 2H), 8.16 (s, 1H), 4.20 (t, 2H), 4.05 (s, 3H), 3.16 (m, 2H), 2.99 (m, 2H), 2.81 (t, 1H), 1.14 (d, 3H).	(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine
45	[A003]	B		Method 1: RT: 1.52 min , MI: 323 [M+H]	(1H, 300MHz, d6-dmso) 8.80 (1H, s), 8.78 – 8.75 (2H, m), 8.34 (1H, s), 8.32 – 8.30 (2H, m), 4.07 (3H, s), 3.94 (2H, br s), 3.82 (1H, br s), 3.72 (1H, br s), 2.15 (1H, br s), 1.10 (1H, br s).	(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
46	[A003]	B		Method 1: RT: 1.32 min, MI:	(1H, 300MHz, d6-dmso): 8.84 (s, 1H), 8.76 (d, 2H), 8.34 (s, 1H), 8.29 (d, 2H), 4.87 (bs, 1H), 4.28 (dd,	[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-

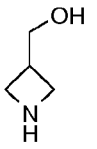
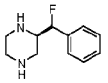
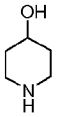
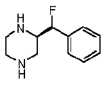
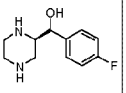
				353.2 [M+H]	2H), 4.06 (s, 3H), 3.43 (m, 1H), 3.07 (m, 3H), 2.82 (m, 3H).	d]pyrimidin-4-yl]piperazin-2-yl]methanol
47	[A003]	B	 [A018]	Method 1: RT: 2.79 min, MI: 405.22 [M+H]	(1H, 300MHz, $CDCl_3$): 8.90 (s, 1H), 8.72 (d, 2H), 8.22 (d, 2H), 8.14 (s, 1H), 7.40 (m, 5H), 5.43 (dd, 1H), 4.18 (m, 1H), 4.10 (s, 3H), 3.53 (m, 2H).	N-[(2R,3R)-2-amino-3-fluoro-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
48	[A003]	B		Method 1: RT: 3.76 min, MI: 470.24 [M+H]	(1H, 300MHz, $CDCl_3$): 8.94 (s, 1H), 8.70 (d, 2H), 8.12 (d, 2H), 8.05 (s, 1H), 7.28 (m, 2H), 7.08 (m, 3H), 4.04 (d, 1H), 3.84 (m, 4H), 3.65 (m, 1H), 3.56 (d, 1H), 3.29 (m, 1H), 3.06 (m, 3H), 2.89 (m, 1H), 2.66 (dt, 1H), 2.53 (dd, 1H).	2-[(2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl]acetamide
49	[A003]	A	 [A009]	Method 1: RT: 5.71 min , MI: 415 [M+H]	(1H, 300MHz, d4-MeOH) 8.63 (1H, s), 8.58 – 8.56 (2H, m), 8.10 (1H, s), 8.06 – 8.04 (2H, m), 7.31 – 7.19 (5H, m), 4.06 (3H, m), 3.98 – 3.91 (1H, m), 3.71 – 3.63 (1H, m), 3.59 – 3.47 (1H, m), 3.20 – 3.14 (1H, m), 2.67 – 2.60 (7H, m).	[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl]dimethylamine
50	[A003]	B		Method 1: RT: 3.69 min, MI: 324.19 [M+H]	(1H, 300MHz, $CDCl_3$) 8.92 (1H, s), 8.74 – 8.72 (2H, m), 8.36 – 8.34 (2H, m), 8.16 (1H, m), 4.62 (1H, br s), 4.26 – 4.16 (1H, m), 4.07 (3H, m), 3.82 – 3.75 (1H, m), 3.63 (1H, d), 2.12 – 2.20 (1H, m), 1.22 – 1.21 (2H, m).	(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol
51	[A003]	B		Method 1: RT: 0.63 min , MI: 351 [M+H]	(1H, 300MHz, $CDCl_3$): 8.97 (s, 1H), 8.78 (d, 2H), 8.31 (d, 2H), 8.19 (s, 1H), 4.23 (m, 2H), 4.07 (s, 3H), 3.08 (m, 2H), 2.75 (t, 2H), 1.16 (m, 6H).	1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3,5-cis-dimethylpiperaz

						inc
52	[A003]	B		Method 1: RT: 4.03 min, MI: 337.37 [M+H]	(1H, 300MHz, $CDCl_3$): 8.98 (s, 1H), 8.77 (d, 2H), 8.32 (d, 2H), 8.19 (s, 1H), 4.22 (t, 2H), 4.07 (s, 3H), 3.19 (m, 2H), 3.05 (m, 2H), 2.82 (m, 1H), 1.15 (d, 3H).	(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine
53	[A003]	B			(1H, 300 MHz, d_6-DMSO) 8.78 – 8.73 (3H, m), 8.30 – 8.28 (3H, m), 4.05 (3H, s), 3.92 (4H, m), 3.36 (3H, m)	(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine
54	[A003]	B	 [A024]	Method 1: RT: 1.48 min, MI: 355.15 [M+H]	(1H, 300MHz, $CDCl_3$) 9.02 (1H, s), 8.80 – 8.78 (2H, m), 8.35 – 8.33 (2H, m), 8.22 (1H, m), 4.59 – 4.57 (1H, m), 4.44 – 4.41 (1H, m), 4.28 (1H, d), 4.22 – 4.16 (1H, m), 4.10 (3H, s), 3.25 – 3.20 (1H, m), 3.12 – 3.03 (1H, m).	3-(fluoromethyl)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
55	[A001]	A		Method 1: RT: 4.22 min, MI: 377.43 [M+H]	(1H, 300MHz, d6-dmso) 9.25 (1H, s), 8.75 (2H, dd), 8.58 (1H, d), 8.31 (2H, dd), 7.89 (1H, d), 7.74 (1H, d), 4.58 (2H, d), 3.86-3.79 (1H, m), 3.33 (3H, m), 1.94-1.78 (4H, m), 1.03 (6H, d).	N-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidine-4-carboxamide
56	[A001]	A		Method 1: RT: 2.42 min, MI: 336.18 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.76 (2H, dd), 8.60 (1H, d), 8.33 (2H, dd), 7.98 (1H, d), 6.11 (2H, s), 4.02-3.99 (4H, m), 3.60-3.56 (4H, m).	4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide
57	[A001]	A		Method 1: RT: 4.8 min , MI: 418.47 [M+H]	(1H, 300MHz, d6-dmso) 9.25 (1H, s), 8.76 (2H, d), 8.58 (1H, d), 8.31 (2H, d), 7.96 (1H, d), 6.27 (1H, d), 4.00 (4H, m), 3.57 (4H, m), 3.47-3.38 (1H, m), 1.77-1.66 (4H, m), 1.56	N-cyclohexyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide

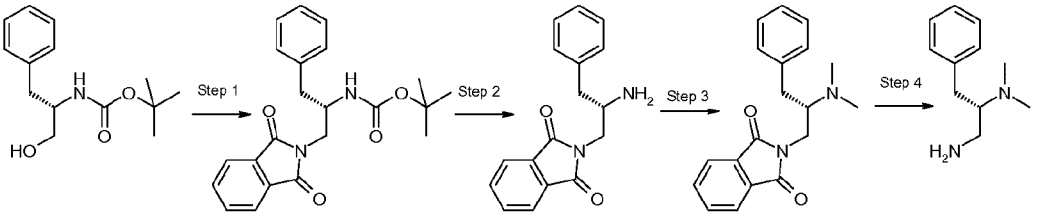
					(1H, d, br), 1.25-1.04 (5H, m).	
58	[A003]	B	 [A028]	Method 1: RT: 0.64 min, MI: 362.18 [M+H]	(1H, 300MHz, $CDCl_3$) 9.03 (1H, s), 8.81 – 7.79 (2H, m), 8.36 – 8.34 (1H, m), 8.24 (1H, s), 4.38 – 4.34 (1H, m), 4.16 – 4.12 (4H, m), 3.42 – 3.33 (1H, m), 3.28 – 3.19 (2H, m), 3.09 – 3.02 (2H, m), 2.60 – 2.58 (2H, m).	2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl}acetonitrile
59	[A001]	A		Method 1: RT: 3.3 min , MI: 361 [M+H]	(1H, 300MHz, d6-dmso) 9.31 (1H, s), 8.80 – 8.78 (2H, m), 8.63 (1H, d), 8.32 – 8.30 (2H, m), 7.97 (1H, d), 4.54 (1H, d), 4.25 (1H, d), 3.78 – 3.56 (3H, m), 3.18 – 3.06 (2H, m), 2.96 – 2.90 (2H, m).	1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
60	[A005]	B		Method 1: RT: 4.43 min , MI: 395 [M+H]		1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
61	[A001]	A		Method 1: RT: 1.30 min , MI: 321 [M+H]	(1H, 300MHz, d6-dmso) 9.33 (s, 1H), 8.78 (d, 2H), 8.65 (d, 1H), 8.33 (d, 2H), 8.01 (d, 1H), 4.55-4.66 (m, 1H), 3.73 (t, 1H), 3.28-3.47 (m, 4H), 1.66-1.75 (m, 2H), 1.04 (t, 3H).	(3S)-3-ethyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
62	[A001]	A		Method 1: RT: 1.76 min , MI: 335 [M+H]	(1H, 300MHz, d6-dmso) 9.21-9.25 (m, 1H), 8.71-8.77 (m, 2H), 8.54-8.60 (m, 1H), 8.22-8.29 (m, 2H), 7.82-7.89 (m, 1H), 4.44-4.62 (m, 2H), 3.31-3.44 (m, 2H), 3.01-3.15 (m, 2H), 2.90 (t, 1H), 2.73 (brs, 1H), 1.68-1.79 (m, 1H), 1.00 (d, 6H).	(3S)-3-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

63	[A008]	B		Method 1: RT: 2.19 min, MI: 341.14 [M+H]	(1H, 300MHz, d4-MeOH) 8.89 (1H, s), 8.61 (1H, d), 8.54 (1H, d), 8.43 (1H, s), 8.35 (1H, s), 8.20 (1H, dd), 4.16 (3H, s), 3.94 (4H, m), 3.36 (4H, m).	1-[2-(3-fluoropyridin-4-yl)-5-methoxypyrido[3,4-d]pyrimidin-4-yl]piperazine
64	[A001]	A		Method 1: RT: 0.66 min , MI: 333 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.78 – 8.76 (2H, m), 8.59 (1H, d), 8.33 – 8.31 (2H, m), 7.94 (1H, d), 4.67 (2H, dd), 3.47 – 3.39 (1H, m), 3.18 – 3.10 (2H, m), 3.08 – 3.04 (1H, m), 2.41 – 2.33 (1H, m), 2.21 – 2.09 (2H, m), 1.94 – 1.83 (1H, m), 1.80 – 1.65 (2H, m), 1.48 – 1.35 (1H, m).	4-{4-[(8aR)-octahydropyrrolo[1,2-a]piperazin-2-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine
65	[A004]	B		Method 1: RT: 1.89 min, MI: 311.15 [M+H]	(1H, 300MHz, d6-dmso) 9.28 (1H, s), 8.73 (1H, d), 8.65 (1H, d), 8.60 (1H, d), 8.13 (1H, dd), 8.00 (1H, d), 4.06 (4H, m), 3.22 (4H, m), 2.97 (1H, s, br).	1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
66	[A004]	B		Method 1: RT: 4.02 min, MI: 379.15 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.73 (1H, d), 8.64 (1H, d), 8.60 (1H, d), 8.11 (1H, dd), 7.97 (1H, dd), 4.53 (1H, dd), 4.21 (1H, d), 3.75 (1H, m), 3.66 (1H, td), 3.51 (1H, dd), 3.15 (1H, d), 3.03 (1H, d), 2.88 (1H, t).	1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine
67	[A001]	A		Method 1: RT: 4.32 min, MI: 333.18 [M+H]	(1H, 300MHz, d6-dmso) 9.27 (1H, s), 8.78 – 8.76 (2H, m), 8.59 (1H, d), 8.33 – 8.31 (2H, m), 7.94 (1H, d), 4.64 (1H, dd), 3.46 (1H, br t), 3.20 – 3.03 (3H, m), 2.41 (1H, br m), 2.18 (2H, br m), 1.94 – 1.04 (1H, br m), 1.78 – 1.68 (2H, br m), 1.49 – 1.36 (1H, m).	4-{4-[(3aS)-octahydro-1H-pyrrolo[3,2-c]pyridin-5-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine

68	[A005]	B		Method 1: RT: 3.05 min , MI: 417 [M+H]	(1H, 300MHz, d6-dmso) 7.79 (d, 2H), 7.53 (brs, 1H), 7.39 (d, 1H), 7.26 (d, 2H), 6.83 (d, 1H), 6.57-6.67 (m, 5H), 3.83 (dd, 1H), 3.04 (t, 1H), 2.82-2.93 (m, 1H), 2.68 (d, 1H), 2.59 (d, 1H), 2.35 (dd, 1H), 2.14 (dd, 1H).	(3S)-3-benzyl-1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
69	[A001]	A		Method 1: RT: 2.32 min , MI: 369 [M+H]	(1H, 300MHz, d6-dmso) 9.23 (s, 1H), 8.74 (d, 2H), 8.56 (d, 1H), 8.26 (d, 2H), 7.89 (d, 1H), 7.51 (d, 2H), 7.25-7.40 (m, 3H), 4.51 (dd, 2H), 3.95 (d, 1H), 3.34-3.46 (m, 1H), 3.13-3.24 (m, 2H), 2.97-3.03 (m, 1H).	3-phenyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
70	[A003]	B		Method 1: RT: 2.47 min, MI: 324.18 [M+H] ;	(1H, 300MHz, $CDCl_3$) 9.00 (1H, s), 8.76 (2H, d), 8.33 (2H, d), 8.20 (1H, s), 4.08 (3H, s), 3.89 (4H, t), 3.77 (4H, t).	4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine
71	[A001]	A	 [A030]	Method 1: RT: 2.72 min, MI: 317.26 [M+H]	(1H, 300MHz, d4-MeOH) 9.24 (1H, s), 8.69 (2H, dd), 8.54 (1H, d), 8.42 (2H, dd), 7.97 (1H, dd), 4.20 (1H, dd), 4.07-3.92 (4H, m), 3.36-3.29 (1H, m), 3.00-2.94 (1H, m), 2.80 (1H, d), 2.65 (1H, s, br).	3-ethynyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
72	[A003]	B	 [A034]	Method 1: RT: 5.36 min, MI: 414.22 [M+H]	(1H, 300MHz, d6-dmso) 8.82 (1H, s), 8.71 (2H, dd), 8.27 (1H, s), 8.10 (2H, dd), 7.34-7.28 (5H, m), 4.27 (1H, d), 4.04 (1H, d), 3.95-3.91 (1H, m), 3.91 (3H, s), 3.81-3.73 (1H, m), 3.59-3.52 (1H, m), 3.38-3.33 (1H, m), 3.04-2.96 (1H, dd), 2.91-2.75 (2H, m).	2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine

73	[A005]	B		Method 1: RT: 3.33 min , MI: 330 [M+H]		{1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]azetidin-3-yl}methanol
74	[A003]	B	 [A036]	Method 1: RT: 1.88 min, MI: 431.18 [M+H]		(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
75	[A005]	B		Method 1: RT: 3.73 min , MI: 342 [M+H]	(1H, 300MHz, d6-dmso) 8.78 (d, 2H), 8.35 (d, 1H), 8.33 (d, 2H), 7.89 (d, 1H), 4.88 (d, 1H), 4.21-4.27 (m, 2H), 3.85-3.91 (m, 1H), 3.64-3.72 (m, 2H), 1.93-1.99 (m, 2H), 1.57-1.65 (m, 2H).	1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidin-4-ol
76	[A003]	B	 [A036]	Method 1: RT: 2.08 min, MI: 431.14 [M+H]	(1H, 500MHz, d6-dmso) 8.81 (1H, s), 8.71 (2H, d), 8.28 (1H, s), 8.10 (2H, d), 7.46-7.45 (5H, m), 5.51 (1H, dd), 4.41 (1H, d, br), 4.02 (1H, m, br), 3.98 (3H, s), 3.20 (2H, t, br), 3.08 (1H, d), 2.99 (1H, d), 2.68 (1H, t).	(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
77	[A003]	B	 [A043]	Method 1: RT: 2.08 min , MI: 447.08 [M+H] (3:1 mixture of diastereomers)	(1H, 500MHz, d6-dmso) 8.79 (0.25H, s), 8.77 (0.75H, s), 8.70 (2H, dd), 8.27 (0.25H, s), 8.22 (0.75H, s), 8.11 (0.75H, d), 8.08 (0.25H, d), 7.99 (1H, d, br), 7.43 (2H, t, br), 7.23 (1.5H, t), 7.20 (0.5H, t), 5.65 (0.75H, d), 5.54 (0.25H, d), 4.54 (0.25H, t), 4.43 (0.75H, t), 3.99 (0.75H, s), 3.93 (2.25H, s), 3.22 (0.75H, t), 3.14 (0.25H, t), 3.94-2.92 (2H, m), 2.85 (1H, t), 2.74 (1H, m), 2.65 (1H, t).	(4-fluorophenyl)[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl]methanol

Synthesis of (S)-N^2,N^2-Dimethyl-3-phenyl-propane-1,2-diamine [A009]



[A010] [A011] [A012] [A009]

Synthesis of [(S)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A010] A mixture of Boc-L-phenylalaninol (25 g, 99.5 mmol), triphenylphosphine (31.3 g, 119.4 mmol), phthalimide (16.1 mg, 109.5 mmol) and THF (300 mL) was chilled to 0°C. A solution of diisopropyl azodicarboxylate (19.5 mL, 99.5mmol) in THF (100 mL) was added over 15 mins. The resulting pale yellow solution was allowed to return to room temperature over night. The reaction mixture was concentrated to approximately 100 mL then partitioned between ethyl acetate and water. A white precipitate formed which was collected by filtration. The organic layer was washed with more water (x1) then brine (x1), dried ($MgSO_4$), filtered and evaporated to yield the title compound as a second white solid and this was material was used in further reactions, without further analysis.

Synthesis of ((S)-1-Aminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A011] A mixture of [(S)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A010] (2 g, 5.25 mmol), 4M HCl in dioxane (5 mL, 20 mmol) and methanol (50 mL) was stirred at room temperature. The reaction mixture was loaded straight on to a methanol conditioned SCX-2 cartridge. The cartridge was washed with methanol (2col cols) and then eluted with 2N ammonia in methanol (2CV). LCMS analysis showed the target material to be predominantly in the methanol wash but also partially in the NH3 elution. The collected fractions were left to stand for a 3 days. After this time, needle like crystals started to form in the methanol fraction. The crystals were collected by filtration and dried in the vac oven to yield the title compound [A011] (400mg): NMR: (1H, 300MHz, d6-DMSO) 8.08 (2H, br s), 7.04 (4H, s), 7.35-7.29 (4H, m), 7.26-7.17 (1H, m), 3.83-3.66 (2H, m), 3.61 (1H, dd), 3.06 (1H, dd), 2.86 (1H, dd); LCMS method: 1, RT:2.50 min, MI 281 [M+H]

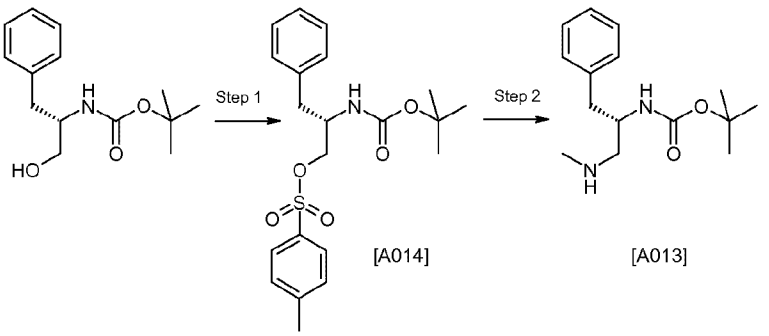
Synthesis of 2-((S)-2-Dimethylamino-3-phenyl-propyl)-isoindole-1,3-dione [A012]

A mixture of 2-((S)-2-Amino-3-phenyl-propyl)-isoindole-1,3-dione [A011] (200 mg, 0.71 mmol), formaldehyde (2 mL, xs) and formic acid (2 mL, xs) was heated to 100°C for 2 hours. The reaction mixture was concentrated under vacuum then partioned between 2M K_2CO_3 and DCM. The organic layer was washed with water then brine, passed through a phase separator and evaporated to yield the title compound [A012] (200mg) which was used without further purification: LCMS method: 1, RT: 2.42 min, MI 309 [M+H]

Synthesis of (S)-N^2,N^2-Dimethyl-3-phenyl-propane-1,2-diamine [A009]

A solution of 2-((S)-2-Dimethylamino-3-phenyl-propyl)-isoindole-1,3-dione [A012] (350mg), hydrazine monohydrate (66.1 ul, 1.36 mmol) and methanol (50 mL) was stirred at room temperature for 20 hours. The solvent was removed under vacuum to yield a white solid. This was then partitioned between 10% citric acid and isopropanol. The aqueous layer was filtered, basified with 2M NaOH, extracted into isoropanol, washed with brine, passed through a phase separator and evaporated to yield title compound [A009] (93mg): LCMS method: 1, RT:0.53 min, MI 179 [M+H]

Synthesis of ((S)-1-Methylaminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A013]



Synthesis of Synthesis of Toluene-4-sulfonicacid(S)-2-tert-butoxycarbonylamino-3-phenyl-propyl ester [A014]

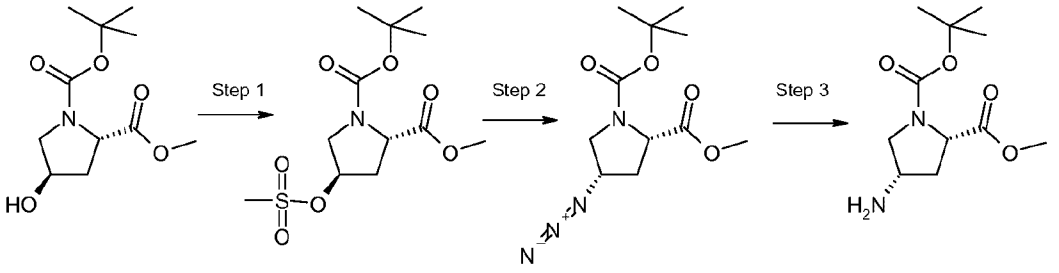
To a solution of Boc-L-phenylalaninol (0.5 g, 1.989 mmol) in DCM (10 mL) at 0°C was added triethylamine (0.83 mL, 5.968 mmol). The reaction mixture was stirred at this temperature for 5minutes. para-Toluenesufonyl chloride (2.188 mmol, 0.42 g) was added dropwise as a solution in DCM (5 mL), and the reaction mixture was allowed to warm up to

room temperature slowly. The reaction mixture stirred at room temperature for 4 hours. The reaction mixture was diluted with DCM (20 mL) and washed with water. Layers separated and the organic layer dried over anhydrous magnesium sulphate. The DCM was evaporated to dryness under reduced pressure to afford the title compound [A014] as a clear oil (0.8g). No further purification was carried out and the crude product was used immediately in the next step.

Synthesis of ((S)-1-Methylaminomethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A013]

Toluene-4-sulfonicacid(S)-2-tert-butoxycarbonylamino-3-phenyl-propyl ester [A014] (0.80 g, 1.973 mmol) was dissolved in THF (10 mL) and methyl amine (2N in THF, 10 mL) was added in one portion. The reaction mixture was stirred at 60°C overnight. The mixture was diluted with ethyl acetate and washed with brine. The layers were separated and the ethyl acetate dried over anhydrous magnesium sulphate. The solvent was removed under reduced pressure to afford the title compound [A013] as a clear oil. No further purification was carried out at this stage. Crude material was used directly in subsequent reactions without further purification.

Synthesis of (2S,4S)-4-Amino-2-hydroxymethyl-pyrrolidine-1-carboxylic acid tert-butyl ester [A015]



[A016] [A017] [A015]

Synthesis of (2S,4R)-4-Methanesulfonyloxy-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A016]

N-Boc-trans-4-hydroxy-L-proline methyl ester (12.28 mmol, 3 g), was dissolved in DCM (30 mL) and triethylamine (13.45 mmol, 1.87 mL) was added. The reaction was cooled to 0°C and methanesulfonyl chloride (24.46 mmol, 1.89mL) was added dropwise over 5 minutes. The reaction mixture was allowed to stir at this temperature for 45 minutes and then warmed

to room temperature for 2 hours. Brine was added and the layers were separated, the aqueous was extracted with dichloromethane (x2). The organics were washed with brine (x1), dried with $MgSO_4$, filtered and evaporated to yield the title compound as a clear oil (3.95g): NMR (1H, 300MHz, $CDCl_3$): 5.22 (m, 1H), 4.39 (m, 1H), 3.74 (s, 3H), 3.73 (m, 2H), 3.65 (s, 3H), 3.07 (s, 3H), 2.51 (m, 1H), 2.22 (m, 2H), 1.41 (d, 9H)

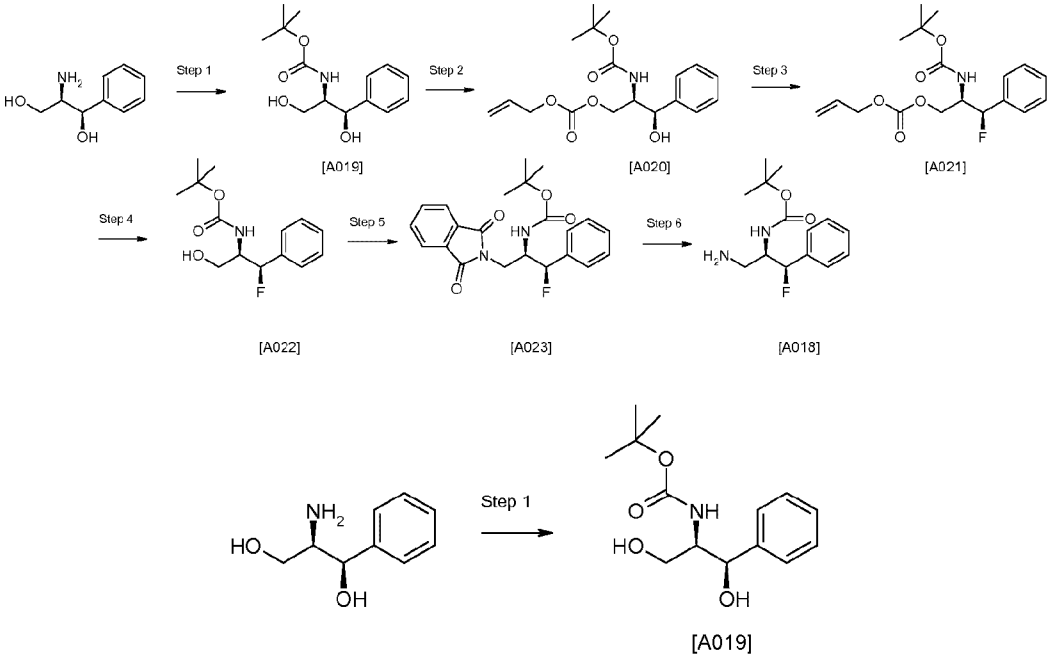
Step 2: Synthesis of (2S,4S)-4-Azido-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A017]

(2S,4R)-4-Methanesulfonyloxy-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A016] (12.28 mmol, 3.95 g), was dissoved in anhydrous DMF (20 mL) and sodium azide (61.14 mmol, 3.97 g) was added in one portion. The reaction was heated to 80°C for 3 hours. Upon cooling the reaction mixture was quenched with water and extracted with ethyl acetate (x3). The organics were washed with brine, dried with $MgSO_4$, filtered and evaporated to a colourless oil. Purified by flash column chromatography using 0 to 40% EtOAc / cyclohexane to yield the title compound [A017] (2.24g): NMR (1H, 300MHz, $CDCl_3$): 4.36 (m, 1H), 4.13 (m, 1H), 3.74 (s, 3H), 3.67 (m, 1H), 3.48 (dt, 1H), 2.47 (m, 1H), 2.14 (m, 2H), 1.43 (d, 9H)

Synthesis of (2S,4S)-4-Amino-2-hydroxymethyl-pyrrolidine-1-carboxylic acid tert-butyl ester [A015]

Water (5 mL) was added to a stirred solution of (2S,4S)-4-azido-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester [A017] (4.44 mmol, 1.2 g) and triphenylphosphine (9.32 mmol 2.45 g), in toluene (40 mL) and the reaction was heated to 60°C overnight. Upon cooling water was added and the layers separated. The aqueous was basified with 2M NaOH added and extracted twice with ethyl acetate, the organics combined, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to give the title compound (200 mg): NMR (1H, 300MHz, $CDCl_3$): 4.20 (m, 1H), 3.71 (s, 3H), 3.62 (m, 1H), 3.50 (m, 1H), 3.22 (m, 1H), 2.43 (m, 1H), 1.78 (m, 1H), 1.43 (d, 9H)

Synthesis of ((1R,2R)-1-Aminomethyl-2-fluoro-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A018]

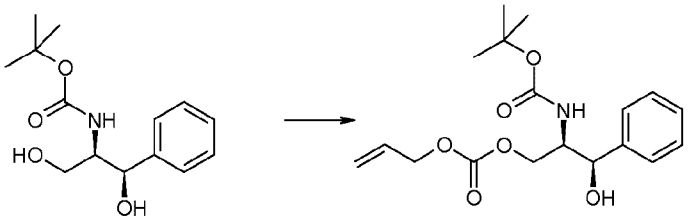


[A019]

Synthesis of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A019]

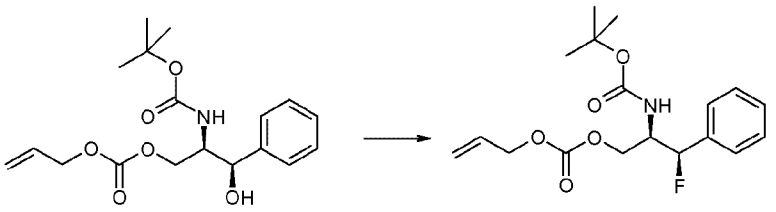
(1R,2R)-(-)-2-Amino-1-phenyl-propane-1,3-diol (5.98 mmol, 1.0 g) was dissolved in methanol (10 mL) and cooled to 0°C. A solution of di-tert-butyl dicarbonate in methanol (4mL) was added and the reaction was warmed to room temperature and stirred for 2 hours. The solvent was removed in vacuo and the product was purified by flash chromatography eluting with 0 to 70% EtOAc / cyclohexane to yield the title compound [A019] (1.20g): NMR (1H, 300MHz, $CDCl_3$): 7.29 (m, 5H), 5.19 (m, 1H), 4.96 (m, 1H), 3.35 (m, 1H), 2.66 (m, 1H), 1.33 (s, 9H); LCMS method: 1, RT:4.35 min, MI: no trace.

Synthesis of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A020]



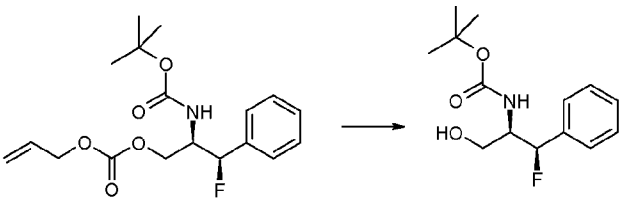
Allyl chloroformate (11.222 mmol, 1.35 g) was added dropwise to a strirred solution of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A019] (1.20 g, 4.48 mmol) and pyridine (15.711mmol, 1.27 mL) in DCM (50mL) at 0°C. The reaction was allowed to warm to room temperature and stirred for an hour. Water was added and the layers separated. The aqueous was extracted twice with DCM. The organics were combined, washed with brine, dried over anhydrous MgSO4, filtered and concentrated in vacuo. The crude product was purified by flash chromatography using 0 to 100% EtOAc / cyclohexane to yield the title compound [A020] (0.93g): NMR (1H, 300MHz, $CDCl_3$): 7.28 (m, 5H), 5.91 (m, 1H), 5.34 (d, 1H), 5.27 (d,1H), 4.99 (m, 1H), 4.84 (t, 1H), 4.61 (d, 2H), 4.27 (dd, 1H), 4.07 (dd, 1H), 4.01 (m, 1H), 3.09 (bs, 1H), 1.33 (s, 9H); LCMS: LC-MS17QC 94% 352+ [M+H] 5.17min

Synthesis of Carbonic acid allyl ester (2R,3R)-2-tert-butoxycarbonylamino-3-phenyl-3-(tetrahydro-pyran-2-yloxy)-propyl ester [A021]



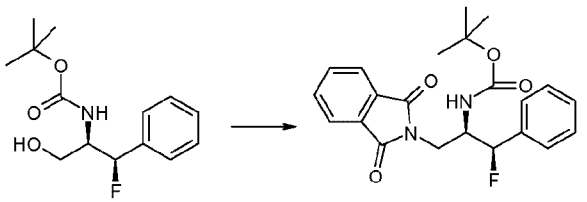
A solution of ((1R,2R)-2-Hydroxy-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A020] (1.42 mmol, 0.50 g) and DIPEA (4.97 mmol 0.865 mL) in DCM (20 mL) was added dropwise to a solution of (diethylamino)sulfur trifluoride (DAST) (4.97 mmol, 0.610 mL) at -78°C under nitrogen. The reaction was slowly warmed to room temperature and stirred for 2 hours. Water was added then extracted twice with DCM. The organics were combined, washed with brine, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo to yield the title compound [A021] which was was used directly in the next step without further purification: LCMS method: 1, RT:3.27 min, MI not seen.

Synthesis of ((1R,2R)-2-Fluoro-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A022]



To a solution of carbonic acid allyl ester (2R,3R)-2-tert-butoxycarbonylamino-3-fluoro-3-phenyl-propyl ester [A021] (2.0 mmol, 0.71 g) in anhydrous THF (15 mL) under nitrogen, was added tetrakis(triphenylphosphine)palladium(0) (0.08 mmol 0.093 g) and morpholine (3.014 mmol, 0.26 mL). The reaction was stirred at rt for 1h under a nitrogen atmosphere. Brine was added and the mixture extracted twice with ethyl acetate. The organics were combined, dried over $MgSO_4$, filtered and concentrated in vacuo. The product was purified by flash chromatography using 0 to 10% MeOH / DCM to yield the the title compound [A022] (0.19g): NMR (1H, 300MHz, $CDCl_3$): 7.32 (m, 5H), 5.68 (d, 1H), 5.11 (m, 1H), 3.99 (m, 1H), 3.86 (m, 1H), 3.67 (m, 1H), 1.39 (s, 9H)

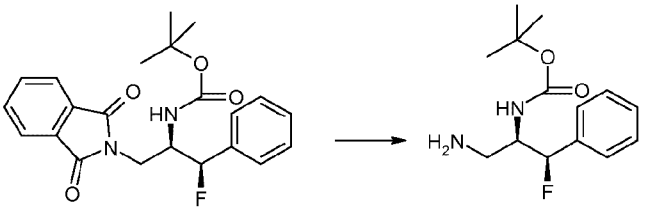
Synthesis of [(1R,2R)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-fluoro-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A023]



A solution of ((1R,2R)-2-Fluoro-1-hydroxymethyl-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A022] (0.705 mmol, 0.19 g), triphenylphosphine (0.988 mmol, 0.259 g) and phthalimide (0.988 mmol, 0.145 g) was cooled to 0°C and diisopropyl azodicarboxylate (DIAD) (0.988 mmol, 0.193 mL) was added dropwise. The reaction was allowed to warm to room temperature and stirred for 1 hour. The solvent was removed in vacuo and the residue was dissolved in DCM. 2M NaOH (aqueous solution) was added and the layers separated using a phase separator. The organic was concentrated in vacuo. The product was purified by flash chromatography using 0 to 30% EtOAc / cyclohexane to yield the title compound [A023] (0.28g): 1LCMS1; 98%, 399.15+ [M+H]+, 5.45min; NMR (1H, 300MHz, $CDCl_3$):

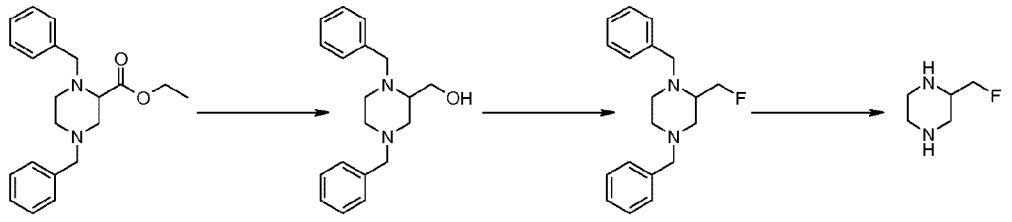
7.80 (m, 2H), 7.65 (m, 2H), 7.40 (m, 4H), 7.31 (m, 1H), 5.72 (dd, 1H), 5.06 (d, 1h), 4.47 (m, 1H), 3.83 (dd, 1H), 3.57 (dd, 1H), 1.20 (s, 9H)

Synthesis of ((1R,2R)-1-Aminomethyl-2-fluoro-2-phenyl-ethyl)-carbamic acid tert-butyl ester [A018]



[(1R,2R)-1-(1,3-Dioxo-1,3-dihydro-isoindol-2-ylmethyl)-2-fluoro-2-phenyl-ethyl]-carbamic acid tert-butyl ester [A023] (0.705 mmol, 0.28 g) was dissolved in methanol (5 mL) and Hydrazine monohydrate (0.916 mmol, 0.045 mL) was added. The reaction was stirred at room temperature for 1 hour then at 60°C overnight. Upon cooling the solvent was removed in vacuo and the residue dissolved in DCM. 2M NaOH (aqueous solution) was added and the mixture extracted twice. The organics were combined, dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The product was purified using an SCX-2 cartridge, applying the crude material as a DCM solution and washing with methanol and DCM. The material was then washed off the SCX-2 cartridge by washing with ammonia (2N in methanol) and the ammonia washes concentrated in vacuo to yield thetitle compound [A018] (0.12g): NMR (1H, 300MHz, $CDCl_3$): 7.34 (m, 5H), 5.62 (d, 1H), 5.19 (d, 1H), 3.89 (m, 1H), 2.83 (m, 2H), 1.40 (s, 9H)

Synthesis of 2-Fluoromethyl-piperazine [A024]



[A025] [A026] [A027] [A024]

(1,4-Dibenzyl-piperazin-2-yl)-methanol [A026]

A solution of 1,4-Dibenzyl-piperazine-2-carboxylic acid ethyl ester [A025] (3.7 g, 10.9 mmol) in THF (10 mL) was added dropwise to a suspension of $LiAlH_4$ (2.24 g, 59 mmol) in THF (20 mL) at 0°C. The reaction was warmed to room temperature and stirred overnight. The reaction was diluted with ether, cooled to 0°C and quenched with water (2.25 mL) and 2M NaOH (4.5 ml) and water (4.5 mL). The suspension was stirred for 15mins and anhydrous MgSO4 was added and stirred for a further 15 mins. The white solid was filtered off (celite) and the solvent remoevd in vacuo. The product was purified by flash chromatography using 0 to 100% EtOAc / cyclohexane to give the title compound [A026] (3.03g, 94 % yield). LCMS method: 1, RT:2.16 min, MI 297.23 [M+H]; NMR (1H, 300MHz, $CDCl_3$): 3.43 (m, 3H), 2.63 (m, 3H), 2.95 (m, 1H), 3.49 (m, 3H), 3.61 (d, 1H), 4.04 (dd, 2H),7.31 (m, 10H)

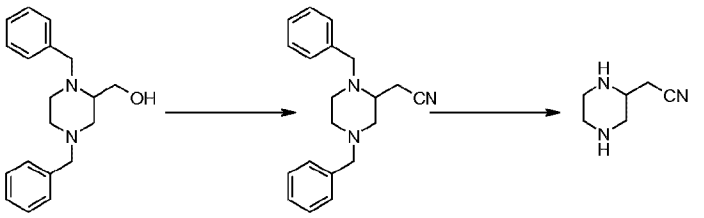
1,4-Dibenzyl-2-fluoromethyl-piperazine [A027]

(1,4-Dibenzyl-piperazin-2-yl)-methanol [A026] (1.09 g, 3.6 mmol) in DCM (5 mL) was added dropwise to a stirred solution of DAST (0.9 mL, 7.35 mmol) in DCM (10 mL) at 0°C. The reaction was warmed to room temperature and stirred overnight. Aqueous 2M NaOH (10 mL) was added the the layers seperated by phase seperator. The solvent was removed in vacuo and the product was purified by flash chromatography using 0 to 30% EtOAc / cyclohexane to give the title compound [A027] (0.42 g, 38% yield). LCMS method: 1, RT:5.88 min, MI 299.38 [M+H]; NMR (1H, 300MHz, $CDCl_3$): 2.28 (m, 3H), 2.50 (m, 2H), 2.70 (m, 2H), 2.83 (m, 1H), 3.49 (m, 3H), 4.11 (d, 1H), 4.53 (ddd, 1H), 4.68 (ddd, 1H), 7.25 (m, 10H)

2-Fluoromethyl-piperazine [A024]

1,4-Dibenzyl-2-fluoromethyl-piperazine [A027] (0.32g, 1.07 mmol) was dissolved in DCE (10 mL) and 1-Chloroethyl chloroformate (0.35 mL, 3.21 mmol) was added. The reaction was heated to reflux overnight. Upon cooling the solvent was removed in vacuo and the intermediate dicarabamate was purified by flash chromatpgraphy eluting with 0 to 50% EtOAc / cyclohexane. The residue was dissolved in methanol (10 mL) and heated to reflux for 1 hour. The solvent was rmoved in vacuo to give the title compound [A024] which was used in the next step and used without further purification

Synthesis of Piperazin-2-yl-acetonitrile [A028]



[A026] [A029] [A028]

(1,4-Dibenzyl-piperazin-2-yl)-acetonitrile [A029]

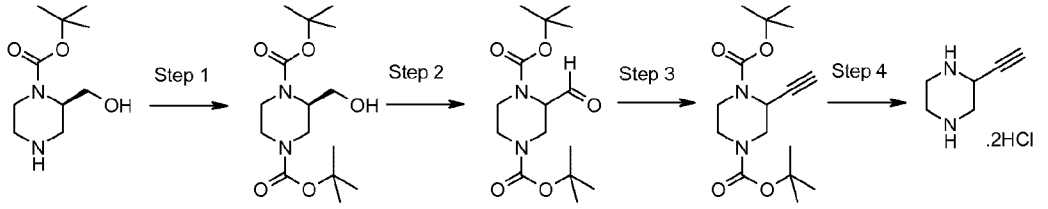
A solution of (1,4-Dibenzyl-piperazin-2-yl)-methanol [A026] (1g, 3.37 mmol) in DCM (10 mL) was added dropwise to a solution of thionyl chloride (0.32 mL, 4.4 mmol) in DCM (5 mL) and the reaction was stirred at room temperature ovenight. The solvent was removed in vacuo and water was added. The aqeous was extracted with ether then bascified with saturated Na2CO3. This was extracted twice with DCM, dried over anhydrous MgSO4, filtered and concentrated in vacuo and used crude in the next step and used without further purification.

To a refluxing solution of KCN (0.244g, 3.7 mmol) in water (10 mL) was added 1,4-Dibenzyl-2-chloromethyl-piperazine (0.91g, 2.9 mmol) in ethanol (10 mL) dropwise. The reaction was heated to reflux for 3 hours. Upon cooling the solvent was removed in vacuo and the residue was was taken up in DCM, washed with water, dried over MgSO4, filtered and concentrated in vacuo. The product was purified by flash chromatography using 0 to 40% EtOAc / cyclohexane, to give the title compound [A029] (0.52 g, 59 % yield). LCMS method: 1, RT:2.87 min, MI 306.26 [M+H]; NMR (1H, 300MHz, $CDCl_3$): 2.43 (m, 3H), 2.58 (m, 4H), 2.87 (dd, 1H), 3.00 (m, 1H), 3.48 (m, 3H), 3.80 (d, 1H), 7.28 (m, 10H).

Piperazin-2-yl-acetonitrile [A028]

(1,4-Dibenzyl-piperazin-2-yl)-acetonitrile [A029] (0.52 g, 1.7 mmol) was dissolved in DCE (10 mL) and 1-Chloroethyl chloroformate (0.55 mL, 5.1 mmol) was added. The reaction was heated to reflux for 2 days. Upon cooling the solvent was removed in vacuo and the intermediate dicarabamate was purified by flash chromatography eluting with 0 to 40% EtOAc / cyclohexane. The residue was dissolved in methanol (10 ml) and heated to reflux for an hour. The solvent was removed in vacuo to give clean product. NMR (1H, 300MHz, d6-dmso): 3.16 (m, 3H), 3.03 (t, 1H), 3.49 (m, 4H), 3.89 (m, 1H), 10.06 (m, 2H)

Synthesis of 2-Ethynyl-piperazine [A030]



[A031] [A032] [A033] [A030]

Synthesis of (R)-2-Hydroxymethyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A031].

To a stirred solution of (R)-1-Boc-2-Hydroxymethyl-piperazine (1 g, 4.62 mmol) and Na_2CO_3 (990 mg, 9.25 mmol) in a mixture of dioxane (8 ml) and water (2 ml) at 0 °C was added Di-tert-butyl dicarbonate and the reaction mixture warmed to room temperature. After 18 hours all solvents were removed *in vacuo* and the resulting residue partitioned between DCM and water. The DCM phase was passed through phase separation cartridge and evaporated to provide a white solid. Purification by column chromatography (0-50% EtOAc:cyclohexane) gave the title compound [A031] as a white solid (1.26g, 86%). 1H-NMR (1H, 300MHz, $CDCl_3$): 4.17 (2H, s, br), 3.93 (1H, s, br), 3.84 (1H, d, br), 3.59 (2H, s, br), 2.95 (3H, s, br), 1.46 (18H, s).

Synthesis of 2-Formyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A032]

A solution of oxalyl chloride (165 µl, 1.90 mmol) in DCM (5 ml) was cooled to -78 °C. DMSO (270 µl, 3.79 mmol) was added dropwise and the reaction mixture stirred for 15mins. A solution of (R)-2-Hydroxymethyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A031] (500 mg, 0.58 mmol) in DCM (1 ml) was added dropwise and the reaction mixture stirred for 1 hour. Triethylamine (1.1 ml, 7.90 mmol) was added and the reaction mixture warmed to room temperature. Saturated $NaHCO_3$ was added, the layers separated and the organic phase collected and evaporated to give the title compound [A032] as a white powder (480mg, 97%). 1H-NMR (1H, 300MHz, $CDCl_3$): 9.58 (1H, s), 4.63-4.45 (2H, m, br), 3.95-3.79 (2H, m, br), 3.15-3.11 (2H, m, br), 2.88 (1H, d, br), 1.44 (18H, s).

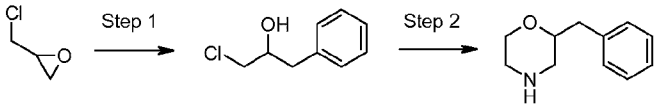
Synthesis of 2-Ethynyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A033]

To a stirred solution of 2-Formyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A032] (480 mg, 0.530 mmol) and K_2CO_3 (425 mg, 3.06 mmol) in MeOH (20 ml) was added Dimethyl (1-diazo-2-oxopropyl)phosphonate (350 mg, 1.83 mmol). After 18 hours the solvent was removed *in vacuo* and the resulting residue partitioned (DCM:water). The organic phase was separated and concentrated to provide the title compound [A033] as a white solid (430mg, 91%).1H-NMR (1H, 300MHz, $CDCl_3$): 4.88 (1H, s, br), 4.25-4.01 (2H, m, br), 3.80 (1H, d, br), 3.18 (1H, t, br), 3.02-2.74 (2H, m), 2.23 (1H, d), 1.47 (18H, s).

Synthesis of 2-Ethynyl-piperazine [A030]

2-Ethynyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A033] (430 mg, 1.39 mmol) was stirred in 4N HCl:dioxane (1 ml) for 4 hours. A pale yellow solid (226 mg, 89%) was collected by filtration and washed with Et_2O then dried in a vacuum oven at 40 °C to yield the title compound [A030]: 1H-NMR (1H, 300MHz, d6-dmso): 4.57 (1H, dt), 4.04 (1H, d), 3.63 (1H, dd), 3.42-3.23 (5H, m).

Synthesis of 2-Benzyl-morpholine [A034]



[A035] [A034]

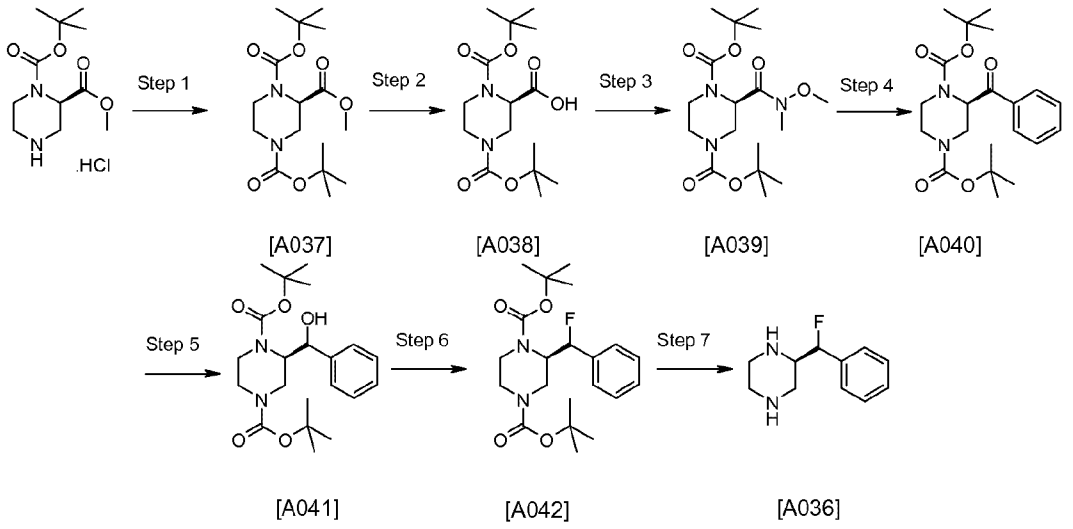
Synthesis of 1-Chloro-3-phenyl-propan-2-ol [A035]

To a stirred solution of Phenyl magnesium bromide (3M in Et_2O, 4.4ml, 13mmol) in Et_2O (14 ml) at 0 °C was added CuI (210mg, 1.08 mmol). Epichlorohydrin (1g, 10.8mmol) in Et_2O (14 ml) was then added and the reaction mixture allowed to warm to room temperature then stirred for 2 hours. Sat. NH_4Cl was added and the solution diluted with water then extracted with EtOAc (x2). The combined organics were washed with brine, dried over $MgSO_4$ and concentrated. Purification by column chromatography (0-20% Et_2O:cyclohexane) provided the title compound [A035] as a colourless oil (1.66g, 90%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.36-7.22 (5H, m), 4.11-4.01 (1H, m), 3.59 (1H, dd), 3.50 (1H, dd), 2.90 (2H, d), 2.18 (1H, d).

Synthesis of 2-Benzyl-morpholine [A034]

To a stirred solution of NaOH (1.63 g, 40.8 mmol) in water3.5 ml) was added 1-Chloro-3-phenyl-propan-2-ol [A035] (1.16 g, 6.8 mmol) in MeOH (7 ml). After 5 min 2-Aminoethane hydrogen sulphate (3.84 g, 27.2mmol) was added and the reaction mixture stirred at 40 °C for 2 hours. NaOH (powdered, 1.63g, 40.8mmol) and PhMe (18 ml) were then added and the reaction heated to 65 °C for 18 hours. Dilution with water (10 ml), was followed by extraction with PhMe (x2). The combined organics were washed (water then brine), dried and concentrated. Purification by column chromatography (0-10% MeOH:DCM) provided the title compound as a colourless oil (360 mg, 30%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.31-7.19 (5H, m), 3.86 (1H, dd), 3.70-3.54 (2H, m), 2.92-2.77 (4H, m), 2.67-2.55 (2H, m).

Synthesis of (R)-2-(Fluoro-phenyl-methyl)-piperazine [A036]



Synthesis of (R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester 2-methyl ester [A037]

To a stirred suspension of (R)-1-N-Boc-piperazine-2-carboxylic acid methyl ester hydrochloride (2 g, 7.12 mmol) and Na_2CO_3 (2.26 g, 21.4 mmol) in dioxane (16ml) and water (4 ml) at 0 °C was added Di-tert-butyl-dicarbonate (1.55 g, 7.12 mmol). After 18 hours all solvents were removed *in vacuo* and the resulting residue partitioned between DCM and water. The organic phase was collected and evaporated to give a colourless oil. Purification by column chromatography (0-30% EtOAc:cyclohexane) gave the title compound [A037] as

a white powder (2.33 g, 95%). 1H-NMR (1H, 300MHz, $CDCl_3$): 5.30 (1H, s), 4.72 (1H, s, br), 4.54 (1H, t, br), 4.08-3.80 (1H, m), 3.73 (3H, s), 3.27-2.73 (3H, m), 1.44 (18H, s).

Synthesis of (R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester [A038]

(R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester 2-methyl ester [A037] (2.33 g, 6.77 mmol) and KOH (1.14 g, 20.3 mmol) were heated to reflux in EtOH (50 ml) for 18 hours. Having cooled to room temperature, solvents were removed *in vacuo* and the residue purified by column chromatography (0-10% MeOH:DCM; 0.1% TEA) to provide the title compound [A038] as a pale orange foam (2.1 g, 94%). 1H-NMR (1H, 300MHz, $CDCl_3$): 4.66-4.50 (2H, m, br), 3.96-3.74 (2H, m, br), 3.47 (1H, s), 3.23 (1H, s, br), 2.85 (1H, s, br), 1.42 (18H, s).

Synthesis of (R)-2-(Methoxy-methyl-carbamoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A039]

(R)-Piperazine-1,2,4-tricarboxylic acid 1,4-di-tert-butyl ester [A038] (2.10 g, 6.36 mmol), O-(7-Azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (2.9 g, 7.63 mmol), N,O-Dimethylhydroxylamine hydrochloride (750 mg, 7.6 3mmol) and TEA (2.2 ml, 15.3 mmol) were stirred in DMA for 18 hours. The reaction mixture was then partitioned between EtOAc and NaOH (1M), and the aqueous phase re-extracted with EtOAc. The combined organics were dried over $MgSO_4$ and concentrated. Purification by column chromatography (0-50% EtOAc:cyclohexane) gave the title compound [A039] as a viscous pale yellow oil (2.15 g, 91%). 1H-NMR (1H, 300MHz, $CDCl_3$): 5.30 (1H, s), 4.86-4.71 (1H, m), 4.47-4.32 (1H, m), 4.06-3.75 (2H, m), 3.85 (3H, s), 3.18 (3H, s), 3.18-2.85 (2H, m), 1.45 (9H, s), 1.42 (9H, s). LCMS method: 1, RT:3.46 min, MI 374.26 [M+H].

Synthesis of (R)-2-Benzoyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A040]

To a stirred solution of (R)-2-(Methoxy-methyl-carbamoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A039] (500 mg, 1.34 mmol) in THF at 0 °C was added Phenylmagnesium chloride solution (3.4 ml, 6.7mmol, 2.0 M in THF) and the reaction mixture allowed to warm to room temperature. Having stirred for 4 hours the solution was quenched (1N NaOH) and solvents removed *in vacuo*. The residue was partitioned between DCM and Rochelles salt (10% aq.) and the organic phase separated and aqueous re-extracted with DCM. The combined organics were then dried ($MgSO_4$) and concentrated. Purification by column chromatography (0-50% EtOAc:cyclohexane) provided the title compound [A040] as a white

solid (416 mg, 80%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.89 (2H, s, br), 7.57 (1H, s, br), 7.47 (2H, s, br), 5.53 (0.6H, s, br), 5.35 (0.4H, s, br), 4.53-4.38 (1H, m, br), 4.06 (0.6H, m, br), 3.87-3.80 (1.4H, m, br), 3.67-3.53 (1H, m, br), 3.41-3.29 (1H, m, br), 2.94-2.81 (1H, m, br), 1.55-1.12 (19H, m, br); LCMS method: 1, RT:3.75 min, MI 391.32 [M+H]

Synthesis of (R)-2-(Hydroxy-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A041]

To a stirred suspension of (R)-2-Benzoyl-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A040] (220 mg, 0.553mmol) in MeOH (4 ml) was added sodium borohydride (41 mg, 1.11 mmol). After 2 hours the reaction mixture was partitioned between EtOAc and water, the organic phase separated and concentrated *in vacuo* to give the title compound [A041] as a white crystalline solid (210 mg, 97%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.43-7.26 (5H, m), 4.74 (1H, s, br), 4.31-3.65 (4H, m), 3.25-2.81 (3H, m), 1.55-1.46 (18H, m), 1.13 (1H, s, br); LCMS method: 1, RT:3.86 min, MI 393.32 [M+H]

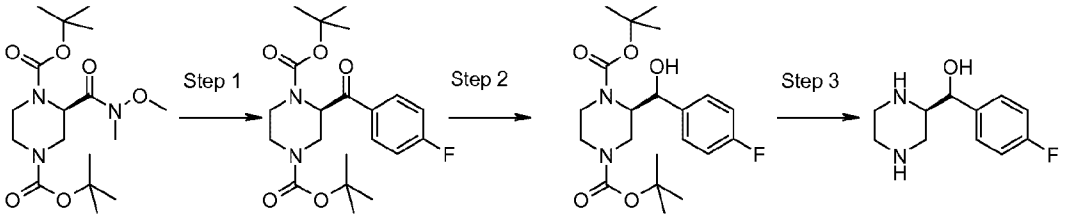
Synthesis of (R)-2-(Fluoro-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A042]

To a stirred solution of (R)-2-(Hydroxy-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A041] (210 mg, 0.535 mmol) in $CHCl_3$ (3 ml) at 0 °C was added (Diethylamino)sulfur trifluoride (330 µl, 2.68 mmol). After 2 hours the reaction mixture was quenched with ice, basified with $NaHCO_3$ (to pH8), then the product extracted into DCM, which was evaporated to give a colourless oil. Purification was achieved by column chromatography (0-50% EtOAc:cyclohexane) to provide the title compound [A042] as a white solid (85mg, 40%). 1H- NMR (1H, 300MHz, $CDCl_3$): 7.34 (5H, m, br), 5.53 (1H, d, br), 4.38-3.84 (4H, m, br), 3.08-2.84 (3H, m, br), 1.49 (9H, s, br), 1.25 (9H, s, br); LCMS method: 1, RT:3.68 min, MI 295.21 [M+H]

Synthesis of (R)-2-(Fluoro-phenyl-methyl)-piperazine [A036]

(R)-2-(Fluoro-phenyl-methyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A042] (85 mg, 0.215 mmol) was stirred in 4N HCl:dioxane (2 ml). After 2 hours the solution was dissolved in MeOH and loaded onto an SCX cartridge which was washed with MeOH followed by 2N NH_3:MeOH. Evaporation provided the title compound [A036] as a yellow gum (35mg, 83%). 1H-NMR (1H, 300MHz, d4-MeOH): 7.49-7.43 (5H, m), 5.25 (1H, d), 3.85 (1H, dd), 3.79-3.726(1H, m), 3.20-3.14 (2H, m), 3.00-2.82 (3H, m).

Synthesis of (4-Fluoro-phenyl)-(R)-piperazin-2-yl-methanol [A043]



[A039] [A044] [A045] [A043]

Synthesis of (R)-2-(4-Fluoro-benzoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A044]

To a stirred solution of (R)-2-(Methoxy-methyl-carbamoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A043] (1.15 g, 3.08 mmol) in THF (24 ml) was added 4-Fluorophenylmagnesium bromide solution (2.0M in Et_2O, 7.7 ml, 15.4 mmol) and the reaction mixture allowed to warm to room temperature. Having stirred for 4 hours the reaction was quenched (1N NaOH) and solvents removed *in vacuo*. The residue was partitioned between DCM and Rochelles salt (10% aq). The organic phase was separated and aqueous phase re-extracted with DCM. Evaporation of the combined organics followed by purification by column chromatography (0-50% EtOAc:cyclohexane) gave the title compound [A044] as a pale yellow oil (800mg, 64%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.94 (2H, s, br), 7.15 (2H, s, br), 5.47 (1H, m, br), 4.48-4.32 (1H, m, br), 4.07-4.03 (1H, m, br), 3.91-3.76 (1H, m, br), 3.61-3.51 (1H, m, br), 3.43-3.31 (1H, m, br), 3.18-3.24 (1H, m, br), 1.56-1.17 (18H, m, br); LCMS method: 1, RT:3.79 min, MI 409.32 [M+H]

Synthesis of (R)-2-[(4-Fluoro-phenyl)-hydroxy-methyl]-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A045]

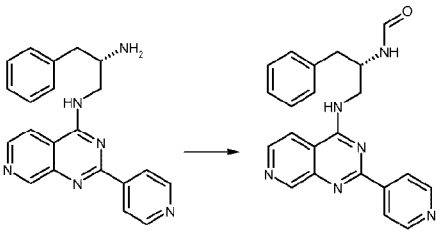
To a stirred solution of (R)-2-(4-Fluoro-benzoyl)-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A044] (520 mg, 1.28 mmol) in MeOH (8 ml) was added sodium borohydride at 0 °C and the reaction mixture allowed to warm to room temperature. After 2 hours the reaction mixture was partitioned between EtOAc and water, the organic phase separated and concentrated *in vacuo* to give a pale yellow oil. Purification by column chromatography (0-50% EtOAc:cyclohexane) provided the title compound [A045] as a white crystalline solid

(330mg, 63%). 1H-NMR (1H, 300MHz, $CDCl_3$): 7.41-7.08 (5H, m), 4.74 (1H, m), 4.27-3.93 (3H, m), 3.64 (1H, m), 3.23-2.84 (1H, m), 1.45 (18H, m), 1.18 (1H, s, br).

Synthesis of (4-Fluoro-phenyl)-(R)-piperazin-2-yl-methanol [A043]

(R)-2-[(4-Fluoro-phenyl)-hydroxy-methyl]-piperazine-1,4-dicarboxylic acid di-tert-butyl ester [A045] (330 mg, 0.808 mmol) was stirred in 4N HCl:dioxane (2 ml). After 2 hours the solution was dissolved in MeOH and loaded onto an SCX cartridge which was washed with MeOH followed by 2N NH_3:MeOH. Evaporation provided the title compound [A043] as a yellow gum which was used without further purification (170mg, 100%).

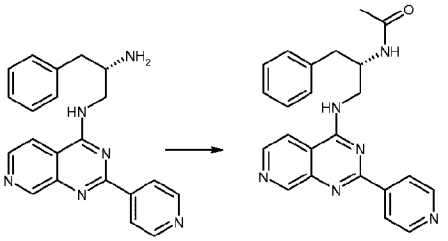
Synthesis of N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide [78]



[6] [78]

A mixture of (S)-3-Phenyl-N^1-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [6] (70 mg, 0.21 mmol) and ethylformate (1.5 mL, 18.6 mmol) was heated in the microwave at 100°C for 1 hour. The reaction mixture was concentrated under vacuum, redissolved in methanol then loaded onto a methanol conditioned SCX-2 cartridge (5g). The cartridge was washed with methanol (2ColVols) then eluted with 2N NH3 in methanol (2CV). The ammonia washes were evaporated to yield the title compound [78]: LCMS method: 1, RT:3.87 min, MI 385 [M+H]; NMR: (1H, 300MHz, d6-dmso) 9.17 (1H, s), 8.90-8.87 (1H, br t), 8.73 (2H, d), 8.63 (1H, d), 8.25 (2H, dd), 8.14 (1H, d), 8.04 (1H, br d), 7.97 (1H, br s), 7.327.20 (5H, m), 4.55-4.46 (1H, m), 3.98-3.90 (1H, m), 3.70-3.62 (1H, m), 3.00-2.93 (1H, dd), 2.85-2.77 (1H, dd)

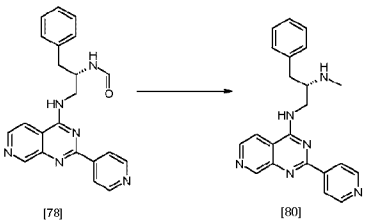
Synthesis of N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-acetamide [79]



[6] [79]

To a stirred solution of (S)-3-Phenyl-N^1-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [6] (70 mg, 0.21 mmol), DIPEA (73 ul, 0.42mmol) and anhydrous DCM (5 mL) at room temperature was added acetic anhydride (29 µl, 0.31 mmol). The reaction mixture was concentrated under vacuum then redissolved in methanol plus formic acid (2 drops) and loaded onto a methanol conditioned SCX-2 cartridge (5 g). The cartridge was washed with methanol (2CV) then eluted with 2N NH_3 in methanol (2CV). The ammonia washes were evaporated to yield the title compound [79]: LCMS method: 1, RT:3.92 min, MI 399 [M+H]; NMR: (1H, 300MHz, d6-dmso) 9.17 (1H, s), 8.85 (1H, br t), 8.72 (2H, dd), 8.63 (1H, d), 7.85 (1H, dd), 7.30-7.17 (5H, m), 4.43-4,33 (1H, m), 4.01-3.92 (1H, m), 3.63-3.55 (1H, m), 2.90 (1H, dd), 2.80 (1H, dd), 1.70 (3H, s)

Synthesis of methyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine [80]

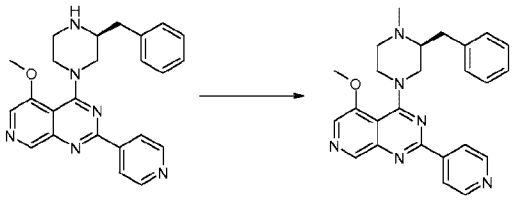


[78] [80]

A stirred suspension of lithium aluminium hydride (19 mg, 0.5 mmol) in anhydrous THF (2.5 mL) was chilled to 0 °C. N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide [78] (40 mg, 0.1 mmol) in THF (2.5 mL) was added over five minutes. The reaction mixture was allowed to warm to room temperature and stirred for 18 h. A further portion of lithium aluminium hydride (10.5mg, 0.28mmol) was added to the reaction mixture and stirring continued at room temperature for 18 hours. Another portion of lithium aluminium hydride (30mg, 0.79mmol) was added to the reaction mixture and stirring continued at room temperature for a further 18 hours. This procedure was repeated on a

second batch of N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide [78] (40 mg, 0.234 mmol) and the crude reaction mixture combined and diluted with ether (20 mL), cooled to 0 °C and quenched by drop-wise addition of water (approx 150 µL), NaOH (approx 300 µL of a 2M solution) and water (approx 300 µL of a 2M solution) again. $MgSO_4$ was added and the mixture filtered and concentrated by rotary evaporation. The crude residue was purified by preparative HPLC (method A). The appropriate fractions were combined, the solvent evaporated and the residue was dissolved in MeOD resulting in precipitation of an impurity which was removed by filtration to give the title compound [80] (2.5 mg). LCMS method: 1, RT:2.39 min, MI 371 [M+H]. ^{1}H NMR (1H, 300MHz, d6-dmso) 9.13 (1H, s), 8.64 – 8.62 (2H, m), 8.54 (1H, d), 8.21 – 8.19 (2H, m), 7.99 (1H, d), 7.32 – 7.21 (5H, m), 3.97 – 3.91 (1H, m), 3.78 – 3.71 (1H, m), 3.29 – 3.22 (1H, m), 3.05 – 2.99 (1H, m), 2.77 – 2.70 (1H, m).

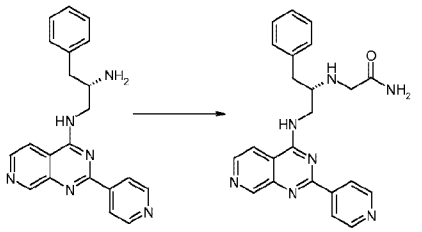
Synthesis of (2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1-methylpiperazine; formic acid [81]



[30] [81]

A stirred solution of 4-((S)-3-Benzyl-piperazin-1-yl)-5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [30] in CH_2Cl_2 (2 mL) was prepared. Paraformaldehyde (55 mg), acetic acid (6 mL, 0.121 mmol) and $CNBH_3$ (180 mg of MP-$CNBH_3$ with 2 mmol/g loading, 0.360 mmol) were added and the reaction was shaken at room temperature overnight. The resin was filtered off and the product was loaded onto a CSX cartridge, washing with methanol and eluting with ammonia in methanol. The ammonia fraction was concentrated and the residue purified then by prep LCMS. The appropriate fractions were combined and concentrated to give the title compound [81]. LCMS method: 1, RT:2.74 min, MI 427.22 [M+H]; ^{1}H NMR (1H, 300MHz, $CDCl_3$) 8.95 (s, 1H), 8.73 – 8.71 (d, 2H), 8.29 (s, 1H), 8.13 - 8.11 (d, 2H), 8.06 (s, 1H), 7.37 – 7.35 (m, 3H), 7.22 – 7.19 (m, 2H), 4.28 (d, 1H), 4.07 (d, 1H), 3.82 (s, 3H), 3.72 – 3.63 (m, 1H), 3.34 (dd, 1H), 3.23 – 3.15 (m, 2H), 2.76 – 2.69 (m, 1H), 2.63 (s, 3H), 2.60 – 2.51 (m, 2H).

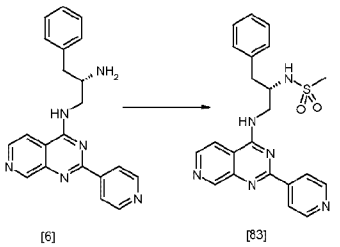
Synthesis of 2-{[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amino}acetamide [82]



[6] [82]

A mixture of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol), 2-Bromoacetamide (38.5 mg, 0.28 mmol), and potassium carbonate (77.5 mg, 0.56 mmol) in DMF (5 mL) was stirred at room temperature for 3 days. A further portion of 2-Bromoacetamide (38.5 mg, 0.28 mmol) was added and the reaction mixture stirred for a further 24 h. The solvent was removed by rotary evaporation and the residue dissolved in methanol (2 mL), filtered then purified by preparative HPLC (method B). The appropriate fractions were combined, evaporated, triturated with diethyl ether and dried in the vac oven to give the title compound [82]: LCMS method: 1, RT:4.49 min, MI 414 [M+H]; ^{1}H NMR (1H, 300MHz, d6-dmso) 9.16 (1H, s), 9.00 (1H, br m), 8.72 – 8.70 (2H, m), 8.64 – 8.62 (1H, m), 8.23 – 8.21 (1H, m), 8.10 – 8.08 (2H, m), 7.32 – 7.26 (5H, m), 7.03 (1H, br s), 3.89 – 3.81 (1H, m), 3.53 – 3.45 (1H, m).

Synthesis of N-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)methanesulfonamide [83]

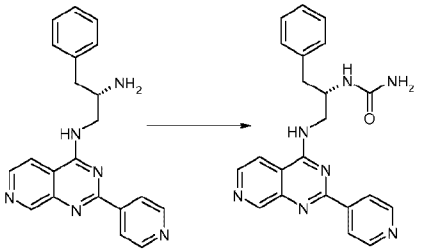


[6] [83]

To a solution of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol) and DIPEA (98 mL, 0.56 mmol) in CH_2Cl_2 (10 mL) at room temperature was added methane sulfonyl chloride (22 mL, 0.28 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with water and the organic phase separated, dried over $MgSO_4$ and purified by column chromatography on silica, eluting with

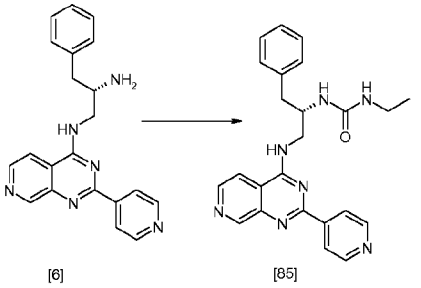
CH_2Cl_2 containing 0 – 10% Methanol. The appropriate fractions were combined and concentrated to give the title compound [83]: LCMS method: 1, RT: 4.04 min, MI 435 [M+H]; ^{1}H NMR (1H, 300MHz, d6-dmso) 9.18 (1H, s), 8.92 (1H, br t), 8.73 – 8.71 (2H, m), 8.65 (1H, d), 8.22 – 8.20 (2H, m), 8.16 (1H, d), 7.39 (1H, br s), 7.33 – 7.31 (4H, m), 7.30 – 7.24 (1H, m), 3.93 – 3.88 (2H, m), 3.69 – 3.61 (1H, m), 2.99 – 2.92 (1H, m), 2.83 – 2.76 (1H, m), 2.35 (3H, s).

Synthesis of (1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea [84]



A mixture of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol), potassium cyanate (227 mg, 2.8 mmol), and acetic acid (4 mL) in water (4 mL) was stirred at 50 °C for 3 hours. A further portion of potassium cyanate (227 mg, 2.8 mmol) was added and the reaction mixture heated in a sealed tube in the microwave at 100 °C for 30 min. The reaction mixture was concentrated under vacuum then partitioned between ethyl acetate and water. The target material was found to partially precipitate on the internal surface of the seperating funnel. This solid was collected and combined with the organic layer which was evaporated to dryness then dissolved in DMSO / Methanol (1 mL), the target material started to precipitate, water (2 mL) was added and the solid was collected by filtration then dried in the vac oven to give (the title compound [84]: LCMS method: 1, RT:4.54 min, MI 398 [M+H];. ^{1}H NMR (1H, 300MHz, d6-dmso) 9.18 (1H, s), 8.99 (1H, br t), 8.74 – 8.72 (2H, m), 8.64 (1H, d), 8.28 – 8.25 (2H, m), 8.12 (1H, d), 7.32– 7.19 (5H, m), 6.05 (1H, d), 5.48 (2H, s), 4.29 – 4.23 (1H, m), 3.88 – 3.80 (1H, m), 3.69 – 3.60 (1H, m), 2.94 – 2.88 (1H, m), 2.83 – 2.76 (1H, m).

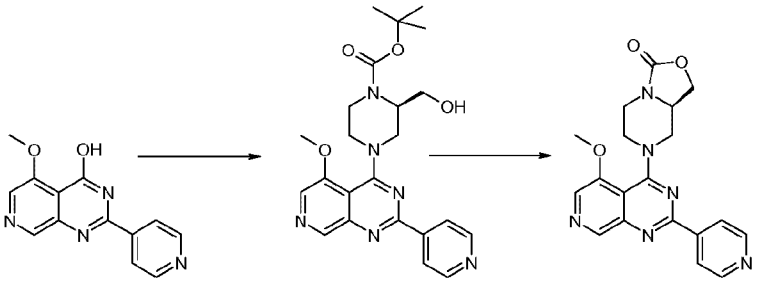
Synthesis of 3-ethyl-1-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea [85]



[6] [85]

A solution of N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine [6] (100 mg, 0.28 mmol) and ethyl isocyanate (19 mg, 0.27 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature for 1 h. The reaction mixture was concentrated by rotary evaporation and the residue purified by column chromatography on silica, eluting with CH_2Cl_2 containing 0 – 10% MeOH. The appropriate fractions were combined, evaporated and the residue triturated with diethyl ether then dried in the vacuum oven to give the title compound [85]. LCMS method: 1, RT:4.20 min, MI 428 [M+H]; ^{1}H NMR (1H, 300MHz, d6-dmso) 9.17 (1H, s), 8.94 (1H, br t), 8.74 – 8.72 (2H, m), 8.64 (1H, d), 8.28 – 8.24 (2H, m), 8.13 (1H, d), 7.32– 7.20 (5H, m), 5.86 (1H, d), 5.79 (1H, t), 4.29 – 4.22 (1H, m), 3.90 – 3.83 (1H, m), 3.70 – 3.61 (1H, m), 2.94 – 2.77 (2H, m), 0.84 (3H, t).

Synthesis of (3aR)-5-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-1H-[1,3]oxazolo[3,4-a]piperazin-1-one [86]



[A003] [A046] [86]

(R)-2-Benzyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A046]

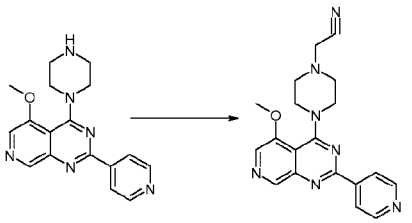
To a solution of 2-Pyridin-4-yl-pyrido[2,3-d]pyrimidin-4-ol [A003] (0.2g, 0.78 mmol) in DMA 93 mL), 2,4,6-Triisopropylbenzenesulfonyl chloride (0.26 g, 0.86 mmol), Et_3N (0.22 mL, 1.57 mmol) and DMAP (10 mg) were added successively. The mixture was stirred at rt

for 2h and (R)-2-Hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester (0.2g, 0.94 mmol) was added. The reaction was stirred overnight and the solvent was removed under reduced pressure. The product was purified by flash chromatography using 0 to 8% MeOH / DCM to give the title compound [A046] (0.14g, 39% yield). LCMS method: 1, RT:4.41 min, MI 453.27 [M+H].

(3aR)-5-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-1H-[1,3]oxazolo[3,4-a]piperazin-1-one [86]

A solution of (R)-2-Hydroxymethyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A046] (20 mg, 0.044 mmol) in CH_2Cl_2 was added drop-wise to a stirred solution of DAST (11 mL, 0.088 mmol) in CH_2Cl_2 (3 mL) at 0 °C. The reaction mixture was warmed to room temperature and stirred overnight. Aqueous $NaHCO_3$ was added the organic phase separated, loaded onto a SCX cartridge, washed with MeOH and eluted with ammonia in methanol. The product was purified purified by preparative HPLC (method A) . The appropriate fractions were combined and concentrated to give the title compound [86]: LCMS method: 1, RT:2.95 min, MI 379 [M+H]; ^1H, NMR (1H, 300MHz, $CDCl_3$): 9.03 (s, 1H), 8.60 (d, 2H), 8.29 (d, 2H), 8.24 (s, 1H), 4.50 (m, 2H), 4.18 (d, 1H), 4.09 (m, 4H), 3.97 (dd, 1H), 3.31 (td, 1H), 3.16 (td, 1H), 3.10 (dd, 1H).

Example [87]: Synthesis of 2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}acetonitrile [87]



[31] [87]

To a stirred mixture of 1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [31] (90 mg, 0.28 mmol) and NEt_3 (78 mL, 0.56 mmol) in DMA (2 mL) was added Chloroacetonitrile (26 mL, 0.42 mmol) and the mixture was stirred at room temperature overnight. The crude reaction mixture was diluted with water and extracted with CH_2Cl_2 (2 x 5 mL), the organic extracts were combined washed with sat $NaHCO_3$ (2 x 10 mL) brine (10 mL) dried $MgSO_4$ filtered and evaporated to give a brown oil which was purified by SXC-2

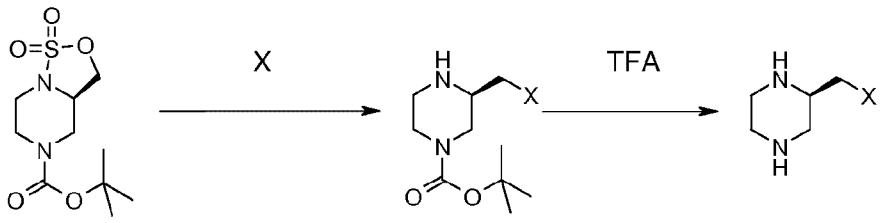
ion exchange (1 g) to give the title compound [87] as a pale yellow solid (0.085 g, 90% yield). LCMS method: 1, RT:4.90 min, MI 362 [M+H]; ^{1}H NMR (1H, 300MHz, $CDCl_3$): 9.02 (1H, s), 8.97 – 8.77 (2H, m), 8.36 – 8.34 (2H, m), 8.22 (s, 1H), 4.11 (3H, s), 3.81 (4H, br t), 3.65 (2H, s), 2.83 (4H, br t).

General synthesis of 2-substituted-piperazine derivatives of general formula [F-008b]

Scheme A2

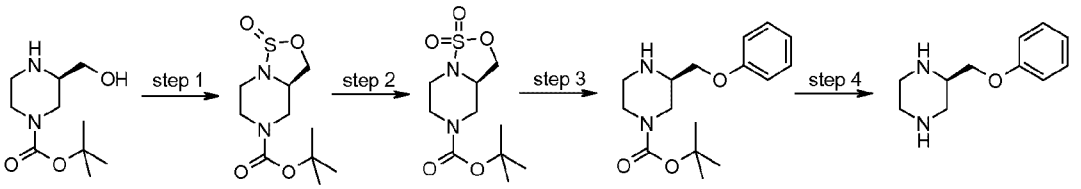
2-substituted piperazine derivatives of general formula [F-008b] were prepared by the reaction of (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A049] with a phenol in the presence of a strong base such as sodium hydride or potassium cyanide in a polar aprotic solvent such as DMF to give the 2-substituted piperazine derivatives of general formula [F-008a]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release resin, followed by chromatographic purification. The N-Boc derivatives of general formula [F-008a] were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC to give the 2-substituted-piperazine derivatives of general formula [F-008b].

Scheme A2



[A049] [F-008a] [F-008b]

Syntheisis of (R)-2-Phenoxymethyl-piperazine [A047]



[A048] [A049] [A050] [A047]

(R)-1-Oxo-tetrahydro-2-oxa-1λ^4-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048]

A solution of (R)-3-Hydroxymethyl-piperazine-1-carboxylic acid tert-butyl ester (5.00 g, 23.118 mmol) in CH_2Cl_2 (330 mL) was prepared and cooled to 0 °C. Imidazole (6.295 g, 92.472 mmol) and triethylamine (7.06 mL, 50.860 mmol) were added followed drop-wise addition of thionyl chloride (1.94 mL, 26.586 mmol) as a solution in CH_2Cl_2 (20 mL) over 20 min. The reaction mixture was allowed to warm to room temperature (ice bath not removed) and the reaction mixture stirred at room temperature for 3 days. The reaction mixture was diluted with water (250 mL) and the organic phase separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic portions dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The residue was purified by chromatography on silica, eluting with cyclohexane containing 0 - 50% EtOAc. The appropriate fractions were combined and concentrated to give the title compound [A048] (5.196 g, 86%) as a pale yellow oil that solidified on standing. ^{1}H NMR (1H, 400MHz, d6-dmso) 4.81 (1H, dd), 4.58 (1H, dd), 4.44 (1H, dd), 4.28 (1H, br d), 4.12 (1H, br d), 4.02 (1H, br d), 3.93 – 3.87 (2H, m), 3.67 – 3.56 (2H, m), 3.46 – 3.34 (2H, m), 3.14 – 3.06 (1H, d), 3.01 – 2.69 (4H, br m), 2.55 (1H, dt), 1.42 (s, 9H), 1.41 (s, 9H).

(R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A049]

A stirred solution of (R)-1-Oxo-tetrahydro-2-oxa-1λ^4-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048] (2.99 g, 11.409 mmol) in anhydrous MeCN (25 mL) was prepared under nitrogen and cooled to 0 °C. Sodium (meta)periodate (2.464 g, 11.523 mmol) was added followed by ruthenium (III) chloride hydrate (24 mg, 0.114 mmol) (reaction mixture turns brown) and water (25 mL). The reaction mixture was stirred at 0 °C for 10 min

and then removed from ice bath and stirred at room temperature for 10 min. TLC shows complete conversion to a new, slightly more polar spot. The reaction mixture was diluted with sat. $NaHCO_3$ (aq) (100 mL) and extracted with CH_2Cl_2 (3 x 40 mL). The combined organic extracts were dried and concentrated by rotary evapoartion. The residue was purified by chromatography on silica, eluting with cyclohexane containing 0 - 50% EtOAc to give the title compound [A049] (1.72 g, 54%) as a pale yellow solid. ^1H NMR (1H, 500MHz, $CDCl_3$) 4.63 (1H, dd,), 4.25 - 4.07 (3H, overlapping t and broad m), 3.67 - 3.61 (1H, m), 3.45 (1H, br. d, J = 11.2 Hz), 3.13 (1H, br. s), 2.98 - 2.94 (2H, br. m), 1.47 (9H, s).

(R)-3-Phenoxymethyl-piperazine-1-carboxylic acid tert-butyl ester [A050]

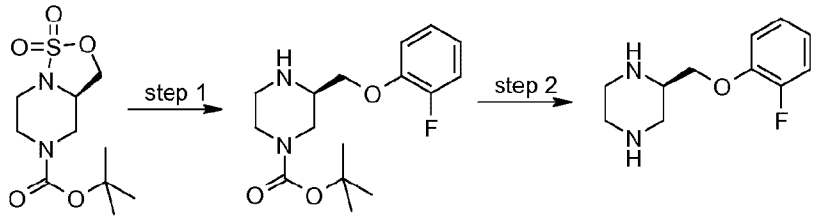
A solution of (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A049] (200 mg, 0.719 mmol) in anhydrous DMF (5 mL) was prepared under nitrogen. Sodium phenolate (88 mg, 0.754 mmol) was added and the reaction mixture heated to 50 °C overnight. A further 0.25 equivalents of sodium phenolate was added and heating continued for a further 5 hours. The reaction mixture was cooled to room temperature and 2 mL of 2M HCl (aq) was added. The mixture was stirred at room temperature for 1 hour. The reaction mixture was loaded onto a 10 g SCX cartridge, washing with methanol and eluting with 7N ammonia in MeOH. The ammonia fractions were combined and concentrated under reduced pressure. The residue was purified by chromatography on silica, eluting with CH_2Cl_2 containing 0 - 10% MeOH. The appropriate fractions were combined and concentrated to give the title compound [A00?] (75 mg, 36%) as a colourless oil. LCMS method: 1, RT:2.85 min, MI 293 [M+H]; ^1H NMR (1H, 500MHz, $CDCl_3$) 7.31 – 7.24 (2H, m), 6.97 (1H, t), 6.91 (2H, d), 4.05 (1H, br s), 3.97 – 3.95 (2H, m), 3.88 – 3.85 (1H, m), 3.09 (1H, br s), 3.04 – 3.01 (1H, br m), 2.96 – 2.91 (1H, br m), 2.83 – 2.74 (1H, br m), 2.74 (1H, br s), 2.14 (1H, br s)1.48 (9H, s).

(R)-2-Phenoxymethyl-piperazine [A047]

A solution of (R)-3-Phenoxymethyl-piperazine-1-carboxylic acid tert-butyl ester [A050] (98 mg, 0.332 mmol) in anhydrous dioxane (1 mL) was prepared and 4M HCl in dioxane (5 mL) was added. The reaction mixture was stirred at room temperature for 2 hours. The reaction mixture was concentrated by rotary evaporation to give a pale pink solid. The product was dissolved in MeOH and loaded onto a SCX cartridge, washing with MeOH and eluting with 7N ammonia in MeOH. The ammonia fraction was concentrated by rotary evaporation to

give the title compound [A047] (58 mg, 91%) as a pale oil that crystalised on standing. LCMS method: 1, RT:0.56 min, MI 193 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.30 – 7.27 (2H, m), 6.97 – 6.94 (1H, m), 6.91 – 6.90 (2H, m), 3.92 – 3.90 (1H, m), 3.83 – 3.83 (1H, m), 3.17 – 3.12 (1H, m), 3.07 – 3.03 (2H, m), 2.99 – 2.96 (1H, m), 2.92 – 2.87 (1H, m), 2.84 – 2.79 (1H, m) 2.63 (1H, dd).

Synthesis of (R)-2-(2-Fluoro-phenoxymethyl)-piperazine [A051]



[A048] [A052] [A051]

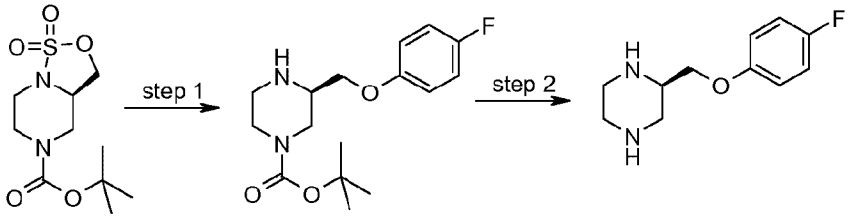
(R)-3-(2-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A052]

A suspension of sodium hydride (69 mg, 1.726 mmol) in anhydrous DMF (5 mL) was prepared and 2-fluorophenol (0.15 mL, 1.726 mmol) added dropwise. The reaction mixture was stirred at room temperature for 10 min then (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A051] (400 mg, 1.438 mmol) was added. The reaction mixture was heated to 50 °C overnight. The reaction mixture was cooled to room temperature and 2M HCl (aq) (1.4 mL, 2.875 mmol) was added. The reaction mixture was stirred at room temperature for 1.5 h. The reaction mixture was loaded onto a SCX cartridge, washing with methanol and eluting with 7N ammonia in MeOH. The ammonia fractions were combined and concentrated by rotary evaporation. The residue was purified by chromatography on silica, eluting with CH_2Cl_2 containing 0 - 10% MeOH. The appropriate fractions were combined and concentrated to give the title compound [A052] (318 mg, 71%) as a colourless oil. LCMS method: 1, RT:2.92 min, MI 311 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.10 – 7.04 (2H, m), 6.99 – 6.91 (2H, m), 4.04 – 3.89 (4H, m and overlapping br s), 3.14 – 3.11 (1H, m), 3.03 (1H, br d), 2.96 (1H, br t), 2.83 – 2.79 (1H, m), 2.75 (1H, br s), 2.23 (1H, br s), 1.48 (9H, s).

(R)-2-(2-Fluoro-phenoxymethyl)-piperazine [A051]

Following the procedure described in scheme A2, (R)-3-(2-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A052] (310 mg, 1.00 mmol) was treated with 4M HCl in dioxane (2 mL) to give the title compound [A051] (196 mg, 93%) as a pale yellow oil. LCMS method: 1, RT:0.75 min, MI 211 [M+H];LCMS method 1LCMS5, RT: 0.75 min, MI: 211 [M+1]. ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.10 – 7.03 (2H, m), 6.98 – 6.89 (2H, m), 4.00 – 3.97 (1H, m), 3.91 – 3.88 (1H, m), 3.23 – 3.18 (1H, m), 3.08 – 3.03 (2H, m), 3.00 – 2.98 (1H, m), 2.94 – 2.89 (1H, m), 2.85 – 2.80 (1H, m), 2.66 – 2.61 (1H, m).

Synthesis of (R)-2-(4-Fluoro-phenoxymethyl)-piperazine [A053]



[A048] [A054] [A053]

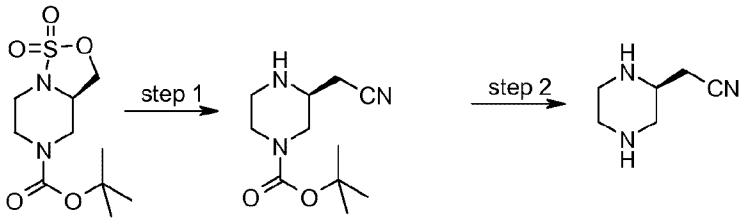
(R)-3-(4-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A054]

Following the procedure described in Scheme A2 step 1, (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048] (400 mg, 1.438 mmol) was reacted with 4-fluorophenol (193 mg, 1.726 mmol) to give the title compound [A054] (100 mg, 22%) as a colourless oil. LCMS method: 1, RT:3.00 min, MI 311 [M+H];. ^{1}H NMR (1H, 500MHz, $CDCl_3$) 6.99 – 6.96 (2H, m), 6.85 – 6.83 (2H, m), 4.06 (1H, br s), 3.95 (1H, br s), 3.95 – 3.90 (1H, m), 3.84 – 3.80 (1H, m), 3.10 – 3.05 (1H, m), 3.03 (1H, br d), 2.93 (1H, br t), 2.83 – 2.78 (1H, m), 2.72 (1H, br s), 2.10 (1H, br s), 1.48 (9H, s).

(R)-2-(4-Fluoro-phenoxymethyl)-piperazine [A053]

Following the procedure described in example Scheme A2, step 4, (R)-3-(4-Fluoro-phenoxymethyl)-piperazine-1-carboxylic acid tert-butyl ester [A054] (100 mg, 0.322 mmol) was treated with 4M HCl in dioxane (2 mL) to give the title compound [A053] (68 mg, 100%) as a colourless oil that solidified on standing. LCMS method: 1, RT:0.59 min, MI 211 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 6.99 – 6.95 (2H, m), 6.85 – 6.82 (2H, m), 3.88 – 3.86 (1H, m), 3.81 – 3.78 (1H, m), 3.15 – 3.10 (1H, m), 3.05 – 3.02 (2H, m), 2.98 – 2.96 (1H, m), 2.91 – 2.86 (1H, m), 2.83 – 2.78 (1H, m), 2.63 – 2.58 (1H, m).

Synthesis of (S)-Piperazin-2-yl-acetonitrile [A055]



[A048] [A056] [A055]

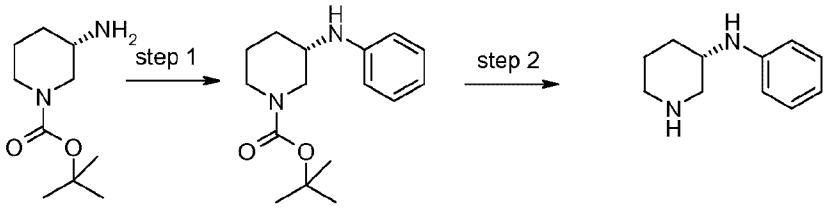
(S)-3-Cyanomethyl-piperazine-1-carboxylic acid tert-butyl ester [A056]

Following the procedure described in Scheme A1, step 3, (R)-1,1-Dioxo-tetrahydro-2-oxa-1λ^6-thia-5,7a-diaza-indene-5-carboxylic acid tert-butyl ester [A048] (1.52 g, 5.46 mmol) was reacted with KCN (356 mg, 5.46 mmol) to give the title compound [A056] (850 mg, 69%). ^{1}H NMR (1H, 500MHz, $CDCl_3$) 3.95 (1H, br s), 3.84 (1H, br d), 3.03 – 2.92 (3H, m), 2.82 – 2.75 (1H, m), 2.70 (1H, br s), 2.51 – 2.41 (2H, m), 1.49 (9H, s). LCMS method: 1, RT:1.39 min, MI 226 [M+H].

(S)-Piperazin-2-yl-acetonitrile [A055]

Following the procedure described in example Scheme A2, step 4, (S)-3-Cyanomethyl-piperazine-1-carboxylic acid tert-butyl ester [A056] (800 mg, 3.55 mmol) was treated with 4M HCl in dioxane to give the title compound [A055] (434 mg, 98%) as a pale orange solid. LCMS method: 1, RT:0.49 min, MI 126 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 3.06 – 2.99 (3H, m), 2.93 – 2.90 (1H, m), 2.87 – 2.82 (1H, m), 2.77 – 2.72 (1H, m), 2.56 – 2.51 (1H, m), 2.44 – 2.42 (2H, m).

Syntheiss of Phenyl-(S)-piperidin-3-yl-amine [A057]



[A058] [A057]

(S)-3-Phenylamino-piperidine-1-carboxylic acid tert-butyl ester [A058]

A solution of (S)-3-Amino-piperidine-1-carboxylic acid tert-butyl ester (500 mg, 2.497 mmol), Pd2(dba)3 (95 mg, 0.104 mmol) and 2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (61 mg, 0.156 mmol) in toluene (5 mL) was prepared under nitrogen. The solvent was degasses and sodium tert-butoxide (280 mg, 2.912 mmol) was added followed by bromobenzene (0.22 mL, 2.080 mmol). The reaction mixture was heated to 100 °C for 24 h. The reaction mixture was cooled to room temperature and concentrated by rotary evaporation. The residue was filtered through a plug of silica, eluting with CH_2Cl_2. The eluent was concentrated by rotary evaporation. The crude residue was purified by chromatography on silica, eluting with cyclohexane containing 5 - 50% EtOAc. The appropriate fractions were combined and concentrated to give the title compound [A058] (535 mg, 78%) as a pale yellow oil that solidified on standing. LCMS method: 1, RT:5.51 min, MI 227 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$) 7.20 – 7.17 (2H, m), 6.71 (1H, t), 6.64 (2H, d), 4.02 (1H, br s), 3.74 – 3.70 (1H, m), 3.63 (1H, br s), 3.39 (1H, br m), 3.09 (1H, br m), 2.89 (1H, br s), 2.02 – 1.99 (1H, m), 1.78 – 1.73 (1H, m), 1.59 – 1.51 (2H, m), 1.46 (9H, s).

Phenyl-(S)-piperidin-3-yl-amine [A057]

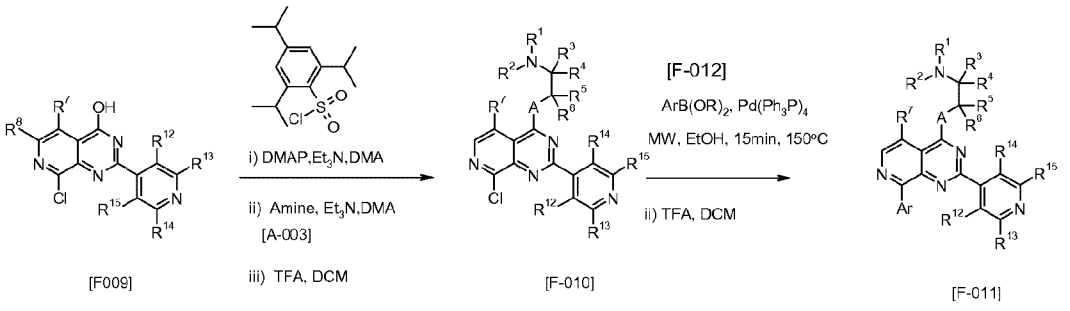
Following the procedure described in Scheme A2, step 4, (S)-3-phenylamino-piperidine-1-carboxylic acid tert-butyl ester [A058] (138 mg, 0.5 mmol) was treated with 4 HCl in dioxane (2 mL) to give the title compound [A057] (85 mg, 97%) as a pale yellow oil. LCMS method: 1, RT:0.96 min, MI 177 [M+H].

General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-011] Scheme A3

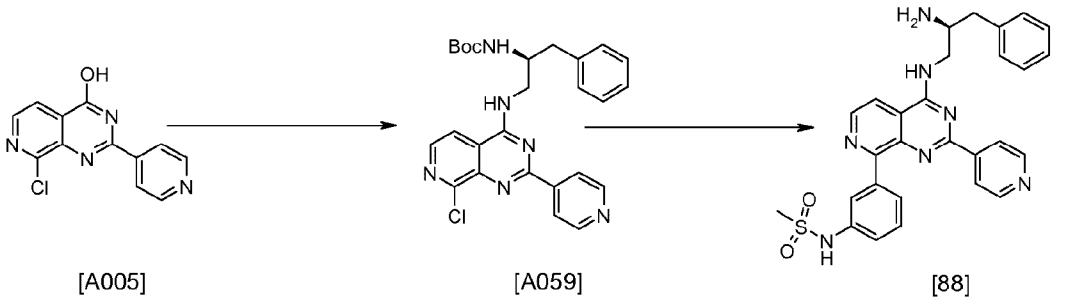
4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] were prepared by the reaction of a 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [F-009] with with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidini-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-003], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature.

After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC. The 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] were reacted in a Suzuki type reaction utilising a suitable boronic acid or boronic ester, of general formula [F-012], a palladium catalyst such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ a base such as Et_3N, KOH, Na_2CO_3 or NaOH in a polar solvent such as EtOH, THF, DMA or dioxane at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme A3



Synthesis of N-{3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-8-yl]-phenyl}-methanesulfonamide [88]



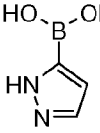
[(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059]

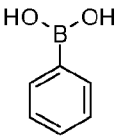
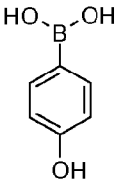
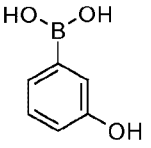
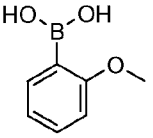
To a solution of 2-Pyridin-4-yl-pyrido[2,3-d]pyrimidin-4-ol [A005] (1 g, 3.8 mmol) in DMA (15 mL), 2,4,6-Triisopropylbenzenesulfonyl chloride (1.3g, 4.25 mmol), Et_3N (1.1 mL, 7.73 mmol) and DMAP (0.1 g) were added successively. The mixture was stirred at rt for 1h then ((S)-2-Amino-1-benzyl-ethyl)-carbamic acid tert-butyl ester (1.16 g, 4.64 mmol) was added. The reaction was stirred overnight and the solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography (SP1 [eluent: DCM/MeOH: 1/0 then 95/5 then 9/1]) to give the title compound: LCMS method: 1, RT:5.76 min, MI 492 [M+H]

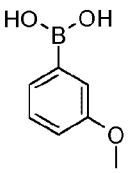
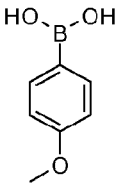
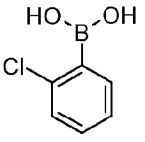
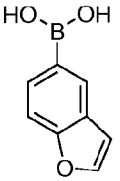
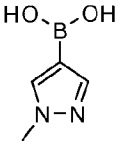
N-{3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-8-yl]-phenyl}-methanesulfonamide [88]

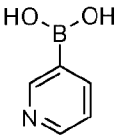
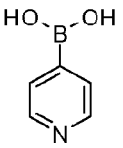
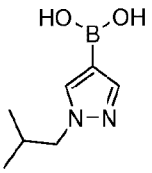
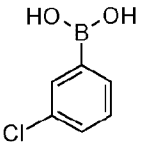
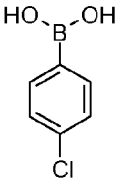
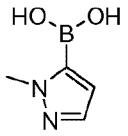
A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07g, 0.142mmol), 3-(methanesulfonylamino)phenylboronic acid pinacol ester (0.06g, 0.2mmol), Pd(Ph3P)4 (0.017g, 0.014mmol), aq K3PO4 (0.5M, 0.57mL, 0.28mmol) and DMA (1mL). The vial was heated under microwave irradiations (150°C, 10min). The solvent was removed under reduced pressure. The crude was purified by Column chromatography (Eluent: DCM/MeOH: 1:0 to 9/1). The purified compound was solubilised in DCM (2mL) and TFA (0.5mL) was added. The solution was stirred 3h and then was poured onto SCX2 column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M which was used without further purification to give the title compound [88]: LCMS method: 1, RT:3.01 min, MI 526 [M+H]; NMR 1H (1H, 300MHz, d6-dmso) 8.70 (d, 2H), 8.68 (d, 1H), 8.25 (d, 2H), 8.14 (d, 1H), 8.04 (d, 2H), 7.37-7.24 (m, 7H), 3.91-3.86 (m, 1H), 3.46-3.33 (m, 2H), 3.10 (s, 3H), 2.77-2.69 (m, 2H).

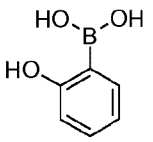
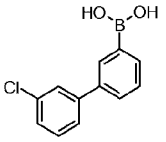
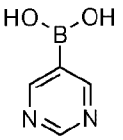
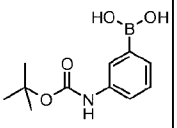
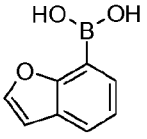
The following compounds were synthesised according to the general synthesis shown in scheme [A3]:

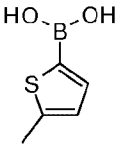
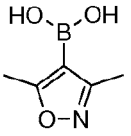
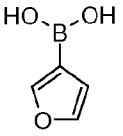
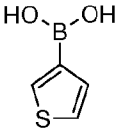
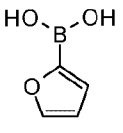
Ex	SM	Boronic acid	Analysis		Name
89	[A059]		Method 1: RT: 3.01 min,	(1H, 300MHz, d6-dmso) 8.76ppm (2H, dd), 8.67ppm (1H,d), 8.29ppm (1H, s), 8.15ppm (1H, d), 8.08ppm	N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-pyrazol-5-yl)-2-(pyridin-4-

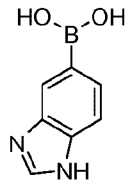
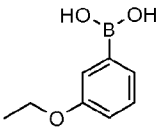
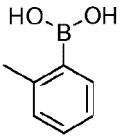
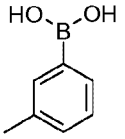
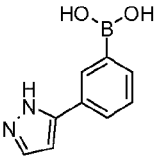
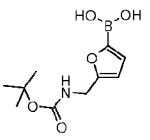
			MI: 423 [M+H]	(2H, dd), 7.71ppm (1H, d), 7.61ppm (1H, d), 7.41-7.30ppm (5H, m), 3.97ppm, (1H, d), 3.58ppm (2H, br s), 3.35ppm (2H, m), 2.97-2.80ppm (2H, m)	yl)pyrido[3,4-d]pyrimidin-4-amine
90	[A059]		Method 1: RT: 3.62 min, MI: 433 [M+H]	(1H, 300MHz, d6-dmso) 9.47ppm (1H, br s), 8.70ppm (1H, d), 8.67ppm (2H, dd), 8.42ppm (1H, br s), 8.18-8.14ppm (3H, m), 7.90ppm (2H, dd), 7.57-7.46ppm (3H, m), 7.42-7.31ppm (5H, m), 3.99ppm (1H, d), 3.67-3.51ppm (2H, m), 3.01ppm (1H, dd), 2.83ppm (1H, dd)	N-[(2S)-2-amino-3-phenylpropyl]-8-phenyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
91	[A059]		Method 1: RT: 2.93 min, MI: 449 [M+H]	(1H, 300MHz, d6-dmso) 8.85-8.85ppm (1H, br s), 8.70ppm (2H, d), 8.62ppm (1H, d), 8.12ppm (2H, d), 8.04ppm (1H, d), 8.00ppm (2H, d), 7.39-7.27ppm (5H, m), 6.91ppm (2H, d), 3.97-3.86ppm (1H, m), 3.54-3.44ppm (2H, m), 2.83ppm (2H, br s)	4-(4-{[(2S)-2-amino-3-phenylpropyl]-amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol
92	[A059]		Method 1: RT: 3.00 min, MI: 449 [M+H]	(1H, 300MHz, d6-dmso) 8.73-8.69ppm (3H, t), 8.16ppm (1H, d), 8.04ppm (2H, d), 7.64-7.62ppm (2H, m), 7.36-7.23ppm (5H, m), 6.88ppm (1H, dd), 3.88ppm (1H, d), 3.46-3.30ppm (2H, m), 2.77-2.74ppm (2H, m)	3-(4-{[(2S)-2-amino-3-phenylpropyl]-amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol
93	[A059]		Method 1: RT: 3.16 min, MI: 463 [M+H]	(1H, 300MHz, d6-dmso) 8.65-8.63ppm (3H, t), 8.19ppm (1H, d), 7.87ppm (2H, d), 7.48ppm (1H, dt), 7.36-7.24ppm (5H, m), 7.17ppm (1H, d), 7.07ppm (1H, t), 3.92-3.84ppm (1H, dd), 3.61ppm (3H, s), 3.44-3.29ppm (2H, m), 2.77-	N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

				2.75ppm (2H, m)	
94	[A059]		Method 1: RT: 3.54 min, MI: 463 [M+H]	(1H, 300MHz, d6-dmso) 8.70ppm (3H, d), 8.18ppm (1H, d), 8.02ppm (2H, d), 7.80-7.76ppm (2H, m), 7.45ppm (1H, t), 7.34-7.24ppm (5H, m), 7.07ppm (1H, dd), 3.88ppm (1H, d), 3.83ppm (3H, s), 3.43-3.33ppm (2H, m), 2.77-2.73ppm (2H, m)	N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
95	[A059]		Method 1: RT: 3.56 min, MI: 463 [M+H]	(1H, 300MHz, d6-dmso) 8.70ppm (2H, d), 8.65ppm (1H, d), 8.24 (2H, d), 8.10ppm (1H, d), 8.04ppm (2H, d), 7.36-7.23ppm (5H, m), 7.09ppm (2H, d), 3.89-3.84ppm (1H, m), 3.85ppm (3H, s), 3.44-3.30ppm (2H, m), 2.74ppm (2H, t)	N-[(2S)-2-amino-3-phenylpropyl]-8-(4-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
96	[A059]		Method 1: RT: 3.46 min, MI: 467 [M+H]	(1H, 300MHz, d6-dmso) 8.69ppm (2H, d), 8.63ppm (2H, dd), 8.28ppm (1H, d), 8.19-8.16ppm (1H, m), 8.01ppm (1H, d), 7.84ppm (2H, dd), 7.64-7.60ppm (1H, m), 7.36-7.23ppm (5H, m), 3.92-3.84ppm (1H, m), 3.44-3.25ppm (2H, m), 2.76-2.74ppm (2H, m)	N-[(2S)-2-amino-3-phenylpropyl]-8-(2-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
97	[A059]		Method 1: RT: 3.69 min, MI: 473 [M+H]	(1H, 300MHz, d6-dmso) 8.68 (d, 3H), 8.48 (d, 1H), 8.18-8.15 (m, 2H), 8.06 (d. 1H), 8.01 (d, 1H), 7.73 (d, 1H), 7.36-7.26 (m, 5H), 7.10 (d, 1H), 3.88 (d, 1H), 3.45-3.37 (m, 2H), 2.77-2.73 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
98	[A059]		Method 1: RT: 2.98 min, MI: 437 [M+H]	(1H, 300MHz, d6-dmso) 8.77 (s, 1H), 8.75 (d, 2H), 8.54 (d, 1H), 8.44 (s, 1H), 8.12 (d, 2H), 7.97 (d, 1H), 7.36-7.27 (m,5H), 3.99 (s, 3H), 3.87 (d, 1H), 3.43-3.35 (m, 2H), 2.77-2.74 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

99	[A059]		Method 1: RT: 2.58 min, MI: 434 [M+H]	(1H, 300MHz, d6-dmso) 9.33 (d, 1H), 8.73-8.66 (m, 3H), 8.51 (td, 1H), 8.21 (d, 1H), 7.98 (d, 2H), 7.57 (dd, 1H), 7.37-7.27 (m, 5H), 3.92-3.84 (m, 1H), 3.47-3.38 (m, 2H), 2.78-2.76 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(pyridin-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
100	[A059]		Method 1: RT: 2.41 min, MI: 434 [M+H]	(1H, 300MHz, d6-dmso) 8.77-2.75 (m, 3H), 8.71 (d, 2H), 8.28 (d, 1H), 8.15 (d, 2H), 8.02 (d, 2H), 7.36-7.26 (m, 5H), 3.91-3.86 (m, 1H), 3.46-3.36 (m, 2H), 2.78-2.73 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-2,8-bis(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
101	[A059]		Method 1: RT: 3.90 min, MI: 479 [M+H]	(1H, 300MHz, d6-dmso) 8.75-8.73 (m, 3H), 8.54 (d, 1H), 8.49 (s, 1H), 8.11 (d, 2H), 7.98 (d, 1H), 7.35-7.25 (m, 5H), 4.07 (d, 2H), 3.88-3.84 (m, 1H), 3.43-3.36 (m, 2H), 2.74-2.70 (m, 2H), 2.23-2.14 (m, 1H), 0.91 (d, 6H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
102	[A059]		Method 1: RT: 4.05 min, MI: 466 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
103	[A059]		Method 1: RT: 4.08 min, MI: 467 [M+H]	(1H, 300MHz, d6-dmso) 8.72-8.62 (m, 3H), 8.35 (s, 1H), 8.23 (d, 2H), 8.19 (d, 1H), 7.94 (d, 2H), 7.62 (d, 2H), 7.39-7.32 (m, 5H), 4.02-3.94 (m, 1H), 3.59-3.50 (m, 2H), 3.00-2.92 (m, 1H), 2.85-2.80 (m, 1H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(4-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
104	[A059]		Method 1: RT: 2.72 min, MI: 437 [M+H]	(1H, 300MHz, d6-dmso) 8.72 (d, 2H), 8.72 (d, 1H), 8.22 (d, 1H), 8.04 (d, 2H), 7.61 (d, 1H), 7.35-7.23 (m, 5H), 7.09 (d, 1H), 4.02 (s, 3H), 3.90-3.85 (m, 1H), 3.44-3.33 (m, 2H), 2.75-2.71 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-

					amine
105	[A059]			(1H, 300MHz, d6-dmso) 8.68-8.74 (m, 3H), 8.38 (d, 1H), 8.35 (s, 1H), 8.22 (d, 1H), 7.96 (d, 2H), 7.32-7.40 (m, 6H), 6.98-7.04 (m, 2H), 3.98 (d, 1H), 3.50-3.58 (m, 2H), 2.95 (dd, 1H), 2.85 (dd, 1H).	2-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol
106	[A059]		Method 1: RT: 4.74 min, MI: 543 [M+H]	(1H, 300MHz, d6-dmso) 8.75 (d, 1H), 8.66 (d, 2H), 8.52 (s, 1H), 8.26-8.18 (m, 2H), 7.99 (d, 2H), 7.83 (d, 1H), 7.80 (s, 1H), 7.72 (d, 1H), 7.67 (t, 1H), 7.52 (t, 1H), 7.46 (d, 1H), 7.38-7.30 (m, 5H), 4.00-3.92 (m, 1H), 3.58-3.52 (m, 2H), 2.91-2.86 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(3-chlorophenyl)-phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
107	[A059]		Method 1: RT: 4.73 min, MI: 543 [M+H]	(1H, 300MHz, d6-dmso) 8.74 (d, 1H), 8.70 (d, 2H), 8.34)d, 2H), 8.27 (d, 2H), 8.18 (d, 1H), 8.01 (d, 2H), 7.88 (d, 2H), 7.83 (d, 2H), 7.57 (d, 2H), 7.40-7.31 (m, 5H), 3.99-3.93 (m, 1H), 3.60-3.53 (m, 2H), 2.89-2.82 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[4-(4-chlorophenyl)-phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
108	[A059]		Method 1: RT: 2.83 min, MI: 435 [M+H]	(1H, 300MHz, d6-dmso) 9.50 (s, 2H), 9.27 (s, 1H), 8.71 (d, 1H), 8.69 (d, 2H), 8.22 (d, 1H), 7.93 (d, 2H), 7.37-7.28 (m, 5H), 3.92-3.85 (m, 1H), 3.47-3.38 (m, 2H), 2.79-2.76 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(pyrimidin-5-yl)pyrido[3,4-d]pyrimidin-4-amine
109	[A059]		Method 1: RT: 2.43 min, MI: 448 [M+H]	(1H, 300MHz, d6-dmso) 8.69 (d, 2H), 8.65 (d, 1H), 8.13 (d, 1H), 8.04 (d, 2H), 7.38-7.26 (m, 7H), 7.17 (t, 1H), 6.68 (d, 1H), 5.16 (brs, 2H), 3.91-3.85 (m, 1H), 3.45-3.35 (m, 2H), 2.77-2.75 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(3-aminophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
110	[A059]		Method 1: RT: 4.07 min, MI:	(1H, 300MHz, d6-dmso) 8.78 (d, 2H), 8.72 (d, 1H), 8.53 (s, 1H), 8.16 (d, 3H), 7.90 (d, 1H), 7.71 (d, 1H), 7.43 (t, 1H), 7.36-7.26 (m, 6H), 3.92-	N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-7-yl)-2-(pyridin-4-yl)pyrido[3,4-

			473 [M+H]	3.84 (m, 1H), 3.52-3.45 (m, 2H), 2.83-2.79 (m, 2H).	d]pyrimidin-4-amine
111	[A059]		Method 1: RT: 1.81 min, MI: 453 [M+H]	(1H, d6-DMSO, 500MHz) 8.67 (d, 2H), 8.30-8.16 (m, 1H), 8.01 (d, 2H), 7.36-7.24 (m, 7H), 6.82 (d, 1H), 3.86-3.73 (m, 1H), 2.75-2.72 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(5-methylthiophen-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
112	[A059]		Method 1: RT: 3.02 min, MI: 452 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(dimethyl-1,2-oxazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
113	[A059]		Method 1: RT: 3.42 min, MI: 426 [M+H] C	(1H, 300MHz, d6-dmso) 8.99 (d, 1H), 8.71 (d, 2H), 8.58 (d, 1H), 8.44 (s, 1H), 8.03 (d, 1H), 7.96 (d, 2H), 7.82 (t, 1H), 7.39-7.29 (m, 5H), 4.00-3.94 (m, 1H), 3.68-3.48 (m, 2H), 303 (dd, 1H), 2.84 (dd, 1H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
114	[A059]		Method 1: RT: 3.55 min, MI: 439 [M+H]	(1H, 300MHz, d6-dmso) 8.96 (d, 1H), 8.74 (d, 2H), 8.63 (d, 1H), 8.13-8.09 (m, 4H), 7.64 (dd, 1H), 7.36-7.25 (m, 5H), 3.92-3.85 (m, 1H), 3.45-3.36 (m, 2H), 2.76-2.71 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(thiophen-3-yl)pyrido[3,4-d]pyrimidin-4-amine
115	[A059]		Method 1: RT: 3.26 min, MI: 423 [M+H]	(1H, 300MHz, d6-dmso) 8.76 (d, 2H), 8.61 (d, 1H), 8.12-8.06 (m, 3H), 7.95 (s, 1H), 7.36-7.26 (m, 5H), 6.80-6.78 (m, 1H), 3.92-3.85 (m, 1H), 3.46-3.39 (m, 2H), 2.78-2.75 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

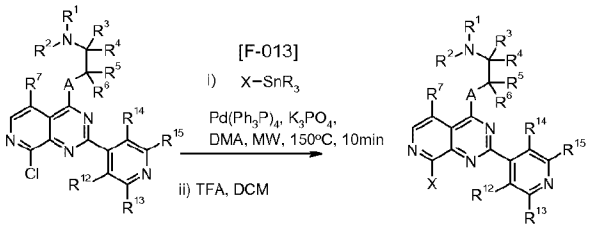
116	[A059]		Method 1: RT: 2.23 min, MI: 473 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-1,3-benzodiazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
117	[A059]		Method 1: RT: 3.72 min, MI: 477 [M+H]		N-[(2S)-2-amino-3-phenylpropyl]-8-(3-ethoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
118	[A059]				N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
119	[A059]				N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
120	[A059]		Method 1: RT: 3.55 min, MI: 499 [M+H]	(1H, 300MHz, d6-dmso) 8.87 (brs, 1H), 8.70 (d, 1H), 8.67 (d, 2H), 8.18 (d, 1H), 8.14-8.09 (m, 3H), 7.91 (d, 1H), 7.77 (brs, 1H), 7.56 (t, 1H), 7.36-7.26 (m, 5H), 6.74 (d, 1H), 3.94-3.85 (m, 1H), 3.44-3.39 (m, 2H), 2.77-2.74 (m, 2H).	N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(1H-pyrazol-5-yl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
121	[A059]				N-[(2S)-2-amino-3-phenylpropyl]-8-[5-(aminomethyl)-furan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-

					d]pyrimidin-4-amine

General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F011] Scheme A4

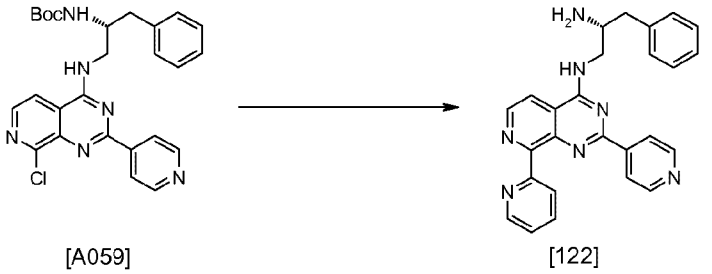
8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F011] were prepared by reaction of a 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] in a Stille type reaction utilising a suitable stannane of general formula [F013], a palladium catalyst such as $Pd(PPh_3)_4$ or $Pd(PPh_3)_2Cl_2$ a base such as K_3PO_4, in a polar solvent such as DMA or dioxane at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme A4



[F-010] [F-011]

Synthesis of (R)-3-Phenyl-N^1-(2-pyridin-4-yl-8-pyridin-2-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [122]



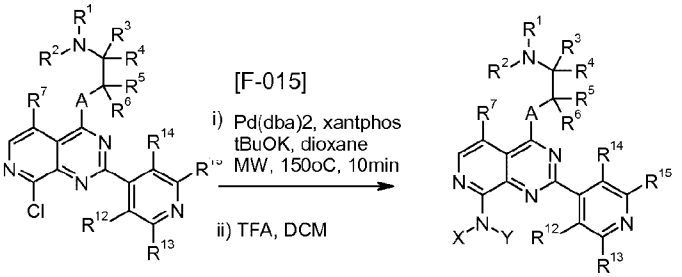
[A059] [122]

(R)-3-Phenyl-N^1-(2-pyridin-4-yl-8-pyridin-2-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [122]

A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07g, 0.142mmol), 2-(Tributylstannyl)pyridine (0.068g, 0.185mmol), $Pd(Ph_3P)_4$ (0.016g, 0.014mmol), LiCl (0.018 g, 0.428mmol) and DMA (1.5 mL). The mixture was heated under microwave irradiation (150oC, 10min) and the solvent was removed under reduced pressure. The crude was purified by Column chromatography (Eluent: DCM/MeOH: 1:0 to 9:1). The purified compound was solubilised in DCM and 0.5mL of TFA was added. The solution was stirred 3h and then was poured on a SCX column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M, the basic solvent was concentrated under reduced pressure to yield the title compound as a yellow solid which was was used without further purification: LCMS method: 1, RT:2.34 min, MI 434 [M+H]; ^{1}H NMR (1H, 500MHz, $CDCl_3$); 8.70-8.76 (m, 2H), 8.63 (d, 2H), 8.42 (brs, 1H), 8.27 (d, 1H), 7.96 (dd, 1H), 7.93 (m, 1H), 7.81 (d, 2H), 7.50 (td, 1H), 7.32-7.52 (m, 5H), 4.00 (d, 1H), 3.51-3.60 (m, 2H), 3.01 (dd, 1H), 2.83 (dd, 1H).

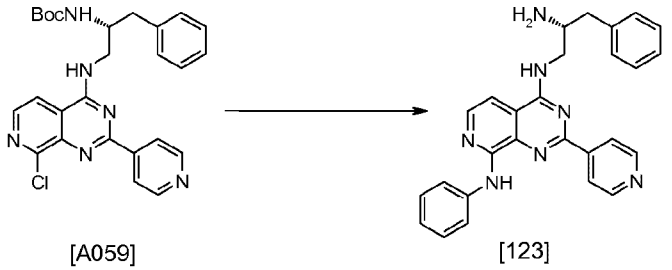
General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] Scheme A5

8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] were prepared by reaction of a 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivatives of general formula [F-010] in a Buchwald type reaction utilising a suitable amine, of general formula [F-015], a palladium catalyst such as $Pd(dba)_2$ or $Pd(OAc)_2$, a ligand such as Xantphos and a base such as NaOtBu or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.



[F-010] [F-014]

Synthesis of N^4-((R)-2-Amino-3-phenyl-propyl)-N^8-phenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine [123]

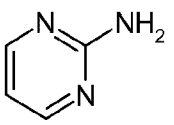
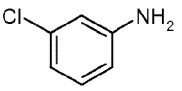
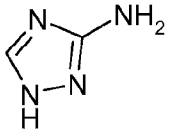


[A059] [123]

N^4-((R)-2-Amino-3-phenyl-propyl)-N^8-phenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine [123]

In a microwave vial, [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.05g 0.1 mmol) Aniline (0.015 g, 0.15 mmol), $Pd(dba)_2$ (0.003 g, 0.005mmol), Xantphos (0.006 g, 0.01 mmol), Sodium tert butoxide (0.02 g, 0. 2mmol) and dioxane (1.3 mL) were added successively. The microwave vial was heated under microwaves (150°C, 10min). The solvent was then removed under reduced pressure, DCM (2 mL) and TFA (0.5 mL) were added successively and the solution was stirred 3h. The solution was poured on a SCX2 column and was washed with MeOH. The compound was released using a 2M NH3/MeOH solution, and then was concentrated under reduce pressure. The crude was purified by preparative HPLC (method A) to yield the title compound [123]: LCMS method: 1, RT:3.53 min, MI 448 [M+H]; NMR (1H, 300MHz, d6-dmso): peaks might be underneath solvent peaks at 2.5 and 3.3 ppm. 9.35 (s, 1H), 8.71 (d, 2H), 8.35 (d, 2H), 8.03-8.08 (m, 3H), 7.46 (d, 1H), 7.27-7.38 (m, 7H), 7.02 (t, 1H), 3.86 (d, 1H), 2.70-2.78 (m, 2H).

The following compounds were synthesised according to the general synthesis shown in scheme [A5]:

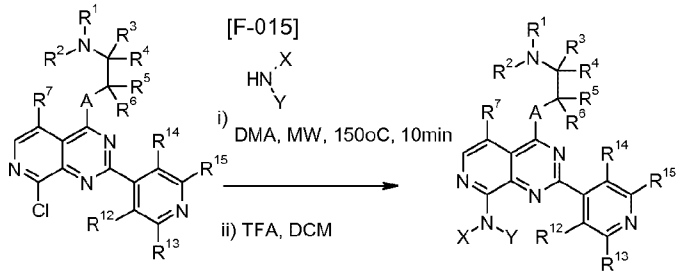
Ex	SM	Amine	Analysis		Name
124	[A059]		Method 1: RT: 2.16 min, MI: 450 [M+H]	(1H, 300MHz, d6-dmso): 8.70 (d, 2H), 8.64 (d, 2H), 8.34 (s, 1H), 8.25 (d, 1H), 8.04 (d, 2H), 7.70 (d, 1H), 7.40-7.33 (m, 5H), 7.10 (t, 1H), 3.97-3.92 (m, 1H), 3.58-3.50 (m, 2H), 2.99-2.93 (m, 1H), 2.87-2.80 (m, 1H).	4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(pyrimidin-2-yl)pyrido[3,4-d]pyrimidine-4,8-diamine
125	[A059]		Method 1: RT: 2.16 min, MI: 482 [M+H]		4-N-[(2S)-2-amino-3-phenylpropyl]-8-N-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidine-4,8-diamine
126	[A059]		Method 1: RT: 2.69 min, MI: 439 [M+H]		4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(1H-1,2,4-triazol-3-yl)pyrido[3,4-d]pyrimidine-4,8-diamine

General synthesis of 8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] Scheme A6

8-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-014] were prepared by reaction of a 4-Substituted 8-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin derivative of general formula [F-010] in a nucleophilic aromatic substitution type reaction utilising a suitable amine [method A], thiol [method B] or phenol [method C] of general formula [F-015], and a base such as NaH in a polar aprotic solvent such as DMA or DMF at high temperature either by heating thermally or using a microwave reactor. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

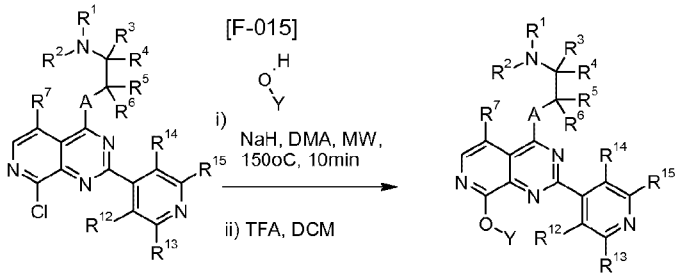
Scheme A6

Method A



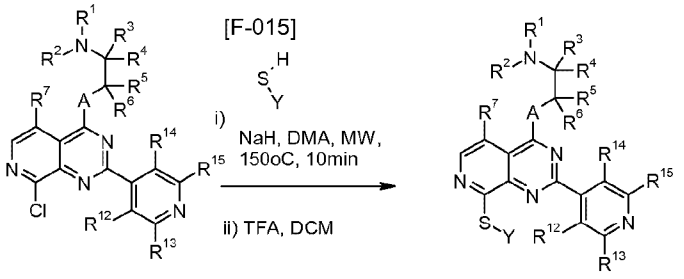
[F-010] [F-014]

Method B



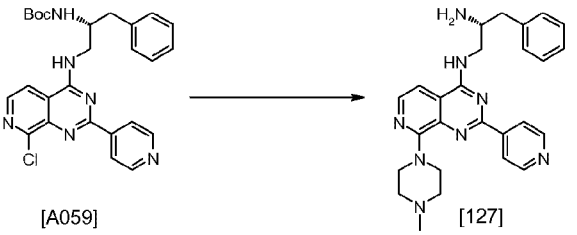
[F-010] [F-014]

Method C



[F-010] [F-014]

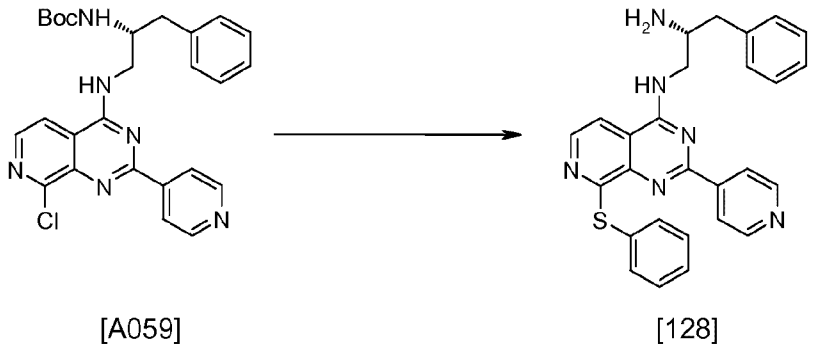
Synthesis of (R)-N^1-[8-(4-Methyl-piperazin-1-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine [127]



(R)-N^1-[8-(4-Methyl-piperazin-1-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine [127]

A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07 g, 0.142 mmol), N-methylpiperazine (0.031 mL, 0.285 mmol) and DMA (2 mL). The solution was heated under microwaves (150°C, 10min). 2 other equivalent of N-methylpiperazine (0.031 mL, 0.285 mmol) was added and the vial was heated again under microwaves (150°C, 10 min). The solvent was removed under reduced pressure and DCM (2 mL) and TFA (0.5 mL) were added successively. The solution was stirred 3h and then was poured on a SCX-2 column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M. The crude was then purified by preparative HPLC (method A) to yield the title compound [127]: LCMS method: 1, RT:1.55 min, MI 455 [M+H]; NMR (1H, 300MHz, d6-dmso): 9.17 (brs, 1H), 8.86 (d, 2H), 8.30 (s, 3H), 8.10 (d, 1H), 7.86 (d, 2H), 7.48 (d, 1H), 7.35-7.41 (m, 5H), 3.83-4.04 (m, 5H), 3.66-3.76 (m, 1H), 3.54-3.64 (m, 1H), 3.12 (dd, 1H), 2.86 (dd, 1H), 2.67-2.72 (m, 4H), 2.53 (s, 3H).

Synthesis of (R)-3-Phenyl-N^1-(8-phenylsulfanyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [128]



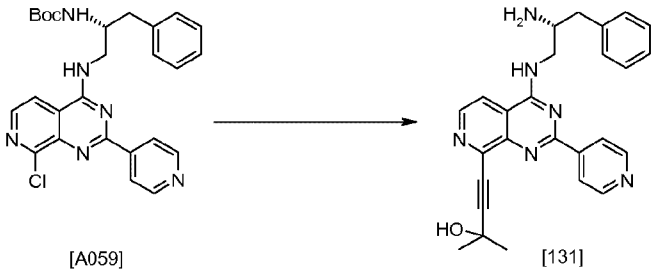
(R)-3-Phenyl-N^1-(8-phenylsulfanyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine [128]

To a suspension of NaH (60% in mineral oil, 0.008 g, 0.2mmol) in DMF (2 mL), Thiophenol (0.02 g, 0.185 mmol) was added. The mixture was stirred 1h and [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.07 g, 0.142 mmol) was added. The mixture was stirred overnight and water (0.3 mL) was added. The solvent were removed under reduced pressure and DCM (2 mL) and TFA (0.5mL) were added successively. The solution was stirred 3h and then was poured on a SCX-2 column, washed with MeOH and the expected product was released using a solution MeOH/NH3 2M. The crude was then purified by preparative HPLC (method A). To yield the title compound [128]: LCMS method: 1, RT:4.06 min, MI 465 [M+H]; NMR (1H, 300MHz, d6-dmso): 9.38 (brs, 1H), 8.72 (d, 2H), 8.23 (s, 3H), 8.03 (d, 2H), 7.89 (d, 1H), 7.58-7.61 (m, 2H), 7.36-7.47 (m, 6H), 3.98 (d, 1H), 3.56-3.73 (m, 2H), 3.05 (dd, 1H), 2.87 (dd, 1H).

The following compounds were synthesised according to the general synthesis shown in scheme [A6]:

Ex	Met-hod	SM	Nuc	Analysis		Name
129	B	[A059]		Method 1: RT: 3.39 min, MI: 449 [M+H]	(1H, 300MHz, d6-dmso): 9.43 (brs, 1H), 8.68 (d, 2H), 8.29 (s, 2H), 8.03 (d, 1H), 7.99 (d, 2H), 7.85 (d, 1H), 7.36-7.48 (m, 6H), 7.21-7.28 (m, 3H), 4.00 (d, 1H), 3.58-3.55 (m, 2H), 3.06 (dd, 1H), 2.81 -2.93 (m, 1H),	N-[(2S)-2-amino-3-phenylpropyl]-8-phenoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
130	C	[A059]		Method 1: RT: 3.43 min, MI: 403 [M+H]	(1H, 300MHz, d6-dmso): 9.58 (brs, 1H), 8.69 (d, 2H), 8.42 (d, 1H), 8.32 (s, 2H), 7.94 (d, 2H), 7.81 (d, 1H), 7.36-7.45 (m, 5H), 3.99 (d, 1H), 3.59-3.70 (m, 2H), 3.07 (dd, 1H), 2.81 (dd, 1H), 2.53 (s, 3H).	N-[(2S)-2-amino-3-phenylpropyl]-8-(methylsulfanyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine

Synthesis of 4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)-2-methylbut-3-yn-2-ol [131]



4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)-2-methylbut-3-yn-2-ol [131]

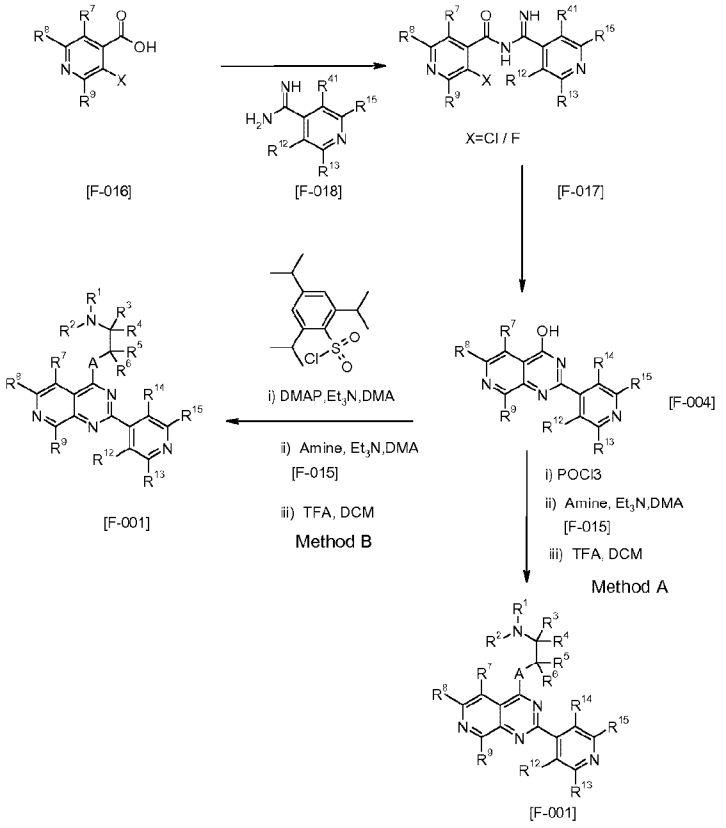
A microwave vial was charged with [(S)-1-Benzyl-2-(8-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [A059] (0.05 g, 0.1 mmol), $Pd(PPh_3)_2Cl_2$ (0.007 g, 0.01 mmol), CuI (0.002 g, 0.01mmol), 2-methyl-3-butyn-2-ol (0.035 g, 0.037 mmol), Triphenylphosphine (0.005g, 0.02 mmol), Triethylamine (0.2 mL) and DMF (0.8 mL). The vial was heated under microwave (150°C, 10min). The solvent was removed under reduced pressure and DCM (2 mL) and TFA (1 mL) were added and the mixture was stirred 3h. The solution was poured on a SCX2 column and was washed with MeOH. The compound was released using a 2M NH3/MeOH solution, and then was concentrated under reduce pressure. The crude was purified by preparative HPLC (method A) to yield the title compound [131]: LCMS method: 1, RT:3.12 min, MI 439 [M+H]; NMR (1H, 300MHz, d6-dmso): 8.71 (d, 2H), 8.56 (d, 1H), 8.31 (brs, 1H), 8.15 (d, 1H), 8.08 (d, 2H), 7.41-7.31 (m, 5H), 3.97-3.92 (m, 1H), 3.59-3.50 (m, 2H), 2.99-2.90 (m, 1H), 2.86-2.79 (m, 1H), 1.59 (s, 6H).

General synthesis of substituted 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A7

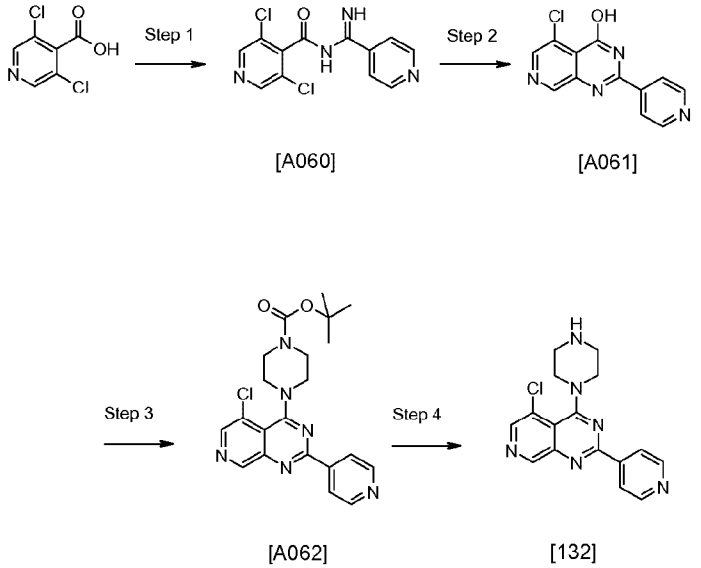
2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] were prepared by coupling of a ortho-halo-isonicotinic acid derivative of general formula [F-016] with an appropriately substituted 4-carbamimidoyl-pyridines of general formula [F-018] with a suitable coupling agent such as O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) in a polar aprotic solvent such as DMA or DMF. The isonicotinoyl-amidine derivative of general formula [F-017] were then cyclised to displace the relevant halogen group to yield the desired 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004]. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-

d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride and the intermediate 4-chloro derivative was then reacted with primary or secondary amino derivative of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A7



Synthesis of 5-Chloro-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [132]



Synthesis of 3,5-Dichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A060]

3,5-Dichloro-isonicotinic acid (10.4mmol, 1.997g), was dissolved in anhydrous DMF (50mL) at room temperature and HATU (10.4mmol, 3.95g), added in one portion and the mixture stirred for 5mins. Then DIPEA (28.6mmol, 5.0mL) was added in one portion and reaction stirred for 40 minutes. Pyridine-4-carboximidamide hydrochloride (9.52mmol, 1.5g) was added in one portion and reaction stirred at room temperature for 18 hours.

The reaction mixture was then poured into water (~250mL in total including rinses of reaction vessel) in a conical flask. The resultant mixture was stirred at room temperature for 90 minutes and the precipitate formed was filtered, washed with water (x2) and ether (x2). Then the solid was dried in vac oven for 4hrs to yield the title compound [A060] (2.359g), as a pale brown powder. LCMS method: 1, RT:3.31 min, MI 295 [M+H].

Synthesis of 5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061]

In a 25mL Biotage microwave vessel, under nitrogen, was added 3,5-Dichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A060] (1.5mmol, 0.443g), cesium carbonate (3.0mmol, 0.978g) and N,N'-Dibenzylethylenediamine (0.3mmol, 0.071mL). The mixture was stirred in anhydrous DMA (10mL), vigorously and iron (III) chloride (0.15mmol, 0.024g) added in one portion. Then the mixture was heated in the microwave at 120°C for 90mins. The reaction was allowed to cool to room temperature and acetic acid (12.0mmol, 0.69mL), added dropwise over about 5 minutes and the resulting mixture diluted with MeOH (10mL) and stirred at RT for 30mins. The mixture was added to a 10g SCX-2 cartridge and washed with methanol (~25-30mL). The cartridge was then washed with ammonia (2N in MeOH, 40mL) and the ammonia washes concentrated in vacuo to yield 5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one (130mg). The non-basic methanol washes of the SCX-2 cartridge were left standing overnight, forming a precipitate. This was filtered, washed with methanol (x1), and dried in a vacuum oven overnight to yield the title compound [A061] (13mg) as an off-white solid. LCMS method: 1, RT:2.12 min, MI 259 [M+H].

Synthesis of 4-(5-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A062]

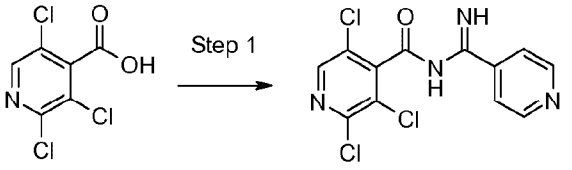
5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061] (0.553mmol, 0.143g), was suspended in anhydrous DCM (14mL) at RT under nitrogen and triethylamine (1.38mmol, 0.193mL), DMAP (approximately 0.005g) and 2,4,6-triisopropylbenzene sulfonyl chloride (0.663mmol, 0.201g) were added sequentially. The reaction was stirred at room temperature

as an off-white suspension for 2hrs. Slowly the mixture becomes a pale green suspension, that was left stirring overnight. Then pyridine (4mL) was added and the reaction vessel sonicated for 5minutes to try to improve the dissolution causing the reaction to change colour from green to brown suspension. The resultant mixture was stirred at room temperature for 1 hour. Boc-piperazine (0.608mmol, 0.113g) was added in one portion and the mixture left stirring for 18 hours.

The reaction was diluted with water and extracted with DCM (x3). Combined organics washed with brine (x1), dried ($MgSO_4$), filtered and concentrated in vacuo. To yield the title compound [A062] which was used in the next reaction without further purification: LCMS method: 1, RT:5.69 min, MI 427 [M+H].

Synthesis of 5-Chloro-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [132] To a solution of 4-(5-Chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A062] (0.47mmol, 0.201g), in anhydrous DCM (8mL), at room temperature was added HCl (4.0N in dioxane, 2mL) to yield an orange suspension that was stirred at room temperature for 3 hours. The mixture was then concentrated in vacuo, redissolved in DCM/MeOH (1:1, 6mL total) and added to an SCX-2 10g cartridge. The cartridge was washed with DCM and MeOH (~35mL total ~2:3 ratio respectively). Then the cartridge was washed with ammonia in methanol (2N, 40mL) and the ammonia washes were concentrated in vacuo to yield 92mg brown oil. The crude material was purified by column chromatography (SP1 4g VWR column with 0-20% MeOH/DCM 15 volumes) to yield the title compound [138] (0.044g) as an orangey-yellow foam. LCMS method: 1, RT:1.60 min, MI 327 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.15 (1H, s), 8.77 (2H, d), 8.61 (1H, s), 8.29 (2H, d), 3.69 (4H, br s), 2.85 (4H, br s)

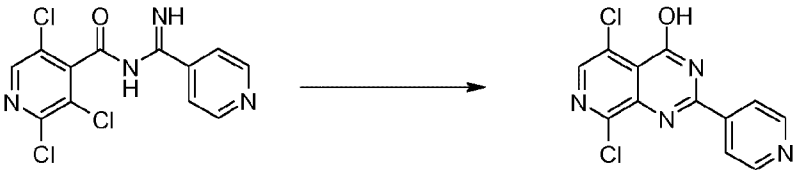
Synthesis of 5,8-Dichloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A063]



[A064]

2,3,5-Trichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A064] was prepared by reaction of 2,3,5-Trichloro-isonicotinic acid, pyridine-4-carboximidamide hydrochloride,

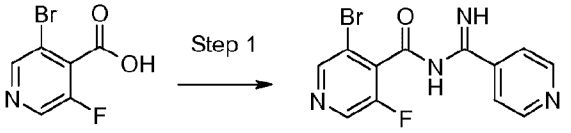
HATU, DIPEA and DMF at room temperature to give the title compound. LCMS method: 1, RT:4.37 min, MI 330 [M+H]; NMR: (1H, 300MHz, d6-dmso); 10.24 (1H, br s), 10.14 (1H, br s), 8.75 (2H, d), 8.60 (1H, s), 7.89 (2H, d).



[A064] [A063]

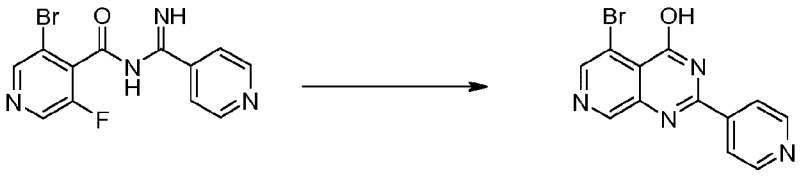
5,8-Dichloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A063] was prepared by reaction of 2,3,5-Trichloro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide[A064], $FeCl_3$, Ce_2CO_3, HCl (4N in dioxane) and DMA in a in μwave for 2hrs at 120°C The reaction mixture was cooled and water (0.5mL) was added followed by MeOH (2mL) and HCl (4eq wrt carbonate, 2.4mmol, 0.6mL 4N HCl in dioxane) and the mixture was stirred for 10mins. The yellow precipitate was collected by filtration and the solid was washed with MeOH (2x, 2mL) then dried in vac oven to give the title compound as a yellow solid (51 mg, 56% yield): LCMS method: 1, RT:4.80 min, MI 293 [M+H]; NMR: (1H, 300MHz, d6-dmso); 13.36 (1H, br s), 8.92 (2H, d), 8.49 (1H, s), 8.14 (2H, br d).

Synthesis of 3-Bromo-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A065]



[A066]

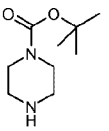
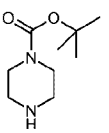
2-Bromo-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A066] was prepare by reaction of 3-Bromo-4-carboxy-5-fluoro-pyridinium; chloride, pyridine-4-carboximidamide hydrochloride, HATU, DIPEA and DMF at room temperature to give the title compound. LCMS method: 1, RT:3.20 min, MI 325 [M+H].



[A066] [A065]

2-Bromo-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A066] (0.05g, 0.155 mmol), DMA (0.5 mL), K_2CO_3 (0.022g, 0.16 mmol), DIPEA (0.28 mL, 0.16 mmol) and DBA (0.024 mL, 0.16 mmol) wa heated at 150°C in μwave for 45mins. The crude reaction mixture was evapourated under reduced pressure and the crude material was purified by column chromatography (SP1 4g VWR column in 0.5%Et3N / DCM / 0-20% MeOH) to yield the title compound [A065] (0.044g, 80% yield) as an orangey-yellow foam: LCMS method: 1, RT:11.57 min, MI 304 [M+H].

The following compounds were synthesised according to the general synthesis shown in scheme [A7]:

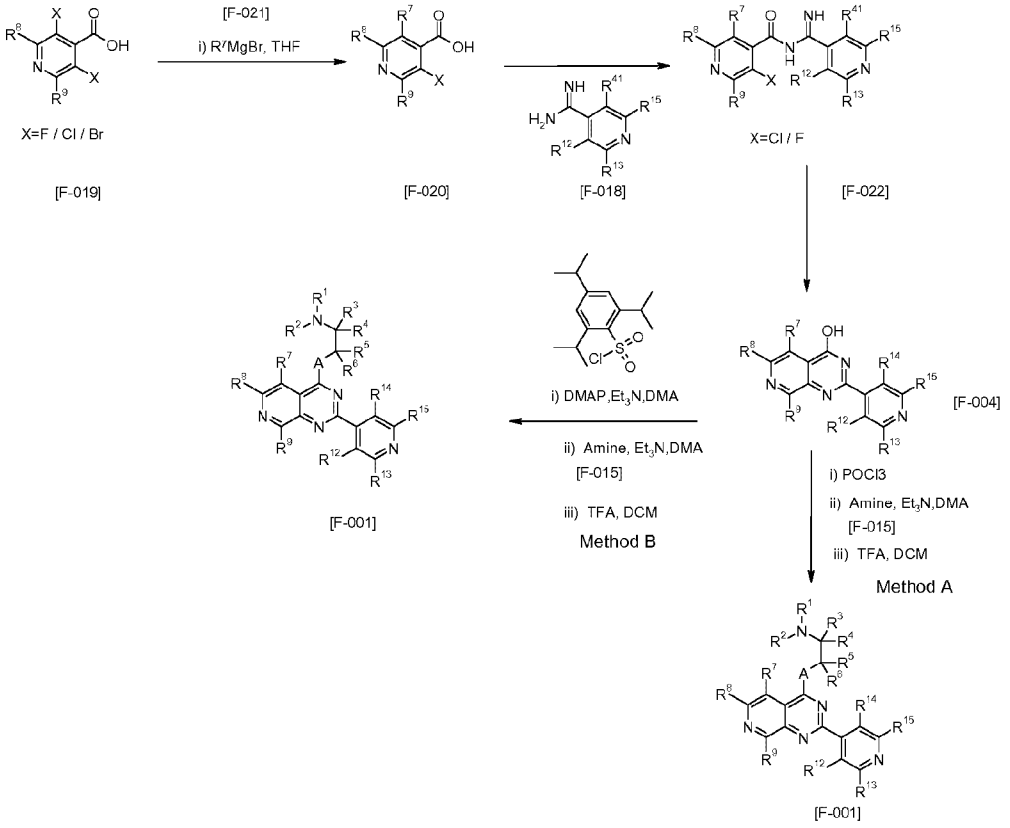
Ex	SM	Met - hod	Amine [F-015]	Analysis		Name
133	[A065]	A		Method 1: RT: 1.77 min, MI: 373 [M+H]	(1H, 500MHz, d6-dmso), 9.17 (1H, s), 8.77 (2H, dd), 8.72 (1H, s), 8.29 (2H, dd), 3.78-3.61 (4H, m), 2.94 (2H, br s), 2.82-2.71 (2H, m)	1-[5-bromo-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
134	[A063]	A		Method 1: RT: 5.02 min, MI: 361 [M+H]	(1H, 500MHz, d6-dmso) 8.79 (2H, dd), 8.41 (1H, s), 8.30 (2H, dd), 3.74 (4H, br s), 2.98-2.75 (4H, m)	1-[5,8-dichloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

General synthesis of substituted 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A8

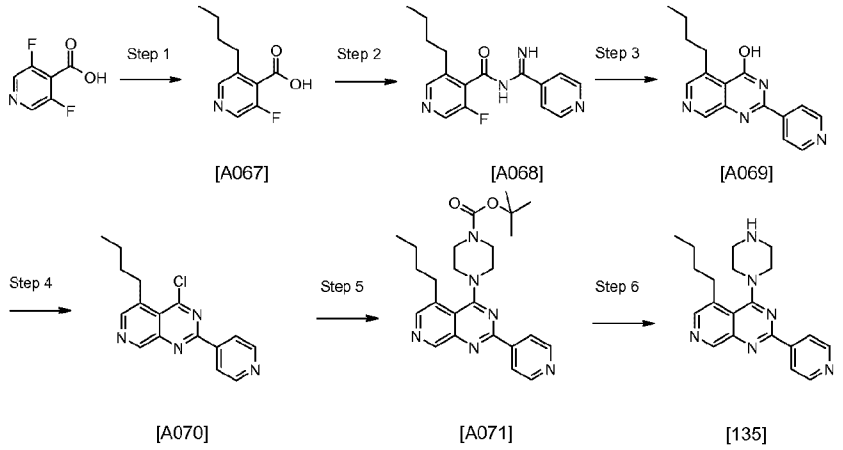
Ortho-halo-isonicotinic acid derivatives of general formula [F-020] were prepared by reaction of a dihalo isoinicotinic acid derivative of general formula [F-019] with a grindard reagent of general formula [F-021] in a polar aprotic solvent such as THF or Et_2O. 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] were prepared by

coupling of a ortho-halo-isonicotinic acid derivative of general formula [F-020] with an appropriately substituted 4-carbamimidoyl-pyridines of general formula [F-018] with a suitable coupling agent such as O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) in a polar aprotic solvent such as DMA or DMF. The isonicotinoyl-amidine derivative of general formula [F-022] were cyclised to displace the relevant halogen group to yield the desired -Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004]. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride and the intermediate 4-chloro derivative was then reacted with primary or secondary amino derivative of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A8



Synthesis of 5-Butyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [135]



Synthesis of 3-Butyl-5-fluoro-isonicotinic acid [A067]

3,5-Difluoro-isonicotinic acid (0.557 g, 3.5 mmol) was suspended in anhydrous THF (8 mL) at 0°C, under an atmosphere of nitrogen. To this was added butyl magnesium chloride (2.0 M in diethyl ether, 5.25 mL, 10.5 mmol) dropwise over 10 minutes. The suspension slowly

changed form during the slow addition with preliminary agglomeration of solid then the solid started to dissolve slowly, achieving full solution around completion of addition of reagent. The reaction mixture was allowed to warm to room temperature and stirred over 72 hours to form a thick yellow suspension. Diluted with water and transferred into a single neck flask and concentrated in vacuo. The yellow solid was diluted with water (10 mL) and EtOAc (10 mL). The pH was adjusted pH~2, by dropwise addition of HCl (conc.) and extracted with EtOAc (x3 - some of the yellow colour goes into organics). Combined organics were washed with brine (x1), dried ($MgSO_4$) and concentrated in vacuo to yield the title compound [A067] as an orange gum/solid (0.402g) that solidifies slowly: NMR: (1H, 300MHz, d6-dmso); 8.52 (1H, s), 8.42 (1H, s), 2.67 (2H, t), 1.58-1.48 (2H, m), 1.35-1.22 (2H, m), 0.87 (3H, t); LCMS method: 1, RT:1.22 min, MI 198 [M+H].

Synthesis of 3-Butyl-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A068]

3-Butyl-5-fluoro-isonicotinic acid [A067] (2.05 mmol, 0.402 g) was dissolved in anhydrous DMF (8 mL) and diisopropylethylamine (DIPEA) (5.95 mmol, 1.04 mL) was added and the mixture stirred at room temperature for 5 minutes. Then O-(7-Azabenzotriazol-1-yl)-N,N,N′,N′-tetramethyluronium hexafluorophosphate (HATU) (2.0 5mmol, 0.78 g) was added in one portion and the resultant mixture stirred for 1 hour. pyridine-4-carboximidamide hydrochloride (1.95 mmol, 0.307 g) was then added portionwise over 5 minutes to the reaction. The resultant solution was stirred at room temperature for 18 hours. The reaction mixture was poured into water (85 mL) and stirred for 30 minutes and then extracted with EtOAc (x3). The combined organics washed with water (x4), brine (x1), dried ($MgSO_4$), filtered and concentrated in vacuo to yield the title compound [A068] (480mg) as a brown solid. The material was used crude in next reaction: NMR: (1H, 300MHz, d6-dmso); 10.28 (1H, br s), 9.93 (1H, br s), 8.74 (2H, d), 8.45 (1H, s), 8.37 (1H, s), 7.90 (2H, d), 2.72-2.66 (2H, m), 1.58-1.48 (2H, m), 1.28-1.15 (2H, m), 0.79 (3H, t); LCMS method: 1, RT:3.90 min, MI 301 [M+H].

Synthesis of 5-Butyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A069]

3-butyl-5-fluoro-N-(imino-pyridin-4-yl-methyl)-isonicotinamide [A068] was placed into 25mL Biotage microwave vessel in solution in anhydrous DMA (5 mL) and heated at 150°C in the microwave for 45mins. The reaction mixture was filtered material through an SCX-2 25g cartridge. The cartridge was washed with methanol (50 mL). Then the cartridge was

washed with ammonia (2N, 40 mL) and the ammonia washes concentrated in vacuo to yield the title compound [A069] (390mg) as a pale brown solid, : NMR: (1H, 300MHz, d6-dmso); 8.95 (1H, s), 8.79 (2H, dd), 8.46 (1H, s), 8.10 (2H, dd), 3.21 (2H, t), 1.63-1.50 (2H, m), 1.43-1.27 (2H, m), 0.91 (3H, t) – also shows one equivalent of DMA; LCMS method: 1, RT:3.29 min, MI 281 [M+H].

Synthesis of 5-Butyl-4-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [A070]

5-Butyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A069] (1.35 mmol, 0.378 g) was suspended in anhydrous 1,2-dichloroethane (DCE) (10 mL) and phosphorus oxychloride ($POCl_3$) (1.4 mmol, 0.131 mL) was added dropwise over 2-3 minutes. Finally DIPEA (2.0 mmol, 0.348 mL) was added and the mixture stirred at RT under nitrogen overnight. The brown solid slowly to change appearance after $POCl_3$ addition, then darkens further on addition of DIPEA to become a dark brown apparent solution. The reaction was left stirring at room temperature overnight under nitrogen. After 20 hours $POCl_3$ (65 µL) was added and stirred at room temperature overnight. The crude mixture was concentrated in vacuo, then azeotroped with toluene (x2) to dryness. The residue was diluted with sodium carbonate (aq. soln., 2N, 20mL) and extracted with DCM (x2), EtOAc (x1). Combined organics washed with brine (x1), dried ($MgSO_4$), filtered through a pad of silica and concentrated in vacuo to yield the title compound [A070] (180mg) as a of a pale brown solid which was used in the next reaction without further purification: LCMS method: 1, RT:5.66 min, MI 299 [M+H].

Synthesis of 4-(5-Butyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A071]

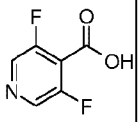
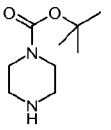
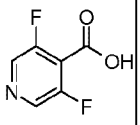
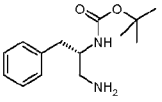
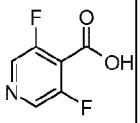
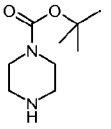
5-Butyl-4-chloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [A070] (0.615 mmol, 0.180 g), was dissolved in anhydrous DCM (5 mL), under nitrogen at room temperature and treated with triethylamine (0.868 mmol, 0.121 mL) and N-Boc-piperazine (0.682 mmol, 0.127 g) in one portion. The resulting mixture was stirred at room temperature for 2 hours. Then sodium carbonate (1N aq. soln, 20 mL) was added and extracted with DCM (x2) and EtOAc (x1). Combined organics washed with brine (x1), dried ($MgSO_4$), filtered and concentrated in vacuo to a dark brown solid, which was purified by column chromatography (SP1 on 25g VWR cartridge in 0-10% MeOH/DCM, 15col vols) to yield the title compound [A071] as a brown gum (0.092g) which was used in the next reaction without further purification: NMR:

(1H, 300MHz, d6-dmso); 9.24 (1H, s), 8.79 (2H, d), 8.49 (1H, s), 8.36 (2H, d), 3.77-3.48 (8H, m), 3.19-3.07 (2H, m), 1.64-1.23 (4H, m), 1.48 (9H, s), 0.96-0.87 (3H, t)

Synthesis of 5-Butyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [135]

4-(5-Butyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A071] (0.20mmol, 0.09g) was dissolved in anhydrous DCM (4 mL) and treated with hydrogen chloride (4N in dioxane, 4 mL) at room temperature and stirred for 2 hours. The reaction was diluted with methanol and poured onto SCX-2 cartridge (5 g), washing with MeOH/DCM (20mL). The cartridge was then washed with ammonia (2N, 20 mL) and the ammonia washes concentrated in vacuo to yield a brown gum (0.059 g). The residue was purified by column chromatography (SP1 4 g column, in a gradient 5-20% MeOH/DCM 15col vols) to yield the title compound [133] as an orangey-brown gum (0.020g).; NMR: (1H, 300MHz, d6-dmso); 9.09 (1H, s), 8.76 (2H, d), 8.51 (1H, s), 8.31 (2H, d), 3.73-3.58 (2H, br s), 3.50-3.37 (2H, br s), 3.07 (2H, t), 2.90-2.79 (4H, br s), 1.51-1.38 (2H, m), 1.28-1.15pm (2H, m), 0.84 (3H, t); LCMS method: 1, RT:2.58 min, MI 349 [M+H].

The following compounds were synthesised according to the general synthesis shown in scheme [A8]:

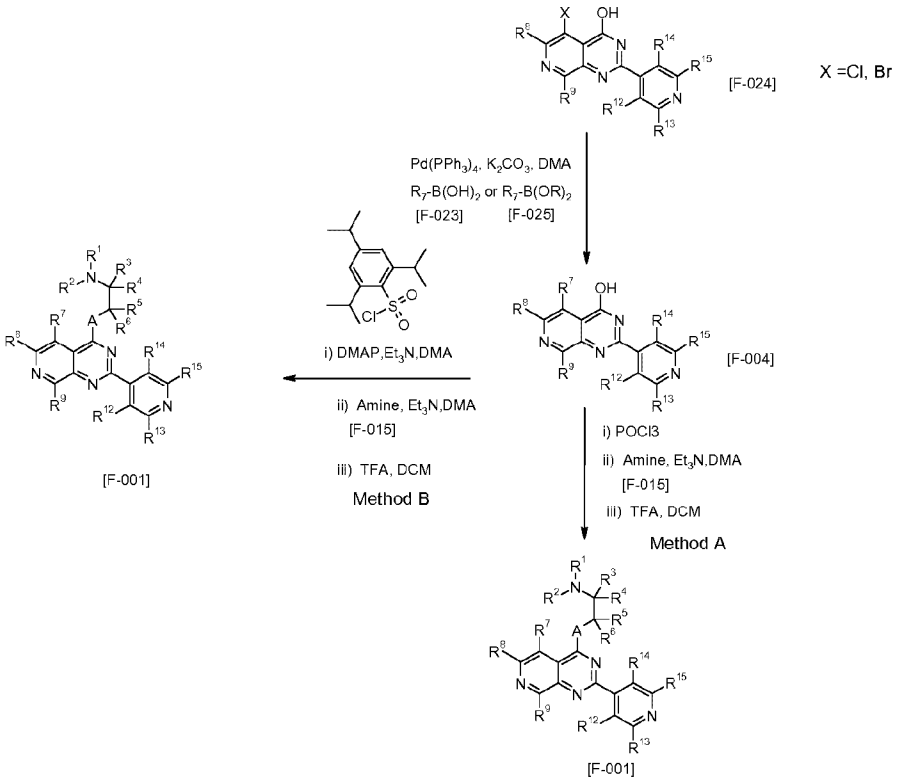
Ex	SM [F-019]	Grig-nard [F-021]	Amine [F-015]	Analysis		Name
136		EtMg Br		Method 1: RT: 1.64 min, MI: 321 [M+H]	(1H, 300MHz, d6-dmso) 9.08 (1H, s), 8.76 (2H, dd), 8.54 (1H, s), 8.30 (2H, dd), 3.72-3.58 (2H, br s), 3.55-3.45 (2H, br s), 3.10 (2H, dd), 2.89-2.77 (4H, br s), 1.17 (3H, t)	1-[5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine
137		EtMg Br		Method 1: RT: 2.90 min, MI: 385 [M+H]	(1H, 300MHz, d6-dmso) 9.02 (1H, s), 8.72 (2H, dd), 8.42 (1H, s), 8.16 (2H, dd), 7.35-7.24 (5H, m), 3.91 (1H, dd), 3.43 (1H, dd), 3.37-3.29 (1H, m), 3.21 (2H, dd), 2.83-2.70 (2H, m), 1.33 (3H, t)	N-[(2S)-2-amino-3-phenylpropyl]-5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine
138		MeMg Br		Method 1: RT: 3.93 min, MI: 307 [M+H]	(1H, 300MHz, d6-dmso) 9.06 (1H, s), 8.76 (2H, dd), 8.43 (1H, s), 8.30 (2H, dd), 3.57 (4H, br s), 2.84 (4H, br s), 2.65 (3H, s)	1-[5-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine

General synthesis of substituted 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] Scheme A9

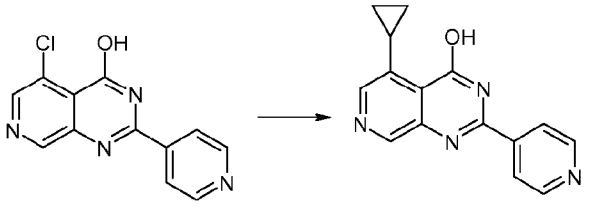
5-Substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] were prepared by reaction of a 5-halo substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-024] (prepared in scheme A7) in a palladium catalysed cross coupling reaction with a boronic acid or boronate ester derivative of general formula [F-023] in the presence of a palladium catalyst such as $Pd(PPh_3)_4$ or $Pd(OAc)_2$, and a base such as K_2CO_3 or Cs_2CO_3 in a polar solvent such as

dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor, or a palladium catalysed cross coupling reaction of a 5-halo substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-024] (prepared in scheme A7) with a fluoroborate derivative of general formula [F-025] in the presence of a catalyst such as $Pd(PPh_3)_4$ or $Pd(OAc)_2$, a ligand such as RuPhos and a base such as K_2CO_3 or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor. 5-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 5-substituted 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with a chlorinatation agent such as phosphorous oxychloride and the intermediated 4-chloro derivative was then reacted with primary or secondary amino derivative of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature [method A]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by normal phase silica gel chromatography or reverse phase preparative HPLC. 4-substituted-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine derivatives of general formula [F-001] were prepared by the reaction of a 2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol derivatives of general formula [F-004] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP [method B]. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [F-015], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, TCA, methanesulfonic acid, HCl or H_2SO_4 in a solvent such as DCM, DCE, THF, EtOH or MeOH and the crude reaction product was purified by reverse phase preparative HPLC

Scheme A9



Synthesis of 1-[5-cyclopropyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [139]

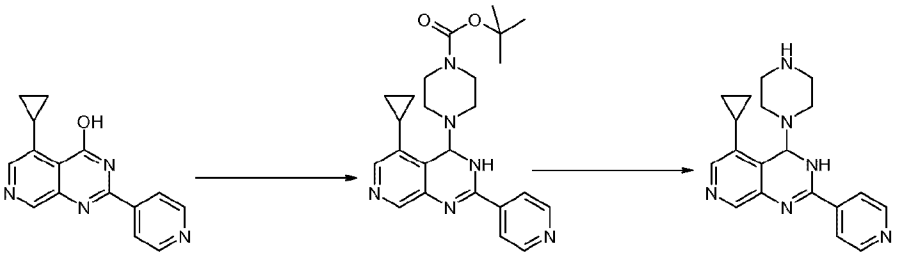


[A061] [A072]

5-Cyclopropyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A060]

5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061] (0.670mmol, 0.173g), potassium carbonate (2.01mmol, 0.278g) and cyclopropyl boronic acid (1.34mmol, 0.115g) was suspended in anhydrous DMA (3mL) and then subjected to vacuum/argon balloon sparge (x3). Then tetrakis(triphenylphosphine)palladium (0.067mmol, 0.077g) was added in one portion and the reaction vessel sealed and heated in a microwave at 150°C for 1hr. The reaction was cooled to room temperature, under nitrogen. Potassium carbonate (2.01mmol, 0.278g) and cyclopropyl boronic acid (1.34mmol, 0.115g) were

added and the reaction mixture subjected to vacuum/argon balloon sparge (x3). Then tetrakis(triphenylphosphine)palladium (0.067mmol, 0.077g) was added in one portion and the reaction vessel sealed and heated in a microwave at 180°C for 1hr. The reaction was cooled to room temperature under air and left standing over 48 hours. The reaction mixture was then poured on to an SCX-2 cartridge (10g) and washed with methanol (~40mL total). Then the cartridge was washed with ammonia (2N in MeOH, ~ 40mL) and the ammonia washes concentrated in vacuo to yield the title compound [A072] (78mg) as a yellow solid which was taken through to next reaction without purification.



[A072] [A073] [139]

4-(5-Cyclopropyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A073]

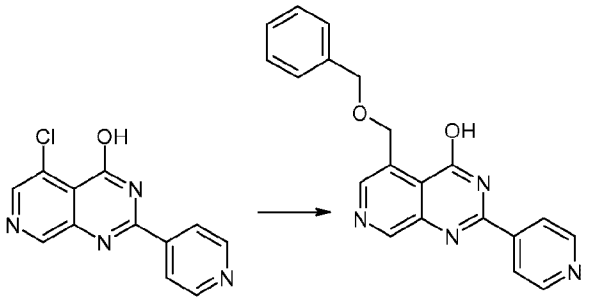
A mixture of 5-Cyclopropyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A072] (0.08 g, 0.3 mmol), DIPEA (0.16 mL, 0.9 mmol), 2,4,6-triisopropylbenzene sulfonyl chloride (0.11 g, 0.36 mmol), DMAP (3 mg) and DMA (2 mL) was stirred at room temperature under nitrogen and left to stir at at RT for 2hrs. Boc-piperazine (0.062 g, 0.33 mmol) was added and the mixture was left to stir at RT overnight. Water was added and the mixture was extracted with EtOAc (x4). The extracts were combined washed with water (x4), brine, dried (MgSO4) and concentrated in vacuo. The crude reaction product was purified by flash column chromatography (SP1, EtOAc:cyclohexane elution) to yield the title compound [A073]: , method: 1, RT:5.57 min, MI 433 [M+H].

1-[5-cyclopropyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine [139]

A mixture of 4-(5-Cyclopropyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A073] (0.9 g, 0.2 mmol) in DCM (3 mL) and 4N HCl dioxane (1 mL) was stirred at RT overnight. The crude reaction mixture was evapourated under reduced pressure then dissolved in MeOH and washed onto SCX-2 (5g) cartridge and washed with MeOH/DCM (1:1, ~ 4 mL) then MeOH (10 mL). Then eluted with ammonia (2N in MeOH, 15mL). The Ammonia elutent was concentrated in vacuo and the

crude product was purified by normal phase chromatography (SiO2, SP1 in MeOH (0-15%)/CHCl3) to give the title compound [139] (30 mg, 43% yield): LCMS method: 1, RT:1.65 min, MI 333 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.99 (1H, s), 8.76 (2H, dd), 8.30 (2H, dd), 8.09 (1H, s), 3.87-3.54 (4H, m), 2.87 (4H, br s), 2.63-2.57 (1H, m), 1.24 (2H, ddd), 1.01 (2H, ddd)

Synthesis of 5-Benzyloxymethyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A074]

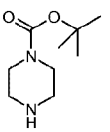


[A061] [A074]

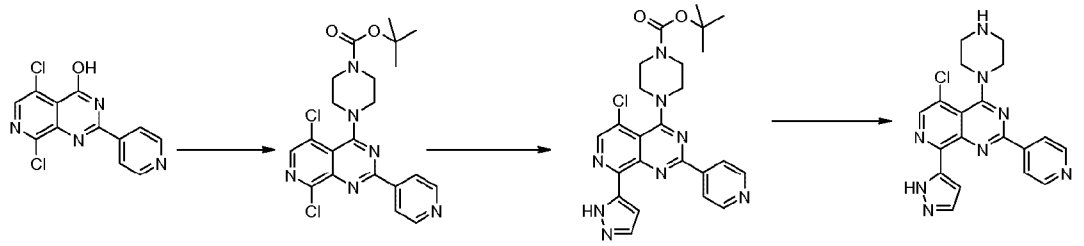
5-Benzyloxymethyl-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A074]
A mixture of5-Chloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A061] (0.1g, 0.4 mmol), Potassium benzyloxymethyltrifluoroborate (0.1 g, 0.45 mmol), cesium carbonate (0.4 g, 1.2 mmol) and RuPhos (12 mg, 0.028 mmol) were placed in Biotage 5mL vessel and suspended in dioxane (1.8 mL) and water (0.2 mL). The mixture was subjected to spurging with vacuum/argon (x3) then the Pd(OAc)2 (3 mg, 0.014 mmol) was added and the vessel sealed and heated at 104°C overnight. DMA (1mL) was added and the mixture was heated in μwave at 150°C for 1hr. The RM was cooled and acetic acid (0.57mL)was added and the mixture and stirred for 10mins. Then flushed down SCX-2 cartridge (10 g) washing with MeOH (30-40mL). Then washed with ammonia (2N in MeOH, 40mL). Ammonia washes concentrated in vacuo to yield the title compound [A074] which was used without further purificatuion: method: 1, RT:3.31 min, MI 345 [M+H].

The following compounds were synthesised according to the general synthesis shown in scheme [A9]:

Ex	SM	Met-hod	Amine	Analysis	Name

140	[A074]	B		Method 1: RT: 4.78 min, MI: 413 [M+H]	(1H, 500MHz, d6-dmso) 9.18 (1H, s), 8.77 (2H, d), 8.69 (1H, s), 8.31 (2H, dd), 7.33-7.25 (5H, m), 4.99 (2H, s), 4.54 (2H, s), 3.51 (4H, br s), 2.79 (4H, t)	1-{5-[(benzyloxy)methyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl}piperazine

Synthesis of 5-Chloro-4-piperazin-1-yl-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [141]



[A063] [A075] [A076] [141]

4-(5,8-Dichloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A075]

A mixture of 5,8-Dichloro-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A063] (0.43 g, 1.47 mmol) Et_3N (0.51 mL, 3.6 mmol), DCM (10 mL), pyridine (2 mL) was sonicated for 2mins. Then DMAP (5 mg) was added followed by 2,4,6-triisopropylbenzene sulfonyl chloride (0.53 g, 1.77 mmol). The reaction mixture was left to stir at RT overnight. The dark brown solution was diluted with water and extracted with DCM (X3) and EtOAc (x1). Combined organics washed with brine (x1). Brine re-extracted with EtOAc (x1). Combined organics dried (MgSO4), filtered and concentrated in vacuo. The crude material was purified by normal phase chromatography (SiO_2 [SP1 (25g vwr cartridge, 0-10% MeOH/DCM]) to give the title compound [A075] (0.19g, 28% yield):. LCMS

method: 1, RT:4.17 min, MI 461 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.81 (2H, d), 8.45 (1H, s), 8.33 (2H, d), 3.76 (4H, br s), 3.33 (4H, br s), 1.40 (9H, br s).

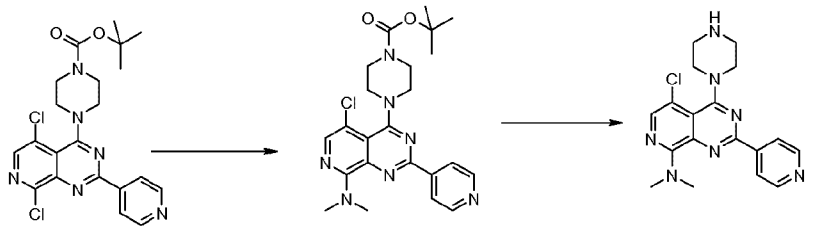
4-[5-Chloro-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [A076]

A mixture of 4-(5,8-Dichloro-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A075] (0.07 g, 0.15 mmol), potassium phosphate tribasic [K_3PO_4 212.27g/mol 21.2g in 100 mL deionised water] (0.3 mL, 0.3 mmol), tetrakis(triphenylphosphine)palladium (17 mg, 0.015 mmol), 1H-Pyrazole-5-boronic acid (24 mg, 0.21 mmol) and DMA (1 mL) were heated in μwave at 150°C for 30min. Acetic acid (0.52 mL) was added and the mixture was left to stir at rt for 20mins and then the crude product was loaded onto an SCX cartridge and the cartridge was washed with methanol then the product was eleuted with 2M ammonia / methanol. The eluent was concentrated under reduced pressure and the crude reaction mixture was purified by normal phase chromatography (SiO_2, ethyl acetate: cyclohexane elution) to give the title compound [A076]: LCMS method: 1, RT:5.62 min, MI 493 [M+H].

Chloro-4-piperazin-1-yl-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [141]

A mixurure of 4-[5-Chloro-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [A076] and HCl dioxane (4N, 1 mL) was stirred at rt for 48 hours. The crude reaction mixture was evapourated under reduced pressure and the crude product loaded onto a SCX-2 cartridge (1 g) and washed with methanol. The product was released from the cartridge using a solution of 2M ammonia / methanol. The ammonia / methanol eluent was concentrated under reduced pressure and the crude product was purified by preparative HPLC (method A) to yield to the title compound: LCMS: method: 1, RT:1.98 min, MI 393 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.76-8.75 (3H, m), 8.50 (1H, s), 8.17 (2H, dd), 7.90 (1H, d), 6.67pm (1H, dd), 3.76 (4H, br s), 2.93 (2H, br s), 2.80 (2H, br s)

Synthesis of 5-chloro-N,N-dimethyl-4-(piperazin-1-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-amine [142]



[A075] [A077] [142]

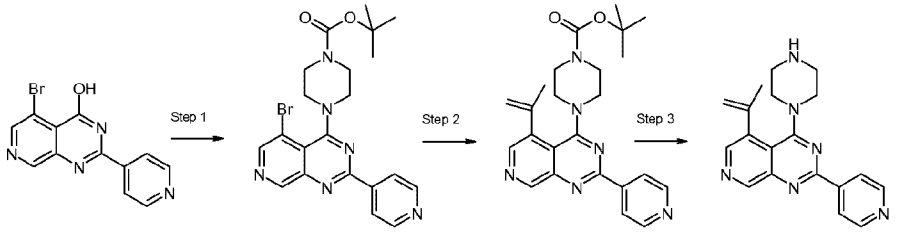
4-(5-Chloro-8-dimethylamino-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A077]

4-[5-Chloro-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [A075] (0.046 g, 0.1 mmol), DMF (2 mL) and dimethylamine in ethanol (0.5 mL) was warmed to 50°C in a sealed vessel and left to stir for 24 h. The crude reaction mixture was evapourated under reduced pressure to yield the title compound [A077] which was used in the next step without further purification: LCMS: method: 1, RT:4.41 min, MI 470 [M+H].

5-chloro-N,N-dimethyl-4-(piperazin-1-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-amine [142]

A mixture of 4-(5-Chloro-8-dimethylamino-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A077] (0.1 g, 0.22 mmol), DCM (3 mL) and HCl (1 mL of a 4N solution in dioxane) was stirred at RT for 2 h. The crude reaction mixture was evpourated under reduced pressure then the crude product was loaded onto an SCX cartridge and the cartridge was washed with methanol then the product was eleuted with 2M ammonia / methanol. The eluent was concentrated under reduced pressure and the crude reaction mixture was purified by normal phase chromatography (SiO_2, SP1 on 4g cartridge in 0-15% MeOH/DCM) to give the title compound: LCMS: method: 1, RT:5.40 min, MI 370 [M+H]; NMR: (1H, 300MHz, d6-dmso); 8.73 (2H, dd), 8.22 (2H, dd), 7.97 (1H, s), 3.76-3.68 (2H, m), 3.56-3.49 (2H, m), 3.16 (3H, s), 3.15 (3H, s), 2.95-2.87 (2H, m), 2.86.2-77 (2H, m)

Synthesis of 5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [143]



[A065] [A078] [A079] [143]

Step 1: Synthesis of 4-(5-Bromo-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A078]

A mixture of 5-Bromo-2-pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A065] (0.74 g, 2.45 mmol) in DMF (15 mL), DIPEA (1.3 mL, 7.3 mmol) and DMAP (5 mg) was stirred at rt for 10 min. 2,4,6-triisopropylbenzene sulfonyl chloride (0.89 g, 2.94 mmol) was added and the mixture was left to stir at rt for 80 mins at RT, then boc-piperazine (0.5g, 2.94 mmol) was added in one portion and the rm was left to stir at rt over night. Water (30mL) was added and the mixture was stirred at RT for 20mins. The resultant solid was collected by filtration and the crude product was purified by column chromatography (SP1 (25 g cartridge) in 0-10% MeOH/DCM (~20vols, 4 vols at 10%MeOH/DCM)) to yield the title compound [A078] (0.69g, 60% yield): LCMS: method: 1, RT:5.83 min, MI 473 [M+H]; NMR: (1H, 300MHz, d6-dmso); 9.22 (1H, s), 8.78 (3H, m), 8.32 (2H, d), 3.79 (4H, br s), 3.61 (4H, br s), 1.41 (9H, br s).

Step 2: Synthesis of 4-(5-Isopropenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A079]

4-(5-Bromo-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A078] (0.2 mmol, 0.094g), potassium phosphate (tribasic) (0.60 mmol, 0.127g), and Isopropenylboronic acid pinacol ester (0.30mmol, 0.057mL) were suspended in anhydrous dioxane (2 mL), in a 5 mL Biotage vessel under nitrogen. The vessel was subjected to vacuum/argon (balloon) sparge (x3) and then dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.01mmol, 0.008 g) added and the reaction sealed and warmed to 96°C for 18 hours. The reaction mixture was cooled to room temperature under air, silica for chromatography added (1g) and the mixture concentrated in vacuo to a brown powder. This was dry loaded onto a silica cartridge and purified by chromatography (SP1 0-10% MeOH/DCM 15 col vols) to yield 4-(5-Isopropenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A079] (85mg) as a 85mg brown glass: NMR: (1H,

500MHz, $CDCl_3$); 9.31 (1H, s), 8.79 (2H, d), 8.50 (1H, s), 8.36 (2H, d), 5.40 (1H, s), 5.32 (1H, s), 3.58 (8H, br s), 2.21 (3H, s), 1.24 (9H, s); LCMS: method: 1, RT:5.66 min, MI 433 [M+H].

Step 3: Synthesis of 5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [143] To a solution of 4-(5-Isopropenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A079] (0.105mmol 0.045 g), in DCM (2 mL) at room temperature was added hydrogen chloride (4N in dioxane, 1mL), to obtain a thick yellowy-brown suspension, that was stirred overnight. The reaction mixture was then concentrated in vacuo, the residue re-dissolved in MeOH and washed onto SCX-2 cartridge. The cartridge was washed with DCM and MeOH (1:1, 20mL total). Then the SCX-2 was washed with ammonia (2N in MeOH, 15mL). The combined ammonia washes were concentrated to an orangey-brown solid, which was purified by column chromatography (SP1 4g cartridge, 0-20% MeOH/DCM, 15 col vols) to yield 5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine [143] (0.011g) as a yellow glass: NMR: (1H, 500MHz, d4-MeOH) 9.15 (1H, s), 8.76 (2H, dd), 8.49 (1H, s), 8.31 (2H, dd), 5.40 (1H, s), 5.20 (1H, s), 3.56 (4H, br s), 2.79 (4H, t), 2.17 (3H, s); LCMS: method: 1, RT:1.88 min, MI 333 [M+H].LC-MS.

Example 151. 5-Methoxy-4-piperidin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine

151a) 3-tert-Butoxycarbonylamino-pyrrolidine-1,3-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester : 3-tert-Butoxycarbonylamino-pyrrolidine-3-carboxylic acid (1.50 g, 6.50 mmol) was added to a solution of Sodium carbonate (1.65 g, 15.6 mmol) in Water (16.7 mL, 926 mmol) and 1,4-Dioxane (9 mL, 100 mmol). The resulting solution was stirred and cooled in an ice bath. To the stirring reaction solution was added a solution of 9-Fluorenylmethyl chloroformate (1.76 g, 6.82 mmol) in 1,4-Dioxane (13 mL, 160 mmol). The mixture was stirred at room temperature for 2 h, poured into Water (300 mL) and extracted twice with ether. The aqueous phase was cooled in an ice bath and slowly treated with 3 M of Hydrogen Chloride in Water (7.80 mL, 23.4 mmol) to neutralize. The resulting mix was extracted with EtOAc (2x), the combined organics dried over Na2SO4, filtered, and concentrated. The residue was pumped under high vacuum for 4 h, leaving 3.12 g (106%) of foam, which was used for subsequent step without further manipulation.

151b) 3-tert-Butoxycarbonylamino-3-carbamoyl-pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester: At rt Di-tert-Butyldicarbonate (655 mg, 3.00 mmol) was added to a mixture of 3-tert-Butoxycarbonylamino-pyrrolidine-1,3-dicarboxylic acid 1-(9H-

fluoren-9-ylmethyl) ester (905 mg, 2.00 mmol) and Pyridine (0.324 mL, 4.00 mmol) in 1,4-Dioxane (5 mL, 60 mmol). After 15 minutes, Ammonium Bicarbonate (0.474 g, 6.00 mmol) was added, and the reaction mixture was stirred for 72 h. Added water (10 mL) to resulting solid mass and swirled. Filtered off solid and rinsed liberally with water. After air drying, dried resulting solid under high vacuum at rt. Obtained 1.12 g (124%) of tannish solid. Proceeded and used this tannish solid for subsequent step without further manipulation.

151c) (3-Carbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester 3-tert-Butoxycarbonylamino-3-carbamoyl-pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester (410 mg, 0.91 mmol) was suspended in Methanol (5 mL, 100 mmol), then at rt added Piperidine (1 mL, 10 mmol) neat. After 16 hours concentrated reaction under reduced pressure, then pumped on residue under high vacuum overnight (to remove as much piperidine as possible), and used crude directly for subsequent reaction.

151d): 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol (127 mg, 0.501 mmol), Triethylamine (216 uL, 1.55 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (167 mg, 0.552 mmol), and 4-Dimethylaminopyridine (6.9 mg, 0.057 mmol) in N,N-Dimethylformamide (2.0 mL, 26 mmol) were stirred at room temperature for 1 h. Gradual dissolution of starting material was observed, intermediate sulfonate observed by hplc . (3-Carbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester (126 mg, 0.550 mmol) was then added as a solution in N,N-Dimethylformamide and the reaction was stirred at room temperature. After 45 minutes concentrated reaction under reduced pressure, then partitioned residue between EtOAc and water. Took organic and washed with 3 mL of 1N HCl. Took aqueous solution, added small amount of DMSO and purified over two runs with preparative reverse phase HPLC. Combined purest fractions of each major product and lyophylized. Obtained 32 mg (14%) of yellow lyophilate of front running material [3-Carbamoyl-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-carbamic acid tert-butyl ester (LC/MS: M+H=466.2). Also obtained 35 mg (22%) of side product 5-Methoxy-4-piperidin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine (LC/MS: M+H=322.1), which was generated from piperidine left over from preparation of starting material (3-Carbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester. Proceeded on with [3-Carbamoyl-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-carbamic acid tert-butyl ester for subsequent reaction without further manipulation.

Example 152. 3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid amide

Added a solution of Trifluoroacetic Acid (1 mL, 10 mmol) in Methylene chloride (2 mL, 30 mmol) to [3-Carbamoyl-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-carbamic acid tert-butyl ester (30 mg, 0.06 mmol) at rt. After 30 minutes concentrated reaction mixture under reduced pressure, then to residue triturate with Et2O to get a solid. Filtered solid and washed liberally with Et2O. Obtainedwith 17 mg of title compound as a solid (LC/MS: +H=366.1).

Example 153. 3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid phenylamide

153a) 3-tert-Butoxycarbonylamino-3-phenylcarbamoyl-pyrrolidine-1-carboxylic acid-9H-fluoren-9-ylmethyl ester : N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (575 mg, 3.00 mmol) was added to a mixture of 3-tert-Butoxycarbonylamino-pyrrolidine-1,3-dicarboxylic acid 1-(9H-fluoren-9-ylmethyl) ester (905 mg, 2.00 mmol), 1-Hydroxybenzotriazole (2.70E2 mg, 2.00 mmol) and Aniline (228 uL, 2.50 mmol) in Tetrahydrofuran (25 mL, 310 mmol). After 10 minutes added N,N-Dimethylformamide (10 mL, 100 mmol) to facilitate dissolution. After 1.5 hour concentrated reaction mixture under reduced pressure. The residue was partitioned between EtOAc (2x) and saturated aqueous NaHCO3. The combined organic phases were dried over Na2SO4, filtered, and concentrated under reduced pressure to yield 0.97 g (92%) of foam (LC/MS: M+H=528.1), which was used for subsequent step without further manipulation.

153b) (3-Phenylcarbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester : 3-tert-Butoxycarbonylamino-3-phenylcarbamoyl-pyrrolidine-1-carboxylic acid 9H-fluoren-9-ylmethyl ester (960 mg, 1.8 mmol) was combined with Methanol (10 mL, 200 mmol), then at toom temperature added Piperidine (2 mL, 20 mmol) neat and the reaction was stirred for 72 h. Concentrated reaction mixture under reduced pressure and Obtained a solid mass. Triturated entire sample with Et2O, filtered and rinsed solid liberally with Et2O. After air drying there remained 0.55 g (99%) of tannish solid. Proceeded and used this material in subsequent reaction without further manipulation.

153c) [1-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenylcarbamoyl-pyrrolidin-3-yl]-carbamic acid tert-butyl ester: 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-

d]pyrimidin-4-ol (254 mg, 1.00 mmol), Triethylamine (431 uL, 3.10 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (334 mg, 1.10 mmol), and 4-Dimethylaminopyridine (14 mg, 0.11 mmol) in N,N-Dimethylformamide (4.0 mL, 52 mmol) were stirred at room temperature for 1 hour. (3-Phenylcarbamoyl-pyrrolidin-3-yl)-carbamic acid tert-butyl ester (335 mg, 1.10 mmol) was added neat and the reaction was stirred at room temperature overnight. The reaction was then concentrated under reduced pressure and partitioned residue between EtOAc and water. Had to filter before separating layers, as precipiated solid causing some problems between layers. The organic phase was dried over Na2SO4, filtered, and concentrated under reduced pressure to give 500 mg of crude product. Dissolved crude in DMSO (3.6 mL), filtered, and purified via preparative reverse phase HPLC. Took purest fractions and basified with saturated aqueous NaHCO3. Solid which crashed from the solution was filtered, and rinsed with water. After air drying there remained 50 mg (9%) off white solid. (LC/MS: M+H=542.1). Proceeded and used material for subsequent step without further manipulation.

153d) At rt dissolved [1-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenylcarbamoyl-pyrrolidin-3-yl]-carbamic acid tert-butyl ester (50.0 mg, 0.0923 mmol) in Methylene chloride (2.0 mL, 31 mmol) then added Trifluoroacetic Acid (1.0 mL, 13 mmol) neat. After 2.5 h concentrated reaction under reduced pressure, dissolved residue in 0.80 mL DMSO, filtered, and purified via preparative reverse phase HPLC. Combined and lyophilized purest fractions. Obtained 32 mg (78%) of title compound as a yellow lyophilate (LC/MS: M+H=442.1).

Example 154. 4-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid [(S)-1-(4-chloro-phenyl)-3-hydroxy-propyl]-amide

154a) 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid methyl ester : 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol (254 mg, 1.00 mmol), Triethylamine (0.432 mL, 3.10 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (334 mg, 1.10 mmol), and 4-Dimethylaminopyridine (14 mg, 0.11 mmol) were combined in N,N-Dimethylformamide (2.0 mL, 26 mmol), and stirred at room temperature. After 45 minutes 4-tert-Butoxycarbonylamino-piperidine-4-carboxylic acid methyl ester (284 mg, 1.10 mmol; Supplier = Oakwood) was added neat and stirred overnight. The reaction mixture was concentrated under reduced pressure and the residue partitioned between CH2Cl2 and water. The organic phase was dried over Na2SO4, filtered, and concentrated under

reduced pressure. Resulting 380 mg (77%) of residue was used for subsequent steps without further manipulation.

154b) 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid : Combined a solution of Lithium hydroxide (180 mg, 7.5 mmol) in water (3 mL, 200 mmol) to a solution of 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid methyl ester (370 mg, 0.75 mmol) in Methanol (10 mL, 200 mmol) at rt and let homogeneous solution stir at rt for 16 hours. After cooling, treated reaction mixture with 1 M of Hydrogen Chloride in Water (7.5 mL, 7.5 mmol), then concentrated off most of MeOH, leaving mostly aqueous as solvent. Filtered resulting solid, then took aqueous filtrate and concentrated. Obtained 292 mg . Added 2.5 mL of DMSO, filtered, then purified via preparative reverse phase HPLC, lyopylized purest fractions to yield 45 mg (12%) of desired product as a yellow lyophilate, which was used for subsequent steps without further manipulation.

154c) [4-[(S)-1-(4-Chloro-phenyl)-3-hydroxy-propylcarbamoyl]-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-4-yl]-carbamic acid tert-butyl ester : 4-tert-Butoxycarbonylamino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid (30.0 mg, 0.0624 mmol) was combined with N,N-Dimethylformamide (1 mL, 10 mmol), then 1-Hydroxybenzotriazole (8.44 mg, 0.0624 mmol) and (S)-3-Amino-3-(4-chloro-phenyl)-propan-1-ol; hydrochloride (27.7 mg, 0.125 mmol; Supplier = Oakwood) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (35.9 mg, 0.187 mmol). After 3 hours concentrated reaction under reduced pressure, then partitioned residue between EtOAc and water. The organic was then washed with saturated aqueous NaHCO3, dried over Na2SO4, filtered and concentrated. The crude residue was used for the subsequent step without further manipulation

154d) At rt dissolved [4-[(S)-1-(4-Chloro-phenyl)-3-hydroxy-propylcarbamoyl]-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-4-yl]-carbamic acid tert-butyl ester (70 mg, 0.1 mmol) in Methylene chloride (2.0 mL) then added Trifluoroacetic Acid (1.0 mL, 13 mmol) neat. After 2 hours concentrated reaction under reduced pressure, dissolved residue in 1 mL DMSO, filtered, and purified via preparative reverse

phase HPLC. Combined purest fractions and lyophylized overnight. Obtained 15 mg (20%) of title compound as a yellow lyophilate (LC/MS: M+H=548.1).

Example 155. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid methyl ester

155a) 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester : 5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ol (508 mg, 2.00 mmol), Triethylamine (863 uL, 6.19 mmol), 2,4,6-Triisopropylbenzenesulfonyl Chloride (668 mg, 2.20 mmol), and 4-Dimethylaminopyridine (28 mg, 0.23 mmol) in N,N-Dimethylformamide (10 mL) were stirred at room temperature for 2 hours. Gradual dissolution of starting material was observed and a considerable darkening of the solution. Piperazine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester (536 mg, 2.20 mmol) was added and the reaction was stirred at room temperature for two hours. Water was added, and the resulting solid product was collected by filtration, washed with water, and dried. Obtained 448 mg (47%) tan colored solid product, which was used for subsequent steps without further manipulation).

155b) At room temperature (rt) dissolved 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester 2-methyl ester (50 mg, 0.1 mmol) in Methylene chloride (2.0 mL) then added Trifluoroacetic Acid (1.0 mL, 13 mmol) neat. After 2.5 hours concentrated reaction solution under reduced pressure, then dissolved residue in 1 mL of DMSO and purified via preparative reverse phase HPLC. Combined desired fractions and lyophylized overnight. Obtained 23 mg (60%) of title compound as a yellow lyophilate (LC/MS: M+H=381.1).

Example 156. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenylamide

156a) 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester : At rt 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester (77.0 mg, 0.165 mmol) was combined with N,N-Dimethylformamide (3 mL), then 1-Hydroxybenzotriazole (22.3 mg, 0.165 mmol), 4-Methylmorpholine (36.3 uL, 0.330 mmol) and Aniline (22.6 uL, 0.247 mmol) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (94.9 mg, 0.495 mmol). After two hours the reaction mixture was concentrated under reduced pressure, and the resulting

residue partitioned between EtOAc and saturated aqueous NaHCO3. The organic phase was dried over Na2SO4, filtered and concentrated. The crude residue was dissolved in 0.95 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 42 mg (47%) of desired product as a yellow lyophilate (LC/MS: M+H=542.2).

156b) Trifluoroacetic Acid (1 mL, 10 mmol) and Methylene chloride (2 mL, 30 mmol) were combined with 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester (42.0 mg, 0.0775 mmol) at rt. After 1.5 h the reaction solution was concentrated under reduced pressure, after which the resulting residue was dissolved in 1.3 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophylized overnight to yield 29 mg (85%) of title compound as a yellow lypohilate (LC/MS: M+H=442.1).

Example 157. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid benzylamide

157a) 2-Benzylcarbamoyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester: At room temperature 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester (77.0 mg, 0.165 mmol) was combined with N,N-Dimethylformamide (3 mL), then 1-Hydroxybenzotriazole (22.3 mg, 0.165 mmol), 4-Methylmorpholine (36.3 uL, 0.330 mmol) and Benzylamine (27.0 uL, 0.247 mmol) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (94.9 mg, 0.495 mmol). After 1.5 h the reaction mixture was concentrated under reduced pressure and the resulting residue partitioned between EtOAc and saturated aqueous NaHCO3. The organic phase was dried over Na2SO4, filtered and concentrated. The crude residue was dissolved in 0.85 mL of DMSO, filtered, then purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 48 mg (52%) of desired product as a yellow lyophilate (LC/MS: M+H=556.2).

157b) A solution of Trifluoroacetic Acid (1 mL, 10 mmol) and Methylene chloride (2 mL, 30 mmol) was combined with 2-Benzylcarbamoyl-4-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester (47.0 mg, 0.0846 mmol) at rt. After 1.5 h concentrated mixture under reduced pressure, then

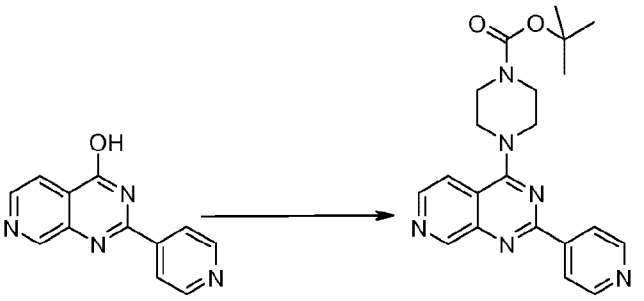
dissolved residue in 1.15 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 38 mg (99%) of title compound as a yellow lypohilate (LC/MS: M+H=456.1).

Example 158. 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenethyl-amide

158a) 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenethylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester : At rt 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1,2-dicarboxylic acid 1-tert-butyl ester (77.0 mg, 0.165 mmol) was combined with N,N-Dimethylformamide (3 mL, 30 mmol), then 1-Hydroxybenzotriazole (22.3 mg, 0.165 mmol), 4-Methylmorpholine (36.3 uL, 0.330 mmol) and Phenethylamine (31.1 uL, 0.248 mmol) were added followed by N-(3-Dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (94.9 mg, 0.495 mmol). After 16 h the reaction mixture was concentrated under reduced pressure and the resulting residue partitioned between EtOAc and saturated aqueous NaHCO3. The organic phase was dried over Na2SO4, filtered and concentrated. The crude residue was dissolved in 0.9 mL of DMSO, filtered, then purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 53 mg (56%) of desired product as a yellow lyophilate (LC/MS: M+H=570.2).

158b) A solution of Trifluoroacetic Acid (1 mL, 10 mmol) and Methylene chloride (2 mL) was combined with 4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-2-phenethylcarbamoyl-piperazine-1-carboxylic acid tert-butyl ester (48.2 mg, 0.0846 mmol) at rt. After 1.5 h concentrated mixture under reduced pressure, then dissolved residue in 1.2 mL of DMSO, filtered, and purified via preparative reverse phase HPLC. The desired fractions were combined and lyophilized to yield 38 mg (96%) of title compound as a yellow lyophilate (LC/MS: M+H=470.2).

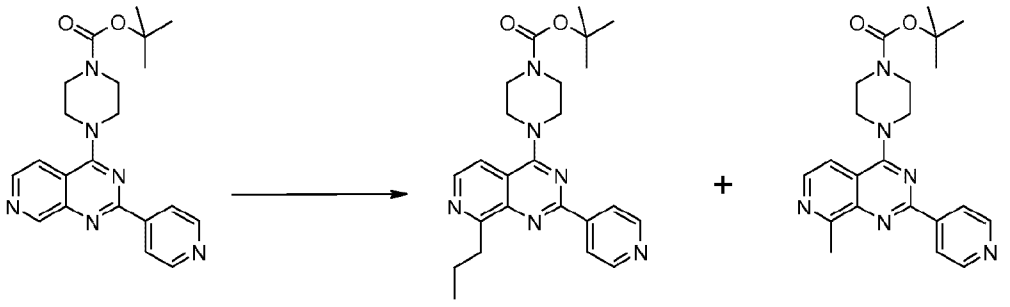
Synthesis of 4-(2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A080]



[A001] [A080]

A mixture of 2-Pyridin-4-yl-3H-pyrido[3,4-d]pyrimidin-4-one [A001] (1.0g, 4.5 mmol), DMF (30 mL) and DIPEA (2.35 mL, 13.5 mmol) was stirred at room temperature under nitrogen. DMAP (5 mg) was added followed by 2,4,6-triisopropylbenzene sulfonyl chloride (1.64g, 5.4 mmol) and the mixture was left to stir for two hours. 1-Boc piperazine (0.83 g, 4.5 mmol) was added and the mixture left to stri at room temperature over night. Water (50 mL) was added and the mixture left to stir for 20 min, filtered and washed with water (x3). The solid was dissolved in DCM (50 mL) and dried (MgSO4), filtered and evaporated under reduced pressure to give the title compound (1.2g, 68% yield) which was used crude in the next step without further purification.

Synthesis of 4-(8-Propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A081] and 4-(8-Methyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A082]



[A080] [A081] [A082]

To a solution of 4-(2-Pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester [A080] (0.196g, 0.5 mmol) , butyraldehyde (0.090 mL, 1.0 mmol), conc sulphuric acid (0.054 mL, 1.0 mmol) and iron sulphate heptahydrate (0.04g, 0.15 mmol) in DMSO (5 mL) was added hydrogen peroxide (35% solution in water, 0.146 mL,

1.5 mmol) dropwise over 2min. The reaction mixture was left to stir at room temperature overnight then water (5 mL) was added and the mixture was basified by addition of NaOH (1N) dropwise to pH ~7-8. The mixture was then extracted with DCM (x3) the organics were combined and washed with water (x1), brine (x1), dried (MgSO4), filtered and evaporated under reduced pressure. The crude residue was purified by column chromatography (SiO2 column, ISCO eluting with 50-90% EtOAc/cHex on 120g column) to give: 4-(8-Propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester (46 mg): LCMS: method: 5, RT:5.79 min, MI 435 [M+H]; ^{1}H NMR (1H, CDCl3, 500MHz), 8.77 (2H, dd), 8.50 (1H, d), 8.38 (2H, dd), 7.46 (1H, d), 3.91-3.89 (4H, m), 3.71-3.69 (4H, m), 3.49 (2H, dd), 2.00-1.92 (2H, dq), 1.51 (9H, s), 1.09 (3H, t) and 4-(8-Methyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid tert-butyl ester (44 mg) as a colourless glass: LCMS: method: 5, RT:5.11 min, MI 407 [M+H]; ^{1}H NMR (CDCl3, 500MHz) 8.78 (2H, dd), 8.46 (1H, d), 8.39 (2H, dd), 7.47 (1H, d), 3.91-3.89 (4H, m), 3.71-3.69 (4H, m), 3.09 (3H, s), 1.51 (9H, s).

Example 159. 4-Piperazin-1-yl-8-propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine

A mixture of 4-(8-Propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid [A081] (0.046g, 0.105 mmol), DCM (3 mL) and HCl (4N in dioxane, 1 mL) was stirred at room temperature for 90 min. The mixture was evaporated under reduced pressure then the crude product was dissolved in methanol and added to SCX-2 cartridge (10g), washed with DCM/MeOH (1:1 10mL) and MeOH (20mL), then eluted with ammonia (7N in methanol, 30mL). The Ammonia washes were evaporated under reduced pressure to give the title compound (34 mg, 75% yield) as a yellow solid: LCMS: method: 5, RT:2.0 min, MI 335 [M+H]; ^{1}H NMR (d6-dmso, 500MHz), 8.76 (2H, dd), 8.45 (1H, d), 8.32 (2H, dd), 7.71 (1H, d), 3.89 (4H, t), 3.37 (2H, t), 2.95 (4H, t), 1.86 (2H, dq), 0.99 (3H, t).

Example 160. 8-Methyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine

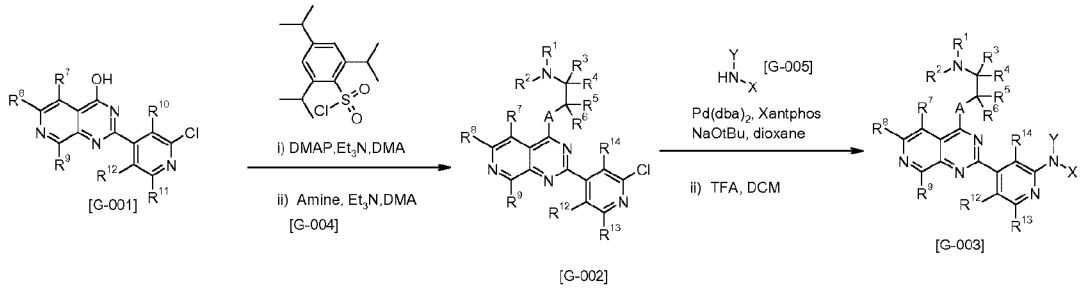
A mixture of 4-(8-Methyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid [A082] (0.045g, 0.11 mmol), DCM (3 mL) and HCl (4N in dioxane, 1 mL) was stirred at room temperature for 90 min. The mixture was evaporated under reduced pressure then the crude product was dissolved in methanol and added to SCX-2 cartridge (10g), washed with DCM/MeOH (1:1 10mL) and MeOH (20mL), then eluted with ammonia (7N in methanol, 30mL). The Ammonia washes were evaporated under reduced pressure to give the title compound (29 mg, 75% yield) as a brown gum: LCMS:

method: 5, RT:2.17 min, MI 307 [M+H]; ^{1}H NMR (d6-dmso, 500MHz), 8.76 (2H, dd), 8.40 (1H, d), 8.33 (2H, dd), 7.70 (1H, d), 3.88 (4H, t), 2.94-2.92 (4H, m), 2.93 (3H, s)

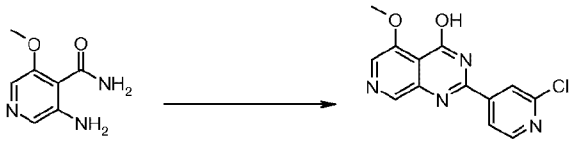
General synthesis of substituted 2-amino pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-003] Scheme B1

2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-002] were prepared by the reaction of a 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol derivative of general formula [G-001] with 2,4,6-triisopropylbenzenesulfonyl chloride in a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP. The intermediate 6,7-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl ester was then reacted with a primary or secondary amino derivative, of general formula [G-004], in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. The 2-(2-chloro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-002] was involved in a Buchwald type reaction utilising a suitable amine, of general formula [G-005], a palladium catalyst such as $Pd(dba)_2$ or $Pd(OAc)_2$, a ligand such as Xantphos and a base such as NaOtBu or Cs_2CO_3 in a polar solvent such as dioxane or a combination of dioxane and DMA at high temperature either by heating thermally or using a microwave reactor, to yield substituted 2-amino pyridyl substituted 2-(2-amino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl amine derivatives of general formula [G-003]. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the intermediate was purified by column chromatography and the N-Boc derivatives were deprotected under acidic conditions with a strong acid such as TFA, HCl in a solvent such as DCM, DCE or 1,4-dioxane or by catch and release sulfonic acidic resins such as polymer supported toluene sulfonic acid and the crude reaction product was purified by normal phase chromatography or reverse phase preparative HPLC.

Scheme B1



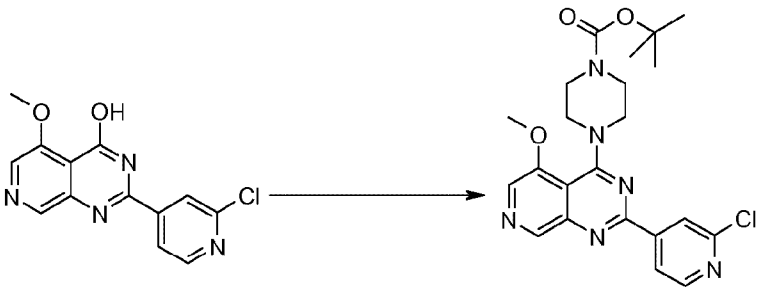
Synthesis of [4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine [200]



[B001]

2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [B001]

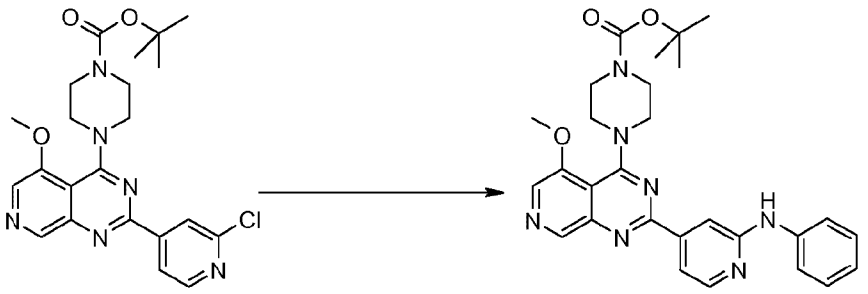
To a solution of 2-chloro-4-pyridinecarbonitrile (0.97g, 7.03 mmol) in MeOH (35 mL) at RT, under nitrogen, was added NaOMe (0.08 g, 1.46 mmol) and left to stir for 60mins. Then a solution of 3-Amino-5-methoxy-isonicotinic acid (1 g, 5.86 mmol) in MeOH (15 mL) was added to the the dark brown mixture dropwise over 5-10mins (via syringe). The solution was stired at rt for 2 h and then overnight at 85° C. After cooling down, the solid was filtered and, washed with methanol and used without further purification to yield the title compound [B001] (0.97 g 57 %yield: LCMS: method: 5, RT:6.32 min, MI 287.34 [M+H].



[B001] [B002]

4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B002].

A mixture of 2-(2-chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-ol [B001] (0.58 g, 2 mmol), anhydrous DMA (5 mL), triethylamine (0.58 mL, 4 mmol) and DMAP (20 mg, 0.16 mmol) was sonicated for 10 min then stirred at room temperature for 10 min. 2,4,6-Triisopropyl -benzenesulfonyl chloride (0.67 g, 2.2 mmol) was added and the mixture was sonicated for 5 min then left to stir at room temperature for 2 hours. During this time the material went into solution to form a viscous solution. A solution of Boc piperazine (0.56 g, 3 mmol) in anhydrous DMA (1 mL) was added and the reaction mixture was left to stir at room temperature overnight. Water (20 mL) was added and the reaction mixture was extracted with DCM (2 x 30 mL), the extracts were combined and washed with water (20 mL), saturated bicarbonate solution (2 x 20 mL) and water (20 mL), dried ($MgSO_4$) filtered and evaporated under reduced pressure to give a pale yellow oil, which was purified by flash column chromatography (SP1, 50 g SiO_2 cartridge 100% EtOAc up to 95% EtOAc : 5 % MeOH gradient) to give the *title compound* [B002] as a colourless solid (0.22g 24% yield). LCMS: method: 5, RT:10.86 min, MI 457 [M+H]; NMR: (1H, 500MHz, $CDCl_3$); 9.0 (1H, s), 8.53 (1H, d), 8.35 (1H, s), 8.28 (1H, 1H, d), 8.23 (1H, s), 3.70 (4H, br s), 3.64 (4H, br s), 1.50 (9H, s)



[B002] [B003]

4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B003]

A mixture of 4-[2-(2-Chloro-pyridin-4-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid tert-butyl ester [B002] (0.100 g, 0.22 mmol), $Pd(dba)_2$ (10 mg, 0.013 mmol), Xantphos (17.5 mg, 0.025 mmol), NaOtBu (43 mg, 0.440 mmol) and anhydrous dioxane (4 ml) was added to a microwave vial. Aniline was then added the vial was sealed and heated at 150°C for 20 min. Water (10 mL) was added and the reaction mixture was extracted with DCM (2 x 10 mL), the extracts were combined and washed

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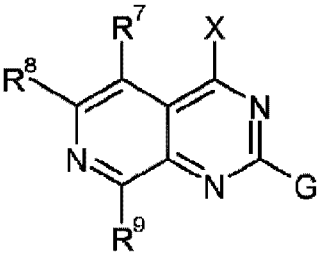
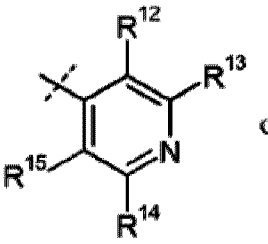
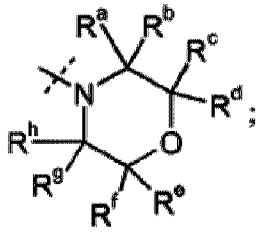
NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

Claims:

1. A compound of formula (I)  or a pharmaceutically acceptable salt form thereof,

wherein (I)

G is a group of formula  or  ;

X is chosen from H, C_{1-10}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-9 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{28}$, $–C(=O)OR^{28}$, $–C(=O)NR^{24}R^{28}$, $–C(O)C(=O)R^{28}$, $–NR^{24}R^{28}$, $–NR^{24}NR^{24}R^{28}$, $–N=NR^{28}$, $–NR^{24}OR^{28}$, $–NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)C(=O)R^{28}$, $–NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)OR^{28}$, $–NR^{24}C(=O)NR^{24}R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{28}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{28}$, $–NR^{24}C(=O)C(=O)NR^{24}R^{28}$, $–NR^{24}S(=O)_2R^{28}$, $–NR^{24}S(=O)_2NR^{24}R^{28}$, $–OR^{28}$, $–OC(=O)R^{28}$, $–OC(=O)NR^{24}R^{28}$, $–OC(=O)OR^{28}$, $–OS(=O)R^{28}$, $–OS(=O)_2R^{28}$, $–OS(=O)_2OR^{28}$, $–OS(=O)_2NR^{24}R^{28}$, $–S(=O)_nR^{28}$, $–S(=O)_2NR^{24}R^{28}$, and $–S(=O)NR^{24}R^{28}$;

R^7, R^8, R^9, R^{12}, R^{13}, R^{14}, R^{15}, R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally

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substituted by 1-11 R^{19}, C_{2-6}alkynyl optionally substituted by 1-9 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–C(=O)C(=O)R^{20}$, $–C(=NR^{25})R^{20}$, $–C(=NR^{25})NR^{22}R^{23}$, $–C(=NOH)NR^{22}R^{23}$, $–C(=NOR^{26})R^{20}$, $–C(=NNR^{22}R^{23})R^{20}$, $–C(=NNR^{24}C(=O)R^{21})R^{20}$, $–C(\ NNR^{24}C(=O)OR^{21})R^{20}$, $–C(=S)NR^{22}R^{23}$, –NC, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{78}R^{78}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P\ (=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, $–OP(=O)(SR^{20})(SR^{20})$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$ $–SP(=O)(OR^{20})(OR^{20})$, $–SP(=O)(SR^{20})(SR^{20})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{22}R^{23})\ (NR^{22}R^{23})$, $–P(=O)(OR^{20})(OR^{20})$, and $–P(=O)(SR^{20})(SR^{20})$;

or any of R^7 and R^8, R^{12} and R^{13}, R^{14} and R^{15}, R^a and R^b, R^a and R^c, R^a and R^e, R^a and R^g, R^b and R^d, R^b and R^f, R^b and R^h, R^c and R^d, R^c and R^e, R^c and R^g, R^d and R^f, R^d and R^h, R^e and R^f, R^e and R^g, R^f and R^h, and R^g and R^h can, together with the atoms linking them, form a $C6_{-11}$aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19};

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R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{2-6}alkenyl optionally substituted by 1-11 R^{39}, C_{2-6}alkynyl optionally substituted by 1-9 R^{39}, C_{6-11} aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{39}, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–C(=O)C(=O)R^{30}$, $–C(=NR^{35})R^{30}$, $–C(=NR^{35})NR^{32}R^{33}$, $–C(=NOH)NR^{32}R^{33}$, $–C(=NOR^{36})R^{30}$, $–C(=NNR^{32}R^{33})R^{30}$, $–C(=NNR^{34}C(=O)R^{31})R^{30}$, $–C(=NNR^{34}C(=O)OR^{31})R^{30}$, $–C(=S)NR^{32}R^{33}$, –NC, $–NO_2$, $–NR^{32}R^{33}$, $–NR^{34}NR^{32}R^{33}$, $–N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $–NR^{34}OR^{36}$, $–NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)C(=O)R^{30}$, $–NR^{34}C(=O)OR^{31}$, $–NR^{34}C(=O)C(=O)OR^{31}$, $–NR^{34}C(=O)NR^{32}R^{33}$, $–NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $–NR^{34}C(=NR^{35})NR^{32}R^{33}$, $–NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $–NR^{34}C(=S)R^{30}$, $–NR^{34}C(=S)OR^{30}$, $–NR^{34}C(=S)NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–NR^{34}S(=O)_2NR^{32}R^{33}$, $–NR^{34}P(=O)R^{78}R^{78}$, $–NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–NR^{34}P(=O)(OR^{30})(OR^{30})$, $–NR^{34}P(=O)(SR^{30})(SR^{30})$, $–OR^{30}$, =O, –OCN, $–OC(=O)R^{30}$, $–OC(=O)NR^{32}R^{33}$, $–OC(=O)OR^{30}$, $–OC(=NR^{35})NR^{32}R^{33}$, $–OS(=O)R^{30}$, $–OS(=O)2R^{30}$, $–OS(=O)_2OR^{30}$, $–OS(=O)_2NR^{32}R^{33}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–OP(=O)(OR^{30})(OR^{30})$, $–OP(=O)(SR^{30})(SR^{30})$, $–Si(R^{34})_3$, –SCN, =S, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–SP(=O)(OR^{30})(OR^{30})$, $–SP(=O)(SR^{30})(SR^{30})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$;

R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{2-6}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl

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optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{28} at each occurrence is independently chosen from C_{1-10}alkyl optionally substituted by 1-13 R^{49}, C_{2-10}alkenyl optionally substituted by 1-11 R^{49}, C_{2-6}alkynyl optionally substituted by 1-9 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49};

R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{59}, C_{2-6}alkenyl optionally substituted by 1-11 R^{59}, C_{2-6}alkynyl optionally substituted by 1-9 R^{59}, C_{6-11}aryl optionally substituted by 1-11 R^{59}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{59}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{59}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{59}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{59}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{59}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{59}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{59}; or any R^{22} and R^{23} and/or R^{32} and R^{33} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{69} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{69};

R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered

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heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, –CN, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–C(=O)C(=O)R^{70}$, $–C(=NR^{75})R^{70}$, $–C(=NR^{75})NR^{72}R^{73}$, $–C(=NOH)NR^{72}R^{73}$, $–C(=NOR^{76})R^{70}$, $–C(=NNR^{72}R^{73})R^{70}$, $–C(=NNR^{74}C(=O)R^{71})R^{70}$, $–C(=NNR^{74}C(=O)OR^{71})R^{70}$, $–C(=S)NR^{72}R^{73}$, –NC, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}NR^{72}R^{73}$, $–N=NR^{74}$, $=NR^{70}$ $=NOR^{70}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}C(=O)NR^{74}C(–O)R^{70}$, $–NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $–NR^{74}C(=NR^{75})NR^{72}R^{73}$, $–NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $–NR^{74}C(=S)R^{70}$, $–NR^{74}C(=S)OR^{70}$, $–NR^{74}C(=S)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–NR^{74}P(=O)R^{78}R^{78}$, $–NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–NR^{74}P(=O)(OR^{70})(OR^{70})$, $–NR^{74}P(=O)(SR^{70})(SR^{70})$, $–OR^{70}$, =O, –OCN, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–OC(=O)OR^{70}$, $–OC(=NR^{75})NR^{72}R^{73}$, $–OS(=O)R^{70}$, $–OS(=O)_2R^{70}$, $–OS(=O)_2OR^{70}$, $–OS(=O)_2NR^{72}R^{73}$, $–OP(=O)R^{78}R^{78}$, $–OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–OP(=O)(OR^{70})(OR^{70})$, $–OP(=O)(SR^{70})(SR^{70})$, $–Si(R^{74})_3$, –SCN, =S, $–S(=O)_nR^{70}$, $–S(=O)_2OR^{70}$, $–SO_3R^{77}$, $–S(=O)_2NR^{72}R^{73}$, $–S(=O)NR^{72}R^{73}$, $–SP(=O)R^{78}R^{78}$, $–SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–SP(=O)(OR^{70})(OR^{70})$, $–SP(=O)(SR^{70})(SR^{70})$, $–P(=O)R^{78}R^{78}$, $–P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $–P(=O)(OR^{70})(OR^{70})$, and $–P(=O)(SR^{70})(SR^{70})$;

R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89};

R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{99}, C_{2-6}alkenyl optionally substituted by 1-11 R^{99}, C_{2-6}alkenyl

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optionally substituted by 1-9 R^{99}, C_{6-11}aryl optionally substituted by 1-11 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{99}; or any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{109} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{109};

R^{78} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{89}, C_{2-6}alkenyl optionally substituted by 1-11 R^{89}, C_{2-6}alkynyl optionally substituted by 1-9 R^{89}, C_{6-11}aryl optionally substituted by 1-11 R^{89}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{89}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{89}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{89}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{89}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{89}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{89}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{89}; or any two R^{78} attached to the same phosphorus atom can, together with the phosphorus atom linking them, form a 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{89};

R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{119}, C_{2-6}alkenyl optionally substituted by 1-11 R^{119} optionally substituted by 1-9 R^{119} C_{6-11}aryl optionally substituted by 1-11 R^{119}, C_{2-6}arylalkyl optionally substituted by 1-19 R^{119}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{119} C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{119}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{119}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{119}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{119}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{119}, halogen, –CN, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{112}R^{113}$, $–C(=O)C(=O)R^{110}$, $–C(=NR^{115})R^{110}$, $–C(=NR^{115})NR^{112}R^{113}$, $–C(=NOH)NR^{112}R^{113}$, $–C(=NOR^{116})R^{110}$, $–C(=NNR^{112}R^{113})R^{110}$, –

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$C(=NNR^{114}C(=O)R^{111})R^{110}$, $-C(=NNR^{114}C(=O)OR^{111})R^{110}$, $-C(=S)NR^{112}R^{113}$, $-NC$, $-NO_2$, $-NR^{112}R^{113}$, $NR^{114}NR^{112}R^{113}$, $-N=NR^{114}$, $=NR^{110}$, NOR^{110}, $-NR^{114}OR^{116}$, $-NR^{114}C(=O)R^{110}$, $-NR^{114}C(=O)C(=O)R^{110}$, $-NR^{114}C(=O)OR^{111}$, $-NR^{114}C(=O)C(=O)OR^{111}$, $-NR^{114}C(=O)NR^{112}NR^{113}$, $-NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $-NR^{114}C(=O)NR^{114}C(=O)OR^{110}$, $NR^{114}C(=NR^{115})NR^{112}R^{113}$, $-NR^{114}C(=O)C(=O)NR^{112}R^{113}$, $-NR^{114}C(=S)R^{110}$, $-NR^{114}C(=S)OR^{110}$, $-NR^{114}C(=S)NR^{114}S(=O)_2R^{111}$, $-NR^{114}S(=O)_2NR^{112}R^{138}$, $-NR^{114}P(=O)R^{118}R^{118}$, $-NR^{114}P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $-NR^{114}P(=O)(OR^{110})(OR^{110})$, $-NR^{114}P(=O)(SR^{110})(SR^{110})$, $-OR^{110}$, $=O$, $-OCN$, $-OC(=O)R^{110}$, $-OC(=O)NR^{112}R^{113}$, $-OC(=O)OR^{110}$, $-OC(=NR^{115})NR^{112}R^{113}$, $-OS(=O)R^{110}$, $OS(=O)_2R^{110}$, $-OS(=O)_2OR^{110}$, $-OS(=O)_2NR^{112}R^{113}$, $-OP(=O)R^{118}R^{118}$ $-OP(=O)(NR^{112}R^{113})(NR^{112}R^{113},)$ $OP(=O)(OR^{110})(OR^{110})$, $OP(=O)(SR^{110})(SR^{110})$, $-Si(R^{114})_3$, $-SCN$, $=S$, $-S(=O)_nR^{110}$, $-S(=O)_2OR^{110}$, $-S(=O)_2NR^{112}R^{113}$, $-S(=O)NR^{112}R^{113}$, $-SP(=O)R^{118}R^{118}$ $-SP(=O)(NR^{112}R^{113})(NR^{112}R^{113})$ $-SP(=O)(OR^{110})(OR^{110})$, $SP(=O)(SR^{110})(SR^{110})$, $-P(=O)R^{118}R^{118}$, $-P(=O)(NR^{112}R^{113})(NR^{112}R^{113})$, $-P(=O)(OR^{110})(OR^{110})$, and $-P(=O)(SR^{110})(SR^{110})$;

R^{110}, R^{111}, R^{114}, R^{115} and R^{116} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{112} and R^{113} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{139}, C_{2-6}alkenyl optionally substituted by 1-11 R^{139}, C_{2-6}alkynyl optionally substituted by 1-9 R^{139}, C_{6-11}aryl optionally substituted by 1-11 R^{139}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{139}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{139}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{139}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{139}, 4-21 membered

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heterocycloalkylalkyl optionally substituted by 1-40 R^{139}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{139}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{139}; or any R^{112} and R^{113} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{149} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{149};

R^{118} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{129}, C_{2-6}alkenyl optionally substituted by 1-11 R^{129}, C_{2-6}alkynyl optionally substituted by 1-9 R^{129}, C_{6-11}aryl optionally substituted by 1-11 R^{129}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{129}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{129}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{129}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{129}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{129}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{129};

R^{119} R^{129}, R^{139} and R^{149} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{159}, C_{2-6}alkenyl optionally substituted by 1-11 R^{159}, C_{2-6}alkynyl optionally substituted by 1-9 R^{159}, C_{6-11}aryl optionally substituted by 1-11 R^{159}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{159}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{159}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{159}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{159}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{159}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{159}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{159}, halogen, –CN, $–C(=O)R^{150}$, $–C(=O)OR^{150}$, $–C(=O)NR^{152}R^{153}$, $–C(=O)C(=O)R^{150}$, $–C(=NR^{155})R^{150}$, $–C(=NR^{155})NR^{152}R^{153}$, $–C(=NOH)NR^{152}R^{153}$, $–C(=NOR^{156})R^{150}$, $–C(=NNR^{152}R^{153})R^{150}$, $–C(=NNR^{154}C(=O)R^{151})R^{150}$, $–C(=NNR^{154}C(=O)OR^{151})R^{150}$, $–C(=S)NR^{152}R^{153}$, –NC, $–NO_2$, $–NR^{152}R^{153}$, $–NR^{154}NR^{152}R^{153}$, $–N=NR^{154}$, $=NR^{150}$, $=NOR^{150}$, $–NR^{154}OR^{156}$, $–NR^{154}C(=O)R^{150}$, $–NR^{154}C(=O)C(=O)R^{150}$, $–NR^{154}C(=O)OR^{151}$, $–NR^{154}C(=O)C(=O)OR^{151}$, $–NR^{154}C(=O)NR^{152}R^{153}$, $NR^{154}C(=O)NR^{154}C(=O)R^{150}$, $–NR^{154}C(=O)NR^{154}C(=O)OR^{150}$, $–NR^{154}C(=NR^{155})NR^{152}R^{153}$, –

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$NR^{154}C(=O)C(=O)NR^{152}R^{153}$, $-NR^{154}C(=S)R^{150}$, $-NR^{154}C(=S)OR^{150}$, $-NR^{154}C(=S)NR^{152}R^{153}$, $-NR^{154}S(=O)_2R^{151}$, $-NR^{154}S(=O)_2NR^{152}R^{153}$, $-NR^{154}P(=O)R^{158}R^{158}$, $-NR^{154}P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-NR^{154}P(=O)(OR^{150})(OR^{150})$, $-NR^{154}P(=O)(SR^{150})(SR^{150})$, $-OR^{150}$, =O, –OCN, $-OC(=O)R^{150}$, $-OC(=O)NR^{152}R^{153}$, $-OC(=O)OR^{150}$, $-OC(=NR^{155})NR^{152}R^{153}$, $-OS(=O)R^{150}$ $-OS(=O)_2R^{150}$, $-OS(=O)_2OR^{150}$, $-OS(=O)_2NR^{152}R^{153}$, $-OP(=O)R^{158}R^{158}$, $-OP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-OP(=O)(OR^{150})(OR^{150})$, $-OP(=O)(SR^{150})(SR^{150})$, $-Si(R^{154})_3$, –SCN, =S, $-S(=O)_nR^{150}$, $-S(=O)_2OR^{150}$, $-S(=O)_2NR^{152}R^{153}$, $-S(=O)NR^{152}R^{153}$, $-SP(=O)R^{158}R^{158}$, $-SP(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-SP(=O)(OR^{150})(OR^{150})$, $-SP(=O)(SR^{150})(SR^{150})$, $-P(=O)R^{158}R^{158}$, $-P(=O)(NR^{152}R^{153})(NR^{152}R^{153})$, $-P(=O)(OR^{150})(OR^{150})$, and $-P(=O)(SR^{150})(SR^{150})$;

R^{150}, R^{151}, R^{154}, R^{155} and R^{156} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{169}, C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{152} and R^{153} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{179}, C_{2-6}alkenyl optionally substituted by 1-11 R^{179}, C_{2-6}alkynyl optionally substituted by 1-9 R^{179}, C_{6-11}aryl optionally substituted by 1-11 R^{179}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{129}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{179}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{179}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{179}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{179}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{179}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{179};

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or any R^{152} and R^{153} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{189} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{189};

R^{158} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{169} C_{2-6}alkenyl optionally substituted by 1-11 R^{169}, C_{2-6}alkynyl optionally substituted by 1-9 R^{169}, C_{6-11}aryl optionally substituted by 1-11 R^{169}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{169}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{169}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{169}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{169}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{169}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{169}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{169};

R^{159}, R^{169}, R^{179} and R^{189} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{199}, C_{2-6}alkenyl optionally substituted by 1-11 R^{199}, C_{2-6}alkynyl optionally substituted by 1-9 R^{199}, C_{6-11}aryl optionally substituted by 1-11 R^{199}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{199}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{199}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{199}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{199}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{199}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{199}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{199}, halogen, –CN, $–C(=O)R^{190}$, $–C(=O)OR^{190}$, $–C(=O)NR^{192}R^{193}$, $–C(=O)C(=O)R^{190}$, $–C(=NR^{195})R^{190}$, $–C(=NR^{195})NR^{192}R^{193}$, $–C(=NOH)NR^{192}R^{193}$, $–C(=NOR^{196})R^{190}$, $–C(=NNR^{192}R^{193})R^{190}$, $–C(=NNR^{194}C(=O)R^{191})R^{190}$, $–C(=NNR^{194}C(=O)OR^{191})R^{190}$, $–C(=S)NR^{192}R^{193}$, –NC, $–NO_2$, $–NR^{192}R^{193}$, $–NR^{194}NR^{192}R^{193}$, $–N=NR^{194}$, $=NR^{190}$, $=NOR^{190}$, $–NR^{194}OR^{196}$, $–NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)C(=O)R^{190}$, $–NR^{194}C(=O)OR^{191}$, $–NR^{194}C(=O)C(=O)OR^{191}$, $–NR^{194}C(=O)NR^{192}R^{193}$, $–NR^{194}C(=O)NR^{194}C(=O)R^{190}$, $–NR^{194}C(=O)NR^{194}C(=O)OR^{190}$, $–NR^{194}C(=NR^{195})NR^{192}R^{193}$, $–NR^{194}C(=O)C(=O)NR^{192}R^{193}$, $–NR^{194}C(=S)R^{190}$, $–NR^{194}C(=S)OR^{190}$, $–NR^{194}C(=S)NR^{192}R^{193}$, $–NR^{194}S(=O)_2R^{191}$, $–NR^{194}S(=O)2NR^{192}R^{193}$, $–NR^{194}P(=O)R^{198}R^{198}$, $–NR^{194}P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, –

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$NR^{194}P(=O)(OR^{190})(OR^{190})$, $-NR^{194}P(=O)(SR^{190})(SR^{190})$, $-OR^{190}$, =O, –OCN, – $OC(=O)R^{190}$, $OC(=O)NR^{192}R^{193}$, $-OC(=O)OR^{190}$, $-OC(=NR^{195})NR^{192}R^{193}$, – $OS(=O)R^{190}$, $-OS(=O)_2R^{190}$, $-OS(=O)_2OR^{190}$, $-OS(=O)_2NR^{192}R^{193}$, – $OP(=O)R^{198}R^{198}$, $-OP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-OP(=O)(OR^{190})(OR^{195})$, – $OP(=O)(SR^{190})(SR^{190})$, $-Si(R^{194})_3$, –SCN, =S, $-S(=O)_nR^{190}$, $-S(=O)_2OR^{190}$, – $S(=O)_2NR^{192}R^{193}$, $-S(=O)NR^{192}R^{193}$, $-SP(=O)R^{198}R^{198}$, – $SP(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $-SP(=O)(OR^{190})(OR^{190})$, $-SP(=O)(SR^{190})(SR^{190})$, – $P(=O)R^{198}R^{198}$, $-P(=O)(NR^{192}R^{193})(NR^{192}R^{193})$, $P(=O)(OR^{190})(OR^{190})$, and – $P(=O)(SR^{190})(SR^{190})$;

R^{190}, R^{191}, R^{194}, R^{195} and R^{196} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{192} and R^{193} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{219}, C_{2-6}alkenyl optionally substituted by 1-11 R^{219}, C_{2-6}alkynyl optionally substituted by 1-9 R^{219}, C_{6-11}aryl optionally substituted by 1-11 R^{219}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{219}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{219}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{219}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{219}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{219}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{219}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{219};

or any R^{192} and R^{193} may form, together with the nitrogen atom to which they are attached, a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{229} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{229};

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R^{198} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{209}, C_{2-6}alkenyl optionally substituted by 1-11 R^{209}, C_{2-6}alkynyl optionally substituted by 1-9 R^{209}, C_{6-11}aryl optionally substituted by 1-11 R^{209}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{209}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{209}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{209}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{209}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{209}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{209}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{209};

R^{199}, R^{209}, R^{219} and R^{229} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 halogen, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl, C_{3-11}cycloalkyl, C_{4-17}cycloalkylalkyl, 3-15 membered heterocycloalkyl, 4-21 membered heterocycloalkylalkyl, 5-15 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $–C(=O)R^{230}$, $–C(=O)OR^{230}$, $–C(=O)NR^{230}R^{230}$, $–C(–O)C(–O)R^{230}$, $–C(=NR^{230})R^{230}$, $–C(=NR^{230})NR^{230}R^{230}$, $–C(=NOH)NR^{230}OR^{230}$, $–C(=NOR^{230})R^{230}$, $–C(=NNR^{230}R^{230})R^{230}$, $–C(=NNR^{230}C(=O)R^{230})R^{230}$, $–C(=NNR^{230}C(=O)OR^{230})R^{230}$, $–C(=S)NR^{230}R^{230}$, –NC, $–NO_2$, $–NR^{230}R^{230}$, $–NR^{230}NR^{230}R^{230}$, $–N=NR^{230}$, $=NR^{230}$, $=NOR^{230}$, $–NR^{230}OR^{230}$, $–NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)C(=O)R^{230}$, $–NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=O)C(=O)OR^{230}$, $–NR^{230}C(=O)NR^{230}R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)R^{230}$, $–NR^{230}C(=O)NR^{230}C(=O)OR^{230}$, $–NR^{230}C(=NR^{230})NR^{230}R^{230}$, $–NR^{230}C(=O)C(=O)NR^{230}R^{230}$, $–NR^{230}C(=S)R^{230}$, $–NR^{230}C(=S)OR^{230}$, $–NR^{230}C(=S)NR^{230}R^{230}$, $–NR^{230}S(=O)_2R^{230}$, $–NR^{230}S(=O)_2NR^{230}R^{230}$, $–NR^{230}P(=O)R^{231}R^{231}$, $–NR^{230}P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–NR^{230}P(=O)(OR^{230})(OR^{230})$, $–NR^{230}P(=O)(SR^{230})(SR^{230})$, $–OR^{230}$, =O, –OCN, $–OC(=O)R^{230}$, $–OC(=O)NR^{230}R^{230}$, $–OC(=O)OR^{230}$, $–OC(=NR^{230})NR^{230}R^{230}$, $–OS(=O)R^{230}$, $–OS(=O)_2R^{230}$, $–OS(=O)_2OR^{230}$, $–OS(=O)_2NR^{230}R^{230}$, $–OP(=O)R^{231}R^{231}$, $–OP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–OP(=O)(OR^{230})(OR^{230})$, $–OP(=O)(SR^{230})(SR^{230})$, $–Si(R^{230})_3$, –SCN, =S, $–S(=O)_nR^{230}$, $–S(=O)_2OR^{230}$, $–SO_3R^{230}$, $–S(=O)_2NR^{230}R^{230}$, $–S(=O)NR^{230}R^{230}$, $–SP(=O)R^{231}R^{231}$, $–SP(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $–SP(=O)(OR^{230})(OR^{230})$, $–SP(=O)(SR^{230})(SR^{230})$, –

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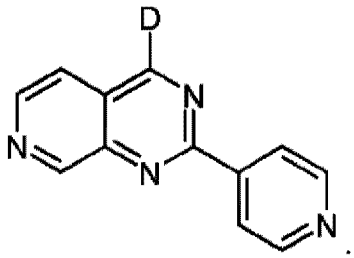
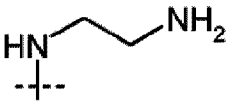
$P(=O)R^{231}R^{231}$, $-P(=O)(NR^{230}R^{230})(NR^{230}R^{230})$, $-P(=O)(OR^{230})(OR^{230})$, and $-P(=O)(SR^{230})(SR^{230})$;

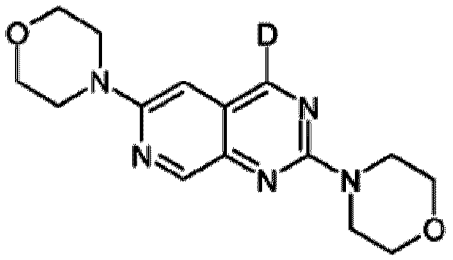
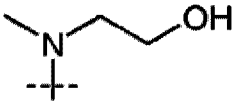
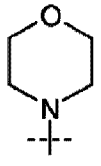
R^{230} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl;

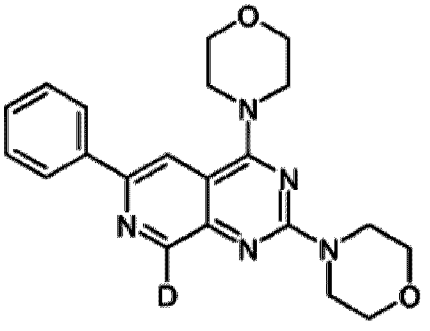
R^{231} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl; and

n at each occurrence is independently chosen from 0, 1, and 2;

with the proviso that the compound is not

(a)  in which D is H or  , or a salt form thereof;

(b)  in which D is  or  , or a salt form thereof; or

(c)  in which D is H or $-CH_3$, or a salt form thereof.

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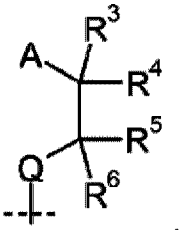
2. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein X is chosen from 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19},–C(=O)R^{28}, –C(=O) $NR^{24}R^{28}$, –$NR^{24}R^{28}$, –$NR^{24}C(=O)R^{28}$, –$NR^{24}S(=O)_2R^{28}$, and –OR^{28}.

3. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein X is chosen from 5-6 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, and –$NR^{24}R^{28}$.

4. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein X is chosen from morpholinyl optionally substituted by 1-6 R^{19}, piperidinyl optionally substituted by 1-6 R^{19}, piperazinyl optionally substituted by 1-6 R^{19}, and –$NR^{24}R^{28}$.

5. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1,

wherein X is 

, and

A is –NR^1R^2, –$CR^iR^jR^k$, –OR^{18a}, or –SR^{18b};

Q is –NR^{11}–, –CR^mR^n–, –O–, or –S–;

R^k is H, halogen, –CN, –NO_2, –$NR^{16}R^{17}$, –OR^{18c}, –SR^{18d}, or –$CR^oR^pR^q$;

R^q is H, halogen, –CN, –NO_2, –$NR^{16a}R^{17a}$ or –OR^{18e};

R^1, R^2, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, and –OR^{70};

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R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{79}, C_{2-6}alkenyl optionally substituted by 1-11 R^{79}, C_{2-6}alkynyl optionally substituted by 1-9 R^{79}, C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{79}, 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{79}, halogen, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-C(=NR^{75})R^{70}$, $-C(=NR^{75})NR^{72}R^{73}$, $-C(=NOH)NR^{72}R^{73}$, $-C(=NOR^{76})R^{70}$, $-C(=NNR^{72}R^{73})R^{70}$, $-C(=NNR^{74}C(=O)R^{71})R^{70}$, $-C(=NNR^{74}C(=O)OR^{71})R^{70}$, $-C(=S)NR^{72}R^{73}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, $-SCN$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, and $-P(=O)(SR^{70})(SR^{70})$;

or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18}d and R^5, R^{18d} and R^5, and R^{18d} and R^n can,

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together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-11 R^{79}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{79}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{79} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{79};

or R^4 and R^5 or R^n and R^5 can together form a double bond;

or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O, =NR^{70}, =NOR^{70}, or =S.

6. The compound or pharmaceutically acceptable salt form thereof as defined in claim 5, wherein R^1, R^2, R^{11} R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^3, R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, –CN, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, and –OR^{70}; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11} R^{16} and R^5, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or R^3 and R^4 can together form =O.

7. The compound or pharmaceutically acceptable salt form thereof as defined in claim 5, wherein R^1, R^{11}, R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d} and R^{18e} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, and C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}; R^4, R^5, R^6, R^i, R^j, R^m, R^n, R^o, and R^p are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –NO_2, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1

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and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4 and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, R^{18a} and R^3, R^{18a} and R^5, R^{18a} and R^{11}, R^{18a} and R^n, R^{18b} and R^3, R^{18b} and R^5, R^{18b} and R^{11}, R^{18b} and R^n, R^{18c} and R^i, R^{18c} and R^3, R^{18c} and R^5, R^{18c} and R^{11}, R^{18c} and R^n, R^{18d} and R^i, R^{18d} and R^3, R^{18d} and R^5, R^{18d} and R^{11}, and R^{18d} and R^n can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^3 and R^6, R^5 and R^6, R^i and R^j, R^i and R^4, R^i and R^5, R^i and R^n, R^m and R^n, R^4 and R^m, and R^6 and R^m can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, or a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

8. The compound or pharmaceutically acceptable salt form thereof as defined in claim 5, wherein R^1, R^{11} R^{16}, R^{17}, R^{16a}, R^{17a}, R^{18a}, R^{18b}, R^{18c}, R^{18d}, and R^{18e} are H; R^2 is chosen from H and C_{1-6}alkyl optionally substituted by 1-6 R^{79}; R^4; R^5; R^6; R^i, R^j, R^m, R°, and R^p are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{79}, C_{2-6}alkynyl optionally substituted by 1-6 R^{79}, C_{7-16}arylalkyl optionally substituted by 1-6 R^{79}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{79}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$NR^{72}R^{73}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}S(=O)_2R^{71}$, –OR^{70}, –$OC(=O)R^{70}$, –$S(=O)_nR^{70}$, and –$S(=O)_2NR^{72}R^{73}$; or any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^1 and R^n, R^4, and R^{11}, R^6 and R^{11}, R^{16} and R^{17}, R^{16} and R^i, R^{16} and R^3, R^{16} and R^5, R^{16} and R^{11}, R^{16} and R^n, R^j and R^{11}, and R^{18a} and R^{11} can, together with the atoms linking them, form a 3-11 membered heterocycloalkyl optionally substituted by 1-6 R^{79}; or any of R^3 and R^4, R^5 and R^6, R^i and R^j, and R^m and R^n can together form =O.

9. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 5-8, wherein R^q is –$NR^{16a}R^{17a}$ or –OR^{18e}.

10. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 5-9, wherein R^k is –$NR^{16}R^{17}$ or –OR^{18c}.

11. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 5-10, wherein A is –NR^1R^2, –$CR^iR^jR^k$, or –OR^{18a}.

12. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 5-10, wherein A is –NR^1R^2.

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13. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 5-12, wherein Q is $-NR^{11}-$, $-CR^mR^n-$, or $-O-$.

14. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 5-12, wherein Q is $-NR^{11}-$.

15. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-14, wherein R^7, R^5, and R^9 are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-7}cycloalkyl, C_{4-8}cycloalkylalkyl, 3-7 membered heterocycloalkyl, 4-8 membered heterocycloalkylalkyl, 5-6 membered heteroaryl, 6-21 membered heteroarylalkyl, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$; $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)R^{20}$,$-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_2R^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^7 and R^8 can, together with the atoms linking them, form a C_{6-10}aryl, C_{3-7}cycloalkyl, 3-7 membered heterocycloalkyl or a 5-6 membered heteroaryl.

16. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-14, wherein R^7, R^8, and R^9 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_nR^{20}$.

17. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-14, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-OR^{20}$; and R^9 is chosen from H, C_{1-6}alkyl optionally substituted by 1-6 R^{19}, C_{2-6}alkenyl optionally substituted by 1-6 R^{19}, C_{2-6}alkynyl optionally substituted by 1-6 R^{19}, C_{6-10}aryl optionally substituted by 1-6 R^{19}, C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally

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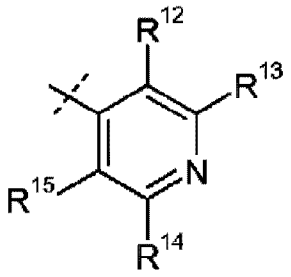
substituted by 1-6 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)OR^{20}, –C(=O)$NR^{22}R^{23}$, –NC, –NO_2, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)OR^{21}, –NR^{24}C(=O)$NR^{22}R^{23}$, –NR^{24}S(=O)$_2R^{21}$, –NR^{24}S(=O)$_2NR^{22}R^{23}$, –OR^{20}, –OC(=O)R^{20}, –OC(=O)$NR^{22}R^{23}$, –S(=O)$_nR^{20}$, and –S(=O)$_2NR^{22}R^{23}$.

18. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-14, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, halogen, –$NR^{22}R^{23}$, and –OR^{20}; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –$NR^{22}R^{23}$, –OR^{20}, and –S(=O)$_nR^{20}$

19. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-18, wherein R^8 is H.

20. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula



, and R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)$NR^{22}R^{23}$, –NO_2, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, –NR^{24}S(=O)$_2R^{21}$, –OR^{20}, –S (=O)$_nR^{20}$ and –S(=O)$_2NR^{22}R^{23}$; or either or both of R^{12} and R^{13}, and/or R^{14} and R^{15}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

21. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula

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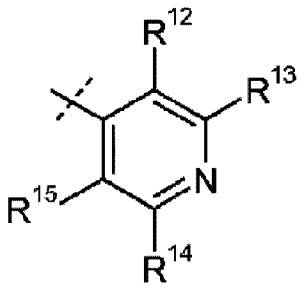
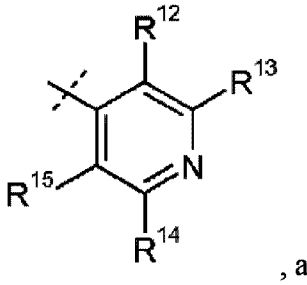


, and R^{12}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-7}cycloalkyl optionally substituted by 1-3 R^{19}, 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

22. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula



, and R^{12} and R^{14} are H; R^{15} is chosen from H and halogen; R^{13} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19} or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

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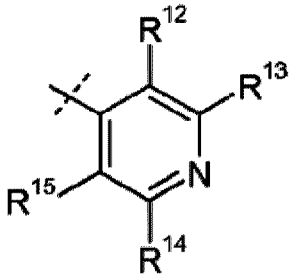
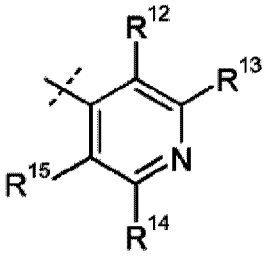
23. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula



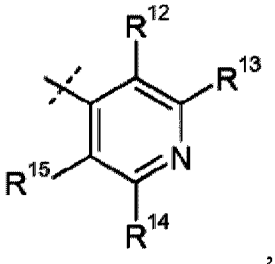
, and R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$; $-NR^{24}C(=O)R^{20}$; $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$; $-NR^{24}S(=O)_2R^{21}$; and $-NR^{24}S(=O)_2NR^{22}R^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-6 membered heteroaryl optionally substituted by 1-6 R^{19}.

24. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-20, wherein G is a group of formula



, and R^{14} and R^{15} are H; R^{12} is chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5 membered heteroaryl optionally substituted by 1-2 R^{19}.

25. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-20, wherein G is a group of formula



, and R^{14} is H; R^{12} and R^{15} are independently chosen from H and halogen; R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a pyrrolyl ring optionally substituted by 1 R^{19}.

26. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-20, wherein G is a group of formula

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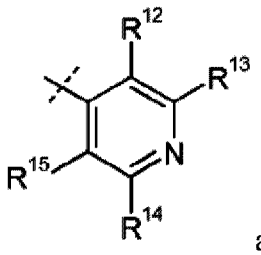
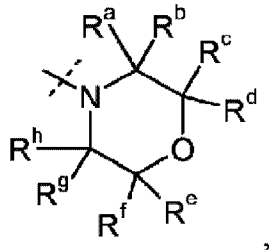


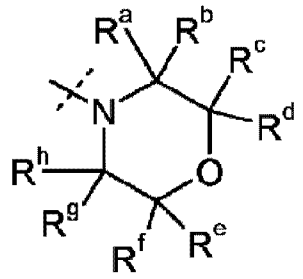
and, and R^{12}, R^{13}, R^{14} and R^{15} are H; or R^{12} and R^{13}, together with the atoms linking them, form a pyrrolyl ring.

27. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula



, and R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

28. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula



, and R^a, R^b, R^c, R^d, R^e, R^f, R^g, and R^h are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and benzyl optionally substituted by 1-3 R^{19}.

29. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula

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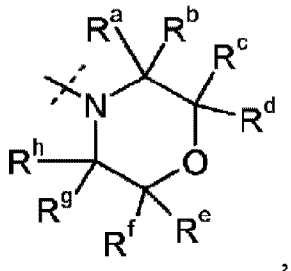
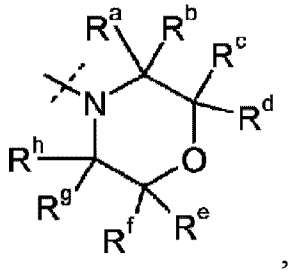


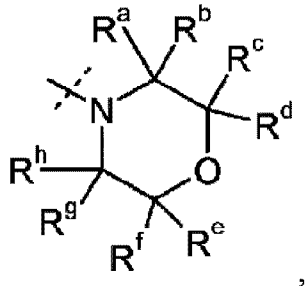
, and R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

30. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula



, and R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H; and R^d is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and benzyl optionally substituted by 1-3 R^{19}.

31. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-19, wherein G is a group of formula



, and R^a, R^b, R^c, R^e, R^f, R^g, and R^h are H.

32. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-31, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkenyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-10}aryl optionally substituted by 1-3 R^{39}, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{39}, 3-6 membered

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heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{39}, halogen, –CN, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NO_2$, $–NR^{32}R^{33}$, $NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–NR^{34}S(=O)_2NR^{32}R^{33}$, $–OR^{30}$, =O, $–OC(=O)R^{30}$, $–OC(=O)NR^{32}R^{33}$, $–Si(R^{34})_3$, =S, $–S(=O)_nR^{30}$, and $–S(=O)_2NR^{32}R^{33}$.

33. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-31, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, $–C(=O)R^{30}$, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, and $–OR^{30}$.

34. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-31, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, 5-6 membered heteroaryl, halogen, $–C(=O)OR^{30}$, $–NR^{32}R^{33}$, and $–OR^{30}$.

35. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-31, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{7-11}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–OR^{30}$, and =O.

36. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-35, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and a R^{37} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, and C_{3-6}cycloalkyl optionally substituted by 1-3 R^{49}.

37. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-35, wherein R^{20} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{49}, phenyl optionally substituted by 1-3 R^{49}, benzyl optionally substituted by 1-3 R^{49}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is H.

38. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-35, wherein R^{20}, R^{21}, R^{24}, R^{25}, R^{26}, R^{27}, R^{30}, R^{31}, R^{34}, R^{35}, R^{36} and R^{37} at each occurrence is independently chosen from H and C_{1-6}alkyl.

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39. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-38, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{59}, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}.

40. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-38, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl optionally substituted by 1-3 R^{59}, and 5-6 membered heteroaryl optionally substituted by 1-3 R^{59}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

41. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-38, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

42. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-41, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}, phenyl optionally substituted by 1-3 R^{79}, benzyl optionally substituted by 1-3 R^{79}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)NR^{72}R^{73}$, $-NR^{72}R^{73}$, $-OR^{70}$, and $-S(=O)_nR^{70}$.

43. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-41, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{79}.

44. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-43, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{89}.

45. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-43, wherein R^{72} and R^{73} at each occurrence is independently chosen from H and C_{1-6}alkyl.

46. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-45, wherein R^{79} and R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl and phenyl.

47. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1-45, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently C_{1-6}alkyl.

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48. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein X is chosen from –NHR^{28} and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}; R^7 is chosen from H, C_{3-6}cycloalkyl, and –OR^{20}; R^8 is chosen from H and halogen; R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19} , halogen, –$NR^{22}R^{23}$, –OR^{20}, and –SR^{20}; R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, –$NR^{22}R^{23}$, and –$NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}; and R^a, R^b, R^c, R^d, R^e, R^f R^g, and R^h are H.

49. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NHR^{28} and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

50. The compound or pharmaceutically acceptable salt form thereof as defined in claim 49, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

51. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NHR^{28} and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{39}, halogen, –CN, –$C(=O)OR^{30}$, –$C(=O)NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}C(=O)R^{30}$, and –OR^{30}.

52. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon

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atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –$NR^{34}C(=O)R^{30}$, and –OR^{30}.

53. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NHR^{28} and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, and –OH.

54. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-6 R^{49}), –NH(3-10 membered heterocycloalkyl optionally substituted by 1-6 R^{49}), –NH(4-11 membered heterocycloalkylalkyl optionally substituted by 1-6 R^{49}), and 3-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

55. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

56. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C1-6alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1-6 R^{19}.

57. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-10 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl optionally substituted by 1-3 R^{39}, C_{6-11}aryl optionally substituted by 1-3 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 3-15 membered heterocycloalkyl optionally

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substituted by 1-3 R^{39}, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, $NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

58. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from -NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl optionally substituted by 1-3 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

59. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl), –NH(6-10 membered heterocycloalkylalkyl), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

60. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(C_{7-11}arylalkyl), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-3 R^{39}, C_{2-6}alkynyl, C_{6-11}aryl, C_{7-16}arylalkyl optionally substituted by 1-3 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{39}, 5-10 membered heterocycloalkyl, halogen, –CN, –C(=O)OR^{30}, –C(=O)$NR^{32}R^{33}$, –$NR^{32}R^{33}$, –NR^{34}C(=O)R^{30}, and –OR^{30}.

61. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}), –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), –NH(6-10 membered

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heterocycloalkylalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms), and 5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms in which the heterocycloalkyl is optionally substituted by 1 or 2 members chosen from C_{1-6}alkyl optionally substituted by 1-6 halogen, halogen, –CN, $–C(=O)OR^{30}$, $–C(=O)NR^{32}R^{33}$, $–NR^{32}R^{33}$, $–NR^{34}C(=O)R^{30}$, and $–OR^{30}$.

62. The compound or pharmaceutically acceptable salt form thereof as defined in claim 48, wherein X is chosen from –NH(C_{1-6}alkyl optionally substituted by 1-6 R^{49}) and –NH(5-6 membered heterocycloalkyl consisting of carbon atoms and 1 or 2 nitrogen atoms).

63. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and –O(C_{1-6}alkyl); R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–SR^{20}$.

64. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1 or 32-62, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $–OR^{20}$; R^8 is H; and R^9 is H.

65. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1 or 32-62, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and –O(C_{1-6}alkyl); R^8 is H; and R^9 is H.

66. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^7 is chosen from H, cyclopropyl, and –O(C_{1-6}alkyl); R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $–NR^{22}R^{23}$, $–OR^{20}$, and $–SR^{20}$.

67. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1 or 32-62, wherein R^7 is chosen from H, cyclopropyl, and –O(C_{1-6}alkyl); R^8 is H; and R^9 is H.

68. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1 or 32-62, wherein R^7 is chosen from H, cyclopropyl, and –O(CH_3); R^8 is H; and R^9 is H.

69. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^7 is chosen from H, cyclopropyl, and –O(C_{1-6}alkyl); R^8 is chosen from H and halogen;

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and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-OR^{20}$, and $-SR^{20}$.

70. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^7 is chosen from H, C_{3-6}cycloalkyl, and $-O(CH_3)$; R^8 is chosen from H and halogen; and R^9 is chosen from H, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5, 6, or 9 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen $-NR^{22}R^{23}$ $-OR^{20}$, and $-SR^{20}$.

71. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-6 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$, or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-6 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-6 R^{19}.

72. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, C_{7-16}arylalkyl optionally substituted by 1-3 R^{19}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, and $NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

73. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

74. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10

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membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

75. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, halogen, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

76. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

77. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NR^{22}R^{23}$, and $-NR^{24}C(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 nitrogen atom, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

78. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a C_{6-11}aryl optionally substituted by 1-3 R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

79. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a phenyl optionally substituted by 1-3

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R^{19}, 5-10 membered heterocycloalkyl optionally substituted by 1-3 R^{19} in which the heterocycloalkyl contains carbon atoms and 1 or 2 nitrogen atoms, or a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

80. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

81. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

82. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H, $-NHR^{23}$, and $-NHC(=O)R^{20}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 nitrogen atom.

83. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19}.

84. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein R^{12}, R^{14}, and R^{15} are H, and R^{13} is chosen from H and $-NHR^{23}$; or R^{12} and R^{13} can, together with the atoms linking them, form a 5-10 membered heteroaryl optionally substituted by 1-3 R^{19} in which the heteroaryl contains carbon atoms and 1 or 2 nitrogen atoms.

85. A compound chosen from:

1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;

N-(2-aminoethyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2R)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-aminopropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

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(3R)-N-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
(3R)-N-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
N-[(2S)-2-amino-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(3S)-3-benzyl-1-[6-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]aminolpropan-2-ol;
(3S)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(3R)-3-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-methyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane;
(2S)-2,4-dibenzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine;
tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxylate;
tert-butyl 4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane-1-carboxylate;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]thiomorpholine;
N,N-Dimethyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine;
N-[(2S)-2-amino-3-phenylpropyl]-N-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-one;
N-[(2S)-1-amino-3-phenylpropan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
(2R)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(3S)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1,4-diazepane;
2-{4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}ethan-1-ol;
(3S)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol;
(3R)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol;

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(3R)-3-benzyl-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(2S)-2-benzyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
methyl(2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-carboxylate;
methyl(2S,4S)-4-[(2S,4S)-4-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}pyrrolidine-2-amido]pyrrolidine-2-carboxylate;
[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl](methyl)amine;
N-[(3R)-oxolan-3-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;
(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine;
(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl]methanol;
N-[(2R,3R)-2-amino-3-fluoro-3-phenylpropyl]-5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
2-[(2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl]acetamide;
[(2S)-1-{[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}-3-phenylpropan-2-yl]dimethylamine;
(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-ol;
1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3,5-cis-dimethylpiperazine;
(3R)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-methylpiperazine;
(3S)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]pyrrolidin-3-amine;
3-(fluoromethyl)-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
N-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidine-4-carboxamide;
4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide;
N-cyclohexyl-4-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine-1-carboxamide;
2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl}acetonitrile;
1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;
1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;
(3S)-3-ethyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

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(3S)-3-(propan-2-yl)-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[2-(3-fluoropyridin-4-yl)-5-methoxypyrido[3,4-d]pyrimidin-4-yl]piperazine;
4-{4-[(8aR)-octahydropyrrolo[1,2-a]piperazin-2-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine;
1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[2-(3-fluoropyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-3-(trifluoromethyl)piperazine;
4-{4-[(3aS)-octahydro-1H-pyrrolo[3,2-c]pyridin-5-yl]pyrido[3,4-d]pyrimidin-2-yl}pyridine;
(3S)-3-benzyl-1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
3-phenyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine;
3-ethynyl-1-[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]morpholine;
{1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]azetidin-3-ylmethanol;
(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[8-chloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperidin-4-ol;
(3R)-3-[fluoro(phenyl)methyl]-1-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
(4-fluorophenyl)[(2R)-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-2-yl]methanol;
N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-formamide;
N-[(S)-1-Benzyl-2-(2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-ylamino)-ethyl]-acetamide;
methyl[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrid[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amine;
(2S)-2-benzyl-4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-1-methylpiperazine;
2-{[(2S)-1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl]amino}acetamide;
N-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)methanesulfonamide;
(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea;
3-ethyl-1-(1-phenyl-3-{[2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]amino}propan-2-yl)urea;
(3aR)-5-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-1H-[1,3]oxazolo[3,4-a]piperazin-1-one;

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2-{4-[5-methoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazin-1-yl}acetonitrile;
N-{3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-8-yl]-phenyl}-methanesulfonamide;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-pyrazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-phenyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol;
3-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol;
N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(4-methoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(2-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(pyridin-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-2,8-bis(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-[1-(2-methylpropyl)-1H-pyrazol-4-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;
N-[(2S)-2-amino-3-phenylpropyl]-8-(4-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

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N-[(2S)-2-amino-3-phenylpropyl]-8-(1-methyl-1H-pyrazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

2-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)phenol;

N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(3-chlorophenyl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-[4-(4-chlorophenyl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(pyrimidin-5-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(3-aminophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(1-benzofuran-7-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(5-methylthiophen-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(dimethyl-1,2-oxazol-4-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-3-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-(thiophen-3-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(furan-2-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(1H-1,3-benzodiazol-5-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(3-ethoxyphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(2-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

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N-[(2S)-2-amino-3-phenylpropyl]-8-(3-methylphenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-[3-(1H-pyrazol-5-yl)phenyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-[5-(aminomethyl)furan-2-yl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

(R)-3-Phenyl-N^1-(2-pyridin-4-yl-8-pyridin-2-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine;

N^4-((R)-2-Amino-3-phenyl-propyl)-N^8-phenyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine;

4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(pyrimidin-2-yl)pyrido[3,4-d]pyrimidine-4,8-diamine;

4-N-[(2S)-2-amino-3-phenylpropyl]-8-N-(3-chlorophenyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidine-4,8-diamine;

4-N-[(2S)-2-amino-3-phenylpropyl]-2-(pyridin-4-yl)-8-N-(1H-1,2,4-triazol-3-yl)pyrido[3,4-d]pyrimidine-4,8-diamine;

(R)-N^1-[8-(4-Methyl-piperazin-1-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine;

(R)-3-Phenyl-N^1-(8-phenylsulfanyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-propane-1,2-diamine;

N-[(2S)-2-amino-3-phenylpropyl]-8-phenoxy-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

N-[(2S)-2-amino-3-phenylpropyl]-8-(methylsulfanyl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

4-(4-{[(2S)-2-amino-3-phenylpropyl]amino}-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-yl)-2-methylbut-3-yn-2-ol;

5-Chloro-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;

1-[5-bromo-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

1-[5,8-dichloro-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

5-Butyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;

1-[5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;

N-[(2S)-2-amino-3-phenylpropyl]-5-ethyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-amine;

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1-[5-methyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-[5-cyclopropyl-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl]piperazine;
1-{5-[(benzyloxy)methyl]-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-4-yl}piperazine;
5-Chloro-4-piperazin-1-yl-8-(1H-pyrazol-3-yl)-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
5-chloro-N,N-dimethyl-4-(piperazin-1-yl)-2-(pyridin-4-yl)pyrido[3,4-d]pyrimidin-8-amine;
5-Isopropenyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
5-Methoxy-4-piperidin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid amide;
3-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3-carboxylic acid phenylamide;
4-Amino-1-(5-methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-4-carboxylic acid; [(S)-1-(4-chloro-phenyl)-3-hydroxy-propyl]-amide;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid methyl ester;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenylamide;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid benzylamide;
4-(5-Methoxy-2-pyridin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-2-carboxylic acid phenethyl-amide;
4-Piperazin-1-yl-8-propyl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
8-Methyl-4-piperazin-1-yl-2-pyridin-4-yl-pyrido[3,4-d]pyrimidine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-oxazol-2-yl)-amine;
(4,5-Dimethyl-oxazol-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(4-Cyclopropyl-thiazol-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

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3-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;
(2-Fluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine;
4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamine;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-morpholin-4-yl-acetamide;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-piperidin-1-yl-acetamide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-4-yl-amine;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-benzamide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-methyl-amine;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;
N-{4-[4-(4-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl)-acetamide;
Cyclopropanecarboxylic acid [4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;
N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2,2-dimethyl-propionamide;
Tetrahydro-pyran-4-carboxylic acid [4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-thiazol-2-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-oxazol-2-yl-amine;
[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-oxazol-2-yl)-amine;
{(S)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol;
1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-4-methyl-piperidin-4-ol;

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{4-[4-((S)-3-Isopropyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

2-{(S)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-ethanol;

N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-N',N'-dimethyl-benzene-1,4-diamine;

{5-Methoxy-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(2-Fluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{5-Methoxy-2-[2-(4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(4-Fluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{4-[5-Methoxy-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{(S)-4-(5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile;

{4-[4-((R)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

Cyclopropanecarboxylic acid {4-[4-(4-hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

{4-[4-((S)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[4-((S)-3-Cyclopropyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[4-((R)-3-Fluoromethyl-piperazin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,3,6-trifluoro-phenyl)-amine;

[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

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{5-Methoxy-2-[2-(pyrazin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

Thiophene-2-carboxylic acid {4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

Cyclopentyl-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

Cyclohexyl-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{2[2-(Pyrazin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl}-methanol;

2-{3-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-R-pyrrolidin-1-yl}-acetamide;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine;

(2-Fluoro-phenyl)-{2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-5-yl}-amine;

4-{5-(4-Cyano-pyridin-2-ylamino)-2-[2-(4-cyano-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine;

{4-[5-Chloro-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

N-[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-difluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine;

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[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5–fluoro-pyridin-2-yl)-amine;

[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;

5-[4-(5-Chloro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;

{4-Piperazin-1-yl-2-[2-(2,3,6-trifluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-5-yl}-(2,3,6-trifluoro-phenyl)-amine;

(2,6-Difluoro-phenyl)-{2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-5-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-pyridin-2-yl)-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,5-dimethyl-oxazol-2-yl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

1-{5-Cyclopropyl-2-[2-(2-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

{4-[5-Cyclopropyl-4-((S)-3-isopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4((S)-3-cyclopropyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine;

(4-{5-Cyclopropyl-4-[3-(1,1-difluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

{(S)-4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile;

Cyclopentyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

Cyclohexyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(tetrahydro-pyran-4-yl)-amine;

Cyclopentyl-{4-[5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

Adamantan-1-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

2-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide;

4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide;

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4-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide;

{4-[(1S,4S)-4-(2,5-Diaza-bicyclo[2.2.1]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

Pyrazine-2-carboxylic acid {4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzamide;

3-Amino-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzamide;

2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide;

2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide;

2-(4-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;

2-(4-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(3-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;

2-(3-Amino-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

{2-[2-(5-Phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(6-Morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

(2-{2-[6-(4-Methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;

2-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

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{2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenoxy)-acetamide;

2-(3-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;

2-(3-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(4-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-phenyl)-acetamide;

2-(4-Amino-phenyl)-N-{4-[5-methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

1-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-1H-pyrrolo[2,3-b]pyridine-4-carbonitrile;

{5-Methoxy-2-[2-(5-phenyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{5-Methoxy-2-[2-(6-morpholin-4-yl-pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

(5-Methoxy-2-{2-[6-(4-methyl-piperazin-1-yl)-pyridin-3-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;

2-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

{2-[2-(4-Imidazol-1-ylmethyl-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

2-Phenyl-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(4-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(2-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

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2-(3-Methoxy-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

{2-[2-(4-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(4-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

6-{4-[4-((R)-Pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile;

2-[4-(4-Piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;

{2-[2-(4-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

6-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-nicotinonitrile;

{2-[2-(5-Methyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(5-Chloro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

2-[2-(Pyrimidin-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

2-(3-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(4-Cyano-phenyl)-N-{4-[4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

(R)-Pyrrolidin-3-yl-{2-[2-(4-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

(R)-Pyrrolidin-3-yl-{2-[2-(5-trifluoromethyl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;

6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinonitrile;

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{4-[5-Methoxy-4-(4-morpholin-4-yl-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

2-(4-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

{2-[2-(5-Morpholin-4-yl-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{2-[2-(2-Methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

(2-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{5-Methoxy-2-[2-(2-methoxy-4-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;

(5-Methoxy-2-{2-[4-(tetrahydro-pyran-4-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(tetrahydro-pyran-4-yl)-phenyl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-2-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-pyridin-2-yl)-amine;

(4-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(5-Chloro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine;

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2-(4-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

2-(3-Chloro-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-acetamide;

2-(3-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(3-trifluoromethyl-phenyl)-acetamide;

2-(4-Methoxy-phenyl)-N-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine;

{2-[2-(Pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl{-(R)-pyrrolidin-3-yl-amine;

{5-Methoxy-2-[2-(pyridin-3-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine;

2-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinamide;

6-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinamide;

(3-Methoxy-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine;

5-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;

{5-Methoxy-2-[2-(pyrimidin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

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[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-5-yl-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-5-yl-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine;

2-[4-(5-Methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-isonicotinonitrile;

2-(3-Cyano-phenyl)-N-[4-(5-methoxy-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,5-trimethoxy-phenyl)-amine;

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-phenyl-pyridin-3-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-3-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-3-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-3-yl)-amine;

N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-pyridin-3-yl-acetamide;

2-{4-[5-Methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

2-(3-Chloro-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-3-yl-acetamide;

N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-pyridin-4-yl-acetamide;

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[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methoxy-pyridin-2-yl)-amine;

2-{4-[4-(4-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

2-(3-Cyano-phenyl)-N-{4-[4-(4-hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(3-Cyano-phenyl)-N-{4-[5-methoxy-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

(6-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(R)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide;

(S)-N-{4-[5-Methoxy-4-((R)-pyrrolidin-3-ylamino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-2-phenyl-propionamide;

(R)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide;

(S)-N-[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-propionamide;

4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methyl-pyridin-2-yl)-amine;

(3-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-piperazin-1-ylpyridin-3-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-methyl-4-(4-methyl-piperazin-1-yl)-phenyl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-piperidin-4-yl-1H-pyrazol-4-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-2-yl)-amine;

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[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl](5-methyl-pyridin-3-yl)-amine;

(5-Chloro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2-Fluoro-4-morpholin-4-yl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

3-Fluoro-4-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;

4-Fluoro-3-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;

(2,6-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2-Fluoro-6-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrimidin-2-yl-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methoxy-pyridin-3-yl)-amine;

(S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol;

2-{4-[4-((S)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;

(R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ol;

2-{4-[4-((R)-3-Hydroxy-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(S)-1-pyrrolidin-2-ylmethyl-amine;

[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-1-pyrrolidin-2-ylmethyl-amine;

2-{4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-ethanol;

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{1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol;

{(R)-4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol;

(R)-7-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-oxazolo[3,4-a]pyrazin-3-one;

(±)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

(±)-trans-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

4-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-one;

(2,3-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2,5-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,6-trifluoro-phenyl)-amine;

((R)-4-{2-[2-(2,6-Difluoro-phenylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl)-methanol;

3-Hydroxymethyl-1-[5-methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-phenyl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-phenyl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethyl-phenyl)-amine;

(6-Fluoro-pyridin-2-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-2-yl)-amine;

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[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-2-yl)-amine;

(2-Fluoro-pyridin-3-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2-Fluoro-3-methyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2-Fluoro-3-trifluoromethyl-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2,4-Difluoro-phenyl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl](2,3,4-trifluoro-phenyl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,5-trifluoro-phenyl)-amine;

(3S,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

(3R,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

3-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-propionamide;

[4-(5-Methoxy-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

{4-[4-(4,4-Difluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile;

{4-[4-(4-Fluoro-piperidin-1-yl)-5-methoxy-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

(3R,4S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

(3S,4R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

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{(R)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol;

{(S)-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl}-methanol;

(meso)-cis-1-[5-Methoxy-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azepane-4,5-diol;

1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

((S)-1-{2-[2-(6-Fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-methoxy-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol;

((S)-1-{5-Methoxy-2-[2-(6-methoxy-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl)-methanol;

2-(4-Cyano-phenyl)-N-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-morpholin-4-yl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-morpholin-4-yl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-3-yl-amine;

(2-Chloro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-methyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

2-{4-[5-Cyclopropyl-4-(4-hydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-phenyl)-amine;

(±)-2-{4-[5-Cyclopropyl-4-cis-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-o-tolyl-amine;

2-{4-[5-Cyclopropyl-4-((3R,4S)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

2-{4-[5-Cyclopropyl-4-((3S,4R)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-N-(1-phenylpyrazol-4-yl)pyridin-2-amine;

(2,3-Dimethyl-2H-indazol-6-yl)-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[1-(2-Fluoro-phenyl)-1H-pyrazol-4-yl]-[4-(5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-phenyl-1H-pyrazol-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dimethyl-2H-indazol-6-yl)-amine;

Phenyl-[4-(4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-pyridin-3-yl)-amine;

[4-(5-Methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methyl-isoxazol-3-yl)-amine;

2-[2-(3-Piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ol;

2-[2-(3-Piperazin-1-ylmethyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ol;

2-[2-(1-Piperidin-4-ylmethyl-1H-pyrazol-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ol;

{5-Methoxy-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;

(5-Methoxy-2-{2-[4-(2-pyrrolidin-1-yl-ethoxy)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-methyl-amine;

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{5-Methoxy-2-[2-(3-piperidin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;

[4-(5-Methoxy-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-dimethyl-phenyl)-amine;

5-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine;

Cyclopropyl-{4-[5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(R)-tetrahydro-furan-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,4-difluoro-cyclohexyl)-amine;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-trifluoromethyl-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-pyridin-3-yl)-amine;

(6-Chloro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxymethyl-phenyl)-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(S)-tetrahydro-furan-3-yl-amine;

2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;

tert-Butyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-trifluoromethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-2-methyl-phenyl)-amine;

3-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-4-methyl-benzonitrile;

7-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-hexahydro-oxazolo[3,4-a]pyrazin-3-one;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-pyridin-2-yl)-amine;

(2-Chloro-6-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

3-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-4-fluoro-benzonitrile;

(4-tert-Butyl-2-chloro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

2-{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-ethyl)-amine;

2-{4-[5-Cyclopropyl-4-(3-oxo-tetrahydro-oxazolo[3,4-a]pyrazin-7-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-isonicotinonitrile;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-trifluoromethyl-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-pyridin-3-yl)-amine;

{4-[5-Cyclopropyl-4-(2,5-diaza-bicyclo[4.1.0]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[5-Cyclopropyl-4-(2,5-diaza-bicyclo[4.1.0]hept-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-dichloro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dimethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-dimethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dichloro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3-dichloro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridazin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methyl-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,6-difluoro-pyridin-2-yl)-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(dimethyl-phosphinoyl)-phenyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(diethyl-phosphinoyl)-phenyl]-amine;

N^5-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-N^2,N^2-dimethyl-pyridine-2,5-diamine;

{4-[5-Cyclopropyl-4-((R)-3-fluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-methoxy-2-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-5-trifluoromethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-trifluoromethoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methanesulfonyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-3-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-isopropyl-2-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pent-deuterio-phenyl-amine;

1-{2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-phenyl}-ethanol;

(1R,2S)-2-Amino-cyclopentanecarboxylic acid [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;

1-{4-[2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-cyclopropanol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-6-yl-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-5-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridazin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-3-methoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-ethoxy-2,6-difluoro-phenyl)-amine;

(2-Chloro-3-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

(2-Chloro-4-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-phenyl)-amine;

(2-Chloro-4-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-dimethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-3-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-methyl-phenyl)-amine;

(2-Chloro-5-fluoro-phenyl)-[4-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2-Chloro-5-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(2-Chloro-3-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

5-Cyclopropyl-2-(6,7-dimethoxy-quinolin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-methoxy-phenyl)-amine;

N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-acetamide;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamine;

N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-isobutyramide;

Cyclopropanecarboxylic acid [4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclobutyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-phenyl-ethyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((S)-1-phenyl-ethyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-methoxy-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-3-methoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-4-methoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-2-methyl-phenyl)-amine;

(2-Chloro-5-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-phenyl)-amine;

(2-Chloro-5-trifluoromethyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-pyrazol-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-cyclohexyl)-amine;

(+/-)-(cis)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;

(4-Cyclopropyl-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-4-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-imidazol-4-yl)-amine;

2-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-ethanol;

(S)-3-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-propane-1,2-diol;

(R)-3-{4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-1-yl}-propane-1,2-diol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methoxy-4-methyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4-dimethoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,5-trimethoxy-phenyl)-amine;

N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-phenyl-acetamide;

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N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-3,3,3-trifluoro-propionamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(1-methyl-4-oxo-4λ^5-[1,4]azaphosphinan-4-yl)-phenyl]-amine;

2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidine;

(2-Chloro-6-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(6-Chloro-2-fluoro-3-methyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(3-Chloro-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclopentyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-isopropyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-ethyl-phenyl)-amine;

2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(1-ethyl-4-oxo-4λ^5-[1,4]azaphosphinan-4-yl)-2-methoxy-phenyl]-amine;

N-(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-acetamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-3-methoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-5-methoxy-phenyl)-amine;

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Cyclopropylmethyl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-methyl-amine;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-fluoro-benzonitrile;
[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenyl-amine;
4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-cyclohexanol;
(2-Chloro-6-fluoro-3-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(2-Chloro-3,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
{4-[5-Cyclopropyl-4-(2,2,3,3,5,5,6,6-octadeuterio-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-y]-phenyl-amine;
(4-Cyclopropyl-3-methoxy-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
4-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acidamide;
N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2-(2,6-difluoro-phenyl)-acetamide;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-propyl-phenyl)-amine;
(4-Cyclopropyl-2-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;
(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(2,6-difluoro-phenyl)-amine;
(4-{5-Cyclopropyl-4-[3-(2,2,2-trifluoro-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;
[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(3-fluoro-phenyl)-ethyl]-amine;

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4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzonitrile;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethyl-phenyl)-amine;

(3-Chloro-2,6-difluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4,6-trifluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-phenyl)-amine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(4-fluoro-phenyl)-ethyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2,6-difluoro-phenyl)-ethyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-phenyl-amine;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid isopropylamide;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid amide;

N-(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-acetamide;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-fluoro-ethyl)-amide;

N-{4-[5-Cyclopropyl-4-((S)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

2-(2-Chloro-pyridin-4-yl)-5-cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

(4-{5-Cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;

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(4-{5-Cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(4-fluoro-phenyl)-amine;

(4-{5-Cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-phenyl-amine;

(4-{5-Cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(4-fluoro-phenyl)-amine;

Cyclopropanecarboxylic acid (4-{5-cyclopropyl-4-[4-(2-methanesulfonyl-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-amide;

Cyclopropanecarboxylic acid (4-{5-cyclopropyl-4-[4-(2-methoxy-ethyl)-piperazin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-amide;

(5-Cyclopropyl-2-fluoro-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

1-{5-Cyclopropyl-4[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-pyrrolidin-1-yl-ethyl)-amide;

1-{5-Cyclopropyl-4[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid methylamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,4-difluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-difluoro-cyclohexyl)-amine;

1-[2-(2-Cyclohexylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carboxylic acid isopropylamide;

(+/-)-(cis)-1-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

(+/-)-(trans)-1-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

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(+/-)-2-{4-[5-Cyclopropyl-4-((trans)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylaminol-isonicotinonitrile;

(+/-)-(trans)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4d]pyrimidin-4-yl)-piperidine-3,4-diol;

1-[2-(2-Cyclopentylamino-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carboxylicacid isopropylamide;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,3,6-trifluoro-pyridin-4-yl)-amine;

Biphenyl-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzoic acid;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-hydroxy-ethyl)-amide;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid dimethylamide;

4-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperazine-1-carboxylic acid amide;

1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-4-ol;

5-Cyclopropyl-2-(2-fluoro-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[4-(4-Amino-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

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{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;

(+/-)-(1RS,2RS,4SR)-Bicyclo[2.2.1]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{4-[4-(4-Aminomethyl-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(S)-1-pyrrolidin-2-ylmethyl-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(S)-1-pyrrolidin-2-ylmethyl-amine;

[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine;

Bicyclo[1.1.1]pent-1-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-3-fluoro-pyridin-2-yl]-phenyl-amine;

[4-(5-Cyclopropyl-4-[1,4]diazepan-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

(+/-)-cis-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-cyclobutyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2,2-trifluoro-1-phenyl-ethyl)-amine;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-3-carboxylic acid methylamide;

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{4-[4-(3-Amino-pyrrolidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-phenyl}-acetic acid;

[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

3-{4-[5-Cyclopropyl-4-((3R,4S)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-benzonitrile;

Chroman-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

N-(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-yl)-acetamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-isopropyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-ethyl-2-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-5-isopropyl-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-ethyl-2-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine;

(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-ol;

[(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-methanol;

[(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-yl]-methanol;

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1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid ethylamide;

(6-Cyclopropyl-2,4-difluoro-pyridin-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(6-Cyclopropyl-2-fluoro-pyridin-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidine-3-carboxylic acid methylamide;

(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-ol;

1-(3-{4-[5-Cyclopropyl-4-(4-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylaminol-phenyl)-piperidin-4-ol;

1-{5-Cyclopropyl-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(1-methyl-1H-pyrazol-4-yl)-ethyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-6-morpholin-4-yl-pyridin-3-yl)-amine;

1-{5-Cyclopropyl-2-[2-(1-piperidin-4-ylmethyl-1H-pyrazol-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

4-((R)-3-Benzyloxymethyl-piperazin-1-yl)-2-(2-chloro-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidine;

(3-Cyclopropyl-phenyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-(4-methyl-piperazin-1-yl)-methanone;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-dimethylamino-ethyl)-amide;

(S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-ol;

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(R)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidin-3-ol;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-methoxy-ethyl)-amide;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-3,5-difluoro-benzonitrile;

(1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl)-piperazin-1-yl-methanone;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-benzamide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl-amine;

1-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-4-carboxylic acid (2-methylamino-ethyl)-amide;

6-{4-[5-Cyclopropyl-4-((cis)-3,4-dihydroxy-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-ylamino}-pyridine-2-carbonitrile;

6-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-pyridine-2-carbonitrile;

1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-3,3-difluoro-piperidine-4,4-diol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,5-difluoro-pyridin-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyridin-2-yl-amine;

(3R,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;

(3R,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;

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(3S,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;

(3S,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-piperidine-3,4-diol;

{4-[5-Cyclopropyl-4-(2-methylamino-ethoxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(piperidin-4-yloxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-pyrazol-4-ylmethyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-phenethyl-amine;

[4-(5-Cyclopropyl-4-pyrrolidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

[4-(4-Azetidin-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-6-methoxy-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-pyridin-2-yl]-(4-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-pyrrolidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine;

[4-(4-Azetidin-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-piperazin-1-yl-phenyl)-amine;

N-{4-[4-((R)-3-Benzyloxymethyl-piperazin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

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{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

N-{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-acetamide;

{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(4-fluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

Cyclopropanecarboxylic acid {4-[5-cyclopropyl-4-((R)-3-methanesulfonylmethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amide;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,6-trifluoro-pyridin-2-yl)-amine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N'-methyl-ethane-1,2-diamine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N',N'-dimethyl-ethane-1,2-diamine;

1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-azetidin-3-ol;

1-{5-Cyclopropyl-2-[2-(3-piperazin-1-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-azetidin-3-ol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-isopropyl-1H-pyrazol-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-ethyl-5-methyl-1H-pyrazol-3-yl)-amine;

[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[6-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperidin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[6-(4-methyl-piperazin-1-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;

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[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,4,6-trifluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

(R)-4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperazine-2-carbonitrile;

{4-[5-Cyclopropyl-4-(1,2,3,6-tetrahydro-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine;

{4-[5-Cyclopropyl-4-(piperidin-4-ylsulfanyl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

(3S,4S)-1-(5-Cyclopropyl-2-{2-[3-(4-methyl-piperazin-1-yl)-phenylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-pyrrolidine-3,4-diol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-cyclopropyl-1H-pyrazol-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(tetrahydro-pyran-4-yl)-1H-pyrazol-4-yl]-amine;

(1-Cyclopentyl-1H-pyrazol-4-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N,N',N'-trimethyl-ethane-1,2-diamine;

{4-[5-Cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,6-difluoro-pyridin-2-yl)-amine;

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{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3-fluoro-pyridin-2-yl)-amine;

(6-Chloro-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(3,6-difluoro-pyridin-2-yl)-ethyl]-amine;

N-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N',N'-dimethyl-butane-1,4-diamine;

[4-(4-Azepan-1-yl-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

1-{5-Cyclopropyl-2-[2-(6-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

(R)-1-{5-Cyclopropyl-2-[2-(6-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-o1;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;

{4-[5-Cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine;

((R)-1-Cyclopropyl-ethyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

((R)-1-Cyclohexyl-ethyl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(5-Cyclopropyl-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

1-{4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-piperidin-1-yl}-2,2-dimethyl-propan-1-one;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine;

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{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methanesulfonyl-piperidin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2-fluoro-phenyl)-1H-pyrazol-4-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,6-difluoro-phenyl)-1H-pyrazol-4-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,4,6-trifluoro-phenyl)-1H-pyrazol-4-yl]-amine;

1-{5-Cyclopropyl-2-[2-(2-methyl-2,3-dihydro-1H-isoindol-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-3,5-difluoro-benzamide;

(1S,2S,4R)-Bicyclo[2.2.1]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(1R,2R,4S)-Bicyclo[2.2.1]hept-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(2-dimethylamino-ethoxy)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-trifluoromethyl-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(4,7-diaza-spiro[2.5]oct-7-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5,6-trifluoro-pyridin-2-yl)-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(7-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-methyl-1H-pyrazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

1-{5-Cyclopropyl-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

((R)-1-Cyclohexyl-ethyl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,6-difluoro-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(5-trifluoromethyl-pyridin-2-yl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3-fluoro-pyridin-2-yl)-amine;

-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-N-methyl-benzamide;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl-amine;

{4-[5-Cyclopropyl-4-((3R,5S)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

6-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-nicotinamide;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(8-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

4-((S)-3-Benzyl-piperazin-1-yl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;

[2-(2-Benzyl-morpholin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

(S)-N^1-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenyl-propane-1,2-diamine;

5-Methoxy-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Methoxy-2-(2-phenoxymethyl-morpholin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[(R)-4-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazin-2-yl]-methanol;

5-Methoxy-2-morpholin-4-yl-4-((R)-3-phenoxymethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

[(S)-1-(5-Methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperidin-3-yl]-phenyl-amine;

4-[(R)-3-(2-Fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;

5-Methoxy-4-((R)-3-methoxymethyl-piperazin-1-yl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;

4-[(R)-3-(4-Fluoro-phenoxymethyl)-piperazin-1-yl]-5-methoxy-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;

(2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine;

[2-Morpholin-4-yl-8-(2H-pyrazol-3-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

N^4-((S)-2-Amino-3-phenyl-propyl)-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine-4,8-diamine;

(S)-N^1-(2-Morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-3-phenyl-propane-1,2-diamine;

5-Bromo-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

Synthesisof5-Cyclopropyl-2-morpholin-4-yl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidine;

[(S)-4-(5-Cyclopropyl-2-morpholin-4-yl-pyrido[3,4-d]pyrimidin-4-yl)-piperazin-2-yl]-acetonitrile;

5-Methoxy-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Methoxy-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(2-Benzyl-1H-pynolo[2,3-b]pyridin-4-yl)-5-methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

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2-[2-(2-Fluoro-benzyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-methoxy-4-piperazin-1-yl pyrido[3,4-d]pyrimidine;

2-(2-Ethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5methoxy-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Methoxy-4-((R)-3-methoxymethyl-piperazin-1-yl)-2-(1H-pynolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{(R)-4-[5-Methoxy-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-methanol;

4-Piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(R)-Pyrrolidin-3-yl-[2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;

5-Cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

8-Chloro-5-cyclopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Isopropyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

[5-Cyclopropyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-((S)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-4-(3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

4-((S)-3-Benzyl-piperazin-1-yl)-5-cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-((S)-3-cyclopropyl-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

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{(S)-4-[5-Cyclopropyl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazin-2-yl}-acetonitrile;

5-Cyclopropyl-4-piperazin-1-yl-2-(2-thiophen-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(2-cyclopropyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

4-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-1-carboxylic acid ethylester;

5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-ol;

5-Cyclopropyl-2-(5-fluoro-1H-pyn-olo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-morpholin-4-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-piperazin-1-yl-2-(2-triduteriomethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-5-chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(4-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(5-fluoro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(+/-)-(cis)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

(+/-)-(trans)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyn-olo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-3,4-diol;

5-Cyclopropyl-4-(3-trifluoromethyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

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5-Cyclopropyl-4-piperidin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;

5-Cyclopropyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidine-4-carbonitrile;

{1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl}-methanol;

{1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-azetidin-3-yl}-methanol;

1-{5-Cyclopropyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ol;

5-Cyclopropyl-4-(1,1-dioxo-1λ^6-thiomorpholin-4-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-thiomorpholin-4-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;

4-Azetidin-1-yl-5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-[1,4]diazepan-5-one;

(R)-1-[2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-pyrrolidin-3-ol;

5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

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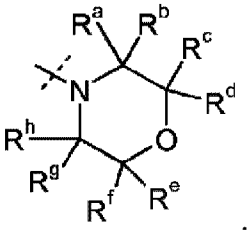
4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)spiro[1,3-dihydropyrrolo[2,3-b]pyridine-2,1'-cyclohexane];

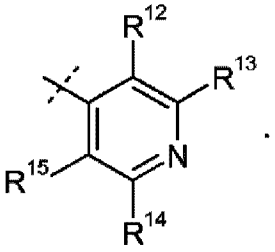
4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

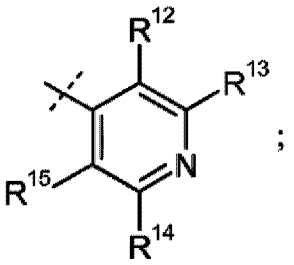
1-[5-Cyclopropyl-2-(9H-pyrido[2,3-b]indo1-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-ol;

or

4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole; or a pharmaceutically acceptable salt form thereof.

86. The compound or pharmaceutically acceptable salt form thereof according to claim 1 wherein G is  .

87. The compound or pharmaceutically acceptable salt form thereof according to claim 1 wherein G is  .

88. The compound or pharmaceutically acceptable salt form thereof according to any one of claims 1 or 87 wherein G is  ;

X is chosen from 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, $-NR^{24}R^{28}$, and $-S(=O)_nR^{28}$;

R^7, R^8, R^9 are each independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{2-6}alkenyl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, and halogen.

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89. The compound of formula (I) or pharmaceutically acceptable salt form thereof according to any one of claims 1, 87 or 88 wherein R^{24} at each occurance is independently chosen from H, and C_{1-6}alkyl optionally substituted by 1-13 R^{49}; and

R^{28} is selected from 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49} and C_{6-11}aryl optionally substituted by 1-11 R^{49}.

90. The compound of formula (I) or pharmaceutically acceptable salt form thereof according to any one of claims 1 or 87-89 wherein R^{12} and R^{13}, together with the atoms linking them, form C_{3-11} cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

91. The compound of formula (I) or pharmaceutically acceptable salt form thereof according to any one of claims 1 or 87-89 wherein R^{12}, R^{14} and R^{15} are each H and R^{13} is $-NR^{22}R^{23}$ or $-NR^{34}C(=O)R^{30}$.

92. The compound of formula (I) or pharmaceutically acceptable salt form thereof according to claim 91 wherein R^{22} and R^{23} are each independently chosen from H,C_{1-6}alkyl optionally substituted by 1-13 R^{49}, C_{6-11}aryl optionally substituted by 1-11 R^{49}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{49}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{49}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{49}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{49}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{49}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{49}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{49}.

93. A compound that is selected from:

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-N,N-dimethyl-benzamide;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine;

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(+/-)-cis-1-{5-Cyclopropyl-2-[2-(3-morpholin-4-yl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidine-3,4-diol;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-((R)-1-cyclopropyl-ethyl)-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-((R)-1-phenyl-ethyl)-amine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-{2-[1-(2-fluoro-phenyl)-cyclopropyl]-1H-pyrrolo[2,3-b]pyridin-4-yl}-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4,6-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-cyclopropyl-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

(5-Cyclobutyl-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

(4-Chloro-1-ethyl-1H-pyrazol-3-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-amine;

{4-[5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-isopropyl-1H-pyrazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl-methyl-piperidin-4-yl-amine;

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{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine;

{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-pyrrolidin-3-yl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1,2,4]triazolo[1,5-a]pyridin-2-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-morpholin-4-yl-phenyl)-amine;

5-Cyclobutyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-pyrrolidin-3-yl-amine;

Azetidin-3-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5,8-difluoro-9H-pyrido[2,3-b]indole;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

Azetidin-3-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;

[4-Chloro-1-(2,2,2-trifluoro-ethyl)-1H-pyrazol-3-yl]-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-8-fluoro-9H-pyrido[2,3-b]indole;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(8-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(7-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(S)-pyrrolidin-3-yl-amine;

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{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-7,8-difluoro-9H-pyrido[2,3-b]indole;

{4-[5-Cyclopropyl-4-((cis)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,4,6-trifluoro-pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(2,2-dimethyl-piperidin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6,8-difluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(5-fluoro-[1,2,4]triazolo[1,5-a]pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-phenyl-ethyl)-amine;

(4-Chloro-1-ethyl-1H-pyrazol-3-yl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

Benzooxazol-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

Benzothiazol-2-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-benzoimidazol-2-yl)-amine;

(5-Cyclopropyl-3,6-difluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

5-Cyclopropyl-2-{2-[1-(4-fluoro-phenyl)-cyclopropyl]-1H-pyrrolo[2,3-b]pyridin-4-yl}-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[5-Cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-naphthalen-2-yl-amine;

Biphenyl-3-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{4-[5-Cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[3-(4-methyl-piperazin-1-yl)-phenyl]-amine;

{4-[5-Cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(1-methyl-1H-pyrazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-fluoro-4-(2-methyl-2H-pyrazol-3-yl)-phenyl]-amine;

{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(R)-pyrrolidin-3-yl-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(R)-pyrrolidin-3-yl-amine;

Azepan-4-yl-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-naphthalen-1-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-iso[D3-4]quinolin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1-methyl-1H-indazol-3-yl)-amine;

{5-Cyclopropyl-2-[2-(3,4,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(1-phenyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

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{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(tetrahydro-furan-2-yl)-ethyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2-fluoro-phenyl)-ethyl]-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-4-yl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

8-Chloro-5-cyclopropyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-2-yl-amine;

{4-[5-Cyclopropyl-4-((cis)-3,5-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine;

2-(2-Chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(2-methoxymethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ylamino}-piperidin-2-one;

[5-Cyclopropyl-2-(1-methyl-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(R)-pyrrolidin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[D3-4]quinolin-2-yl-amine;

(±)-2-((endo)-2-Bicyclo[2.2.1]hept-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

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5-Cyclobutyl-2-(2-methoxymethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-(1-methyl-piperidin-4-yl)-amine;

5-Cyclobutyl-4-piperazin-1-yl-2-(1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(1-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(1-methyl-piperidin-4-yl)-amine;

1-(4-{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-ylamino}-piperidin-1-yl)-ethanone;

5-Cyclopropyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(3-Chloro-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-(R)-pyrrolidin-3-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-iso[D3-4]quinolin-1-yl-amine;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

4-(4-Piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

8-Chloro-5-cyclopropyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-exo-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]--7-oxa-bicyclo[2.2.1]hept-2-yl-amine;

(2,6-Difluoro-phenyl)-[4-(4-piperazin-1-yl-5-vinyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

1-[4-({5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidin-1-yl]-ethanone;

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1-[4-({5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidin-1-yl]-ethanone;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(R)-indan-1-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(S)-indan-1-yl-amine;

[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-8-fluoro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

5-Cyclopropyl-8-fluoro-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(1-Cyclobutyl-piperidin-4-ylmethyl)-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

Benzo[1,2,5]oxadiazol-4-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

5-Cyclopentyl-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-(2-difluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-4-ylmethyl-amine;

5-Cyclopropyl-2-[2-(2-methoxy-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(2-methoxy-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(1-Cyclobutyl-piperidin-4-yl)-{5-cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(tetrahydro-pyran-4-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

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5-Cyclobutyl-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(1-phenyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2-difluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(1-isopropyl-piperidin-4-yl)-methyl-amine;

Benzo[1,2,5]oxadiazol-5-yl-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

5-Bromo-4-piperazin-1-yl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-8-chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-8-fluoro-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Bromo-2-(2-tert-butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-exo-5-Cyclopropyl-2-[2-(7-oxa-bicyclo[2.2.1]hept-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-exo-5-Cyclobutyl-2-[2-(7-oxa-bicyclo[2.2.1]hept-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2,6-difluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-[1-(2,2-difluoro-ethyl)-piperidin-4-yl]-methyl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-indan-5-yl-amine;

(5-Cyclopropyl-3,6-difluoro-pyridin-2-yl)-{4-[5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-amine;

N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-2,2-difluoro-2-phenyl-acetamide;

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5-Cyclopropyl-2-[2-(1-fluoro-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[5-Cyclopropyl-4-(1-methyl-piperidin-4-ylsulfanyl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(2,6-difluoro-phenyl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(1-methyl-piperidin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[2-fluoro-4-(1-methyl-1H-pyrazol-4-yl)-phenyl]-amine;

{4-[5-Cyclopropyl-4-(hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[5-Cyclopropyl-4-(hexahydro-pyrrolo[3,4-c]pyrrol-2-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethyl-benzooxazol-5-yl)-amine;

5-Cyclopropyl-4-(piperidin-4-ylsulfanyl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(±)-endo-2-(2-Bicyclo[2.2.1]hept-2-yl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[8-Chloro-5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(1,2,3,4-tetrahydro-naphthalen-2-yl)-amine;

{5-Cyclopropyl-2-[2-([D3-4]quinolin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-ylmethyl-amine;

(1S,2R)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

(1S,2S)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

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(1R,2S)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

(1R,2R)-1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-2-ol;

5-Cyclobutyl-2-[2-(2,6-difluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(2,6-difluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-(2-Cyclobutyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2-cyclobutyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-methyl-3H-benzoimidazol-5-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-amine;

{2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

5-Cyclopropyl-2-(2-cyclohexyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2-cyclohexyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[3-Chloro-1-(5-trifluoromethyl-pyridin-2-yl)-1H-pyrazol-4-yl]-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-difluoro-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-difluoro-piperidin-4-yl)-amine;

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{5-Cyclobutyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

trans-2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-indan-1-ol;

(R)-2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-phenyl-ethanol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-naphthalen-2-yl-ethyl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2-fluoro-phenyl)-ethyl]-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethoxy-phenyl)-amine;

{5-Cyclobutyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

(S)-2-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-ylamino]-2-phenyl-ethanol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-naphthalen-1-yl-ethyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,2-difluoro-2-phenyl-ethyl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-ylmethyl-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(tetrahydro-pyran-4-yl)-amine;

{8-Chloro-5-cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

{8-Chloro-5-cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

(5-Chloro-3-fluoro-pyridin-2-yl)-[4-(5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

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{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-(tetrahydro-pyran-4-yl)-amine;

(4-{5-Cyclopropyl-4-[3-(tetrahydro-pyran-4-yl)-pyrrolidin-1-yl]-pyrido[3,4-d]pyrimidin-2-yl}-pyridin-2-yl)-(3,5-difluoro-pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(3,5,6-trifluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,3-dimethyl-indan-1-yl)-amine;

[4-(8-Chloro-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;

5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(1-phenyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-4-piperazin-1-yl-2-[2-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3-fluoro-piperidin-4-yl)-amine;

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[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;

[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5-difluoro-pyridin-2-yl)-amine;

[4-(5,8-Dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2,6-difluoro-phenyl)-amine;

2-(2-tert-Butyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5,8-dicyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridazin-3-yl)-amine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(tetrahydro-furan-3-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

(2,6-Difluoro-phenyl)-[4-(4-piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

(3,5-Difluoro-pyridin-2-yl)-[4-(4-piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-amine;

[4-(4-Piperazin-1-yl-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3,5,6-trifluoro-pyridin-2-yl)-amine;

{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

5-Cyclopropyl-2-(2,2-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[4-(3-Amino-piperidin-1-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]indole;

6-Chloro-4-(5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

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5-Cyclobutyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{4-[5-Cyclopropyl-4-(3-methylamino-piperidin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

N-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-N'-methyl-benzene-1,4-diamine;

5-Cyclopropyl-4-piperazin-1-yl-2-[2-(1-trifluoromethyl-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidine;

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6,7,8,9-tetrahydro-5H-pyrido[2,3-b]indole;

2-(3-Chloro-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(tetrahydro-pyran-4-yl)-amine; or

4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-3,3-dimethyl-1,3-dihydro-pyrrolo[2,3-b]pyridin-2-one;

or a pharmaceutically acceptable salt thereof.

94. A compound selected from:

4-({8-Chloro-2-[2-(5-chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidinedi-trifluoroacetate;

4-{8-Chloro-2-[2-(5-chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-piperazinedi-trifluoroacetate;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-pyridin-2-yl-ethyl)-amine;

2-(2-Cyclopentyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2-cyclopentyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

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5-Cyclobutyl-2-[2-(3,3-difluoro-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(3,3-difluoro-cyclobutyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-((R)-1-phenyl-propyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[(R)-1-(2-methoxy-phenyl)-ethyl]-amine;

4-{2-[2-(5-Chloro-3-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclobutyl-pyrido[3,4-d]pyrimidin-4-yl}-piperazine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-fluoro-quinolin-2-yl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-phenoxy-ethyl)-amine;

4-({2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridn-4-yl]-5-cyclobutyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-piperidine;

((R)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl);

5-Cyclobutyl-2-(3-methoxy-2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(2,2-dimethyl-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

4-{[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino)-piperidine;

{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

5-cyclobutyl-2-(6-fluoro-9H-pyrido[2,3-b]indol-4-yl)-N-methyl-N-(4-piperidyl)pyrido[3,4-d]pyrimidin-4-amine;

{5-Cyclopropyl-2-[2-((R)-1-phenyl-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

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[5-Cyclobutyl-2-(7-fluoro-9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

{5-Cyclopropyl-2-[2-(4-trifluoromethoxy-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

{5-Cyclopropyl-2-[2-(3-methyl-3H-benzimidazol-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

((S)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl);

((R)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl)-methyl;

[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

{5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethoxy-phenyl)-amine;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6-fluoro-9H-pyrido[2,3-b]indole;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-7-fluoro-9H-pyrido[2,3-b]indole;

((S)-1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-yl)-methyl;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5-fluoro-9H-pyrido[2,3-b]indole;

4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-3-methyl-piperidine;

{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

1-(5-cyclopropyl-2-spiro[1,3-dihydropyrrolo[2,3-b]pyridine-2,1'-cyclohexane]-4-yl-pyrido[3,4-d]pyrimidin-4-yl)piperidin-3-amine;

4-({2-[2-(5-Chloro-3-fluoro-pyridin-2-ylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-3,3-dimethyl-piperidine;

(5-Cyclopropyl-2-{2-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-ylamino]-pyridin-4-yl}-pyrido[3,4-d]pyrimidin-4-yl)-methyl-piperidin-4-yl-amine;

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{5-Cyclopropyl-2-[2-(1-cyclopropyl-piperidin-4-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

(1-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-4-fluoro-piperidin-3-yl);

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-phenyl-amine;

5-Cyclopropyl-2-(3-phenyl-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-3,4-trans-4-{[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-1-methyl-pyrrolidin-3-ol;

(±)-3,4-trans-4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-1-methyl-pyrrolidin-3-ol;

(±)-3,4-trans-4-({5-Cyclopropyl-2-[2-((R)-1-phenyl-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-1-methyl-pyrrolidin-3-ol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-(2,6-difluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-(3,5-difluoro-pyridin-2-yl)-amine;

2-[2-(2-tert-Butyl-thiazol-4-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2-phenoxy-ethylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

2-(3-Bromo-pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-fluoro-4-trifluoromethoxy-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methoxy-4-trifluoromethoxy-phenyl)-amine;

(±)-{5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

4-({5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-3-methoxy-cyclohexane;

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2-(3-Bromo-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

N*1*-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-ethane-1,2-diamine;

(±)-{5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;

N(1)-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-ethane-1,2-diamine;

{4-[5-Cyclopropyl-4-(1-oxy-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;

(S)-1-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

4-[5-Cyclobutyl-4-(1-oxy-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole;

4-[5-Cyclobutyl-7-oxy-4-(1-oxy-piperazin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-5,6,7,8-tetrahydro-cyclopenta[4,5]pyrrolo[2,3-b]pyridine;

{4-[4-((S)-3-Amino-piperidin-1-yl)-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-phenyl-amine;

{4-[4-((S)-3-Amino-piperidin-1-yl)-5-trifluoromethyl-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-(3,5-difluoro-pyridin-2-yl)-amine;

5-Cyclopropyl-4-((S)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-4-((S)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

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[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;

5-Cyclopropyl-2-[3-(3-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[3-(4-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[3-(2-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-((R)-3-trifluoromethyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

(±)-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;

(±)-(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;

(±)-(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;

5-cyclopropyl-2-[2-[(1R,2S,4S)-norbornan-2-yl]-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-cyclopropyl-2[2-[(1S,2R,4R)-norbornan-2-yl]-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[5-Cyclopropyl-2-(3-phenyl-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

[2-(3-Bromo-pyridin-4-yl)-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl]-methyl-piperidin-4-yl-amine;

(±)-3,4-trans-4-{[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-pyrrolidin-3-ol;

(±)-(3,4-trans)-4-{[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-methyl-amino}-pyrrolidin-3-ol;

1-[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-cyclobutanol;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(3-trifluoromethoxy-phenyl)-amine;

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[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-methyl-4-trifluoromethoxy-phenyl)-amine;

(S)-1-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

(R)-1-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

4-(5-Cyclobutyl-4-morpholin-4-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole;

(5-Aza-spiro[2.5]oct-8-yl)-[5-cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-amine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-((S)-3-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

N-{5-Cyclopropyl-2-[2-(3,5-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-cyclohexane-1,3-diamine;

N-[5-Cyclopropyl-2-(2-phenylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-cyclohexane-1,3-diamine;

2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-4-((S)-2-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

(±)-(3,4-trans)-4-({2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-pyrrolidin-3-ol;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((R)-3-trifluoromethyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;compoundwithtrifluoro-acetic acid;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(2-trifluoromethoxy-phenyl)-amine;

(±)-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

(±)-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

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(±)-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

(±)-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-3-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]ipyrimidine;

5-Cyclopropyl-4-(3,3-dimethyl-piperazin-1-yl)-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-5-yl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazolo[1,5-a]pyridin-6-yl-amine;

(±)-(3,4-trans)-4-({5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-methyl-amino)-pyrrolidin-3-ol;

5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-2-methyl-piperazin-1-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidine;

(S)-1-{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ylamine;

(S)-1-{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ylamine;

5-Cyclobutyl-2-[2-(2-methyl-tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(2-methyl-tetrahydro-furan-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

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1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-cyclobutanol;

1-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-3-phenyl-urea;

5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

(±)-{5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

(5-Aza-spiro[2.5]oct-8-yl)-{5-cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

{2-[2-(4-Chloro-phenylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

2-(3-Chloro-2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(±)-[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3,4-trans)-4-methoxy-pyrrolidin-3-yl)-amine;

(±)-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3,4-trans)-4-methoxy-pyrrolidin-3-yl)-amine;

[5-Cyclopropyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3R,4S)-3-methoxy-piperidin-4-yl)-amine;

[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-((3R,4S)-3-methoxy-piperidin-4-yl)-amine;

[5-Cyclopropyl-2-(2-p-tolylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;

5-Cyclopropyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-2-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[2-(3-fluoro-pyridin-2-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-((S)-2-methyl-piperazin-1-yl)-pyrido[3,4-d]pyrimidine;

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{5-Cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

(5-Aza-spiro[2.5]oct-8-yl)-{5-cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-amine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine;

{5-Cyclobutyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

5-Cyclobutyl-2-[2-(1-fluoromethyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

3-[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-1H-pyrrolo[2,3-b]pyridin-2-yl]-tetrahydro-furan-3-ol;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-3,4-dihydro-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-5-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

(S)-1-[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

5-Cyclopropyl-4-(2,6-diaza-spiro[3.3]hept-2-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(pyrazolo[1,5-a]pyridin-6-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

4-[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperazine-2-carboxylic acid;

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{5-Cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(4-methyl-piperidin-4-yl)-amine;

{5-Cyclopropyl-2-[2-(2,2-difluoro-1-methyl-cyclopropyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-methyl-piperidin-4-yl-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-fluoro-phenyl)-amine;

[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-oxetan-3-yl-phenyl)-amine;

5-cyclobutyl-N-methyl-2-[2-(1-methyl-1-phenyl-ethyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-N-(4-piperidyl)pyrido[3,4-d]pyrimidin-4-amine;

5-Cyclopropyl-4-(octahydro-pyrrolo[3,2-c]pyridin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

(S)-1-[5-Cyclobutyl-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-piperidin-3-ylamine;

2-[3-(2-Chloro-phenyl)-pyridin-4-yl]-5-cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-4-piperazin-1-yl-2-(3-o-tolyl-pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclopropyl-2-[3-(2-methoxy-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

(S)-2-Amino-6-[5-cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-ylamino]-hexanoic acid;

5-Cyclopropyl-4-((R)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-4-((R)-2-methyl-piperazin-1-yl)-2-(2-trifluoromethyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(4-fluoro-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

{2-[2-(4-Chloro-phenylamino)-pyridin-4-yl]-5-cyclopropyl-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

{5-Cyclopropyl-2-[2-(4-isopropyl-phenylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

{5-Cyclopropyl-2-[2-([1,2,4]triazolo[1,5-a]pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

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5-Cyclobutyl-4-((S)-2-methyl-piperazin-1-yl)-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-4-((R)-2-methyl-piperazin-1-yl)-2-(2-methyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-pyrazin-2-yl-amine;

2-(3-Bromo-pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-[3-(2-fluoro-phenyl)-pyridin-4-yl]-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

5-Cyclobutyl-2-(3-phenyl-pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

[5-Cyclopropyl-2-(2-p-tolylamino-pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-6-trifluoromethoxy-9H-pyrido[2,3-b]indole;

[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-methyl-amine;

[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;

4-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-3-yl]-benzamide;

[5-Cyclopropyl-2-(2-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(4-methyl-piperidin-4-yl)-amine;

[5-Cyclobutyl-2-(9H-pyrido[2,3-b]indol-4-yl)-pyrido[3,4-d]pyrimidin-4-yl]-(3,3-dimethyl-piperidin-4-yl)-amine;

5-Cyclobutyl-2-(2-phenylsulfanyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

N-[4-(5-Cyclopropyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-benzenesulfonamide;

5-Cyclopropyl-2-(3-phenyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

{5-Cyclopropyl-2-[2-(2-fluoro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-((3R,4R)-4-methoxy-pyrrolidin-3-yl)-amine;

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{2-[2-(2-Chloro-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-5-cyclopropyl-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-((3R,4R)-4-methoxy-pyrrolidin-3-yl)-amine;

5-Cyclobutyl-4-piperazin-1-yl-2-(1H-pyrazolo[3,4-b]pyridin-4-yl)-pyrido[3,4-d]pyrimidine;

4-[5-Cyclobutyl-4-(octahydro-pyrrolo[3,2-c]pyridin-1-yl)-pyrido[3,4-d]pyrimidin-2-yl]-9H-pyrido[2,3-b]indole;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(4-trifluoromethyl-pyridin-2-yl)-amine;

N-{4-[5-Cyclopropyl-4-(methyl-piperidin-4-yl-amino)-pyrido[3,4-d]pyrimidin-2-yl]-pyridin-2-yl}-benzenesulfonamide;

5-Cyclopropyl-2-[2-(2-methoxy-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-4-piperazin-1-yl-3,4-dihydro-pyrido[3,4-d]pyrimidine;

(S)-1-{5-Cyclopropyl-2-[2-(2-methoxy-phenyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]-3,4-dihydro-pyrido[3,4-d]pyrimidin-4-yl}-piperidin-3-ylamine;

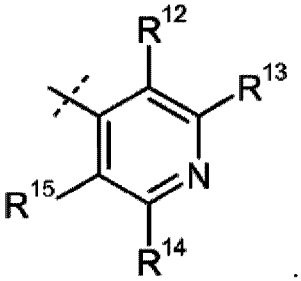
[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-(6-fluoro-pyridin-2-yl)-amine;

[4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-pyridin-2-yl]-[1-(2,2,2-trifluoro-ethyl)-piperidin-4-yl]-amine; or

2-(2-Benzenesulfonyl-1H-pyrrolo[2,3-b]pyridin-4-yl)-5-cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidine;

or a pharmaceutically acceptable salt thereof.

95. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1,



wherein G is a group of formula ; X is chosen from 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19}, $-OR^{28}$, $-S(=O)_nR^{28}$ and $-NR^{24}R^{28}$; R^7, R^8, R^9 R^{12}, R^{13}, R^{14} and R^{15} are independently chosen from H,C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, halogen, and$-OR^{20}$; or any of R^{12} and R^{13} or R^{14} and R^{15} can, together with the atoms linking them, form a 3-15 membered

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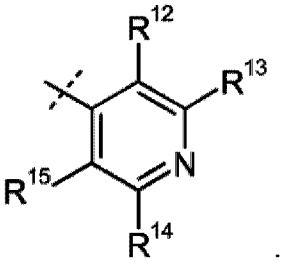
heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

96. The compound or pharmaceutically acceptable salt form thereof as defined in claim 95 where R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}, C_{6-11}aryl optionally substituted by 1-11 R^{39}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{39}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{39}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{39}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-40 R^{39}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{39}, halogen, –CN,–$C(=O)OR^{30}$, $–NR^{32}R^{33}$, $–OR^{30}$, =O, and $–S(=O)_nR^{30}$, where n is 0, 1, or 2.

97. The compound or pharmaceutically acceptable salt form thereof as defined in any one of claims 1, 5, 87-90 and 95-96, wherein G is a group of formula  ; and R^7 is C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19} and R^8 and R^9 are H.

98. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein the compound is {5-Cyclopropyl-2-[2-(3,6-difluoro-pyridin-2-ylamino)-pyridin-4-yl]-pyrido[3,4-d]pyrimidin-4-yl}-(3,3-dimethyl-piperidin-4-yl)-amine, or a pharmaceutically acceptable salt form thereof.

99. The compound or pharmaceutically acceptable salt form thereof as defined in claim 1, wherein the compound is 4-(5-Cyclobutyl-4-piperazin-1-yl-pyrido[3,4-d]pyrimidin-2-yl)-9H-pyrido[2,3-b]indole, or a pharmaceutically acceptable salt form thereof.

100. A pharmaceutical composition comprising the compound or pharmaceutically acceptable salt form thereof according to any one of claims 1-99, and a pharmaceutically acceptable excipient.

101. A pharmaceutical composition comprising the compound or pharmaceutically acceptable salt form thereof according to claim 98, and a pharmaceutically acceptable excipient.

102. A pharmaceutical composition comprising the compound or pharmaceutically acceptable salt form thereof according to claim 99, and a pharmaceutically acceptable excipient.

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103. The compound or pharmaceutically acceptable salt form thereof according to any one of claims 1-99 for use in the treatment of an aPKC-dependent disorder or condition.

104. The compound or pharmaceutically acceptable salt form thereof according to claim 98 for use in the treatment of an aPKC-dependent disorder or condition.

105. The compound or pharmaceutically acceptable salt form thereof according to claim 99 for use in the treatment of an aPKC-dependent disorder or condition.

106. The compound or pharmaceutically acceptable salt form thereof for use according to any one of claims 103 to 105, wherein the aPKC-dependent disorder or condition is cancer.

107. The compound or pharmaceutically acceptable salt form thereof for use according to claim 106, wherein the cancer is non-small cell lung cancer (NSCLC), squamous cell carcinoma, leukemia, prostate cancer, non-Hodgkin's lymphoma, endometrial cancer, lung cancer, or breast cancer.

108. The compound or pharmaceutically acceptable salt form thereof for use according to claim 107, wherein the squamous cell carcinoma is esophageal squamous cell carcinoma.

109. The compound or pharmaceutically acceptable salt form thereof for use according to claim 107, wherein the non-Hodgkin's lymphoma is follicular lymphoma.

110. Use of the compound or pharmaceutically acceptable salt form thereof according to any one of claims 1-99 for the treatment of an aPKC-dependent disorder or condition.

111. Use of the compound or pharmaceutically acceptable salt form thereof according to any one of claims 1-99 for the manufacture of a medicament for the treatment of an aPKC-dependent disorder or condition.

112. Use of the compound or pharmaceutically acceptable salt form thereof according to claim 98 for the treatment of an aPKC-dependent disorder or condition.

113. Use of the compound or pharmaceutically acceptable salt form thereof according to claim 98 for the manufacture of a medicament for the treatment of an aPKC-dependent disorder or condition.

114. Use of the compound or pharmaceutically acceptable salt form thereof according to claim 99 for the treatment of an aPKC-dependent disorder or condition.

115. Use of the compound or pharmaceutically acceptable salt form thereof according to claim 99 for the manufacture of a medicament for the treatment of an aPKC-dependent disorder or condition.

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116. The use according to any one of claims 110 to 115, wherein the aPKC-dependent disorder or condition is cancer.

117. The use according to claim 116, wherein the cancer is non-small cell lung cancer (NSCLC), squamous cell carcinoma, leukemia, prostate cancer, non-Hodgkin's lymphoma, endometrial cancer, lung cancer, or breast cancer.

118. The use according to claim 117, wherein the squamous cell carcinoma is esophageal squamous cell carcinoma.

119. The use according to claim 117, wherein the non-Hodgkin's lymphoma is follicular lymphoma.

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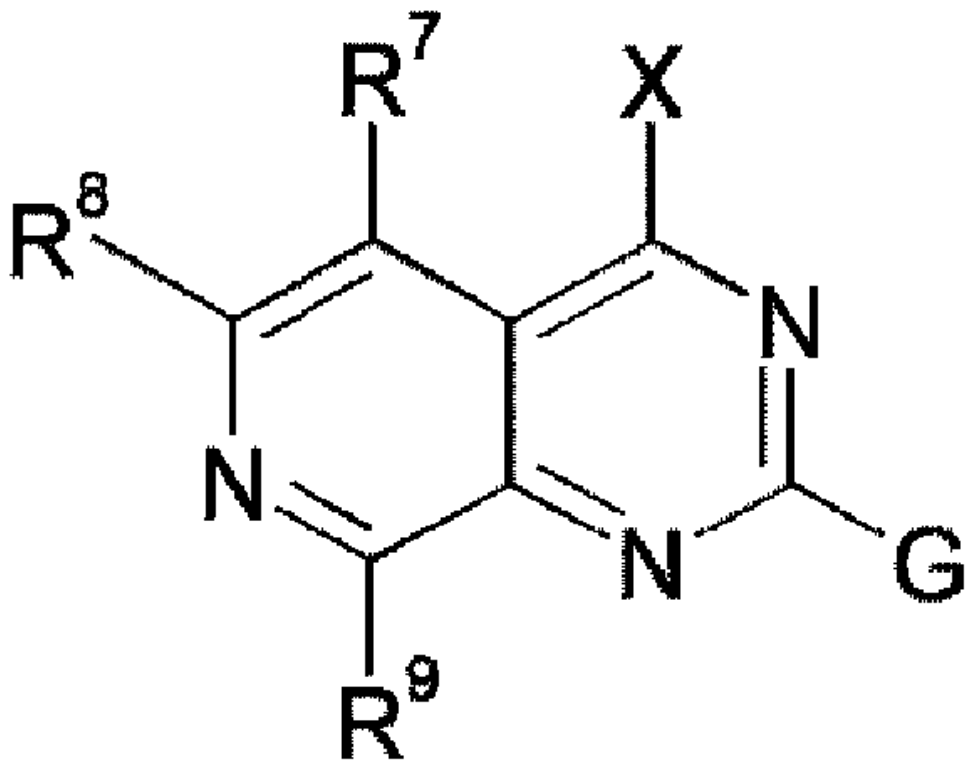

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