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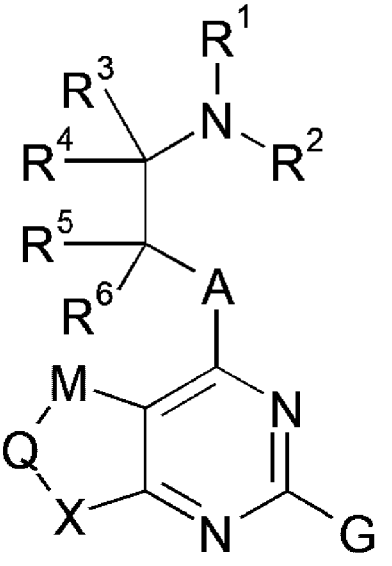

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(57) Abrégé/Abstract:
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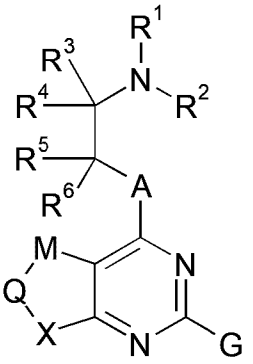
Abstract

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



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THIENOPYRIMIDINE 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., 2005) 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 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.

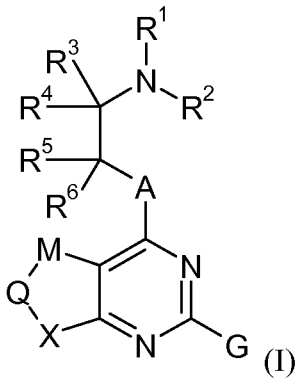
Further evidence that small molecule inhibition of PKCζ could have important therapeutic benefits has recently emerged from tumour models that link PKCζ signalling to the mTOR pathway. PKCζ is constitutively activated in follicular lymphoma and has been identified as a novel target for the anti-CD20 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^1, R^2, R^3, R^4, R^5, R^6, A, G, M, Q 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 ($C_6H_{11}CH_2$–).

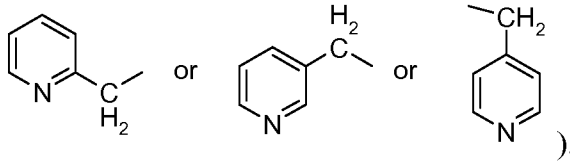
"Haloalkyl" or "haloalkyl group" refers to alkyl groups in which one or more hydrogen atoms are replaced by halogen atoms. Haloalkyl includes both saturated alkyl groups and unsaturated alkenyl and alkynyl groups, such as for example $–CF_3$, $–CHF_2$, $–CH_2F$, $–CF_2CF_3$, $–CHFCF_3$, $–CH_2CF_3$,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

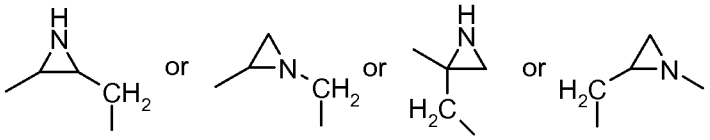
"Heteroarylalkyl" or "heteroarylalkyl group" refers to an alkyl group in which a hydrogen atom is replaced by a heteroaryl group, wherein alkyl group and heteroaryl group are as previously defined (i.e., heteroarylalkyl–). Heteroarylalkyl groups can be

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]heptane, 8-oxa-3-aza-bicyclo[3.2.1]octane, 3,8-diaza-bicyclo[3.2.1]octane, 2,5-diaza-bicyclo[2.2.1]heptane, 3,8-diaza-bicyclo[3.2.1]octane, 3,9-diaza-bicyclo[4.2.1]nonane, 2,6-diaza-bicyclo[3.2.2]nonane, [1,4]oxaphosphinane 4-oxide, [1,4]azaphosphinane 4-oxide, [1,2]oxaphospholane 2-oxide, phosphinane 1-oxide, [1,3]azaphospholidine 3-oxide, and [1,3]oxaphospholane 3-oxide. 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 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.

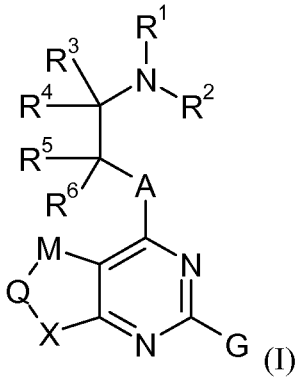
"Treatment" refers to the acute or prophylactic diminishment or alleviation of at least one symptom or characteristic associated or caused by a disorder being treated. For example, treatment can include diminishment of several symptoms of a disorder or complete eradication of a disorder.

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 referes 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 1, 2 and 4, an explicit description of a genus having the limitations of Embodiments 1, 3 and 4, and an explicit description of a genus having the limitations of Embodiments 1, 2, 3 and 4. By way of example, if Embodiment 1 is a compound of formula (I) defining R^1, R^2 and R^3 independently as alkyl or aryl, and Embodiment 2 is a compound of Embodiment 1 defining R^1 as alkyl, and Embodiment 3 is a compound of Embodiments 1 or 2 defining R^2 as alkyl, and Embodiment 4 is a compound of any of Embodiments 1-3 defininining R^3 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^1 and R^2 are alkyl or aryl, and R^3 is alkyl), an explicit description of a genus having the limitations of Embodiments 1, 2 and 4 (i.e., a compound of formula (I) in which R^2 is alkyl or aryl, and R^1 and R^3 are alkyl), an explicit description of a genus having the limitations of Embodiments 1, 3 and 4 (i.e., a compound of formula (I) in which R^1 is alkyl or aryl, and R^2 and R^3 are alkyl), and an explicit description of a genus having the limitations of Embodiments 1, 2, 3 and 4 (i.e., a compound of formula (I) in which R^1, R^2 and R^3 are 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 A is NR^{11}, O, or S, Embodiment 2 recites a compound of Embodiment 1 in which A is O or S, and Embodiment 3 recites a compound of Embodiments 1 or 2 in which R^{11} is alkyl, then Embodiment 3 defines a genus having the limitations of Embodiments 1 and 3 and a genus having the limitation of Embodiments 1, 2 and 3. In the genus defined by the limitations of Embodiments 1, 2 and 3, A cannot be NR^{11}; therefore this genus should be interpreted to ignore and omit the Embodiment 3 defintion of R^{11} = alkyl.

Embodiment 1. A compound of formula (I)

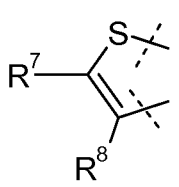
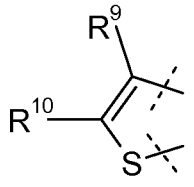


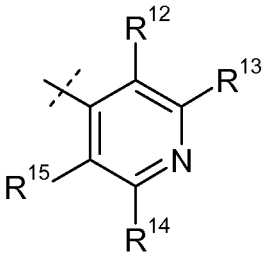
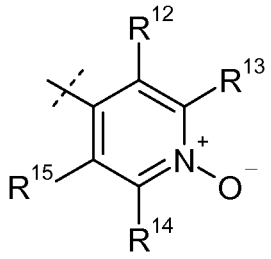
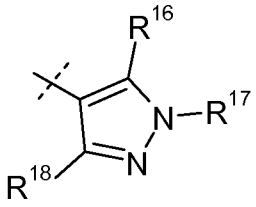
(I)

or a salt form thereof,

wherein

A is NR^{11}, O, or S;

M-Q-X is a group of formula  or  ;

G is a group of formula  ,  , or  ;

R^1, R^2, R^{11}, and R^{17} 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}, and $-OR^{20}$;

R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, and R^{18} 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, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}NR^{22}R^{23}$, $–N=NR^{24}$, $–NR^{24}OR^{26}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $–NR^{24}C(=NR^{25})NR^{22}R^{23}$, $–NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $–NR^{24}C(=S)R^{20}$, $–NR^{24}C(=S)OR^{20}$, $–NR^{24}C(=S)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–NR^{24}P(=O)R^{28}R^{28}$, $–NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–NR^{24}P(=O)(OR^{20})(OR^{20})$, $–NR^{24}P(=O)(SR^{20})(SR^{20})$, $–OR^{20}$, –OCN, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–OC(=NR^{25})NR^{22}R^{23}$, $–OS(=O)R^{20}$, $–OS(=O)_2R^{20}$, $–OS(=O)_2OR^{20}$, $–OS(=O)_2NR^{22}R^{23}$, $–OP(=O)R^{28}R^{28}$, $–OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–OP(=O)(OR^{20})(OR^{20})$, $–OP(=O)(SR^{20})(SR^{20})$, $–Si(R^{24})_3$, –SCN, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–SP(=O)R^{28}R^{28}$, $–SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–SP(=O)(OR^{20})(OR^{20})$, $–SP(=O)(SR^{20})(SR^{20})$, $–P(=O)R^{28}R^{28}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $–P(=O)(OR^{20})(OR^{20})$, and $–P(=O)(SR^{20})(SR^{20})$;

any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, R^6 and R^{11}, and R^{16} and R^{17} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19};

any of R^3 and R^6, R^7 and R^8, R^9 and R^{10}, R^{12} and R^{13}, and R^{14} and R^{15} 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^3 and R^5 or R^4 and R^6 can together form a double bond;

any of R^3 and R^4, and R^5 and R^6 can together form =O, =NR^{20}, =NOR^{20}, or =S;

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, –$NO_2$, –$NR^{32}R^{33}$, –$NR^{34}NR^{32}R^{33}$, –$N=NR^{34}$, =$NR^{30}$, =$NOR^{30}$, –$NR^{34}OR^{36}$, –$NR^{34}C(=O)R^{30}$, –$NR^{34}C(=O)C(=O)R^{30}$, –$NR^{34}C(=O)OR^{31}$, –$NR^{34}C(=O)C(=O)OR^{31}$, –$NR^{34}C(=O)NR^{32}R^{33}$, –$NR^{34}C(=O)NR^{34}C(=O)R^{30}$, –$NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, –$NR^{34}C(=NR^{35})NR^{32}R^{33}$, –$NR^{34}C(=O)C(=O)NR^{32}R^{33}$, –$NR^{34}C(=S)R^{30}$, –$NR^{34}C(=S)OR^{30}$, –$NR^{34}C(=S)NR^{32}R^{33}$, –$NR^{34}S(=O)_2R^{31}$, –$NR^{34}S(=O)_2NR^{32}R^{33}$, –$NR^{34}P(=O)R^{38}R^{38}$, –$NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, –$NR^{34}P(=O)(OR^{30})(OR^{30})$, –$NR^{34}P(=O)(SR^{30})(SR^{30})$, –$OR^{30}$, =O, –OCN, –$OC(=O)R^{30}$, –$OC(=O)NR^{32}R^{33}$, –$OC(=O)OR^{30}$, –$OC(=NR^{35})NR^{32}R^{33}$, –$OS(=O)R^{30}$, –$OS(=O)_2R^{30}$, –$OS(=O)_2OR^{30}$, –$OS(=O)_2NR^{32}R^{33}$, –$OP(=O)R^{38}R^{38}$, –$OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, –$OP(=O)(OR^{30})(OR^{30})$, –$OP(=O)(SR^{30})(SR^{30})$, –$Si(R^{34})_3$, –SCN, =S, –$S(=O)_nR^{30}$, –$S(=O)_2OR^{30}$, –$SO_3R^{37}$, –$S(=O)_2NR^{32}R^{33}$, –$S(=O)NR^{32}R^{33}$, –$SP(=O)R^{38}R^{38}$, –$SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, –$SP(=O)(OR^{30})(OR^{30})$, –$SP(=O)(SR^{30})(SR^{30})$, –

$P(=O)R^{38}R^{38}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, 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} and R^{38} 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};

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};

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 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, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{110}R^{110}$, $–C(=O)C(=O)R^{110}$, $–C(=NR^{110})R^{110}$, $–C(=NR^{110})NR^{110}R^{110}$, $–C(=NOH)NR^{110}R^{110}$, $–C(=NOR^{110})R^{110}$, $–C(=NNR^{110}R^{110})R^{110}$, $–C(=NNR^{110}C(=O)R^{110})R^{110}$, $–C(=NNR^{110}C(=O)OR^{110})R^{110}$, $–C(=S)NR^{110}R^{110}$, –NC, $–NO_2$, $–NR^{110}R^{110}$, $–NR^{110}NR^{110}R^{110}$, $–N=NR^{110}$, $=NR^{110}$, $=NOR^{110}$, $–NR^{110}OR^{110}$, –

$NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)C(=O)R^{110}$, $-NR^{110}C(=O)OR^{110}$, $-NR^{110}C(=O)C(=O)OR^{110}$, $-NR^{110}C(=O)NR^{110}R^{110}$, $-NR^{110}C(=O)NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)NR^{110}C(=O)OR^{110}$, $-NR^{110}C(=NR^{110})NR^{110}R^{110}$, $-NR^{110}C(=O)C(=O)NR^{110}R^{110}$, $-NR^{110}C(=S)R^{110}$, $-NR^{110}C(=S)OR^{110}$, $-NR^{110}C(=S)NR^{110}R^{110}$, $-NR^{110}S(=O)_2R^{110}$, $-NR^{110}S(=O)_2NR^{110}R^{110}$, $-NR^{110}P(=O)R^{111}R^{111}$, $-NR^{110}P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-NR^{110}P(=O)(OR^{110})(OR^{110})$, $-NR^{110}P(=O)(SR^{110})(SR^{110})$, $-OR^{110}$, =O, –OCN, $-OC(=O)R^{110}$, $-OC(=O)NR^{110}R^{110}$, $-OC(=O)OR^{110}$, $-OC(=NR^{110})NR^{110}R^{110}$, $-OS(=O)R^{110}$, $-OS(=O)_2R^{110}$, $-OS(=O)_2OR^{110}$, $-OS(=O)_2NR^{110}R^{110}$, $-OP(=O)R^{111}R^{111}$, $-OP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-OP(=O)(OR^{110})(OR^{110})$, $-OP(=O)(SR^{110})(SR^{110})$, $-Si(R^{110})_3$, –SCN, =S, $-S(=O)_nR^{110}$, $-S(=O)_2OR^{110}$, $-SO_3R^{110}$, $-S(=O)_2NR^{110}R^{110}$, $-S(=O)NR^{110}R^{110}$, $-SP(=O)R^{111}R^{111}$, $-SP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-SP(=O)(OR^{110})(OR^{110})$, $-SP(=O)(SR^{110})(SR^{110})$, $-P(=O)R^{111}R^{111}$, $-P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-P(=O)(OR^{110})(OR^{110})$, and $-P(=O)(SR^{110})(SR^{110})$;

R^{110} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl;

R^{111} 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.

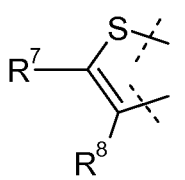
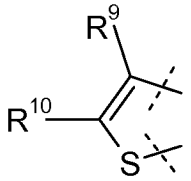
Embodiment 2. The compound of Embodiment 1, wherein A is NR^{11}, O, or S.

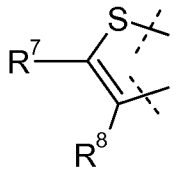
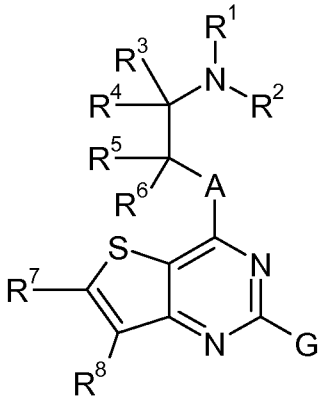
Embodiment 3. The compound of Embodiment 1, wherein A is NR^{11} or O.

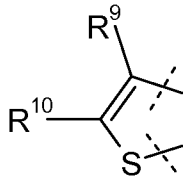
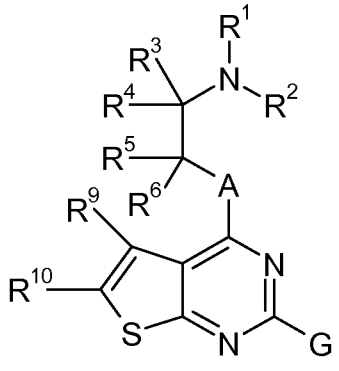
Embodiment 4. The compound of Embodiment 1, wherein A is NR^{11}.

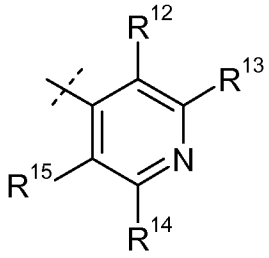
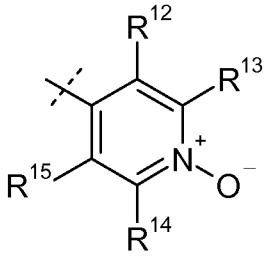
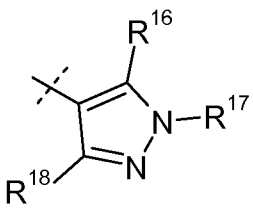
Embodiment 5. The compound of Embodiment 1, wherein A is O.

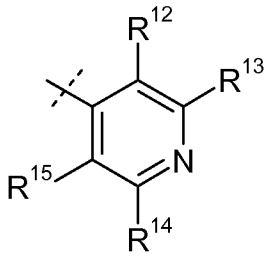
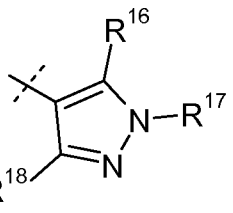
Embodiment 5. The compound of Embodiment 1, wherein A is S.

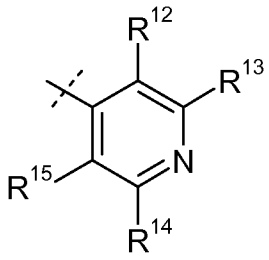
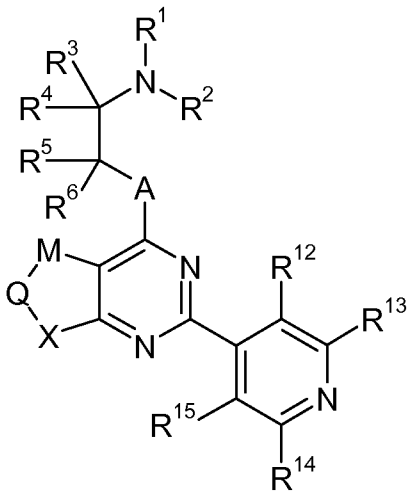
Embodiment 6. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  or  .

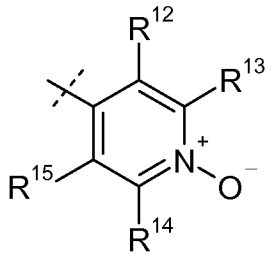
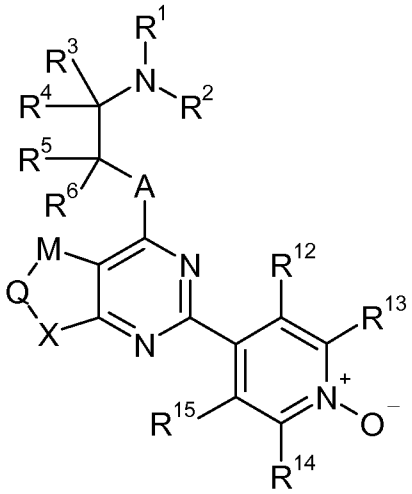
Embodiment 7. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , and the compound of formula (I) is a compound of formula (Ia)  (Ia).

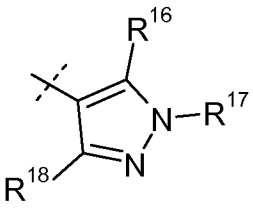
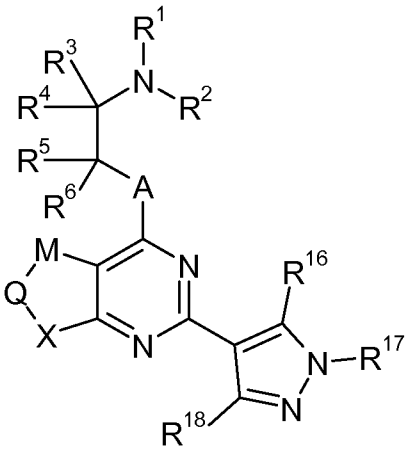
Embodiment 8. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , and the compound of formula (I) is a compound of formula (Ib)  (Ib).

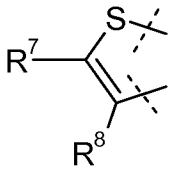
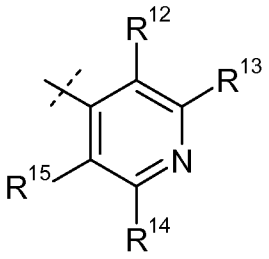
Embodiment 9. The compound of any of Embodiments 1-8, wherein G is a group of formula  ,  , or  .

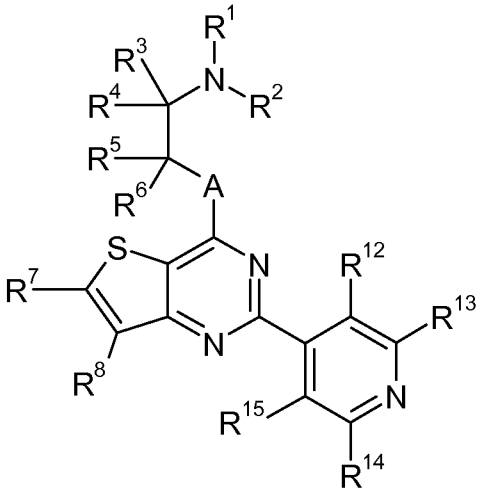
Embodiment 10. The compound of any of Embodiments 1-8, wherein G is a group of formula  or  .

Embodiment 11. The compound of any of Embodiments 1-8, wherein G is a group of formula  , and the compound of formula (I) is a compound of formula (Ic)  (Ic).

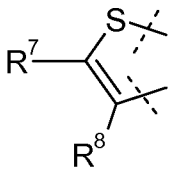
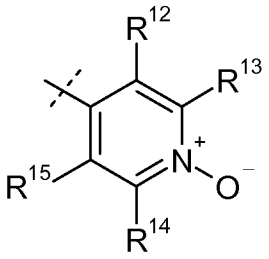
Embodiment 12. The compound of any of Embodiments 1-8, wherein G is a group of formula  , and the compound of formula (I) is a compound of formula (Id)  (Id).

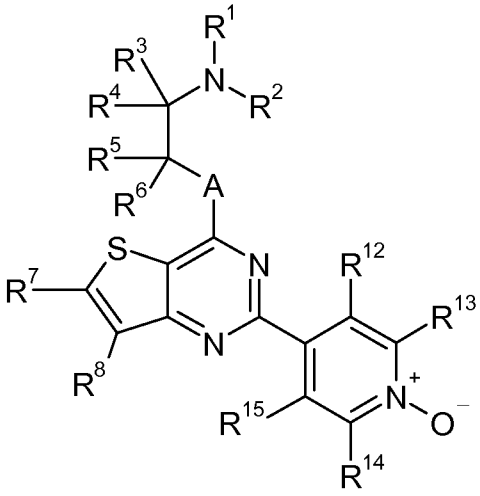
Embodiment 13. The compound of any of Embodiments 1-8, wherein G is a group of formula  , and the compound of formula (I) is a compound of formula (Ie)  (Ie).

Embodiment 14. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , G is a group of formula  , and the compound of formula (I) is a compound of formula (If)

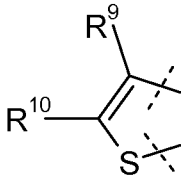
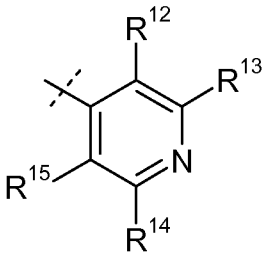


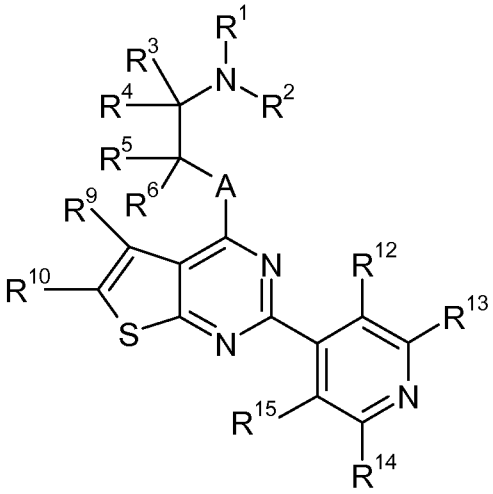
(If).

Embodiment 15. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , G is a group of formula  , and the compound of formula (I) is a compound of formula (Ig)

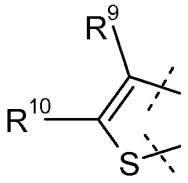
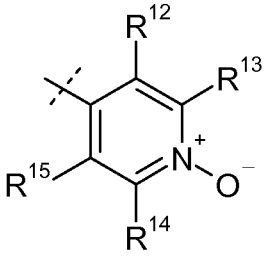


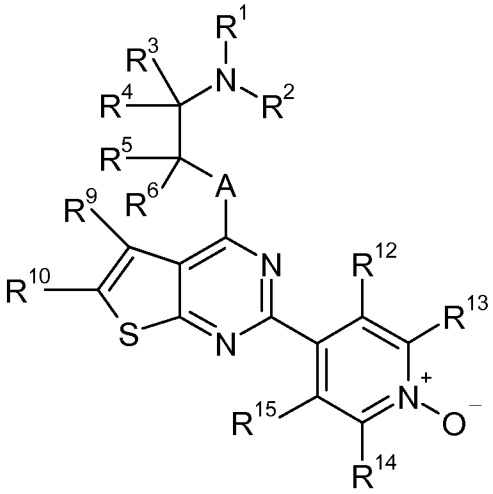
(Ig).

Embodiment 16. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , G is a group of formula  , and the compound of formula (I) is a compound of formula (Ih)

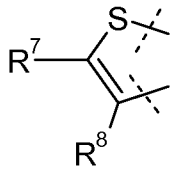
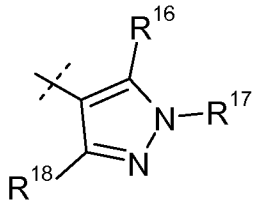


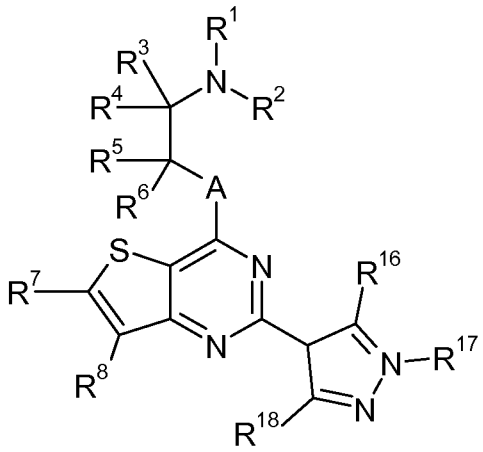
(Ih).

Embodiment 17. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , G is a group of formula  , and the compound of formula (I) is a compound of formula (Ii)

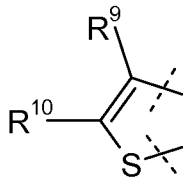
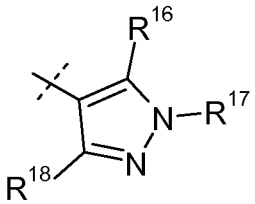


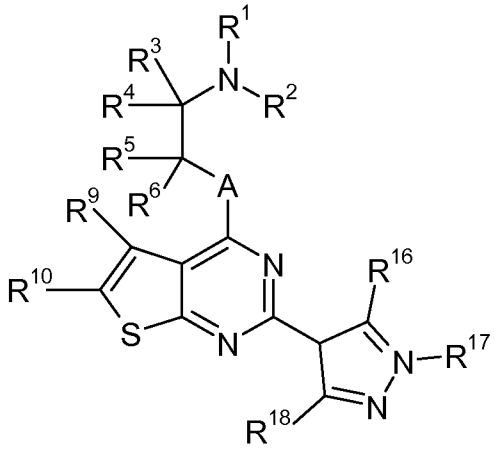
(Ii).

Embodiment 18. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , G is a group of formula  , and the compound of formula (I) is a compound of formula (Ij)



(Ij).

Embodiment 19. The compound of any of Embodiments 1-5, wherein M-Q-X is a group of formula  , G is a group of formula  , and the compound of formula (I) is a compound of formula (Ik)



(Ik).

Embodiment 20. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} 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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5

and R^6 can together form =O, =NR^{20}, =NOR^{20}, or =S; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 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 21. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} 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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-$

$SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 22. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} 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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(OR^{20})(OR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 23. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} 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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(OR^{20})(OR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can

together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-6 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-6 R^{19}.

Embodiment 24. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} 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}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-15 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, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(OR^{20})(OR^{20})$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered

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

Embodiment 25. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} 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_{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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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_{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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(OR^{20})(OR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 26. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} 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_{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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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_{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, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 27. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, 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}, and 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, 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}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 28. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3

R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, 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}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 29. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, 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}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 30. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 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_{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, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 31. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 32. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; alternatively, any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 33. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; alternatively, any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 34. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$;

alternatively, any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 35. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$,$-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 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 36. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$,$-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 37. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$,$-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 38. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$,$-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively any of R^1 and R^2,

R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 39. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and 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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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 $-OR^{20}$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can together form =O, $=NR^{20}$, $=NOR^{20}$, or =S; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 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 40. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and 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}, and $-OR^{20}$; R^3, R^4, R^5, and R^6 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 $-OR^{20}$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; alternatively any of R^3 and R^4, and R^5 and R^6 can together form =O, $=NR^{20}$, $=NOR^{20}$, or =S; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 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 41. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively, R^3 and R^6 can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 42. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted

by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively, R^3 and R^6 can, together with the atoms linking them, form a C_{3-10}cycloalkyl optionally substituted by 1-6 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 43. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively, R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 44. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively, R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 45. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted

by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively, R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}.

Embodiment 46. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^4, R^5, and R^6 are H; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 47. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^4, R^5, and R^6 are H; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-6 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 48. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^4, R^5, and R^6 are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13

R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 49. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^4, R^5, and R^6 are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^4 and R^{11}, and R^6 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 50. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^4, R^5, and R^6 are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{4-17}cycloalkylalkyl optionally substituted by 1-32 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 51. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 52. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 53. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-12}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 54. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-12}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 55. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-12}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 56. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-12}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 57. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-12}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 58. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 59. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-22 R^{19}.

Embodiment 60. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-16}arylalkyl optionally substituted by 1-19 R^{19}, C_{6-10}cycloalkylalkyl optionally substituted by 1-10 R^{19}, and 6-21 membered heteroarylalkyl optionally substituted by 1-27 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl.

Embodiment 61. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4

and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 62. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 63. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl.

Embodiment 64. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 65. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl

optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl; alternatively R^3 and R^4 can together form =O; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 66. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a C_{3-6}cycloalkyl; alternatively R^3 and R^4 can together form =O.

Embodiment 67. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a cyclopropyl group optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 68. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a cyclopropyl group optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^3, R^1 and R^5, and

R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 69. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^2 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-6 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-6 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; alternatively R^3 and R^6 can, together with the atoms linking them, form a cyclopropyl group optionally substituted by 1-3 R^{19}.

Embodiment 70. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a cyclopropyl group; and alternatively any of R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 71. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; R^4, R^5, and R^6 are H; alternatively R^3 and R^6 can, together with the atoms linking them, form a cyclopropyl group; and alternatively any of R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-11 R^{19}.

Embodiment 72. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; R^4, R^5, and R^6 are

H; alternatively R^3 and R^6 can, together with the atoms linking them, form a cyclopropyl group.

Embodiment 73. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 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}, and 6-10 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 74. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 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}, and 6-10 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 75. The compound of any of Embodiments 1-19, wherein R^1, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 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}, and 6-10 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 76. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3

R^{19}; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{7-11}arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7}cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; R^4, R^5, and R^6 are H.

Embodiment 77. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 78. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; and alternatively any of R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 79. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}.

Embodiment 80. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; and alternatively any of R^1 and R^3, R^1 and R^5, R^1 and R^{11}, and R^4 and R^{11} can, together with the atoms linking them, form a 5-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 81. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3

R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; and alternatively any of R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 5-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 82. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H.

Embodiment 83. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively any of R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 5-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 84. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively any of R^1 and R^3, R^1 and R^5, and R^4 and R^{11} can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 85. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively any of R^1 and R^3, and R^4 and R^{11} can, together with the atoms linking

them, form a 5 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 86. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively any of R^1 and R^3, and R^4 and R^{11} can, together with the atoms linking them, form a 5 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 87. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 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}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively any of R^1 and R^3, and R^4 and R^{11} can, together with the atoms linking them, form a 5 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 88. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 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}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively any of R^1 and R^3, and R^4 and R^{11} can, together with the atoms linking them, form a 5 membered heterocycloalkyl optionally substituted by 1-3

R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 89. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 is H; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 90. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 is H; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 91. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 92. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 93. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 94. The compound of any of Embodiments 1-19, wherein R^1, R^2, and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 95. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 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}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 96. The compound of any of Embodiments 1-19, wherein R^1 and R^{11} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^2 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}; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^4, R^5, and R^6 are H; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 97. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 5-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 98. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 99. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5 membered heterocycloalkyl optionally substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a 6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 100. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 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}, C_{6-7}cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a 5 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

Embodiment 101. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, benzyl optionally substituted by 1-3 R^{19}, C_7cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-7 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group optionally

substituted by 1-3 R^{19}; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a piperidinyl group optionally substituted by 1-3 R^{19}.

Embodiment 102. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, benzyl optionally substituted by 1-3 R^{19}, C_7cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-7 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group optionally substituted by 1-3 R^{19}.

Embodiment 103. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, benzyl optionally substituted by 1-3 R^{19}, C_7cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-7 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a piperidinyl group.

Embodiment 104. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, benzyl optionally substituted by 1-3 R^{19}, C_7cycloalkylalkyl optionally substituted by 1-3 R^{19}, and 6-7 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group.

Embodiment 105. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is benzyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a piperidinyl group.

Embodiment 106. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is benzyl optionally substituted by 1-3 R^{19}; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group.

Embodiment 107. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is benzyl; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group; and alternatively R^1 and R^{11} can, together with the atoms linking them, form a piperidinyl group.

Embodiment 108. The compound of any of Embodiments 1-19, wherein R^1, R^2, R^4, R^5, R^6, and R^{11} are H; R^3 is benzyl; alternatively R^1 and R^5 can, together with the atoms linking them, form a pyrrolidinyl group.

Embodiment 109. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 110. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 111. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 112. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 113. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 114. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 115. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 116. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 117. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 118. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 119. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 120. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 –$S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{3-7}cycloalkyl, or a 3-7 membered heterocycloalkyl.

Embodiment 121. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 122. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 123. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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 $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 124. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} 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 $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 125. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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 and R^9 are independently chosen from 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 $-OR^{20}$;alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 126. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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 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 $-OR^{20}$; R^9 is chosen from 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 $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 127. The compound of any of Embodiments 1-108, wherein 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^7 and R^{10} are independently chosen from 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 $–OR^{20}$;alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 128. The compound of any of Embodiments 1-108, wherein 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 $–OR^{20}$; 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_{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^7 and R^{10} are independently chosen from 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};alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 129. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 130. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} 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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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 1-3 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_{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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 131. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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 and R^9 are independently chosen from 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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 132. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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 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_{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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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^9 is chosen from 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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 133. The compound of any of Embodiments 1-108, wherein 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_{6-11}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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 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^7 and R^{10} are independently chosen from 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}, 6-21

membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)N$R^{22}R^{23}$, –N$R^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 134. The compound of any of Embodiments 1-108, wherein R^8 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_{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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)N$R^{22}R^{23}$, –N$R^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; R^9 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_{6-11}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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)N$R^{22}R^{23}$, –N$R^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; R^7 and R^{10} are independently chosen from 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}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, –C(=O)R^{20}, –C(=O)N$R^{22}R^{23}$, –N$R^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 135. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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}, 6-11 membered heteroarylalkyl optionally substituted by 1-3 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 136. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} 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}, 6-11 membered heteroarylalkyl optionally substituted by 1-3 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 1-3 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_{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}, 6-11 membered heteroarylalkyl optionally substituted by 1-3 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 137. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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)$NR^{22}R^{23}$, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –OR^{20}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 138. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 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_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 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 $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 139. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^8 and R^9 are independently chosen from 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 140. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^8 is chosen from 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_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 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^9 is chosen from 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 141. The compound of any of Embodiments 1-108, wherein 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_{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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^7 and R^{10} are independently chosen from 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 142. The compound of any of Embodiments 1-108, wherein R^8 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_{3-10}cycloalkyl optionally substituted by 1-3 R^{19}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 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^9 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_{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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^7 and R^{10} are independently chosen from 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 143. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, 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, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 144. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, 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, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 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, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 145. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 146. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 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, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 147. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 148. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, 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, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{6-10}aryl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 149. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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}, phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 150. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} 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}, phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^8 is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 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_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 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 $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6

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

Embodiment 151. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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}, phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^8 and R^9 are independently chosen from 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}, phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 152. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} 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}, phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; R^8 is chosen from 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_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 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^9 is chosen from 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}, phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–OR^{20}$; alternatively, either

or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl optionally substituted by 1-3 R^{19}, 3-6 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{19}.

Embodiment 153. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 154. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 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, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 155. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 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 and R^9 are independently chosen from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 156. The compound of any of Embodiments 1-108, wherein R^7 and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6

membered heteroaryl, 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 C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 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^9 is chosen from C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl optionally substituted by 1-3 R^{19}, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 157. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 158. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 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, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl or a 5-6 membered heteroaryl.

Embodiment 159. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkynyl, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 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}; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{3-6}cycloalkyl or a 3-6 membered heterocycloalkyl.

Embodiment 160. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} are independently chosen from H, C_{1-6}alkyl, C_{2-6}alkynyl, phenyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, 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, C_{2-6}alkynyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{3-6}cycloalkyl or a 3-6 membered heterocycloalkyl.

Embodiment 161. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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, $-C(=O)NR^{22}R^{23}$, and $-NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 162. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} 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, $-C(=O)NR^{22}R^{23}$, and $-NR^{22}R^{23}$; 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_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, halogen, $-C(=O)NR^{22}R^{23}$, and $-NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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 163. The compound of any of Embodiments 1-108, wherein R^7 and R^8 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)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; alternatively, 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}, or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 164. The compound of any of Embodiments 1-108, 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_{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)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; 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_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; alternatively, 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}, or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 165. The compound of any of Embodiments 1-108, wherein R^9 and R^{10} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, C_{6-11}aryl optionally substituted by 1-11 R^{19}, and –C(=O)$NR^{22}R^{23}$; alternatively, R^9 and R^{10} can, together with the atoms linking them, form a C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, or a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}.

Embodiment 166. The compound of any of Embodiments 1-108, wherein R^7, R^8, R^9, and R^{10} 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}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, a C_{6-11}aryl optionally substituted by 1-11 R^{19}, a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, or a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}.

Embodiment 167. The compound of any of Embodiments 1-108, wherein R^7, R^9, and R^{10} 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}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; 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_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, can, together with the atoms linking them, form a C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, a C_{6-11}aryl optionally substituted by 1-11 R^{19}, a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, or a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}.

Embodiment 168. The compound of any of Embodiments 1-108, wherein R^7 and R^8 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}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; alternatively, 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}, or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 169. The compound of any of Embodiments 1-108, 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_{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}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; 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_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, halogen, –CN, –C(=O)$NR^{22}R^{23}$, and –$NR^{22}R^{23}$; alternatively, 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}, or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 170. The compound of any of Embodiments 1-108, wherein R^9 and R^{10} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, and –C(=O)$NR^{22}R^{23}$; alternatively, R^9 and R^{10} can, together with the atoms linking them, form

a C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, or a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}.

Embodiment 171. The compound of any of Embodiments 1-108, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, and halogen; 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_{6-11}aryl optionally substituted by 1-11 R^{19}, C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}, halogen, –CN, $-C(=O)NR^{22}R^{23}$, and $-NR^{22}R^{23}$; alternatively, 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}, or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 172. The compound of any of Embodiments 1-108, wherein R^7 is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, and halogen; 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_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, halogen, –CN, $-C(=O)NR^{22}R^{23}$, and $-NR^{22}R^{23}$; alternatively, 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}, or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}.

Embodiment 173. The compound of any of Embodiments 1-108, wherein R^9 is chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^{10} is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, and $-C(=O)NR^{22}R^{23}$; alternatively, R^9 and R^{10} can, together with the atoms linking them, form a C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, or a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}.

Embodiment 174. The compound of any of Embodiments 1-108, wherein R^9 is C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^{10} is chosen from H, C_{1-6}alkyl optionally substituted by 1-13 R^{19}, and $-C(=O)NR^{22}R^{23}$; alternatively, R^9 and R^{10} can, together with the atoms linking them, form a C_{3-11}cycloalkyl optionally substituted by 1-21 R^{19}, or a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19}.

Embodiment 175. The compound of any of Embodiments 1-174, wherein 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_{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, –$NO_2$, –$NR^{22}R^{23}$, –$NR^{24}NR^{22}R^{23}$, –$N=NR^{24}$, –$NR^{24}OR^{26}$, –$NR^{24}C(=O)R^{20}$, –$NR^{24}C(=O)C(=O)R^{20}$, –$NR^{24}C(=O)OR^{21}$, –$NR^{24}C(=O)C(=O)OR^{21}$, –$NR^{24}C(=O)NR^{22}R^{23}$, –$NR^{24}C(=O)NR^{24}C(=O)R^{20}$, –$NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, –$NR^{24}C(=NR^{25})NR^{22}R^{23}$, –$NR^{24}C(=O)C(=O)NR^{22}R^{23}$, –$NR^{24}C(=S)R^{20}$, –$NR^{24}C(=S)OR^{20}$, –$NR^{24}C(=S)NR^{22}R^{23}$, –$NR^{24}S(=O)_2R^{21}$, –$NR^{24}S(=O)_2NR^{22}R^{23}$, –$NR^{24}P(=O)R^{28}R^{28}$, –$NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$NR^{24}P(=O)(OR^{20})(OR^{20})$, –$NR^{24}P(=O)(SR^{20})(SR^{20})$, –$OR^{20}$, –OCN, –$OC(=O)R^{20}$, –$OC(=O)NR^{22}R^{23}$, –$OC(=O)OR^{20}$, –$OC(=NR^{25})NR^{22}R^{23}$, –$OS(=O)R^{20}$, –$OS(=O)_2R^{20}$, –$OS(=O)_2OR^{20}$, –$OS(=O)_2NR^{22}R^{23}$, –$OP(=O)R^{28}R^{28}$, –$OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$OP(=O)(OR^{20})(OR^{20})$, –$OP(=O)(SR^{20})(SR^{20})$, –$Si(R^{24})_3$, –SCN, –$S(=O)_nR^{20}$, –$S(=O)_2OR^{20}$, –SO_3R^{27}, –$S(=O)_2NR^{22}R^{23}$, –$S(=O)NR^{22}R^{23}$, –$SP(=O)R^{28}R^{28}$, –$SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$SP(=O)(OR^{20})(OR^{20})$, –$SP(=O)(SR^{20})(SR^{20})$, –$P(=O)R^{28}R^{28}$, –$P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, –$P(=O)(OR^{20})(OR^{20})$, and –$P(=O)(SR^{20})(SR^{20})$; alternatively, 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 1-11 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 176. The compound of any of Embodiments 1-174, wherein 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_{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, –$NR^{22}R^{23}$, –$NR^{24}NR^{22}R^{23}$, –

$N{=}NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, 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 $C_{6\text{-}11}$aryl optionally substituted by 1-11 R^{19}, $C_{3\text{-}11}$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 177. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, $C_{1\text{-}6}$alkyl optionally substituted by 1-6 R^{19}, $C_{2\text{-}6}$alkenyl optionally substituted by 1-6 R^{19}, $C_{2\text{-}6}$alkynyl optionally substituted by 1-6 R^{19}, $C_{6\text{-}11}$aryl optionally substituted by 1-6 R^{19}, $C_{7\text{-}16}$arylalkyl optionally substituted by 1-6 R^{19}, $C_{3\text{-}11}$cycloalkyl optionally substituted by 1-6 R^{19}, $C_{4\text{-}17}$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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N{=}NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, 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 $C_{6\text{-}11}$aryl optionally substituted by 1-6 R^{19}, $C_{3\text{-}11}$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 178. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, $C_{1\text{-}6}$alkyl optionally substituted by 1-6 R^{19}, $C_{2\text{-}6}$alkenyl optionally substituted by 1-6 R^{19}, $C_{2\text{-}6}$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, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, 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 179. The compound of any of Embodiments 1-174, 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}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $-P(=O)(OR^{20})(OR^{20})$; alternatively, 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 180. The compound of any of Embodiments 1-174, 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_{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, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–P(=O)R^{28}R^{28}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $–P(=O)(OR^{20})(OR^{20})$; alternatively, 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 181. The compound of any of Embodiments 1-174, 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, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–P(=O)R^{28}R^{28}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $–P(=O)(OR^{20})(OR^{20})$; alternatively, 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 182. The compound of any of Embodiments 1-174, 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}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{19}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{19}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}, 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, –

$NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, 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 183. The compound of any of Embodiments 1-174, 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_{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, $-CN$, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, 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 184. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} 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_{6-11}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}, 5-15 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 $-S(=O)_2NR^{22}R^{23}$; alternatively, 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 185. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} 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_{6-11}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}, 5-15 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, 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 186. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} 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_{6-11}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}, 5-15 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 $–S(=O)_2NR^{22}R^{23}$.

Embodiment 187. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} 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_{6-11}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}, 5-15 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 $–S(=O)_2NR^{22}R^{23}$.

Embodiment 188. The compound of any of Embodiments 1-174, 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; alternatively, 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 189. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} 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_{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 $–S(=O)_2NR^{22}R^{23}$; alternatively, 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 190. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} 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_{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 $–S(=O)_2NR^{22}R^{23}$; alternatively, 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 191. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} 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_{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 $–S(=O)_2NR^{22}R^{23}$.

Embodiment 192. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} 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_{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 $-S(=O)_2NR^{22}R^{23}$.

Embodiment 193. The compound of any of Embodiments 1-174, 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}, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 194. The compound of any of Embodiments 1-174, 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}, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-NR^{24}C(=O)NR^{22}R^{23}$.

Embodiment 195. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 196. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, and $-NR^{24}C(=O)NR^{22}R^{23}$.

Embodiment 197. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 198. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen.

Embodiment 199. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}.

Embodiment 200. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_2NR^{22}R^{23}$.

Embodiment 201. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, C_{1-6}alkyl, halogen, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–NR^{24}C(=O)NR^{22}R^{23}$.

Embodiment 202. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} is chosen from H, C_{1-6}alkyl, halogen, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 203. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} is chosen from H, C_{1-6}alkyl, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, and $–NR^{24}C(=O)NR^{22}R^{23}$.

Embodiment 204. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl, halogen, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–OR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

Embodiment 205. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} is chosen from H, C_{1-6}alkyl, and halogen.

Embodiment 206. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H and C_{1-6}alkyl.

Embodiment 207. The compound of any of Embodiments 1-174, wherein 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_{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 $–OR^{20}$; alternatively, 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 1-11 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 208. The compound of any of Embodiments 1-174, wherein 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_{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}; alternatively, 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 1-11 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 209. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, halogen, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)$NR^{22}R^{23}$, –OR^{20}, and –$S(=O)_2NR^{22}R^{23}$.

Embodiment 210. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently chosen from H, halogen, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –NR^{24}C(=O)$NR^{22}R^{23}$.

Embodiment 211. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} is chosen from H, halogen, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)$NR^{22}R^{23}$, –OR^{20}, and –$S(=O)_2NR^{22}R^{23}$.

Embodiment 212. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{15} are H; R^{14} is chosen from H, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, and –NR^{24}C(=O)$NR^{22}R^{23}$.

Embodiment 213. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} is chosen from H, halogen, –$NR^{22}R^{23}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)$NR^{22}R^{23}$, –OR^{20}, and –$S(=O)_2NR^{22}R^{23}$.

Embodiment 214. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} is chosen from H and halogen.

Embodiment 215. The compound of any of Embodiments 1-174, wherein R^{12}, R^{13}, R^{14}, and R^{15} are H.

Embodiment 216. The compound of any of Embodiments 1-215, wherein R^{17} 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_{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}, and $-OR^{20}$; R^{16} and R^{18} 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, or $-P(=O)(SR^{20})(SR^{20})$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl optionally substituted by 1-13 R^{19}; R^{16} and R^{18} 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, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, or $-P(=O)(SR^{20})(SR^{20})$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 218. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}; R^{16} and R^{18} 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, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, –

$C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, or $-P(=O)(SR^{20})(SR^{20})$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 219. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-$

$NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, or $-P(=O)(SR^{20})(SR^{20})$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 220. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} 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, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-OR^{20}$, –OCN, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, –SCN, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, and $-S(=O)NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 221. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{2-6}alkenyl optionally substituted by 1-1 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)N$R^{22}R^{23}$, –C(=O)C(=O)R^{20}, –NC, –NO_2, –N$R^{22}R^{23}$, –NR^{24}N$R^{22}R^{23}$, –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)N$R^{22}R^{23}$, –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)N$R^{22}R^{23}$, –NR^{24}S(=O)$_2R^{21}$, –NR^{24}S(=O)$_2$N$R^{22}R^{23}$, –OR^{20}, –OCN, –OC(=O)R^{20}, –OC(=O)N$R^{22}R^{23}$, –OC(=O)OR^{20}, –OS(=O)R^{20}, –OS(=O)$_2R^{20}$, –OS(=O)$_2$OR^{20}, –OS(=O)$_2$N$R^{22}R^{23}$, –SCN, –S(=O)$_n R^{20}$, –S(=O)$_2$OR^{20}, –SO_3R^{27}, –S(=O)$_2$N$R^{22}R^{23}$, and –S(=O)N$R^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 222. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} 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}, 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)N$R^{22}R^{23}$, –NC, –NO_2, –N$R^{22}R^{23}$, –NR^{24}N$R^{22}R^{23}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)OR^{21}, –NR^{24}C(=O)N$R^{22}R^{23}$, –NR^{24}S(=O)$_2R^{21}$, –NR^{24}S(=O)$_2$N$R^{22}R^{23}$, –OR^{20}, –OCN, –OC(=O)R^{20}, –OC(=O)N$R^{22}R^{23}$, –OC(=O)OR^{20}, –OS(=O)R^{20}, –OS(=O)$_2R^{20}$, –OS(=O)$_2$OR^{20}, –OS(=O)$_2$N$R^{22}R^{23}$, –SCN, –S(=O)$_n R^{20}$, –S(=O)$_2$OR^{20}, –SO_3R^{27}, –S(=O)$_2$N$R^{22}R^{23}$, and –S(=O)N$R^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 223. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} 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}, 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)N$R^{22}R^{23}$, –NC, –NO_2, –N$R^{22}R^{23}$, –NR^{24}C(=O)R^{20}, –NR^{24}C(=O)OR^{21}, –NR^{24}C(=O)N$R^{22}R^{23}$, –NR^{24}S(=O)$_2R^{21}$, –OR^{20}, –OCN, –OC(=O)R^{20}, –OC(=O)N$R^{22}R^{23}$, –SCN, –S(=O)$_n R^{20}$, –S(=O)$_2$OR^{20}, –SO_3R^{27}, –S(=O)$_2$N$R^{22}R^{23}$, and –S(=O)N$R^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 224. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} 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}, 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, $-C(=O)R^{20}$, $-C(=O)NR^{22}R^{23}$, –NC, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}S(=O)_2R^{21}$, $-OR^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 225. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} 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}, 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 $-S(=O)_2NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 226. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} 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}, 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 $-S(=O)_2NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 227. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered

heterocycloalkyl, 5-10 membered heteroaryl, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 228. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, 5-10 membered heteroaryl, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 229. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 230. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 3-10 membered heterocycloalkyl or a 5-10 membered heteroaryl.

Embodiment 231. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl 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 $–S(=O)_2NR^{22}R^{23}$.

Embodiment 232. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl 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 $–S(=O)_2NR^{22}R^{23}$.

Embodiment 233. The compound of any of Embodiments 1-215, wherein R^{17} is chosen from H and C_{1-6}alkyl; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, and $–OR^{20}$.

Embodiment 234. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, halogen, and $-OR^{20}$.

Embodiment 235. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl optionally substituted by 1-3 R^{19}, and halogen.

Embodiment 236. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H, C_{1-6}alkyl, and halogen.

Embodiment 237. The compound of any of Embodiments 1-215, wherein R^{16}, R^{17}, and R^{18} are independently chosen from H and C_{1-6}alkyl.

Embodiment 238. The compound of any of Embodiments 1-215, wherein R^{17} 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_{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}, and $-OR^{20}$; R^{16} and R^{18} 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 $-OR^{20}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 239. The compound of any of Embodiments 1-215, wherein R^{17} 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_{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}, and $-OR^{20}$; R^{16} and R^{18} 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 $-OR^{20}$; alternatively, R^{16} and R^{17} can, together with the atoms linking them, form a 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 240. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H and C_{1-6}alkyl optionally substituted by 1-3 R^{19}.

Embodiment 241. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H and C_{1-6}alkyl.

Embodiment 242. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H and C_{1-4}alkyl.

Embodiment 243. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H and C_{1-3}alkyl.

Embodiment 244. The compound of any of Embodiments 1-215, wherein R^{17} is H; R^{16} and R^{18} are independently chosen from H and methyl.

Embodiment 245. The compound of any of Embodiments 1-215, wherein R^{16}, R^{17}, and R^{18} are H.

Embodiment 246. The compound of any of Embodiments 1-240, 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, $–NO_2$, $–NR^{32}R^{33}$, $–NR^{34}NR^{32}R^{33}$, $–N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $–NR^{34}OR^{36}$, $–NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)C(=O)R^{30}$, $–NR^{34}C(=O)OR^{31}$, $–NR^{34}C(=O)C(=O)OR^{31}$, $–NR^{34}C(=O)NR^{32}R^{33}$, $–NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $–NR^{34}C(=NR^{35})NR^{32}R^{33}$, $–NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $–NR^{34}C(=S)R^{30}$, $–NR^{34}C(=S)OR^{30}$, $–NR^{34}C(=S)NR^{32}R^{33}$, $–NR^{34}S(=O)_2R^{31}$, $–NR^{34}S(=O)_2NR^{32}R^{33}$, $–NR^{34}P(=O)R^{38}R^{38}$, $–NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–NR^{34}P(=O)(OR^{30})(OR^{30})$, $–NR^{34}P(=O)(SR^{30})(SR^{30})$, $–OR^{30}$, =O, –OCN, $–OC(=O)R^{30}$, $–OC(=O)NR^{32}R^{33}$, $–OC(=O)OR^{30}$, $–OC(=NR^{35})NR^{32}R^{33}$, $–OS(=O)R^{30}$, $–OS(=O)_2R^{30}$, $–OS(=O)_2OR^{30}$, $–OS(=O)_2NR^{32}R^{33}$, $–OP(=O)R^{38}R^{38}$, $–OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–OP(=O)(OR^{30})(OR^{30})$, $–OP(=O)(SR^{30})(SR^{30})$, $–Si(R^{34})_3$, –SCN, =S, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–SP(=O)R^{38}R^{38}$, $–SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–SP(=O)(OR^{30})(OR^{30})$, $–SP(=O)(SR^{30})(SR^{30})$, $–P(=O)R^{38}R^{38}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$.

Embodiment 247. The compound of any of Embodiments 1-240, 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, $–NO_2$, $–NR^{32}R^{33}$, $–NR^{34}NR^{32}R^{33}$, $–N=NR^{34}$, $=NR^{30}$, $=NOR^{30}$, $–NR^{34}OR^{36}$, $–NR^{34}C(=O)R^{30}$, $–NR^{34}C(=O)C(=O)R^{30}$, $–NR^{34}C(=O)OR^{31}$, $–NR^{34}C(=O)C(=O)OR^{31}$, $–NR^{34}C(=O)NR^{32}R^{33}$, –

$NR^{34}C(=O)NR^{34}C(=O)R^{30}$, $-NR^{34}C(=O)NR^{34}C(=O)OR^{30}$, $-NR^{34}C(=NR^{35})NR^{32}R^{33}$, $-NR^{34}C(=O)C(=O)NR^{32}R^{33}$, $-NR^{34}C(=S)R^{30}$, $-NR^{34}C(=S)OR^{30}$, $-NR^{34}C(=S)NR^{32}R^{33}$, $-NR^{34}S(=O)_2R^{31}$, $-NR^{34}S(=O)_2NR^{32}R^{33}$, $-NR^{34}P(=O)R^{38}R^{38}$, $-NR^{34}P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-NR^{34}P(=O)(OR^{30})(OR^{30})$, $-NR^{34}P(=O)(SR^{30})(SR^{30})$, $-OR^{30}$, =O, –OCN, $-OC(=O)R^{30}$, $-OC(=O)NR^{32}R^{33}$, $-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-OS(=O)R^{30}$, $-OS(=O)_2R^{30}$, $-OS(=O)_2OR^{30}$, $-OS(=O)_2NR^{32}R^{33}$, $-OP(=O)R^{38}R^{38}$, $-OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-OP(=O)(OR^{30})(OR^{30})$, $-OP(=O)(SR^{30})(SR^{30})$, $-Si(R^{34})_3$, –SCN, =S, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-SP(=O)R^{38}R^{38}$, $-SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-SP(=O)(OR^{30})(OR^{30})$, $-SP(=O)(SR^{30})(SR^{30})$, $-P(=O)R^{38}R^{38}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 248. The compound of any of Embodiments 1-240, 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, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-P(=O)R^{38}R^{38}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$.

Embodiment 249. The compound of any of Embodiments 1-240, 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, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–P(=O)R^{38}R^{38}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$.

Embodiment 250. The compound of any of Embodiments 1-240, 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, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–P(=O)R^{38}R^{38}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$.

Embodiment 251. The compound of any of Embodiments 1-240, 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, $–S(=O)_nR^{30}$, $–S(=O)_2OR^{30}$, $–SO_3R^{37}$, $–S(=O)_2NR^{32}R^{33}$, $–S(=O)NR^{32}R^{33}$, $–P(=O)R^{38}R^{38}$, $–P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $–P(=O)(OR^{30})(OR^{30})$, and $–P(=O)(SR^{30})(SR^{30})$.

Embodiment 252. The compound of any of Embodiments 1-240, 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 253. The compound of any of Embodiments 1-240, 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 254. The compound of any of Embodiments 1-240, 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 255. The compound of any of Embodiments 1-240, 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 256. The compound of any of Embodiments 1-240, 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 257. The compound of any of Embodiments 1-240, 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 258. The compound of any of Embodiments 1-240, 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 259. The compound of any of Embodiments 1-240, 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 260. The compound of any of Embodiments 1-240, 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 261. The compound of any of Embodiments 1-240, wherein R^{19} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{39}.

Embodiment 262. The compound of any of Embodiments 1-240, 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 263. The compound of any of Embodiments 1-240, 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 264. The compound of any of Embodiments 1-240, 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 265. The compound of any of Embodiments 1-240, 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 266. The compound of any of Embodiments 1-240, 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 267. The compound of any of Embodiments 1-266, 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 268. The compound of any of Embodiments 1-266, 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 269. The compound of any of Embodiments 1-266, 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 270. The compound of any of Embodiments 1-266, 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 271. The compound of any of Embodiments 1-266, 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 272. The compound of any of Embodiments 1-266, 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 273. The compound of any of Embodiments 1-266, 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, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 274. The compound of any of Embodiments 1-266, 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 275. The compound of any of Embodiments 1-266, 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.

Embodiment 276. The compound of any of Embodiments 1-266, 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 277. The compound of any of Embodiments 1-266, 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 278. The compound of any of Embodiments 1-266, 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 279. The compound of any of Embodiments 1-266, 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 280. The compound of any of Embodiments 1-266, 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}, 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 281. The compound of any of Embodiments 1-266, 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}, 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}.

Embodiment 282. The compound of any of Embodiments 1-266, 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}, 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}.

Embodiment 283. The compound of any of Embodiments 1-266, 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}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 284. The compound of any of Embodiments 1-266, 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}, C_{3-6}cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

Embodiment 285. The compound of any of Embodiments 1-266, 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 286. The compound of any of Embodiments 1-266, 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 287. The compound of any of Embodiments 1-266, 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 288. The compound of any of Embodiments 1-266, 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 289. The compound of any of Embodiments 1-266, 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 290. The compound of any of Embodiments 1-266, 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 291. The compound of any of Embodiments 1-266, 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 292. The compound of any of Embodiments 1-266, 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 293. The compound of any of Embodiments 1-266, 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 294. The compound of any of Embodiments 1-266, 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 optionally substituted by 1-3 R^{49}.

Embodiment 295. The compound of any of Embodiments 1-266, 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}, 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 296. The compound of any of Embodiments 1-266, 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 297. The compound of any of Embodiments 1-266, 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 298. The compound of any of Embodiments 1-266, 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 299. The compound of any of Embodiments 1-266, 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 300. The compound of any of Embodiments 1-266, wherein R^{20} at each occurrence is independently chosen from H, 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 301. The compound of any of Embodiments 1-266, 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 302. The compound of any of Embodiments 1-266, 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 303. The compound of any of Embodiments 1-266, 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 304. The compound of any of Embodiments 1-266, 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 305. The compound of any of Embodiments 1-266, 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 306. The compound of any of Embodiments 1-266, 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 307. The compound of any of Embodiments 1-266, 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 308. The compound of any of Embodiments 1-266, 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 309. The compound of any of Embodiments 1-266, 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}, 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 310. The compound of any of Embodiments 1-266, 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 311. The compound of any of Embodiments 1-266, 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.

Embodiment 312. The compound of any of Embodiments 1-266, 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 313. The compound of any of Embodiments 1-266, 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 314. The compound of any of Embodiments 1-266, wherein R^{20} at each occurrence is independently chosen from H, 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 315. The compound of any of Embodiments 1-266, 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.

Embodiment 316. The compound of any of Embodiments 1-266, 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.

Embodiment 317. The compound of any of Embodiments 1-266, 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 318. The compound of any of Embodiments 1-266, 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 319. The compound of any of Embodiments 1-266, 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 320. The compound of any of Embodiments 1-266, 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 321. The compound of any of Embodiments 1-266, 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 322. The compound of any of Embodiments 1-266, 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 H.

Embodiment 323. The compound of any of Embodiments 1-266, 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}, 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 H.

Embodiment 324. The compound of any of Embodiments 1-266, 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 H.

Embodiment 325. The compound of any of Embodiments 1-266, 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 H.

Embodiment 326. The compound of any of Embodiments 1-266, 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 H.

Embodiment 327. The compound of any of Embodiments 1-266, 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 H.

Embodiment 328. The compound of any of Embodiments 1-266, wherein R^{20} at each occurrence is independently chosen from H, 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 H.

Embodiment 329. The compound of any of Embodiments 1-266, 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 330. The compound of any of Embodiments 1-266, 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 H.

Embodiment 331. The compound of any of Embodiments 1-266, 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 332. The compound of any of Embodiments 1-266, 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 H.

Embodiment 333. The compound of any of Embodiments 1-266, 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 334. The compound of any of Embodiments 1-266, 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 335. The compound of any of Embodiments 1-266, 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 336. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} 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 337. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from 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_{6-11}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 338. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from 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 339. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from 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 340. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, C_{7-}

$_{11}$arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 341. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from C_{1-6}alkyl, C_{6-10}aryl, and C_{7-11}arylalkyl.

Embodiment 342. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 343. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from C_{1-6}alkyl and C_{6-10}aryl.

Embodiment 344. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is independently chosen from C_{1-6}alkyl and phenyl.

Embodiment 345. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{49}.

Embodiment 346. The compound of any of Embodiments 1-335, wherein R^{28} and R^{38} at each occurrence is C_{1-6}alkyl.

Embodiment 347. The compound of any of Embodiments 1-346, 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}; alternatively, 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 348. The compound of any of Embodiments 1-346, 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}; alternatively, 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 349. The compound of any of Embodiments 1-346, 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}; alternatively, 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 350. The compound of any of Embodiments 1-346, 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 351. The compound of any of Embodiments 1-346, 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}; alternatively, 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 352. The compound of any of Embodiments 1-346, 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 353. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl; alternatively, 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 or a 5-10 membered heteroaryl.

Embodiment 354. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H, C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 355. The compound of any of Embodiments 1-346, 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}, and 5-10 membered heteroaryl optionally substituted by 1-3 R^{59}.

Embodiment 356. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} 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}.

Embodiment 357. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} 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}.

Embodiment 358. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} 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}.

Embodiment 359. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} 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}.

Embodiment 360. The compound of any of Embodiments 1-346, 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 independently chosen from H and C_{1-6}alkyl; alternatively, 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 361. The compound of any of Embodiments 1-346, 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 independently chosen from H and C_{1-6}alkyl; alternatively, 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 362. The compound of any of Embodiments 1-346, 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 independently chosen from H and C_{1-6}alkyl; alternatively, 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 363. The compound of any of Embodiments 1-346, 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 independently chosen from H and C_{1-6}alkyl.

Embodiment 364. The compound of any of Embodiments 1-346, wherein R^{22} 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}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl; alternatively, 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 365. The compound of any of Embodiments 1-346, wherein R^{22} 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}; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 366. The compound of any of Embodiments 1-346, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl; alternatively, 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 or a 5-10 membered heteroaryl.

Embodiment 367. The compound of any of Embodiments 1-346, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl; R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 368. The compound of any of Embodiments 1-346, wherein R^{22} 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}, 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 369. The compound of any of Embodiments 1-346, 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 370. The compound of any of Embodiments 1-346, 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 371. The compound of any of Embodiments 1-346, 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 independently chosen from H and C_{1-6}alkyl.

Embodiment 372. The compound of any of Embodiments 1-346, 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 373. The compound of any of Embodiments 1-346, 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; alternatively, 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 374. The compound of any of Embodiments 1-346, 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; alternatively, 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 375. The compound of any of Embodiments 1-346, 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; alternatively, 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 376. The compound of any of Embodiments 1-346, 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.

Embodiment 377. The compound of any of Embodiments 1-346, wherein R^{22} 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}; R^{23}, R^{32} and R^{33} at each occurrence is H; alternatively, 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 378. The compound of any of Embodiments 1-346, wherein R^{22} 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}; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 379. The compound of any of Embodiments 1-346, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl; R^{23}, R^{32} and R^{33} at each occurrence is H; alternatively, 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 or a 5-10 membered heteroaryl.

Embodiment 380. The compound of any of Embodiments 1-346, wherein R^{22} at each occurrence is independently chosen from H, C_{1-6}alkyl, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl; R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 381. The compound of any of Embodiments 1-346, wherein R^{22} 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}, 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 382. The compound of any of Embodiments 1-346, 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 383. The compound of any of Embodiments 1-346, 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 384. The compound of any of Embodiments 1-346, 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 385. The compound of any of Embodiments 1-346, 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 386. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 387. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is H.

Embodiment 388. The compound of any of Embodiments 1-346, 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}; alternatively, 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 389. The compound of any of Embodiments 1-346, 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}; alternatively, 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 390. The compound of any of Embodiments 1-346, 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}; alternatively, 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 391. The compound of any of Embodiments 1-346, 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}; alternatively, 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 392. The compound of any of Embodiments 1-346, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently chosen from H and C_{1-6}alkyl

optionally; alternatively, 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 393. The compound of any of Embodiments 1-392, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 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 $–P(=O)(SR^{70})(SR^{70})$.

Embodiment 394. The compound of any of Embodiments 1-392, 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 395. The compound of any of Embodiments 1-392, 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}, 3-15 membered heterocycloalkyl optionally substituted by 1-6 R^{79}, 5-15 membered heteroaryl optionally substituted by 1-6 R^{79}, halogen, –CN, –$C(=O)R^{70}$, –$C(=O)OR^{70}$, –$C(=O)NR^{72}R^{73}$, –$C(=O)C(=O)R^{70}$, –NC, –NO_2, –$NR^{72}R^{73}$, –$NR^{74}NR^{72}R^{73}$, –$N=NR^{74}$, $=NR^{70}$, $=NOR^{70}$, –$NR^{74}OR^{76}$, –$NR^{74}C(=O)R^{70}$, –$NR^{74}C(=O)C(=O)R^{70}$, –$NR^{74}C(=O)OR^{71}$, –$NR^{74}C(=O)C(=O)OR^{71}$, –$NR^{74}C(=O)NR^{72}R^{73}$, –$NR^{74}C(=O)NR^{74}C(=O)R^{70}$, –$NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, –$NR^{74}C(=NR^{75})NR^{72}R^{73}$, –$NR^{74}C(=O)C(=O)NR^{72}R^{73}$, –$NR^{74}S(=O)_2R^{71}$, –$NR^{74}S(=O)_2NR^{72}R^{73}$, –$NR^{74}P(=O)R^{78}R^{78}$, –$NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, –$NR^{74}P(=O)(OR^{70})(OR^{70})$, –$OR^{70}$, =O, –OCN, –$OC(=O)R^{70}$, –$OC(=O)NR^{72}R^{73}$, –$OC(=O)OR^{70}$, –$OC(=NR^{75})NR^{72}R^{73}$, –$OS(=O)R^{70}$, –

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

Embodiment 396. The compound of any of Embodiments 1-392, 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_{6-10}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, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $=NR^{70}$, $=NOR^{70}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-OR^{70}$, =O, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-Si(R^{74})_3$, $-SCN$, =S, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, and $-P(=O)(OR^{70})(OR^{70})$.

Embodiment 397. The compound of any of Embodiments 1-392, 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_{2-6}alkenyl optionally substituted by 1-3 R^{79}, C_{2-6}alkynyl 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, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-OR^{70}$, =O, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OS(=O)_2NR^{72}R^{73}$, $-Si(R^{74})_3$, $-SCN$, $-S(=O)_nR^{70}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, and $-P(=O)(OR^{70})(OR^{70})$.

Embodiment 398. The compound of any of Embodiments 1-392, 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_{2-6}alkenyl optionally substituted by 1-3 R^{79}, C_{2-6}alkynyl 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, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}OR^{76}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)OR^{71}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–NR^{74}S(=O)_2NR^{72}R^{73}$, $–OR^{70}$, =O, $–OC(=O)R^{70}$, $–OC(=O)NR^{72}R^{73}$, $–OS(=O)_2NR^{72}R^{73}$, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$.

Embodiment 399. The compound of any of Embodiments 1-392, 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_{2-6}alkenyl optionally substituted by 1-3 R^{79}, C_{2-6}alkynyl 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, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–OR^{70}$, =O, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$.

Embodiment 400. The compound of any of Embodiments 1-392, 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, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–OR^{70}$, =O, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$.

Embodiment 401. The compound of any of Embodiments 1-392, 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}, 3-10 membered heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-10 membered heteroaryl optionally substituted by 1-3 R^{79}, –CN, and $–C(=O)R^{70}$.

Embodiment 402. The compound of any of Embodiments 1-392, 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}, 5-6 membered

heterocycloalkyl optionally substituted by 1-3 R^{79}, 5-9 membered heteroaryl optionally substituted by 1-3 R^{79}, –CN, and –C(=O)R^{70}.

Embodiment 403. The compound of any of Embodiments 1-392, 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 R^{79}, phenyl, 6 membered heterocycloalkyl optionally substituted by 1 R^{79}, 5-9 membered heteroaryl optionally substituted by 1-3 R^{79}, –CN, and –C(=O)R^{70}.

Embodiment 404. The compound of any of Embodiments 1-392, wherein R^{39} at each occurrence is independently chosen from C_{1-6}alkyl and 5-9 membered heteroaryl optionally substituted by 1-3 R^{79}; R^{59} and R^{69} at each occurrence is independently C_{1-6}alkyl; R^{49} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1 R^{79}, phenyl, 6 membered heterocycloalkyl optionally substituted by 1 R^{79}, 5 membered heteroaryl optionally substituted by 1-3 R^{79}, –CN, and –C(=O)R^{70}.

Embodiment 405. The compound of any of Embodiments 1-392, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, 5-6 membered heterocycloalkyl, 5-9 membered heteroaryl, –CN, and –C(=O)R^{70}.

Embodiment 406. The compound of any of Embodiments 1-392, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, 5-6 membered heterocycloalkyl, and 5-9 membered heteroaryl.

Embodiment 407. The compound of any of Embodiments 1-392, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 R^{79}.

Embodiment 408. The compound of any of Embodiments 1-392, 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}.

Embodiment 409. The compound of any of Embodiments 1-392, 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 410. The compound of any of Embodiments 1-392, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently C_{1-6}alkyl.

Embodiment 411. The compound of any of Embodiments 1-410, 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 412. The compound of any of Embodiments 1-410, 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 413. The compound of any of Embodiments 1-410, 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 414. The compound of any of Embodiments 1-410, 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_{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 415. The compound of any of Embodiments 1-410, 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, C_{6-10}aryl, C_{7-11}arylalkyl, C_{3-10}cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

Embodiment 416. The compound of any of Embodiments 1-410, 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 417. The compound of any of Embodiments 1-410, 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 418. The compound of any of Embodiments 1-410, 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 1-3 R^{89}, and 5-6 membered heteroaryl.

Embodiment 419. The compound of any of Embodiments 1-410, 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 420. The compound of any of Embodiments 1-410, 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, and 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}.

Embodiment 421. The compound of any of Embodiments 1-410, 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, and 5-6 membered heterocycloalkyl optionally substituted by C_{1-6}alkyl.

Embodiment 422. The compound of any of Embodiments 1-410, 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, and 5-6 membered heterocycloalkyl.

Embodiment 423. The compound of any of Embodiments 1-410, wherein R^{70} at each occurrence is independently chosen from H, C_{1-6}alkyl, and 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{89}; R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is H.

Embodiment 424. The compound of any of Embodiments 1-410, wherein R^{70} at each occurrence is independently chosen from H, C_{1-6}alkyl, and 5-6 membered

heterocycloalkyl optionally substituted by C_{1-6}alkyl; R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is H.

Embodiment 425. The compound of any of Embodiments 1-410, wherein R^{70} at each occurrence is independently chosen from H, C_{1-6}alkyl, and 5-6 membered heterocycloalkyl; R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is H.

Embodiment 426. The compound of any of Embodiments 1-410, 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 427. The compound of any of Embodiments 1-410, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is H.

Embodiment 428. The compound of any of Embodiments 1-427, 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}; alternatively, 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 429. The compound of any of Embodiments 1-427, 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}; alternatively, 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 430. The compound of any of Embodiments 1-427, 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}, C_{2-6}alkenyl optionally substituted by 1-3 R^{99}, C_{2-6}alkynyl optionally substituted by 1-3 R^{99}, C_{6-11}aryl optionally substituted by 1-3 R^{99}, C_{7-16}arylalkyl optionally substituted by 1-3 R^{99}, C_{3-11}cycloalkyl optionally substituted by 1-3 R^{99}, C_{4-17}cycloalkylalkyl optionally substituted by 1-3 R^{99}, 3-15 membered heterocycloalkyl optionally substituted by 1-3 R^{99}, 4-21 membered heterocycloalkylalkyl optionally substituted by 1-3 R^{99}, 5-15 membered heteroaryl optionally substituted by 1-3 R^{99}, and 6-21 membered heteroarylalkyl optionally substituted by 1-3 R^{99}; alternatively, 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 431. The compound of any of Embodiments 1-427, 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}, C_{2-6}alkenyl optionally substituted by 1-3 R^{99}, C_{2-6}alkynyl optionally substituted by 1-3 R^{99}, C_{6-10}aryl optionally substituted by 1-3 R^{99}, C_{7-11}arylalkyl 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}; alternatively, 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 432. The compound of any of Embodiments 1-427, 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}, C_{6-10}aryl optionally substituted by 1-3 R^{99}, C_{7-11}arylalkyl 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}; alternatively, 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 433. The compound of any of Embodiments 1-427, 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}; alternatively, any R^{72} and R^{73} may form, together with the nitrogen atom to which they are attached, a 5-6 membered heterocycloalkyl optionally substituted by 1-3 R^{109} or a 5-6 membered heteroaryl optionally substituted by 1-3 R^{109}.

Embodiment 434. The compound of any of Embodiments 1-427, 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 435. The compound of any of Embodiments 1-427, 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; alternatively, 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 436. The compound of any of Embodiments 1-427, 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 437. The compound of any of Embodiments 1-427, 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 438. The compound of any of Embodiments 1-427, 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 439. The compound of any of Embodiments 1-427, wherein R^{72} and R^{73} at each occurrence is independently chosen from H, C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 440. The compound of any of Embodiments 1-427, wherein R^{72} and R^{73} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 441. The compound of any of Embodiments 1-427, wherein R^{72} and R^{73} at each occurrence is H.

Embodiment 442. The compound of any of Embodiments 1-441, 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}.

Embodiment 443. The compound of any of Embodiments 1-441, 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}.

Embodiment 444. The compound of any of Embodiments 1-441, 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}.

Embodiment 445. The compound of any of Embodiments 1-441, 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}.

Embodiment 446. The compound of any of Embodiments 1-441, 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}.

Embodiment 447. The compound of any of Embodiments 1-441, 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.

Embodiment 448. The compound of any of Embodiments 1-441, 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}.

Embodiment 449. The compound of any of Embodiments 1-441, wherein R^{78} at each occurrence is independently chosen from C_{1-6}alkyl, phenyl, and benzyl.

Embodiment 450. The compound of any of Embodiments 1-441, wherein R^{78} at each occurrence is C_{1-6}alkyl optionally substituted by 1-3 R^{89}.

Embodiment 451. The compound of any of Embodiments 1-441, wherein R^{78} at each occurrence is C_{1-6}alkyl.

Embodiment 452. The compound of any of Embodiments 1-451, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl optionally substituted by 1-13 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, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{110}R^{110}$, $–C(=O)C(=O)R^{110}$, $–C(=NR^{110})R^{110}$, $–C(=NR^{110})NR^{110}R^{110}$, $–C(=NOH)NR^{110}R^{110}$, $–C(=NOR^{110})R^{110}$, $–C(=NNR^{110}R^{110})R^{110}$, $–C(=NNR^{110}C(=O)R^{110})R^{110}$, $–C(=NNR^{110}C(=O)OR^{110})R^{110}$, $–C(=S)NR^{110}R^{110}$, –NC, $–NO_2$, $–NR^{110}R^{110}$, $–NR^{110}NR^{110}R^{110}$, $–N=NR^{110}$, $=NR^{110}$, $=NOR^{110}$, $–NR^{110}OR^{110}$, $–NR^{110}C(=O)R^{110}$, $–NR^{110}C(=O)C(=O)R^{110}$, $–NR^{110}C(=O)OR^{110}$, $–NR^{110}C(=O)C(=O)OR^{110}$, $–NR^{110}C(=O)NR^{110}R^{110}$, $–NR^{110}C(=O)NR^{110}C(=O)R^{110}$, $–NR^{110}C(=O)NR^{110}C(=O)OR^{110}$, $–NR^{110}C(=NR^{110})NR^{110}R^{110}$, $–NR^{110}C(=O)C(=O)NR^{110}R^{110}$, $–NR^{110}C(=S)R^{110}$, $–NR^{110}C(=S)OR^{110}$, $–NR^{110}C(=S)NR^{110}R^{110}$, $–NR^{110}S(=O)_2R^{110}$, $–NR^{110}S(=O)_2NR^{110}R^{110}$, $–NR^{110}P(=O)R^{111}R^{111}$, $–NR^{110}P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $–NR^{110}P(=O)(OR^{110})(OR^{110})$, $–NR^{110}P(=O)(SR^{110})(SR^{110})$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–OC(=O)NR^{110}R^{110}$, –

$OC(=O)OR^{110}$, $-OC(=NR^{110})NR^{110}R^{110}$, $-OS(=O)R^{110}$, $-OS(=O)_2R^{110}$, $-OS(=O)_2OR^{110}$, $-OS(=O)_2NR^{110}R^{110}$, $-OP(=O)R^{111}R^{111}$, $-OP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-OP(=O)(OR^{110})(OR^{110})$, $-OP(=O)(SR^{110})(SR^{110})$, $-Si(R^{110})_3$, –SCN, =S, $-S(=O)_nR^{110}$, $-S(=O)_2OR^{110}$, $-SO_3R^{110}$, $-S(=O)_2NR^{110}R^{110}$, $-S(=O)NR^{110}R^{110}$, $-SP(=O)R^{111}R^{111}$, $-SP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-SP(=O)(OR^{110})(OR^{110})$, $-SP(=O)(SR^{110})(SR^{110})$, $-P(=O)R^{111}R^{111}$, $-P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-P(=O)(OR^{110})(OR^{110})$, and $-P(=O)(SR^{110})(SR^{110})$.

Embodiment 453. The compound of any of Embodiments 1-451, 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 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, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{110}R^{110}$, $-C(=O)C(=O)R^{110}$, –NC, $-NO_2$, $-NR^{110}R^{110}$, $-NR^{110}NR^{110}R^{110}$, $-NR^{110}OR^{110}$, $-NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)C(=O)R^{110}$, $-NR^{110}C(=O)OR^{110}$, $-NR^{110}C(=O)C(=O)OR^{110}$, $-NR^{110}C(=O)NR^{110}R^{110}$, $-NR^{110}C(=O)NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)NR^{110}C(=O)OR^{110}$, $-NR^{110}C(=O)C(=O)NR^{110}R^{110}$, $-NR^{110}S(=O)_2R^{110}$, $-NR^{110}S(=O)_2NR^{110}R^{110}$, $-NR^{110}P(=O)R^{111}R^{111}$, $-NR^{110}P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-NR^{110}P(=O)(OR^{110})(OR^{110})$, $-OR^{110}$, =O, –OCN, $-OC(=O)R^{110}$, $-OC(=O)NR^{110}R^{110}$, $-OC(=O)OR^{110}$, $-OS(=O)R^{110}$, $-OS(=O)_2R^{110}$, $-OS(=O)_2OR^{110}$, $-OS(=O)_2NR^{110}R^{110}$, $-OP(=O)R^{111}R^{111}$, $-OP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-OP(=O)(OR^{110})(OR^{110})$, $-Si(R^{110})_3$, –SCN, =S, $-S(=O)_nR^{110}$, $-S(=O)_2OR^{110}$, $-SO_3R^{110}$, $-S(=O)_2NR^{110}R^{110}$, $-S(=O)NR^{110}R^{110}$, $-P(=O)R^{111}R^{111}$, $-P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, and $-P(=O)(OR^{110})(OR^{110})$.

Embodiment 454. The compound of any of Embodiments 1-451, 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 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, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{110}R^{110}$, –NC, $-NO_2$, $-NR^{110}R^{110}$, $-NR^{110}OR^{110}$, $-NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)OR^{110}$, $-NR^{110}C(=O)NR^{110}R^{110}$, $-NR^{110}C(=O)NR^{110}C(=O)R^{110}$, $-NR^{110}S(=O)_2R^{110}$, $-NR^{110}S(=O)_2NR^{110}R^{110}$, $-NR^{110}P(=O)R^{111}R^{111}$, $-NR^{110}P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-NR^{110}P(=O)(OR^{110})(OR^{110})$, $-OR^{110}$, =O, –OCN, $-OC(=O)R^{110}$, $-OC(=O)NR^{110}R^{110}$, $-OS(=O)_2NR^{110}R^{110}$, –

$OP(=O)R^{111}R^{111}$, $-OP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, –SCN, =S, $-S(=O)_nR^{110}$, $-S(=O)_2NR^{110}R^{110}$, $-S(=O)NR^{110}R^{110}$, $-P(=O)R^{111}R^{111}$, and $-P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$.

Embodiment 455. The compound of any of Embodiments 1-451, 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 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, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{110}R^{110}$, $-NO_2$, $-NR^{110}R^{110}$, $-NR^{110}OR^{110}$, $-NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)NR^{110}R^{110}$, $-NR^{110}S(=O)_2R^{110}$, $-NR^{110}S(=O)_2NR^{110}R^{110}$, $-OR^{110}$, =O, –OCN, $-OC(=O)R^{110}$, $-S(=O)_nR^{110}$, $-S(=O)_2NR^{110}R^{110}$, and $-S(=O)NR^{110}R^{110}$.

Embodiment 456. The compound of any of Embodiments 1-451, 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 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, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{110}R^{110}$, $-NO_2$, $-NR^{110}R^{110}$, $-NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)NR^{110}R^{110}$, $-NR^{110}S(=O)_2R^{110}$, $-NR^{110}S(=O)_2NR^{110}R^{110}$, $-OR^{110}$, =O, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{110}R^{110}$.

Embodiment 457. The compound of any of Embodiments 1-451, 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 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, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{110}R^{110}$, $-NR^{110}R^{110}$, $-NR^{110}C(=O)R^{110}$, $-NR^{110}S(=O)_2R^{110}$, $-OR^{110}$, =O, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{110}R^{110}$.

Embodiment 458. The compound of any of Embodiments 1-451, 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 halogen, phenyl, benzyl, C_{3-6}cycloalkyl, 3-6 membered heterocycloalkyl, 5-6 membered heteroaryl, halogen, –CN, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{110}R^{110}$, $-NR^{110}R^{110}$, $-OR^{110}$, =O, $-S(=O)_nR^{110}$, and $-S(=O)_2NR^{110}R^{110}$.

Embodiment 459. The compound of any of Embodiments 1-451, 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 halogen, halogen, and $-NR^{110}R^{110}$.

Embodiment 460. The compound of any of Embodiments 1-451, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl, halogen, and $-NR^{110}R^{110}$.

Embodiment 461. The compound of any of Embodiments 1-451, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{110}R^{110}$.

Embodiment 462. The compound of any of Embodiments 1-451, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is $-NR^{110}R^{110}$.

Embodiment 463. The compound of any of Embodiments 1-451, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is C_{1-6}alkyl.

Embodiment 464. The compound of any of Embodiments 1-451, wherein R^{79} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{110}R^{110}$; R^{89}, R^{99} and R^{109} at each occurrence is C_{1-6}alkyl.

Embodiment 465. The compound of any of Embodiments 1-451, wherein R^{79} at each occurrence is independently chosen from C_{1-6}alkyl and $-NR^{110}R^{110}$; R^{89}, R^{99} and R^{109} at each occurrence is $-NR^{110}R^{110}$.

Embodiment 466. The compound of any of Embodiments 1-451, wherein R^{79} at each occurrence is $-NR^{110}R^{110}$; R^{89}, R^{99} and R^{109} at each occurrence is C_{1-6}alkyl.

Embodiment 467. The compound of any of Embodiments 1-466, wherein R^{110} at each occurrence is independently chosen from H, C_{1-6}alkyl and C_{1-6}-haloalkyl.

Embodiment 468. The compound of any of Embodiments 1-466, wherein R^{110} at each occurrence is independently chosen from H and C_{1-6}alkyl.

Embodiment 469. The compound of any of Embodiments 1-466, wherein R^{110} at each occurrence is C_{1-6}alkyl.

Embodiment 470. The compound of any of Embodiments 1-466, wherein R^{110} at each occurrence is H.

Embodiment 471. The compound of any of Embodiments 1-470, wherein R^{111} at each occurrence is independently chosen from C_{1-6}alkyl and C_{1-6}-haloalkyl.

Embodiment 472. The compound of any of Embodiments 1-470, wherein R^{111} at each occurrence is C_{1-6}alkyl.

Embodiment 473. The compound of any of Embodiments 1-470, wherein R^{111} at each occurrence is C_{1-6}-haloalkyl.

Embodiment 474. The compound of any of Embodiments 1-473, wherein n at each occurrence is independently chosen from 0, 1, and 2.

Embodiment 475. The compound of any of Embodiments 1-473, wherein n at each occurrence is independently chosen from 0 and 2.

Embodiment 476. The compound of any of Embodiments 1-473, wherein n at each occurrence is independently chosen from 1 and 2.

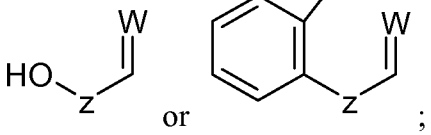
Embodiment 477. The compound of any of Embodiments 1-473, wherein n at each occurrence is independently chosen from 0 and 1.

Embodiment 478. The compound of any of Embodiments 1-473, wherein n at each occurrence is 0.

Embodiment 479. The compound of any of Embodiments 1-473, wherein n at each occurrence is 1.

Embodiment 480. The compound of any of Embodiments 1-473, wherein n at each occurrence is 2.

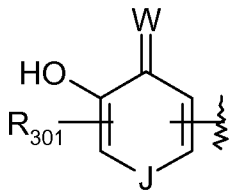
Embodiment 481. The compound of any of Embodiments 1-480, wherein neither R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, nor R^{28} contain either of the following chemical moieties



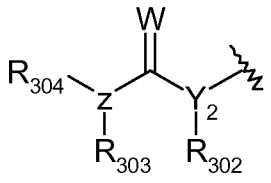
;

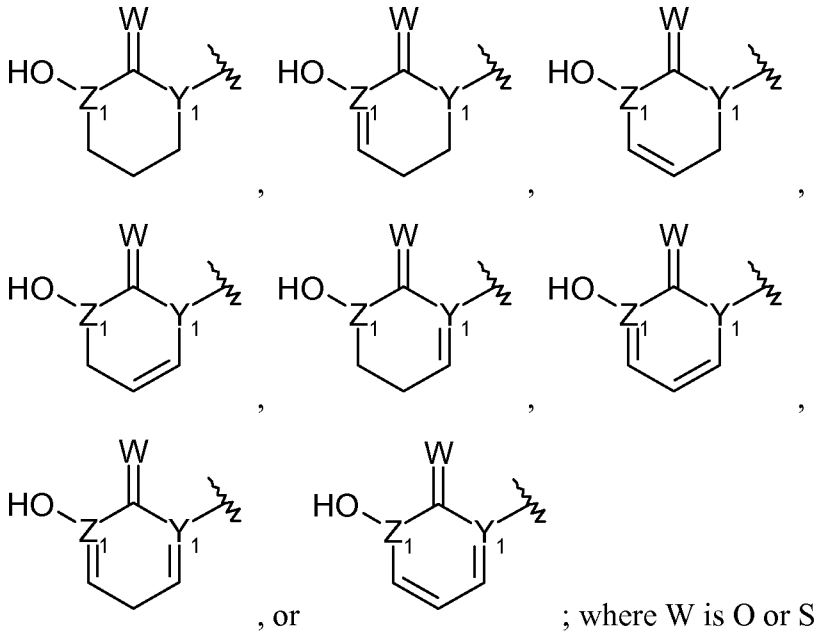
wherein W is O or S, and Z is N or C.

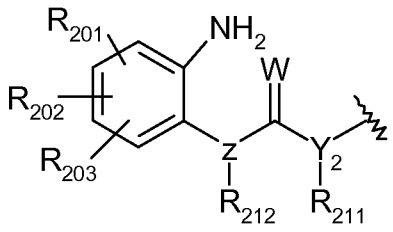
Embodiment 482. The compound of any of Embodiments 1-481, wherein neither R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17}, R^{18}, R^{19}, R^{20}, R^{21}, R^{22}, R^{23}, R^{24}, R^{25}, R^{26}, R^{27}, nor R^{28} is:

(a) 

; where W is O or S; J is O, NH or NCH_3; and R_{301} is hydrogen or alkyl;

(b)  ; where W is O or S; Y_2 is absent, N, or CH; Z is N or CH; R_{302} and R_{304} are independently hydrogen, hydroxyl, or an aliphatic group; provided that if R_{302} and R_{304} are both present, one of R_{302} or R_{304} must be hydroxyl and if Y_2 is absent, R_{304} must be hydroxyl; and R_{303} is hydrogen or aliphatic group;

(c)  ; where W is O or S; Y_1 and Z_1 are independently N, C or CH; or

(d)  , where Z is N or CH; Y_2 is absent, N, or CH; W is O or S; R_{211} and R_{212} are independently selected from hydrogen or aliphatic group; R_{201}, R_{202} and R_{203} are independently selected from hydrogen, hydroxyl, amino, halogen, alkoxy, alkylamino, dialkylamino, CF_3, CN, NO_2, sulfonyl, acyl, aliphatic group, substituted aliphatic group, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic;

wherein for the purpose of this Embodiment, the following definitions apply:

an aliphatic group is a non-aromatic moiety that may be saturated (e.g. single bond) or contain one or more units of unsaturation, e.g., double and/or triple bonds; an aliphatic group may be straight chained, branched or cyclic, contain carbon, hydrogen or, optionally, one or more heteroatoms and may be substituted or unsubstituted;

"acyl" refers to hydrogen, alkyl, partially saturated or fully saturated cycloalkyl, partially saturated or fully saturated heterocycle, aryl, and heteroaryl substituted carbonyl groups;

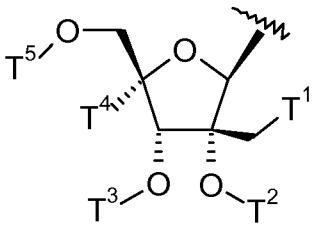
"alkoxy" embraces linear or branched oxy-containing radicals each having alkyl portions of one to about twenty carbon atoms or, preferably, one to about twelve carbon atoms; and

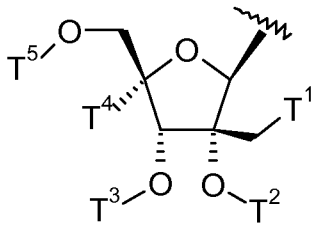
"heterocyclic" refers to saturated, partially unsaturated and unsaturated heteroatom-containing ringshaped radicals, where the heteroatoms may be selected from nitrogen, sulfur and oxygen;

Embodiment 483. The compound of any of Embodiments 1-482, wherein A is not S.

Embodiment 484. The compound of any of Embodiments 1-483, wherein R^1 is not $-OR^{20}$.

Embodiment 485. The compound of any of Embodiments 1-484, wherein R^8 is not tetrahydrofuranyl substituted by 4 or 5 R^{19}.

Embodiment 486. The compound of any of Embodiments 1-484, wherein R^8 is not  , wherein T^1 is R^{39}; T^2, T^3, and T^5 are independently chosen from R^{30}, $-C(=O)R^{30}$, $-C(=O)NR^{32}R^{33}$, $-C(=O)OR^{30}$, $-C(=NR^{35})NR^{32}R^{33}$, $-S(=O)R^{30}$, $-S(=O)_2R^{30}$, $-S(=O)_2OR^{30}$, $-S(=O)_2NR^{32}R^{33}$, $-P(=O)R^{38}R^{38}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, and $-P(=O)(SR^{30})(SR^{30})$; and T^4 is R^{19}.

Embodiment 487. The compound of any of Embodiments 1-484, wherein R^8 is not  , wherein T^1 is hydrogen, fluoro, azido, amino, hydroxyl, C_{1-3}alkoxy, mercapto, or C_{1-3}alkylthio; T^2, T^3, and T^5 are independently chosen from R^{30}, –$C(=O)R^{30}$, –$C(=O)NR^{32}R^{33}$, –$C(=O)OR^{30}$, –$C(=NR^{35})NR^{32}R^{33}$, –$S(=O)R^{30}$, –$S(=O)_2R^{30}$, –$S(=O)_2OR^{30}$, –$S(=O)_2NR^{32}R^{33}$, –$P(=O)R^{38}R^{38}$, –$P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, –$P(=O)(OR^{30})(OR^{30})$, and –$P(=O)(SR^{30})(SR^{30})$; and T^4 is hydrogen, azido, methyl, hydroxymethyl, or fluoromethyl.

Embodiment 488. The compound of any of Embodiments 1-487, wherein R^{10} is not –CN.

Embodiment 489. The compound of any of Embodiments 1-488, wherein none of R^1 and R^2, R^1 and R^3, R^1 and R^5, or R^1 and R^{11}, together with the atoms linking them, form a heterocycloalkyl optionally substituted by one or more R^{19} or a heteroaryl optionally substituted by one ore more R^{19}.

Embodiment 490. The compound of any of Embodiments 1-488, wherein R^1 and R^{11} do not, together with the atoms linking them, form a heterocycloalkyl optionally substituted by one or more R^{19} or a heteroaryl optionally substituted by one or more R^{19}.

Embodiment 491. The compound of any of Embodiments 1-490, wherein neither R^7 nor R^{10} is H, or neither R^8 nor R^9 is H.

Embodiment 492. The compound of Embodiment 491, wherein neither R^7 nor R^{10} is H.

Embodiment 493. The compound of Embodiment 491, wherein neither R^8 nor R^9 is H.

Embodiment 494. The compound of any of Embodiments 1-493, wherein neither R^3 and R^4 nor R^5 and R^6 together form =O, =NR^{20}, =NOR^{20}, or =S.

Embodiment 495. The compound of any of Embodiments 1-494, wherein neither R^3 and R^4 nor R^5 and R^6 together form =O.

Embodiment 496. The compound of any of Embodiments 1-495, wherein

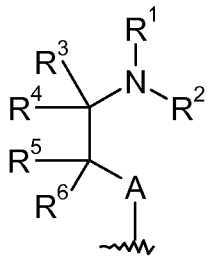
(a) when R^1 is H, R^2 is neither aryl optionally substituted by one or more R^{19} nor heteroaryl optionally substituted by one or more R^{19},

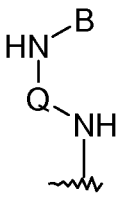
(b) when R^2 is H, R^1 is neither optionally substituted by one or more R^{19} nor heteroaryl optionally substituted by one or more R^{19},

(c) R^3, R^4, R^5, and R^6 are not $-NHR^{22}$, $-NHR^{23}$, $-SO_2NHR^{22}$, $-SO_2NHR^{23}$, $-C(=O)NHR^{22}$, or $-C(=O)NHR^{23}$, wherein R^{22} and R^{23} are either aryl optionally substituted by one or more R^{59} or heteroaryl optionally substituted by one or more R^{59}, and

(d) R^3, R^4, R^5, and R^6 do not contain a group of formula $-NHR$, $-SO_2NHR$, or $-C(=O)NHR$, wherein R is optionally substituted aryl, or optionally substituted heteroaryl.

Embodiment 497. The compound of any of Embodiments 1-496, wherein the



group of formula does not together form a group of formula  , wherein

B is an optionally substituted aryl, or optionally substituted heteroaryl;

Q is a C_{1-4}alkylidene chain in which each methylene unit of said Q is substituted by R^2 and $R^{2'}$, and up to two non-adjacent methylene units of said Q are optionally and independently replaced by $-SO_2$ or $-C(=O)$;

each R^2 is independently selected from H, $-OH$, C_{1-10}alkyl, C_{1-10} aliphatic, (C_{1-10} aliphatic)-NH-(C_{1-10} aliphatic); -O-(C_{1-10} aliphatic); $-NH_2$, -NH(C_{1-10} aliphatic), $-N(C_{1-10}$ aliphatic$)_2$, -C(=O)R, aryl, or heteroaryl, wherein said aliphatic, aryl, or heteroaryl is optionally substituted;

each $R^{2'}$ is independently selected from H and an optionally substituted C_{1-10} aliphatic group; and

R is selected from an optionally substituted group selected from C_{1-10} aliphatic, aryl, aralkyl, heteroaryl, and heteroaralkyl;

wherein for the purpose of this Embodiment, the following definitions apply:

"alkylidene chain" refers to a straight or branched carbon chain that may be fully saturated or have one or more units of un saturation and has two points of attachment to the rest of the molecule;

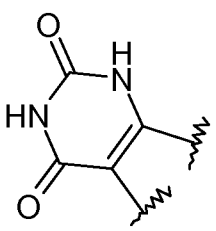
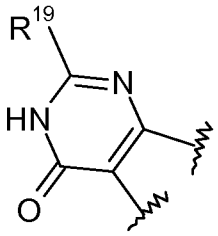
"aliphatic" or "aliphatic group" means a straight-chain or branched, substituted or unsubstituted C_1-C_8 hydrocarbon chain that is completely saturated or that contains one or more units of unsaturation, or a monocyclic C_3-C_8 hydrocarbon or bicyclic C_8-C_{12} hydrocarbon that is completely saturated or that contains one or more units of unsaturation, but which is not aromatic, that has a single point of attachment to the rest of the molecule wherein any individual ring in said bicyclic ring system has 3-7 members.

Embodiment 498. The compound of any of Embodiments 1-497, wherein R^8 is neither aryl optionally substituted by one or more R^{19} nor heteroaryl optionally substituted by one or more R^{19}.

Embodiment 499. The compound of any of Embodiments 1-498, wherein:

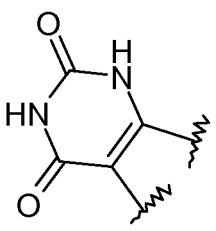
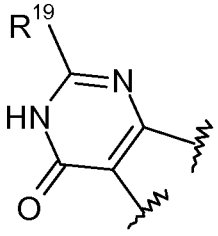
(a) when R^9 is $-NH_2$, R^{10} is not $-C(=O)NH_2$;

(b) when R^9 is $-NHC(=S)NHCOPh$, R^{10} is not $-C(=O)OR^{20}$, wherein R^{20} is alkyl optionally substituted by R^{49}; and

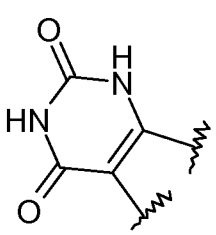
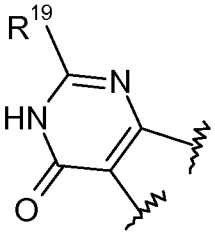
(c) R^9 and R^{10} do not, together with the atoms linking them, form a group of formula  or  , wherein R^{19} is as defined herein.

Embodiment 500. The compound of any of Embodiments 1-499, wherein:

(a) when R^9 is $-NH_2$, R^{10} is not $-C(=O)NH_2$; and

(b) R^9 and R^{10} do not, together with the atoms linking them, form a group of formula  or  , wherein R^{19} is as defined herein.

Embodiment 501. The compound of any of Embodiments 1-500, wherein R^9 and R^{10} do not, together with the atoms linking them, form a group of formula


or

, wherein R^{19} is as defined herein.

Embodiment 502. The compound of any of Embodiments 1-501, wherein neither R^1 and R^2 nor R^1 and R^3, together with the atoms linking them, form a heterocycloalkyl optionally substituted by one or more R^{19} or a heteroaryl optionally substituted by one or more R^{19}, wherein R^{19} is as defined herein.

Embodiment 503. The compound of any of Embodiments 1-502, wherein R^{10} is not –CN, aryl optionally substituted by one or more R^{19}, heterocycloalkyl optionally substituted by one or more R^{19}, or heteroaryl optionally substituted by one or more R^{19}, wherein R^{19} is as defined herein.

Embodiment 504. The compound of any of Embodiments 1-503, wherein R^9 is neither $–NH_2$ nor –OH when R^{10} is $–C(=O)R^{20}$, $–C(=O)OR^{20}$, or $–C(=O)NR^{22}R^{23}$, wherein R^{20}, R^{22}, and R^{23} are as defined herein.

Embodiment 505. The compound of any of Embodiments 1-504, wherein when

(a) R^9 is chosen from H, C_1-C_6alkyl, C_3-C_7cycloalkyl and $-(CH_2)_{n1}-R^{411}$ wherein the subscript n1 is an integer of from 0 to 3 and R^{411} is selected from C_1-C_6alkoxy, C_1-C_6alkylthio, mono- or di-(C_1-C_6alkyl)amino, amino, phenyl, pyridyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, thiazolyl, pyrazolyl, and thienyl, wherein each of the rings is optionally substituted with from 1 to 3 substituents selected from halogen, N_3, NO_2, CN, C_1-C_6alkyl, OR^{412}, $N(R^{412})_2$, CO_2R^{412} and $CON(R^{412})_2$, wherein each R^{412} is independently H or C_1-C_6alkyl; and

(b) R^{10} is chosen from $–R^{401}$, $–OR^{401}$, $–SR^{401}$, $–N(R^{410})R^{401}$, $–C(=O)R^{401}$, and $–CH(OH)R^{401}$, wherein R^{410} is selected from H, C_1-C_6alkyl and $C(=O)C_1$-C_6alkyl; and R^{401} is chosen from H, halo, CN, NO_2, N_3, C_1-C_6alkyl, C_3-C_7cycloalkyl, $-C(R^{413})=C(R^{413})_2$, $-C\equiv CR^{413}$ or $-(CH_2)_{n2}-R^{414}$; wherein each R^{413} is independently selected from H, F, CI, Br, CN, C_1-C_6alkyl, C_3-C_7cycloalkyl, $(CH_2)_{n2}-R^{414}$ and $C(O)-(CH_2)_{n2}-R^{414}$; and wherein each subscript n2 is independently an integer of from 0 to 3 and each R^{414} is independently selected from C_1-C_6alkoxy, C_1-C_6alkylthio, mono- or di-(C_1-C_6)alkylamino, amino, phenyl, pyridyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl,

thiazolyl, pyrazolyl, and thienyl, wherein each of the rings is optionally substituted with from 1 to 3 substituents selected from halogen, NO_2, N_3, CN, $(C_1$-$C_6)$alkyl, OR^{415}, $N(R^{415})_2$, CO_2R^{415} and $CON(R^{415})_2$, wherein each R^{415} is independently H or C_1-C_6alkyl; and wherein any alkyl or cycloalkyl portions of R^{401} are optionally substituted with from one to five F substituents;

R^1 and R^{11} do not, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by one or more R^{19}, wherein R^{19} is as defined herein.

Embodiment 506. The compound of any of Embodiments 1-504, wherein when

(a) R^9 is chosen from H, C_1-C_6alkyl, C_3-C_7cycloalkyl and $-(CH_2)_{n1}$-R^{411} wherein the subscript n1 is an integer of from 0 to 3 and R^{411} is selected from C_1-C_6alkoxy, C_1-C_6alkylthio, mono- or di-$(C_1$-C_6alkyl)amino, amino, phenyl, pyridyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, thiazolyl, pyrazolyl, and thienyl, wherein each of the rings is optionally substituted with from 1 to 3 substituents selected from halogen, N_3, NO_2, CN, C_1-C_6alkyl, OR^{412}, $N(R^{412})_2$, CO_2R^{412} and $CON(R^{412})_2$, wherein each R^{412} is independently H or C_1-C_6alkyl; and

(b) R^{10} is chosen from $-R^{401}$, $-OR^{401}$, $-SR^{401}$, $-N(R^{410})R^{401}$, $-C(=O)R^{401}$, and $-CH(OH)R^{401}$, wherein R^{410} is selected from H, C_1-C_6alkyl and $C(=O)C_1$-C_6alkyl; and R^{401} is chosen from H, halo, CN, NO_2, N_3, C_1-C_6alkyl, C_3-C_7cycloalkyl, $-C(R^{413})=C(R^{413})_2$, $-C{\equiv}CR^{413}$ or $-(CH_2)_{n2}$-R^{414}; wherein each R^{413} is independently selected from H, F, CI, Br, CN, C_1-C_6alkyl, C_3-C_7cycloalkyl, $(CH_2)_{n2}$-R^{414} and $C(O)$-$(CH_2)_{n2}$-R^{414}; and wherein each subscript n2 is independently an integer of from 0 to 3 and each R^{414} is independently selected from C_1-C_6alkoxy, C_1-C_6alkylthio, mono- or di-$(C_1$-$C_6)$alkylamino, amino, phenyl, pyridyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, thiazolyl, pyrazolyl, and thienyl, wherein each of the rings is optionally substituted with from 1 to 3 substituents selected from halogen, NO_2, N_3, CN, $(C_1$-$C_6)$alkyl, OR^{415}, $N(R^{415})_2$, CO_2R^{415} and $CON(R^{415})_2$, wherein each R^{415} is independently H or C_1-C_6alkyl; and wherein any alkyl or cycloalkyl portions of R^{401} are optionally substituted with from one to five F substituents;

R^1 and R^{11} do not, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-4 R^{403}, wherein each R^{403} is independently chosen from C_1-C_6alkyl, C_3-C_7cycloalkyl, $-(CH_2)_{n4}$-R^{419} and $-C(O)$-$(CH_2)_{n4}$-R^{419}; wherein the subscript n4 is an integer of from 0 to 4 and each R^{419} is independently selected from C_1-C_6alkoxy, C_1-C_6alkylthio, mono- or di-$(C_1$-$C_6)$alkylamino, amino, phenyl, pyridyl,

furanyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, thiazolyl, pyrazolyl, and thienyl, wherein each of the rings is optionally substituted with from 1 to 3 substituents selected from halogen, N_3, NO_2, CN, C_1-C_6alkyl, -OR^{420}, -$N(R^{420})_2$, CO_2R^{420} and $CON(R^{420})_2$, wherein each R^{420} is independently H or C_1-C_6alkyl; and wherein any alkyl or cycloalkyl portions of R^{403} are optionally substituted with from one to five F substituents.

Embodiment 507. The compound of any of Embodiments 1-504, wherein R^1 and R^{11} do not, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by 1-4 R^{403}, wherein each R^{403} is independently chosen from C_1-C_6alkyl, C_3-C_7cycloalkyl, -$(CH_2)_{n4}$-R^{419} and -C(O)-$(CH_2)_{n4}$-R^{419}; wherein the subscript n4 is an integer of from 0 to 4 and each R^{419} is independently selected from C_1-C_6alkoxy, C_1-C_6alkylthio, mono- or di-(C_1-C_6)alkylamino, amino, phenyl, pyridyl, furanyl, pyrrolyl, imidazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, thiazolyl, pyrazolyl, and thienyl, wherein each of the rings is optionally substituted with from 1 to 3 substituents selected from halogen, N_3, NO_2, CN, C_1-C_6alkyl, -OR^{420}, -$N(R^{420})_2$, CO_2R^{420} and $CON(R^{420})_2$, wherein each R^{420} is independently H or C_1-C_6alkyl; and wherein any alkyl or cycloalkyl portions of R^{403} are optionally substituted with from one to five F substituents.

Embodiment 508. The compound of any of Embodiments 1-504, wherein R^1 and R^{11} do not, together with the atoms linking them, form a 6-7 membered heterocycloalkyl optionally substituted by one or more R^{19}, wherein R^{19} is as defined herein.

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 therefor. 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

HCl for hydrochloric acid

H_2SO_4 for sulfuric acid

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

NMR

Proton NMR spectra are recorded using a Bruker AMX-300 NMR machine at 300 MHz or a Bruker Avance NMR machine at 400 MHz. Shifts are reported in ppm values relative to an internal standard of tetramethylsilane (TMS) or residual protic solvent. The following abbreviations are used to describe the splitting patterns: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (double-doublet), dt (double-triplet), br (broad).

LCMS Methods

Samples analysed by High Performance Liquid Chromatography-Mass Spectrometry employed the following conditions.

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

Method 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

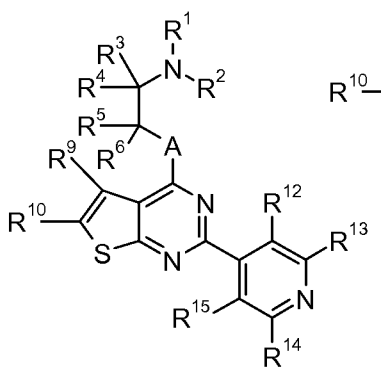
Several methods for the chemical synthesis of 4-substituted-2-(pyridin-4-yl)-thieno[2,3-d]pyrimidine compounds ("4PT23P compounds") and 4-substituted-2-(pyridin-4-yl)-thieno[3,2-d]pyrimidine compounds ("4PT32P compounds") of the present invention are described herein. These and/or other well known methods 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. Unless otherwise stated, compounds are of commercial origin or readily synthesized by standard methods well known to one skilled in the art of organic synthesis.

It is understood that the examples and embodiments described herein are for illustrative purposes only and that various modifications or changes in light thereof will be suggested to persons skilled in the art and are to be included within the spirit and purview of this invention. Specific chemical transformations are listed in the ensuing schemes and one skilled in the art appreciates that a variety of different reagents may be used in place of those listed. Common replacements for such reagents can be found in texts such as "Encyclopedia of Reagents for Organic Synthesis" Leo A. Paquette , John Wiley & Son Ltd (1995) or "Comprehensive Organic Transformations: A Guide to Functional Group Preparations" Richard C. Larock. Wiley-VCH and "Strategic Applications of Named

Reactions in Organic Synthesis" Kurti and Czako, Elsevier, 2005 and references cited therein.

4PT23P compounds

In one approach, compounds of formula [F-1] (where A = NH or N alkyl) are prepared by reacting a compound of formula [F-2] (where X is a halogen such as chlorine or sulfonate) with a compound of formula [F-3] (where A is NH or NH_2 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.



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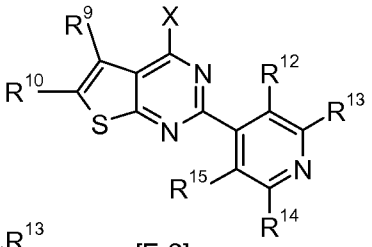

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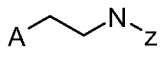
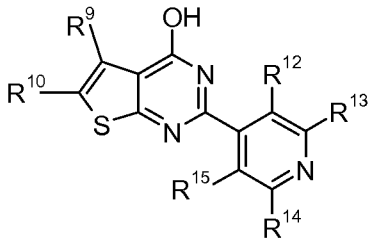


[F-3]

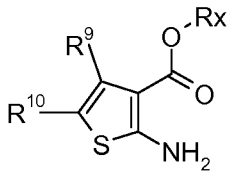
The reaction is suitably conducted at an elevated temperature for example 40 °C. Where Z is a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc, compounds of formula [F-1] are prepared by a suitable deprotection reaction. For example: where Z is a Boc protecting group reaction with 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-1] (where A is O) are prepared by reacting a compound of formula [F-2] (where X is a halogen such as chlorine or sulfonate) with a compound of formula [F-2] (where A = 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-1] 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-2] (where X is a halogen such as chlorine) are prepared by reacting a compound of formula [F-4] 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-2] (where X is a sulfonate) are prepared by reacting a compound of formula [F-4] with a suitably substituted sulfonyl chloride such as 2,4,6-triisopropylbenzenesulfonyl 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.

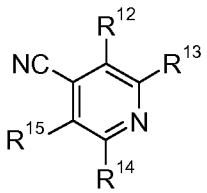


[F-4]

In one approach, compounds of formula [F-4] are prepared by reacting a compound of formula [F-5] (where Rx is an alkyl group such as methyl or ethyl) with a compound of formula [F-6] in a suitable solvent such as dioxane with a suitable base such as potassium-tert-pentylate. The reaction is suitably conducted at ambient temperature.

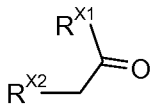


[F-5]

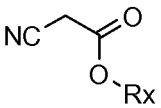


[F-6]

In one approach, compounds of formula [F-5] are prepared by reacting a ketone derivative of formula [F-7] (where R^{x1} and R^{x2} are H, alkyl, aryl or form a cyclic saturated ring) with a cyanoacetic acid derivative of formula [F-8] (where Rx is an alkyl group such as methyl or ethyl) with elemental sulphur in the presence of a base such as morpholine in a suitable solvent such as ethanol. The reaction is suitably conducted at an elevated temperature for example 80-90 °C.



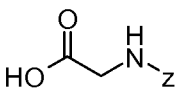
[F-7]



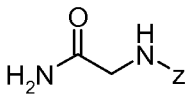
[F-8]

In one approach, compounds of formula [F-3] (where A is OH) are prepared by reacting a compound of formula [F-9] (where Z on the terminal nitrogen is H, alkyl or a

suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) with a reducing agent such as borane-THF complex in a suitable solvent such as THF. The reaction is suitably conducted at low temperature for example 0 °C. In one approach, compounds of formula [F-3] (where A is NH_2) are prepared by reacting a compound of formula [F-10] (where Z on the terminal nitrogen is H, alkyl or a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) with a reducing agent such as borane-THF complex in a suitable solvent such as THF. The reaction is suitably conducted at low temperature for example 0 °C. In one approach, compounds of formula [F-10] are prepared by reacting compounds of formula [F-9] with Boc anhydride in the presence of a suitable base such as pyridine, ammonium carbonate in a suitable solvent such as dioxane. The reaction is suitably conducted at ambient temperature.

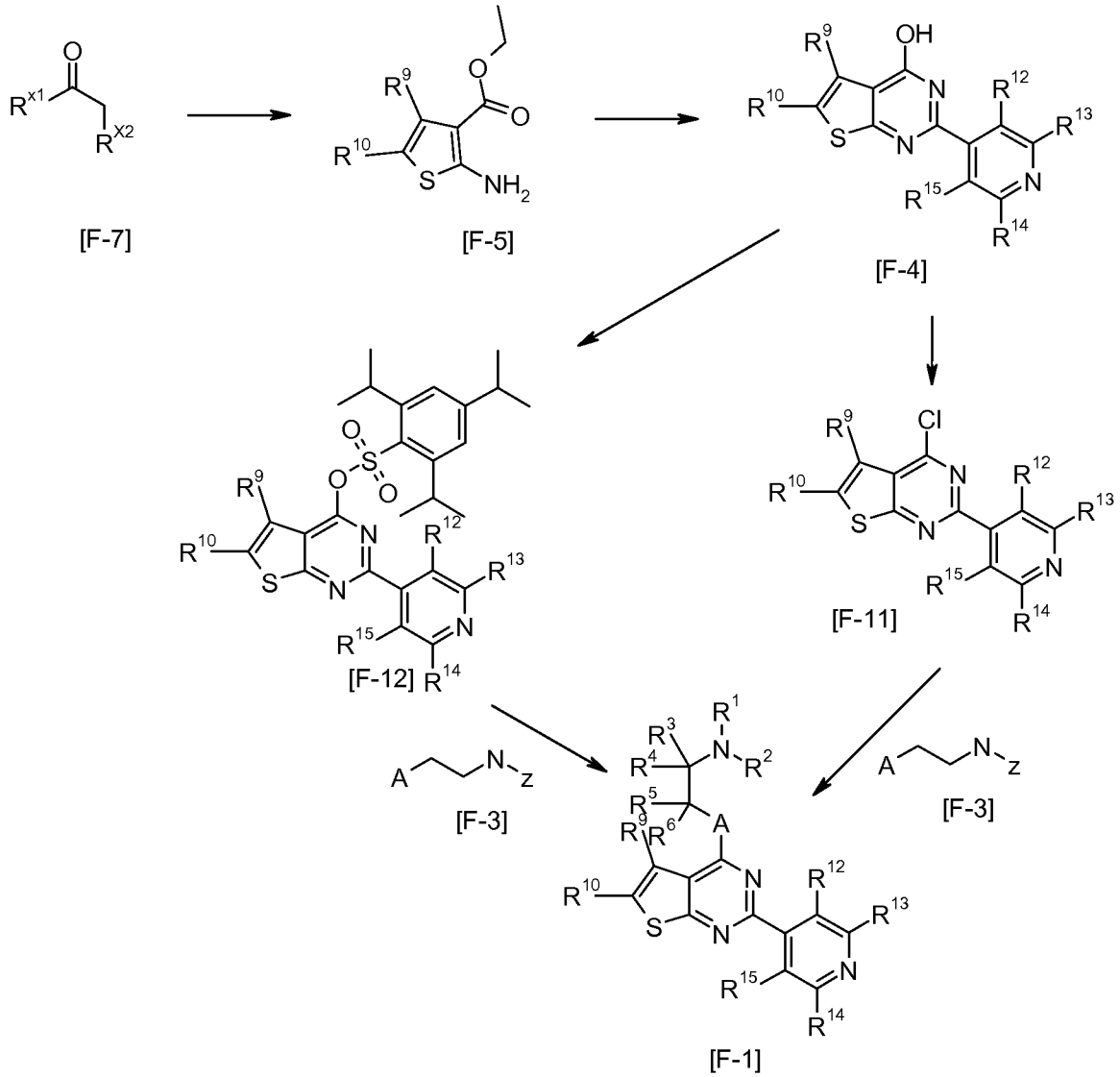


[F-9]



[F-10]

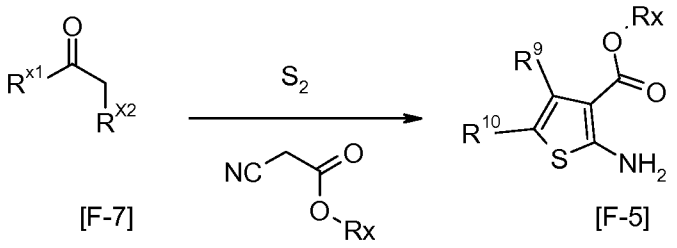
An example of a method as described above is illustrated in the following scheme.



General synthesis of 2-amino-4,5-substitued-thiophene-3-carboxylic acid ethyl esters of general formula [F-5] (Scheme A1)

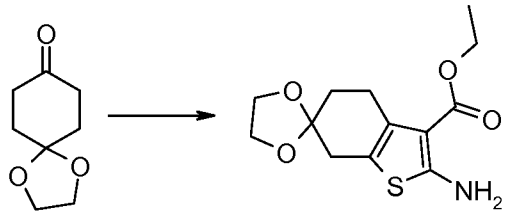
2-amino-4,5-substitued-thiophene-3-carboxylic acid ethyl esters of general formula [F-5] were synthesised by a cyclisation reaction with cyano-acetic acid ethyl ester of general formula [F-8], a substituted ketone of general formula [F-7] and elemental sulphur in the presence of morpholine in a polar protic solvent such as ethanol at reflux (scheme A1).

Scheme A1



[F-7] [F-8] [F-5]

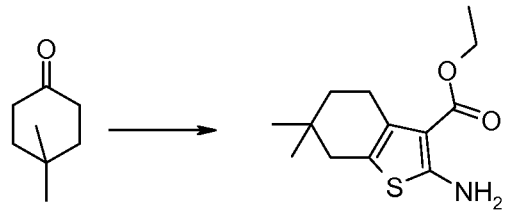
Synthesis of 2-Amino-1,4-Dioxa-spiro[6.6]4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester [AA-1]



[AA-1]

To a mixture of 1,4-Dioxa-spiro[4.5]decan-8-one (1.56 g, 10 mmol), cyano-acetic acid ethyl ester (1.13 g, 10 mmol) and elemental sulphur (320 mg, 10 mmol) in ethanol (20 ml) was added morpholine (870 mg, 10 mmol). The reaction was heated at reflux overnight. The mixture was left to cool down and a precipitate formed which was recovered by filtration and washed with cold ethanol (40 ml), then dried under reduced pressure to give the title compound (2.1 g ,76 %) which was used without further purification. LCMS method: 3, RT: 5.24 min, MI: 284 [M+1]. 1H NMR (300MHz, DMSO): 4.21 (m, 1H), 4.17 (q, 2H), 4.01 (m, 1H,), 3.82 (m, 2H,), 3.08 (m, 1H), 2.68 (m, 1H), 1.91(m, 4H), 1.21 (t, 3H).

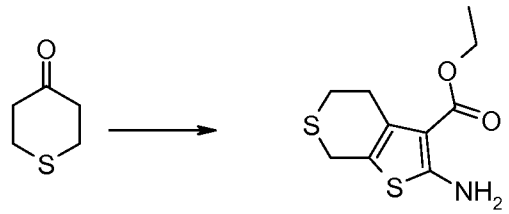
Synthesis of 2-amino-6,6-dimethyl-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester [AA-2]



[AA-2]

To a mixture of 4,4-Dimethyl-cyclohexanone, cyano-acetic acid ethyl ester and elemental sulphur in ethanol was added morpholine. The reaction was reflux overnight. The mixture was left to cool down and a precipitate appeared. The solid was recovered by filtration and to give the title compound as a yellow solid. LCMS method: 3, RT: 5.64 min, MI: 254 [M+1].

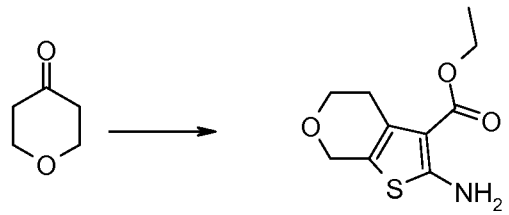
Synthesis of 2-amino-4,7-dihydro-5H-thieno[2,3-c]thiopyran-3-carboxylic acid ethyl ester [AA-3]



[AA-3]

To a mixture of tetrahydro-thiopyran-4-one, cyano-acetic acid ethyl ester and elemental sulphur in ethanol was added morpholine. The reaction was reflux overnight. The mixture was left to cool down and a precipitate appeared. The solid was recovered by filtration and to give the title compound as a yellow solid. LCMS method: 3, RT: 5.78 min, MI: 244 [M+1].

Synthesis of 2-amino-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid ethyl ester [AA-4]



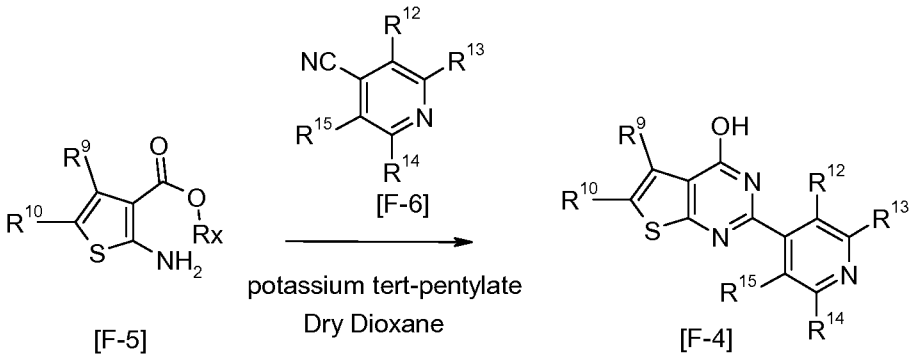
[AA-4]

To a mixture of tetrahydro-pyran-4-one, cyano-acetic acid ethyl ester and elemental sulphur in ethanol was added morpholine. The reaction was reflux overnight. The mixture was left to cool down and a precipitate appeared. The solid was recovered by filtration and to give the title compound as a yellow solid. LCMS method: 3, RT: 5.86 min, MI: 228 [M+1].

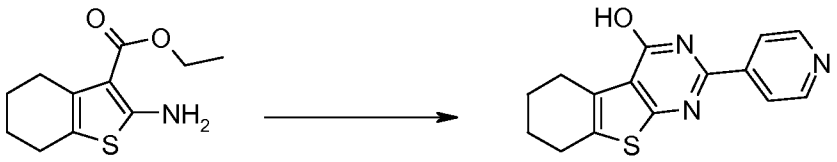
General synthesis of 5, 6-substituted 2-pyridin-4-yl-thieno [2, 3-d] pyrimidin-4-ols of general formula [F-4] (Scheme A2)

4,5-substituted-2-amino-thiophene-3-carboxylic acid alkyl esters of general formula [F-5] were subjected to a cyclisation reaction with 4-cyanopyridine of general formula [F-6] in the presence of a hindered alkoxide base such as potassium-tert-pentylate 1.7M in toluene or potassium-tert-butoxide in a dry non-aprotic solvent such as dioxane or THF at ambient temperature.

Scheme A2

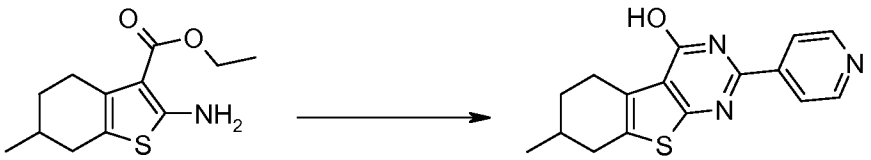


Synthesis of 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-5]



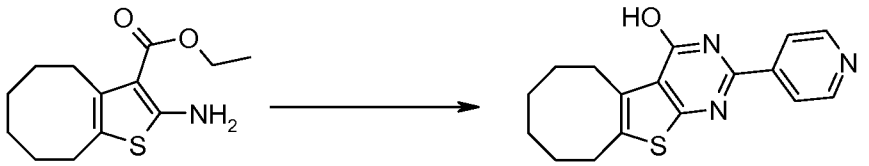
To a solution of 4-cyanopyridine (1.25 g, 12 mmol) in dry dioxane (10 ml) was added 2-amino-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester (2.25 g,10 mmol) followed by potassium-tert-pentylate 1.7M in toluene (12 ml, 20 mmol). The reaction mixture was stirred at room temperature overnight. After completion the precipitate formed was filtered and washed with diethyl ether. The residue was used without any further purification in the next step. LCMS method: 1, RT: 3.54 min, MI: 284 [M+1]. 1H 1 H NMR (300MHz, DMSO): 8.56 (d,2H), 8.12 (d,2H), 2.90 (m,2H), 2.67 (m,2H), 1.76 (m,4H).

The following compounds were prepared according to the general synthesis shown in scheme A2:



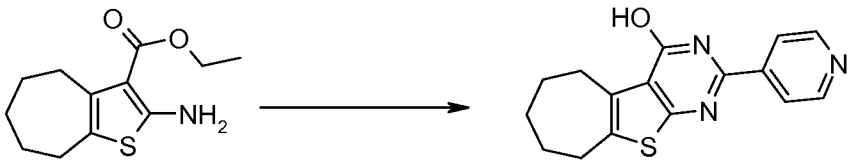
[AA-6]

7-methyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-6] was prepared by reaction of 2-amino-6-methyl-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as an off-white solid. LCMS method: 1, RT: 3.68min, MI: 298 [M+1].



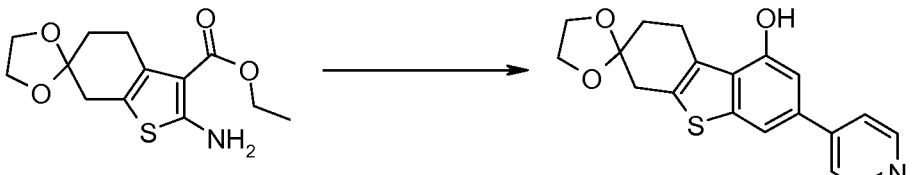
[AA-7]

2-pyridin-4-yl-5,6,7,8,9,10-hexahydro-11-thia-1,3-diaza-cycloocta[a]inden-4-ol [AA-7] was prepared by reaction of 2-amino-4,5,6,7,8,9-hexahydro-cycloocta[b]thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as an off-white solid. LCMS method: 1, RT: 3.72 min, MI: 312 [M+1].



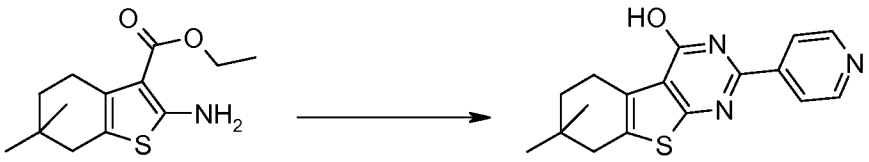
[AA-8]

2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-ol [AA-8] was prepared by reaction of 2-amino-5,6,7,8-tetrahydro-4H-cyclohepta[b]thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 2, RT: 3.87 min, MI: 298 [M+1].



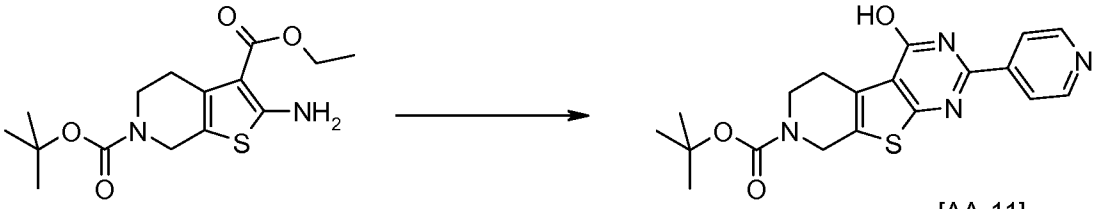
[AA-1] [AA-9]

1,4-Dioxa-spiro[7.7]-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-9] was prepared by reaction of 2-Amino-1,4-Dioxa-spiro[6.6]4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester [AA-1], 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 3, RT: 2.80 min, MI: 342 [M+1].



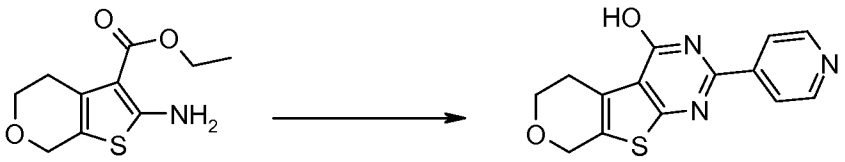
[AA-2] [AA-10]

7,7-dimethyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-10] was prepared by reaction of 2-amino-6,6-dimethyl-4,5,6,7-tetrahydro-benzo[b]thiophene-3-carboxylic acid ethyl ester [AA-2], 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as an off-white solid. LCMS method: 3, RT: 4.24 min, MI: 312 [M+1].



[AA-11]

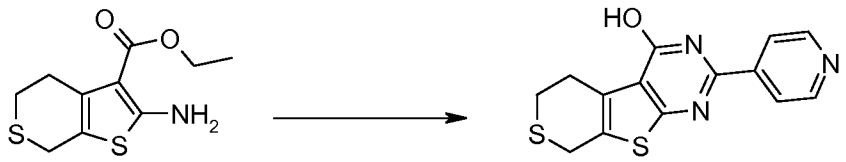
4-hydroxy-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5]thieno[2,3-d]pyrimidine-7-carboxylic acid tert-butyl ester [AA-11] was prepared by reaction of 2-amino-4,7-dihydro-5H-thieno[2,3-c]pyridine-3,6-dicarboxylic acid 6-tert-butyl ester 3-ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as an off-white solid. LCMS method: 1, RT: 3.50 min, MI: 384 [M+1].



[AA-4] [AA-12]

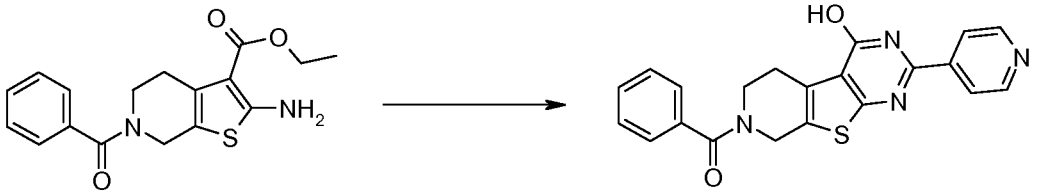
2-pyridin-4-yl-5,8-dihydro-6H-pyrano[4',3':4,5]thieno[2,3-d]pyrimidin-4-ol [AA-12] was prepared by reaction of 2-amino-4,7-dihydro-5H-thieno[2,3-c]pyran-3-carboxylic acid ethyl ester [AA-4], 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and

dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 3, RT: 3.50 min, MI: 286 [M+1].



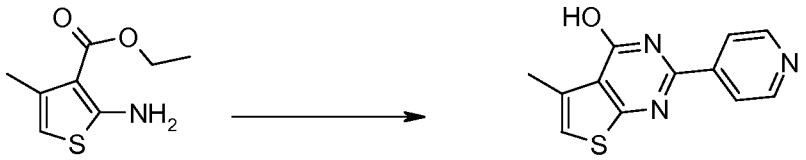
[AA-3] [AA-13]

2-pyridin-4-yl-5,8-dihydro-6H-thiopyrano[4',3':4,5]thieno[2,3-d]pyrimidin-4-ol [AA-13] was prepared by reaction of 2-amino-4,7-dihydro-5H-thieno[2,3-c]thiopyran-3-carboxylic acid ethyl ester [AA-3], 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 2, RT: 3.14 min, MI: 302 [M+1].



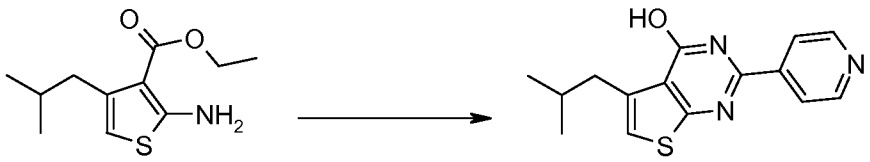
[AA-14]

(4-Hydroxy-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-7-yl)-phenyl-methanone [AA-14] was prepared by reaction of 2-Amino-6-benzoyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and THF at room temperature to give the title compound as a yellow solid. LCMS method: 3, RT: 3.02 min, MI: 389[M+1].



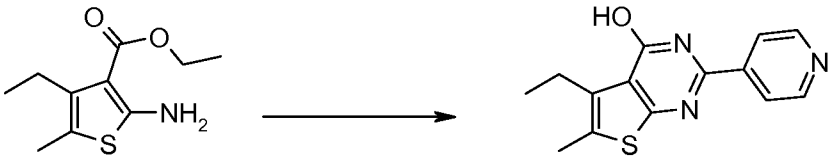
[AA-15]

5-Methyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-15] was prepared by reaction of ethyl 2-amino-4-methylthiophene-3-carboxylate, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and THF at room temperature to give the title compound as a yellow solid. LCMS method: 3, RT: 2.56 min, MI: 244[M+1].



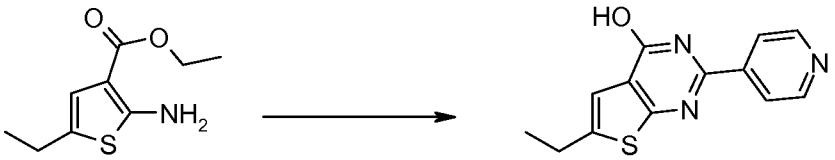
[AA-16]

5-isobutyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-16] was prepared by reaction of 2-amino-4-isobutyl-thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a brown solid. LCMS method: 2, RT: 3.14 min, MI: 286 [M+1].



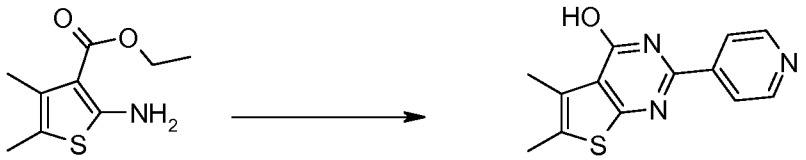
[AA-17]

5-ethyl-6-methyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-17] was prepared by reaction of 2-amino-4-ethyl-5-methyl-thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a brown solid. LCMS method: 2, RT: 3.26 min, MI: 272 [M+1].



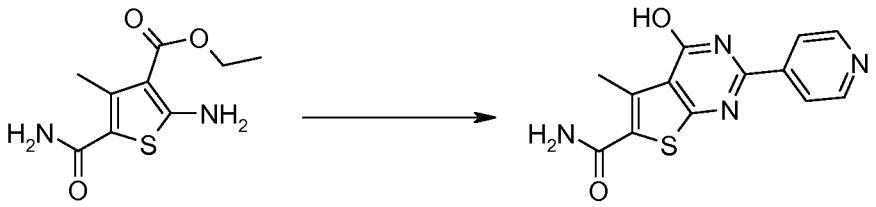
[AA-18]

6-ethyl-2-pyridin-4-yl-thieno [2, 3-d] pyrimidin-4-ol [AA-18] was prepared by reaction of 2-amino-5-ethyl-thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a brown solid. LCMS method: 2, RT: 3.15 min, MI: 258 [M+1].



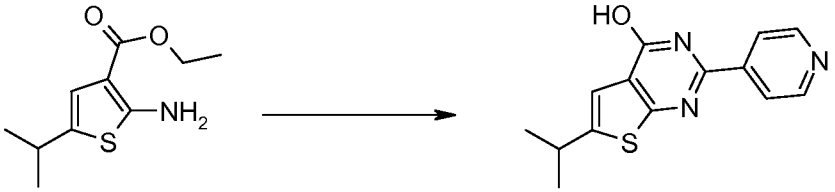
[AA-19]

5,6-dimethyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-19] was prepared by reaction of 2-amino-4,5-dimethyl-thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 3, RT: 3.05 min, MI: 258 [M+1].



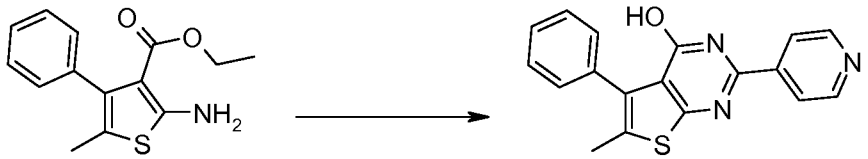
[AA-20]

4-hydroxy-5-methyl-2-pyridin-4-yl-thieno [2, 3-d]pyrimidine-6-carboxylic acid amide [AA-20] was prepared by reaction of 2-amino-5-carbamoyl-4-methyl-thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a brown solid. LCMS method: 2, RT: 3.02 min, MI: 287 [M+1].



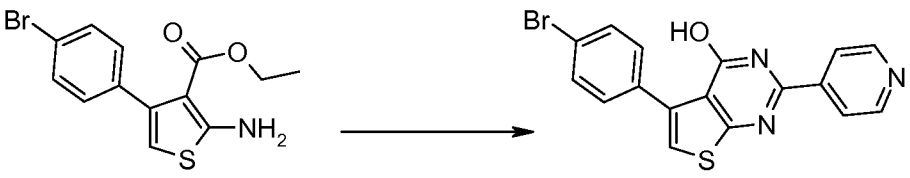
[AA-21]

6-isopropyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-21] was prepared by reaction of 2-amino-5-isopropyl-thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a brown solid. LCMS method: 2, RT: 3.29 min, MI: 272 [M+1].



[AA-22]

6-methyl-5-phenyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-22] was prepared by reaction of 2-amino-5-methyl-4-phenyl-thiophene-3-carboxylic acid ethyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 2, RT: 3.79 min, MI: 320 [M+1].



[AA-23]

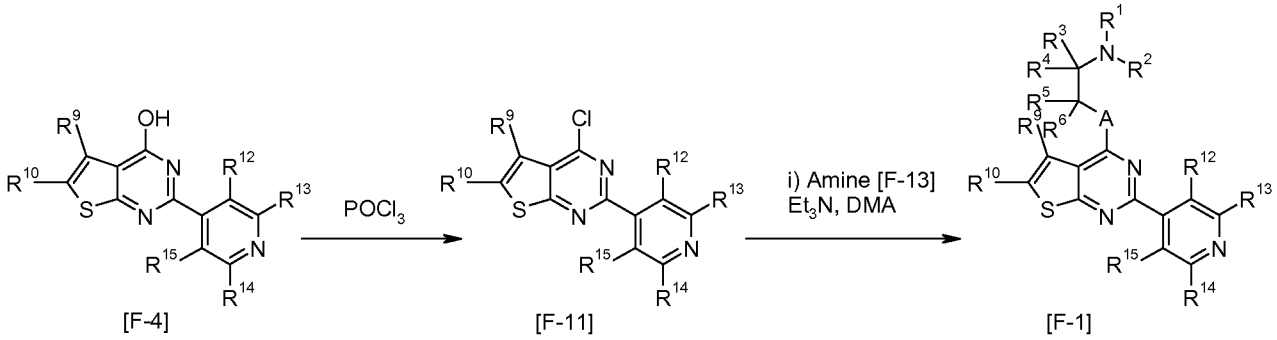
5-(4-bromo-phenyl)-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-23] was prepared by reaction of 2-amino-4-(4-bromo-phenyl)-thiophene-3-carboxylic acid ethyl ester, 4-

cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a brown solid. LCMS method: 2, RT: 4.16 min, MI: 384-386 [M+1].

General synthesis of 5,6 substituted 4-amino-2-pyridin-4-yl-thieno[2,3-d]pyrimidines of general formula [F-1] (Scheme A3)

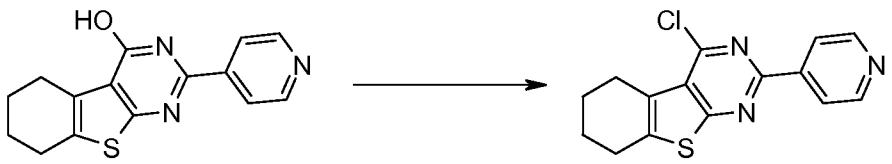
5,6-substituted 2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol derivatives of general formula [F-4] were reacted in an activation step using a chlorinating reagent such as phosphorus oxychloride or phosphorous pentachloride to yield the 5,6-substituted 4-chloro-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-11], which were reacted with primary or secondary amine derivative of general formula [F-13] at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A3



[F-4] [F-11] [F-1]

Synthesis of 4-chloro-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [AA-24]

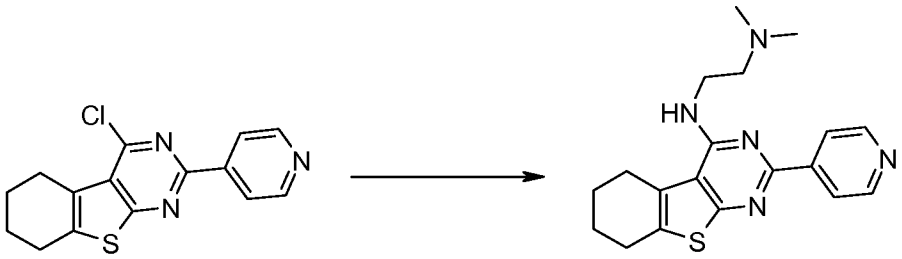


[AA-5] [AA-24]

2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-5] (1 g, 3.6 mmol) was stirred in $POCl_3$ (10 ml,109 mmol) at reflux at 125 °C overnight. The mixture was allowed to cool down to room temperature and the excess of $POCl_3$ was removed under reduced pressure. The residue was carefully poured into ice-water and the solution

was basified with a saturated solution of sodium hydrogen carbonate (50 ml) and the product was extracted into DCM (2x25 ml). The combined extracts were dried with magnesium sulfate, filtered and evaporated under reduced pressure to yield the title compound as a yellow-orange solid, which was was used without further purification. LCMS method: 2, RT: 5.46 min, MI: 302 [M+1].

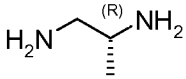
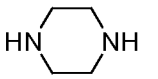
Synthesis of N,N-dimethyl-N'-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl)-ethane-1,2-diamine [1]

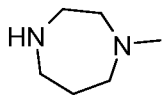
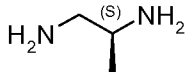
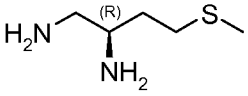
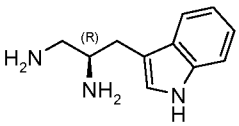
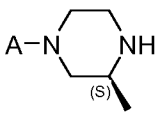
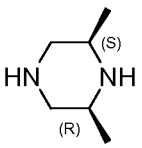
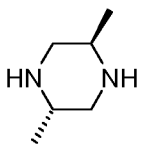
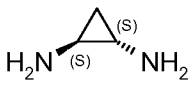


[AA-24] [1]

To a solution of 4-chloro-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine (50mg, 0.166 mmol) [AA-24] in DMA (1 ml) was added N,N-dimethylethylenediamine (20µl, 0.166 mmol) followed by Et_3N (32 µl, 0.232 mmol) and the mixture was stirred at room temperature for 2 hours. The reaction mixture was loaded onto a SCX-2 cartridge, 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: 2,: RT: 2.1min, MI: 354 [M+1]. 1H NMR (300MHz, DMSO): 8.70 (d,2H) 8.20 (d,2H), 3.7 (m,2H), 2.9 (m,2H), 2.8 (m,2H), 2.6 (m,2H), 2.3 (s,6H), 1.8 (m,4 H).

The following compounds were prepared according to the general synthesis shown in scheme A3:

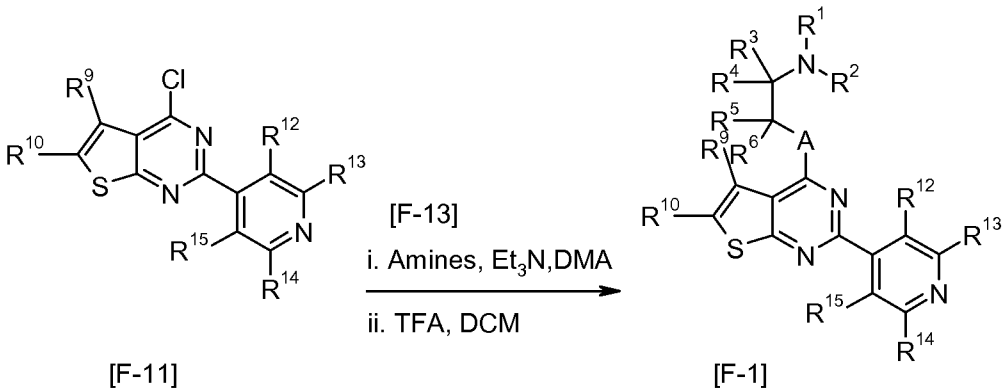
Ex	SM	Amine [F-13]	Characterisation	
2	[AA-24]		method: 2, RT: 2.05 min, MI: 340 [M+1]	
3	[AA-24]		method: 2, RT: 2.13 min, MI: 352 [M+1]	

Ex	SM	Amine [F-13]	Characterisation	
4	[AA-24]		method: 2, RT: 2.15 min, MI: 380 [M+1]	1H NMR (300MHz, DMSO): 8.70 (d,2H) 8.20 (d,2H), 4 (m,2H), 3.8 (m,2H), 3.2 (m,2H), 3 (m,2H), 2.9 (m,4H), 2.1 (m,2H), 1.9 (m,2H), 1.7 (m,2H), 0.8 (s,3H)
5	[AA-24]		method: 2,RT: 2.10 min, MI: 340 [M+1]	
6	[AA-24]		method: 2, RT: 2.33 min, MI: 400 [M+1]	
7	[AA-24]		method: 2, RT: 2.46 min, MI: 455 [M+1]	
8	[AA-24]		method: 2, RT: 2.20 min, MI: 366 [M+1]	
9	[AA-24]		method: 2, RT: 2.23 min, MI: 380[M+1]	
10	[AA-24]		method: 2, RT: 2.30 min, MI: 380 [M+1]	1H NMR (300MHz, DMSO): 8.8 (d,2H), 8.2 (d,2H), 3.4 (m,2H), 3.2 (m,2H), 3.1 (m,2H), 2.90 (m,2H), 2.68 (m,2H) , 1.9 (m,4H), 1.13 (d,6H)
11	[AA-24]		method: 2, RT: 2.10 min, MI: 338 [M+1]	

General synthesis of 5,6 substituted 4-amino-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-1] (Scheme A4)

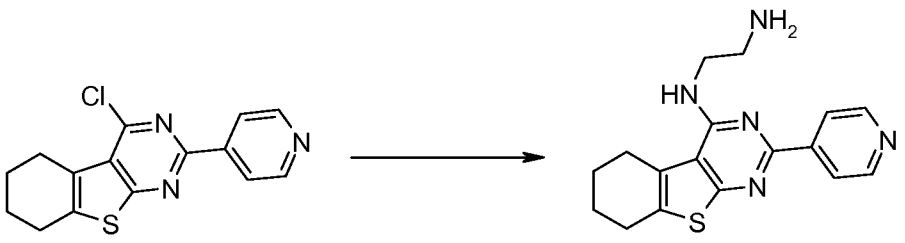
5,6 substituted 4-chloro-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-11] were reacted with N-Boc protected primary or secondary diamine derivatives of general formula [F-13] at ambient temperature. After reaction work up, typically by a liquid-liquid extraction or purification 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 A4



[F-11] [F-1]

Synthesis of N*1*-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl)-ethane-1,2-diamine [12]

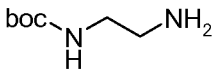
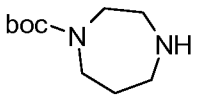
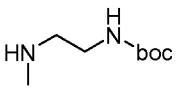
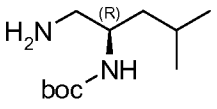
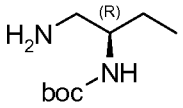
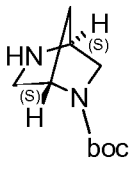


[AA-24] [12]

To a solution of 4-chloro-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine (50 mg, 0.166 mmol) [AA-24] in DMA (1 ml) was added (2-amino-ethyl)-carbamic acid tert-butyl ester (28 µl, 0.182 mmol) followed by Et_3N (32 µl, 0.232 mmol) , the mixture was stirred at room temperature for 2 hours. The product was extracted with DCM (1 ml) and washed with brine (2 ml). To the organic phase was added TFA (1 ml)

and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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: 2, RT: 2.07min, MI: 326 [M+1]. 1H NMR (300MHz, DMSO): 8.70 (d,2H)., 8.28 (d,2H), 3.88 (m,2H), 3.14 (m,2H), 2.94 (m,2H), 2.78 (m,2H), 1.84 (m,4H).

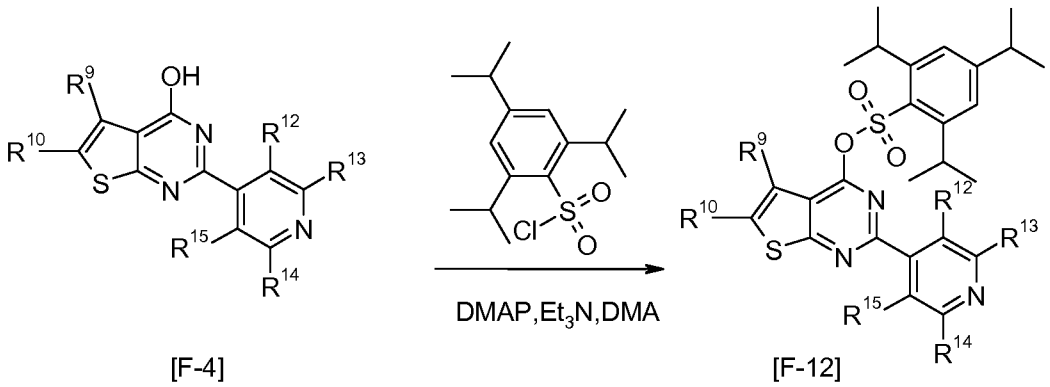
The following compounds were prepared according to the general synthesis shown in Scheme A4:

Ex	SM	Amine [F-13]	Characterisation	
13	[AA-5]		method: 2, RT: 2.05 min, MI: 340 [M+1]	1H NMR (300MHz, DMSO): 8.7 (d,2H), 8.2 (d,2H), 3.9 (m,2H), 3.1 (m,2H), 3 (m,2H), 2.8 (m,2H), 2.45 (s,3H) , 1.8 (m,4H)
14	[AA-5]		method: 2, RT: 2.10 min, MI: 366 [M+1]	
15	[AA-5]		method: 2, RT: 2.17 min, MI: 340 [M+1]	
16	[AA-5]		method: 2, RT: 2.35 min, MI: 382 [M+1]	
17	[AA-5]		method: 2, RT: 2.18 min, MI: 354 [M+1]	
18	[AA-5]		method: 2, RT: 2.13 min, MI: 364 [M+1]	

General synthesis of 5,6-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester derivatives of general formula [F-12] (Scheme A5)

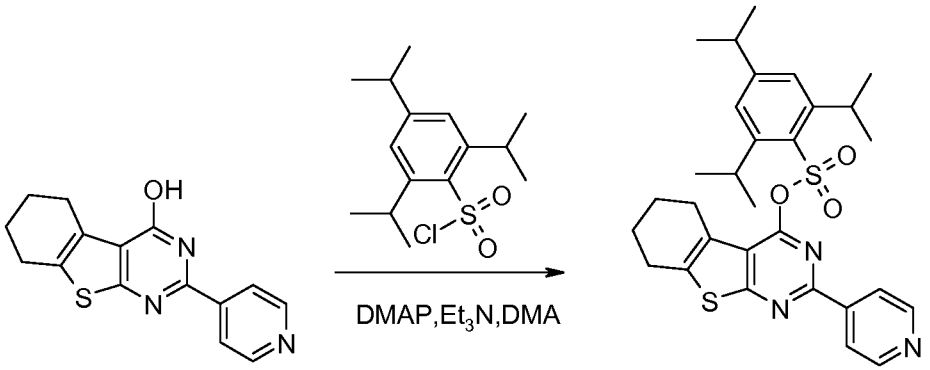
Compounds were prepared by the reaction of 5,6-substituted 2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol derivatives of general formula [F-4] (described in scheme A2) with 2,4,6-triisopropylbenzenesulfonyl chloride in halogenated solvent such as DCM or a polar aprotic solvent such as DMA, DMF, NMP with a tertiary alkylamine base such as Et_3N, DIPEA or NMM and a catalytic amount of DMAP.

Scheme A5



[F-4] [F-12]

Synthesis of 2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-25].

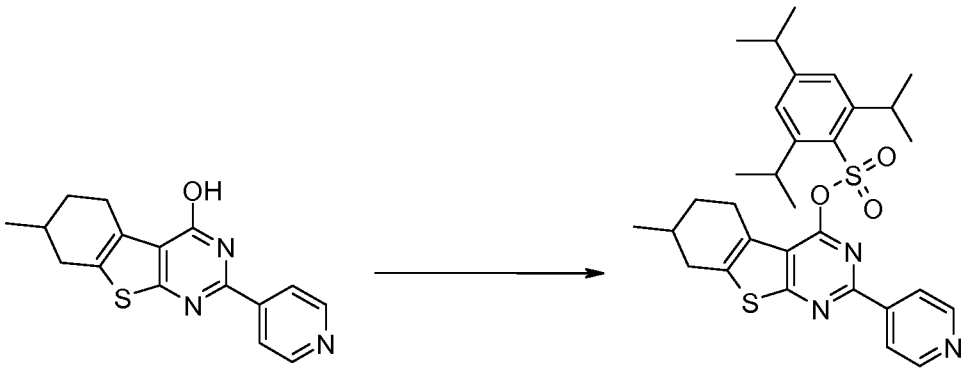


[AA-5] [AA-25]

To a solution of 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol (1 g, 3.5 mmol) [AA-5] in DCM (10 ml) was added 2,4,6-triisopropylbenzenesulfonyl chloride (1.3 g, 4.2 mmol), Et_3N (1.5 ml, 10.5 mmol) and DMAP (6 mg, 0.05 mmol). The mixture was stirred for at room temperature for one hour. After completion the mixture was diluted with water and the product was extracted into

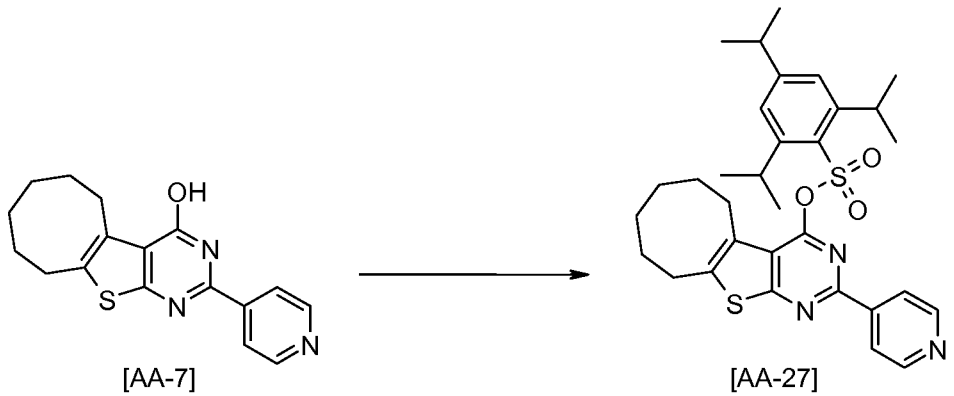
DCM (2x2 ml). The combined extracts were dried with magnesium sulfate, filtered and evaporated under reduced pressure to yield the title compound as a brown solid, which was used without further purification in the next step. LCMS method: 3, RT: 6.23 min, MI: 550 [M+1].

The following compounds were prepared according to the general synthesis shown in scheme A5:



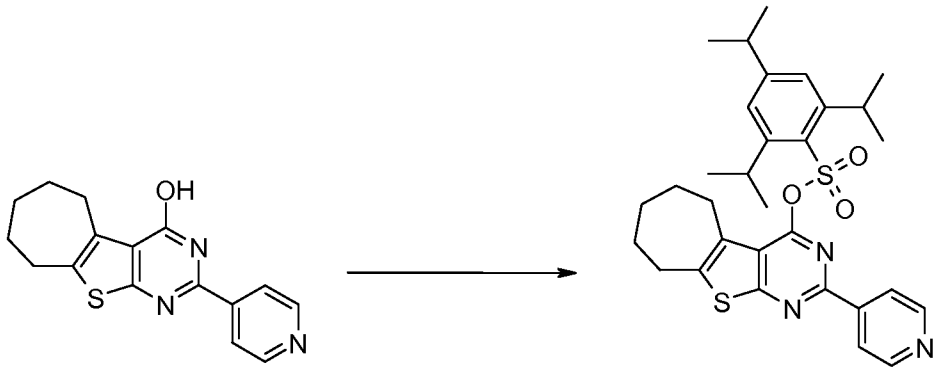
[AA-6] [AA-26]

2,4,6-triisopropyl-benzenesulfonic acid 7-methyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-26] was prepared by reaction of 7-methyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-6], 2,4,6-triisopropyl benzene sulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.34 min, MI: 564 [M+1].



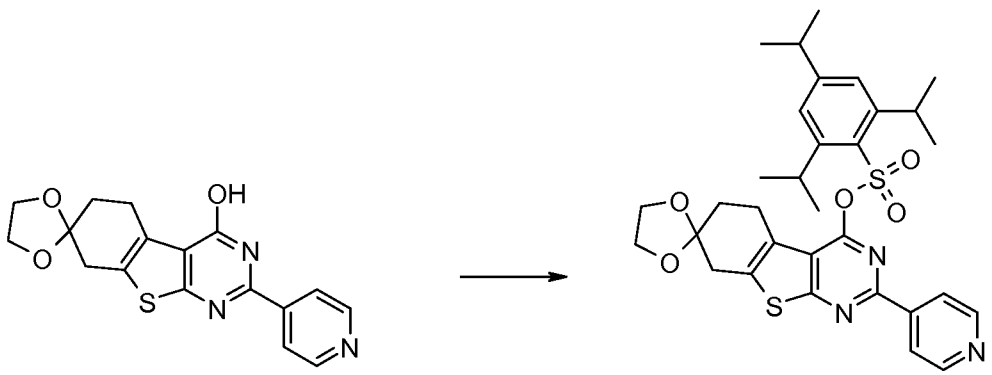
[AA-7] [AA-27]

2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8,9,10-hexahydro-11-thia-1,3-diaza-cycloocta[a]inden-4-yl ester [AA-27] was prepared by reaction of 2-pyridin-4-yl-5,6,7,8,9,10-hexahydro-11-thia-1,3-diaza-cycloocta[a]inden-4-ol [AA-7], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.47 min, MI: 578 [M+1].



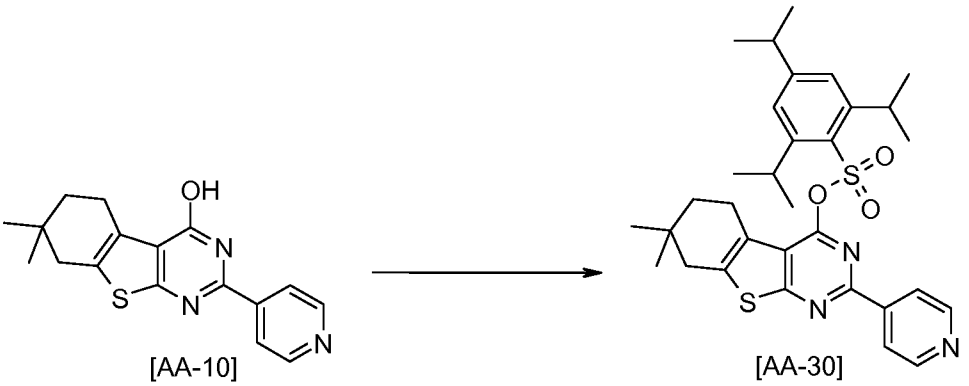
[AA-8] [AA-28]

2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-yl ester [AA-28] was prepared by reaction of 2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-ol [AA-8], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the title compound as a brown solid. LCMS method: 3, RT: 6.39 min, MI: 564 [M+1].



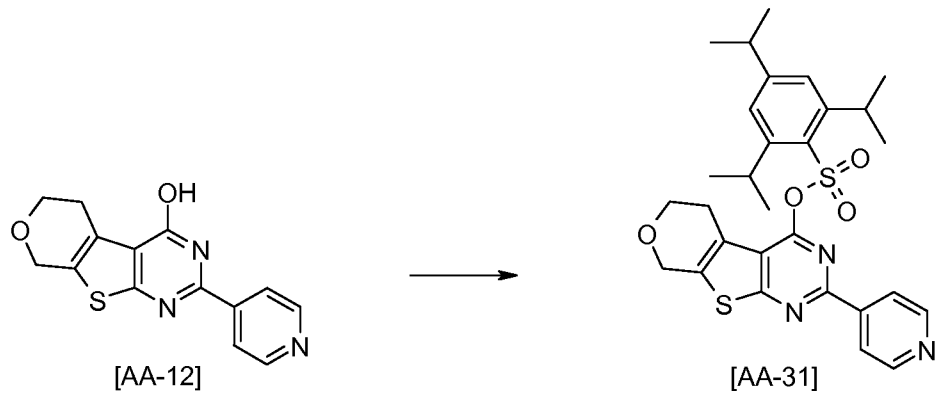
[AA-9] [AA-29]

2,4,6-triisopropyl-benzenesulfonic acid 1,4-Dioxa-spiro[7.7]-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol ester [AA-29] was prepared by reaction of 1,4-Dioxa-spiro[7.7]-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-9], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.56 min, MI: 608 [M+1].



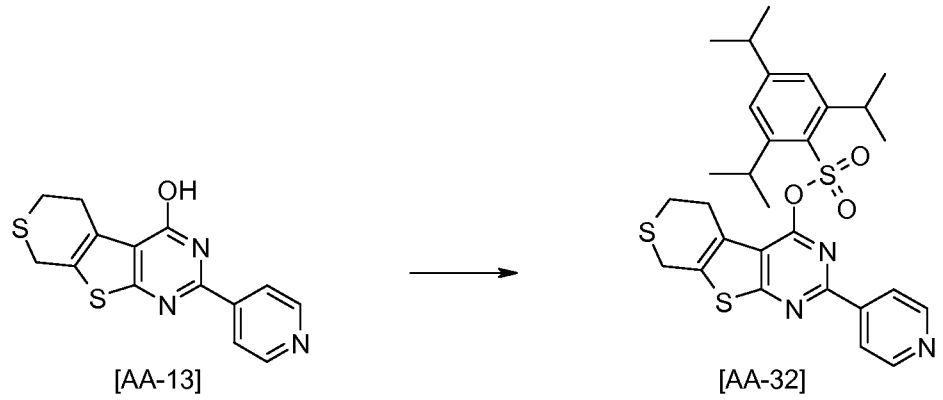
[AA-10] [AA-30]

2,4,6-triisopropyl-benzenesulfonic acid 7,7-dimethyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-30] was prepared by reaction of 7,7-dimethyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ol [AA-10], 2,4,6-triisopropyl benzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.37 min, MI: 578 [M+1].



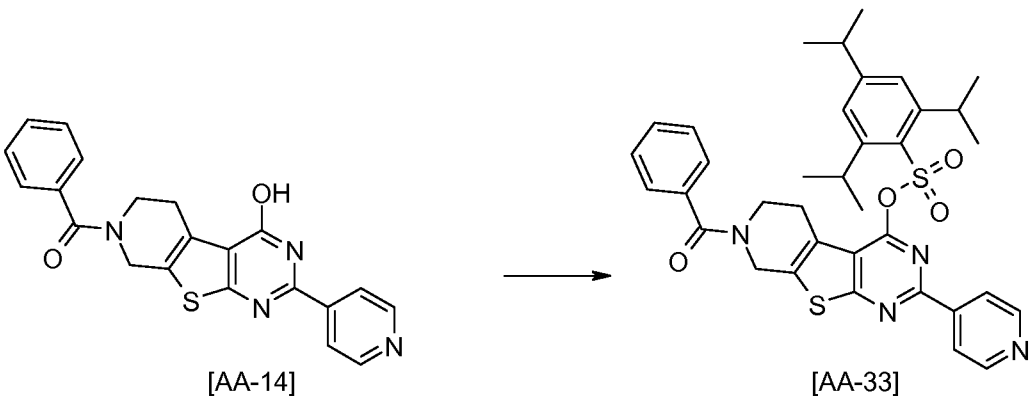
[AA-12] [AA-31]

2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,8-dihydro-6H-pyrano [4',3':4,5]thieno [2,3-d]pyrimidin-4-yl ester [AA-31] was prepared by reaction of 2-pyridin-4-yl-5,8-dihydro-6H-pyrano[4',3':4,5]thieno[2,3-d]pyrimidin-4-ol [AA-12], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.29 min, MI: 552 [M+1].



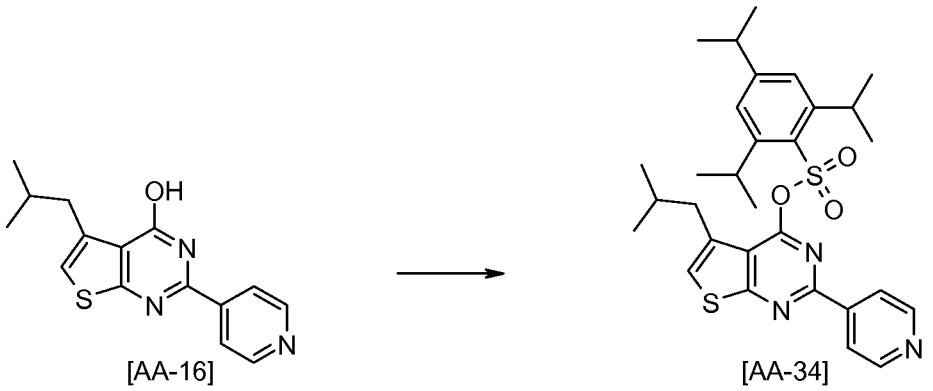
[AA-13] [AA-32]

2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,8-dihydro-6H-thiopyrano [4',3':4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-32] was prepared by reaction of 2-pyridin-4-yl-5,8-dihydro-6H-thiopyrano[4',3':4,5]thieno[2,3-d]pyrimidin-4-ol [AA-13], 2,4,6-triisopropyl benzene sulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.58 min, MI: 568 [M+1].



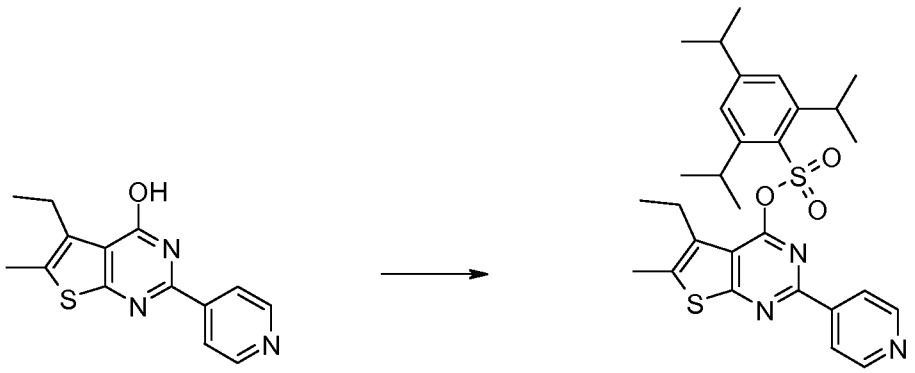
[AA-14] [AA-33]

2,4,6-Triisopropyl-benzenesulfonic acid 7-benzoyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-33] was prepared by reaction of (4-Hydroxy-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-7-yl)-phenyl-methanone [AA-14], 2,4,6-triisopropyl benzene sulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.67 min, MI: 655 [M+1].



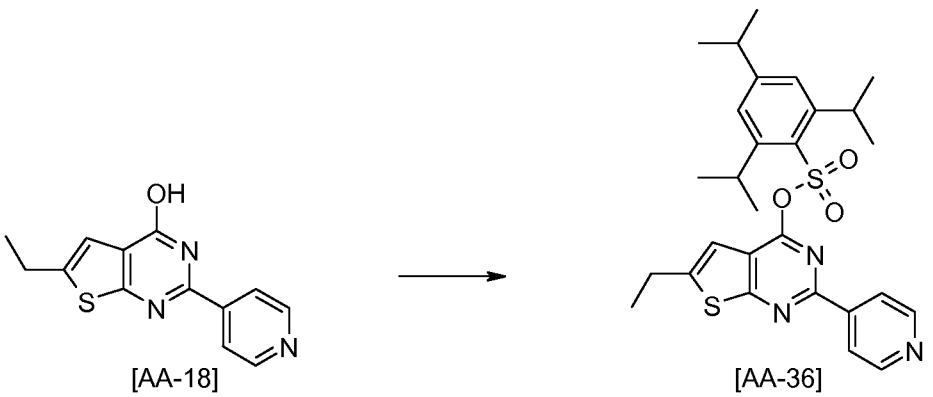
[AA-16] [AA-34]

2,4,6-triisopropyl-benzenesulfonic acid 5-isobutyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-34] was prepared by reaction of 5-Isobutyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-16], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.36 min, MI: 552 [M+1].



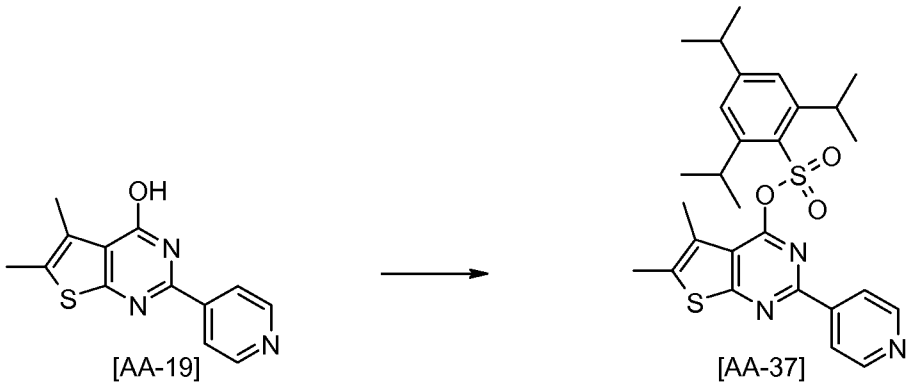
[AA-17] [AA-35]

2,4,6-triisopropyl-benzenesulfonic acid 5-ethyl-6-methyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-35] was prepared by reaction of 5-ethyl-6-methyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-17], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.29 min, MI: 538 [M+1].



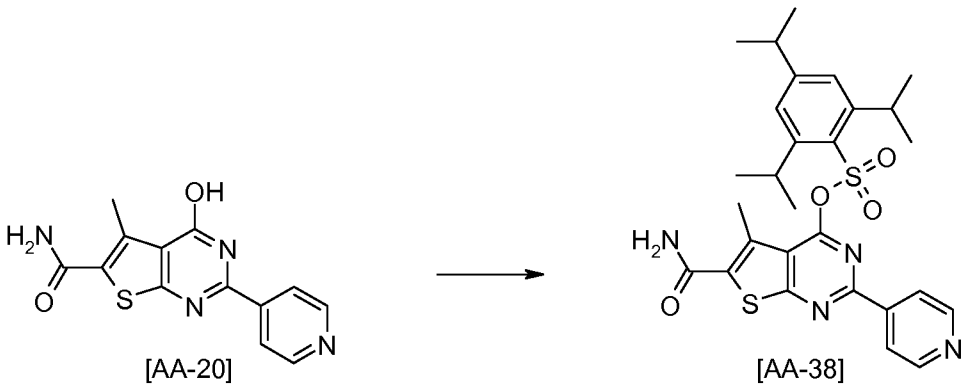
[AA-18] [AA-36]

2,4,6-triisopropyl-benzenesulfonic acid 6-ethyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-36] was prepared by reaction of 6-ethyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-18], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.22 min, MI: 524 [M+1].



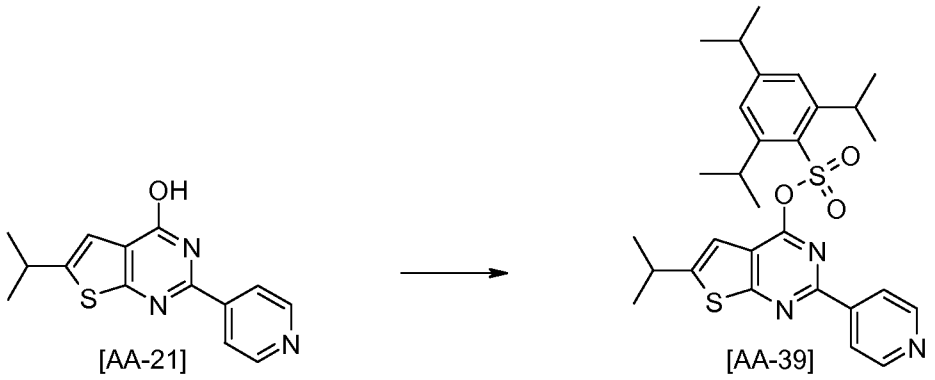
[AA-19] [AA-37]

2,4,6-triisopropyl-benzenesulfonic acid 5,6-dimethyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-37] was prepared by reaction of 5,6-dimethyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-19], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.18 min, MI: 524 [M+1].



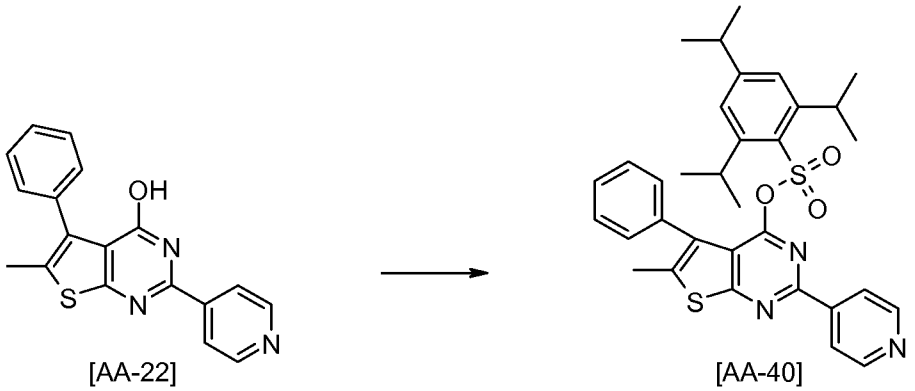
[AA-20] [AA-38]

2,4,6-triisopropyl-benzenesulfonic acid 6-carbamoyl-5-methyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-38] was prepared by reaction of 4-hydroxy-5-methyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidine-6-carboxylic acid amide [AA-20], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.12 min, MI: 553 [M+1].



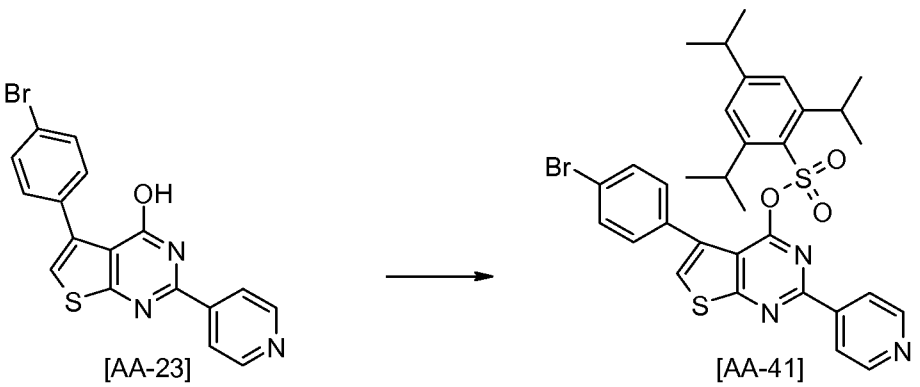
[AA-21] [AA-39]

2,4,6-triisopropyl-benzenesulfonic acid 6-isopropyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-39] was prepared by reaction of 6-isopropyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-21], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.24 min, MI: 538 [M+1].



[AA-22] [AA-40]

2,4,6-triisopropyl-benzenesulfonic acid 6-methyl-5-phenyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-40] was prepared by reaction of 6-methyl-5-phenyl-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-22], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.55 min, MI: 586 [M+1].



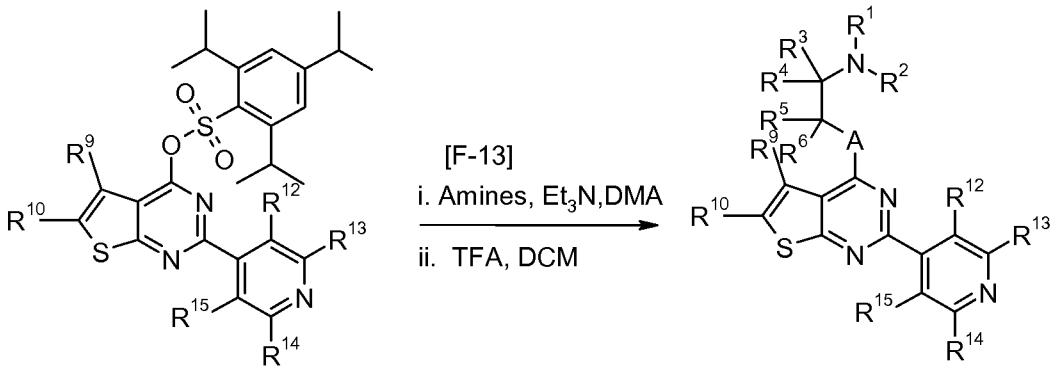
[AA-23] [AA-41]

2,4,6-triisopropyl-benzenesulfonic acid 5-(4-bromo-phenyl)-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-41] was prepared by reaction of 5-(4-bromo-phenyl)-2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-ol [AA-23], 2,4,6-triisopropylbenzenesulfonyl chloride, Et_3N, DMAP and DCM at room temperature to give the desired compound as a brown solid. LCMS method: 3, RT: 6.66 min, MI: 651 [M+1].

General synthesis of 5,6 substituted 4-amino-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-1] (Scheme A6)

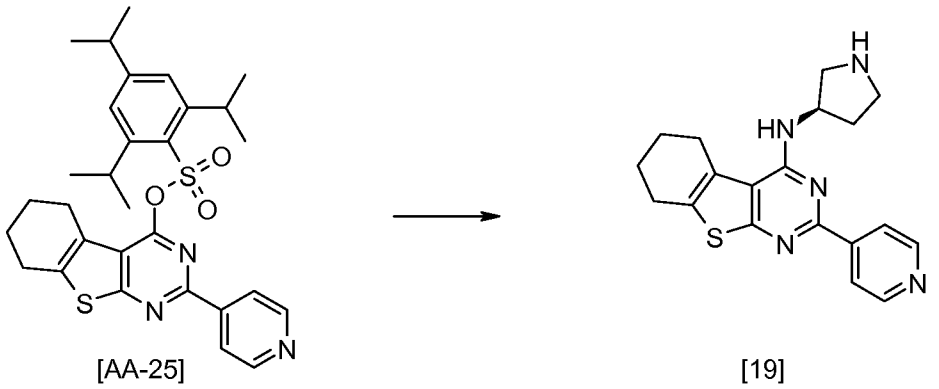
5,6-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[2,3-d] pyrimidin -4-yl ester derivatives of general formula [F-12] [prepared in scheme A5] were reacted with a primary or secondary amino derivative of general formula [F-13] in a polar aprotic solvent such as DMA, DMF, 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 A6



[F-12] [F-1]

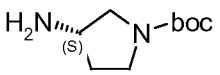
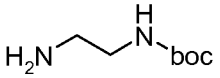
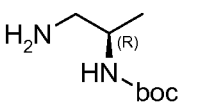
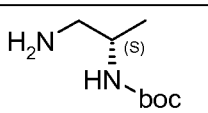
(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl)-(R)-pyrrolidin-3-yl-amine [19]

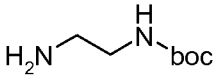
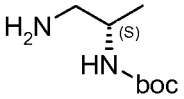
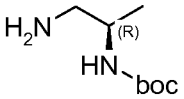
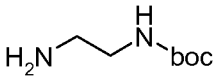
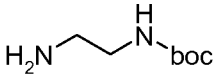
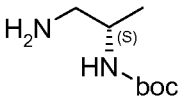
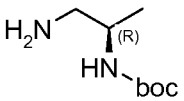
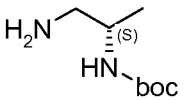
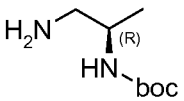
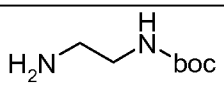
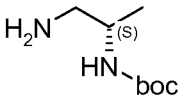
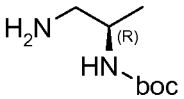
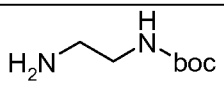
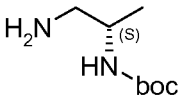


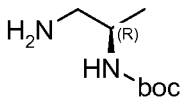
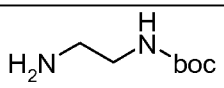
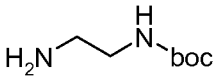
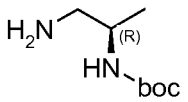
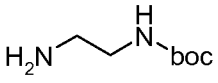
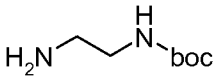
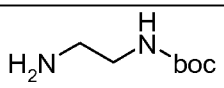
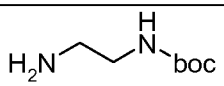
[AA-25] [19]

To a solution of 2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester (60 mg, 0.110 mmol) [AA-25] in DMA (1 ml) was added (R)-(+)-1-Boc-3-aminopyrrolidine (23 mg, 0.121 mmol) followed by Et_3N (30 µl, 0.220 mmol) and the mixture was stirred at room temperature for 2 hours. Water (1 ml) was added and the mixture was extracted with DCM (2 x ml), the extracts were combined and washed with brine (2 ml). To the organic phase was added TFA (1 ml) and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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 B) to yield to the desired compound. LCMS method: 4, RT: 4.43 min, MI: 352 [M+1]. 1H NMR (300MHz, DMSO): 8.70 (d,2H), 8.24 (d,2H), 3.53 (m,2H), 3.33 (m,1H), 3.22 (m,2H), 3.03 (m,2H), 2.81 (m,2H), 2.34 (m,1H), 2.10 (m,1H), 1.83 (m,4H).

The following compounds were prepared according to the general synthesis shown in scheme A6:

Ex	SM	Amine	Characterisation	
20	[AA-25]		method: 4, RT: 4.14 min, MI: 352 [M+1]	
21	[AA-26]		method: 2, RT: 2.32 min, MI: 340 [M+1]	
22	[AA-26]		method: 2, RT: 2.73 min, MI: 354 [M+1]	
23	[AA-26]		method: 2, RT: 2.66 min, MI: 354 [M+1]	

Ex	SM	Amine	Characterisation	
24	[AA-27]		method: 2, RT: 2.36 min, MI: 354 [M+1]	
25	[AA-27]		method: 2, RT: 2.68 min, MI: 368 [M+1]	
26	[AA-27]		method: 2, RT: 2.57 min, MI: 368 [M+1]	
27	[AA-33]		method: 3, RT: 2.16 min, MI: 431 [M+1]	
28	[AA-34]		method: 2, RT: 2.37 min, MI: 328 [M+1]	
29	[AA-34]		method: 2, RT: 2.41min, MI: 342 [M+1]	
30	[AA-34]		method: 2, RT: 2.51 min, MI: 342 [M+1]	
31	[AA-35]		method: 2, RT: 2.30 min, MI: 328 [M+1]	
32	[AA-35]		method: 2, RT: 2.32 min, MI: 328 [M+1]	
33	[AA-36]		method: 2, RT: 2.01 min, MI: 300 [M+1]	
34	[AA-36]		method: 2, RT: 2.12 min, MI: 314 [M+1]	
35	[AA-36]		method: 2, RT: 2.12 min, MI: 314 [M+1]	
36	[AA-37]		method: 2, RT: 1.92 min, MI: 300 [M+1]	
37	[AA-37]		method: 2, RT: 2.08 min, MI: 314 [M+1]	

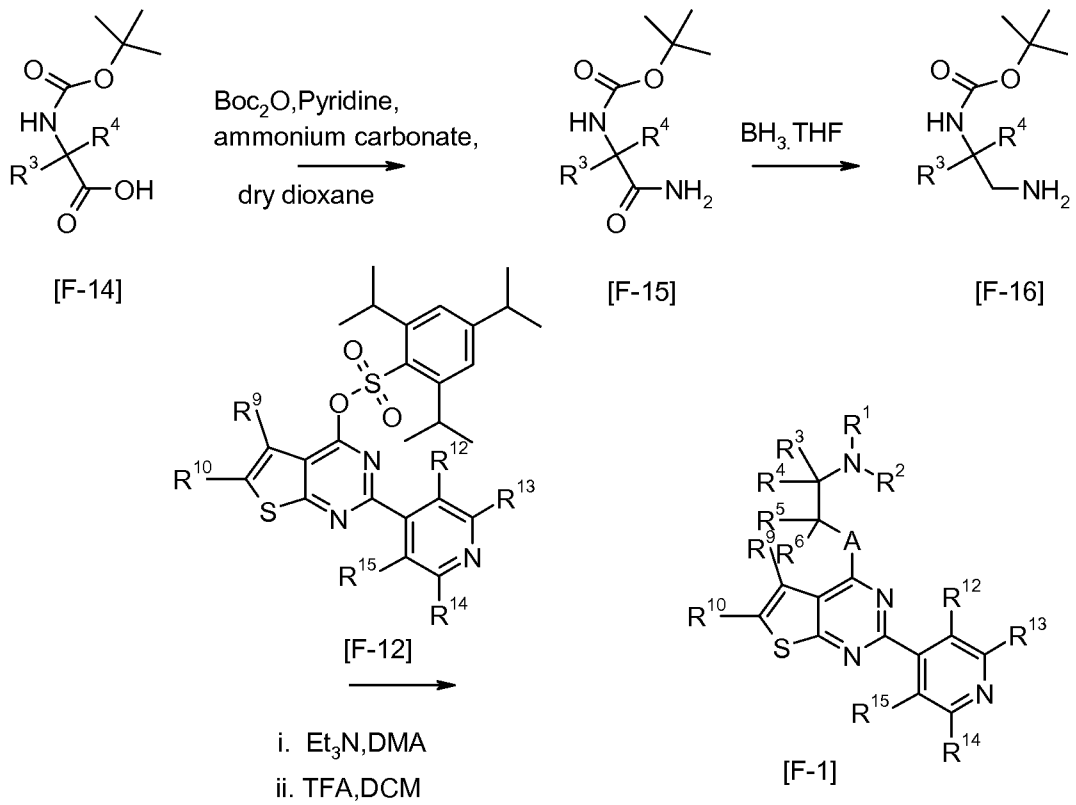
Ex	SM	Amine	Characterisation	
38	[AA-37]		method: 2, RT: 2.52 min, MI: 314 [M+1]	
39	[AA-38]		method: 2, RT: 1.60 min, MI: 329 [M+1]	
40	[AA-39]		method: 2, RT: 2.07 min, MI: 314 [M+1]	
41	[AA-39]		method: 2, RT: 2.16 min, MI: 328 [M+1]	
42	[AA-29]		method: 3, RT: 1.48 min, MI: 384 [M+1]	1H NMR (300MHz, DMSO): 8.7 (d, 2H) 8.42 (s, HCOOH, 1H) 8.26 (d, 2H), 3.94(bs,2H), 3.86 (bm,4H), 3.86(bm, 2H), 3.30 (m, 2H), 3.22 (m, 4H),
43	[AA-30]		method: 3, RT: 2.33 min, MI: 354 [M+1]	
44	[AA-32]		method: 3, RT: 2.07 min, MI: 344 [M+1]	
45	[AA-31]		method: 3, RT: 1.81 min, MI: 328 [M+1]	

General synthesis of 5,6 substituted 4-amino-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-1] (Scheme A7)

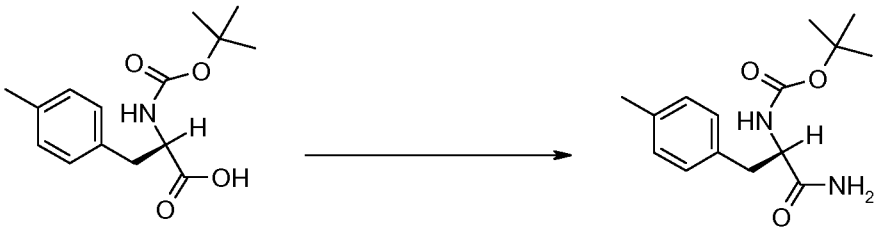
Compounds were synthesised starting from an N-Boc protected amino acid derivative of general formula [F-14] which was converted to a primary carboxamide derivative of general formula [F-15] by reaction with di-tert-butyl dicarbonate in the presence of a base such as pyridine or 2,6-lutidine and ammonium carbonate in an anhydrous solvent such as dioxane, THF or diethylether. The resultant primary carboxamide derivative was reduced to the amino derivativeof general formula [F-16] with a borane reducing agent such as BH_3.THF or BH_3.SMe_2 in an anhydrous solvent such as

THF, dioxane or diethylether. The resultant amino derivative was then reacted with a 5,6-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [F-12] [prepared in scheme A5] 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



((S)-1-carbamoyl-2-p-tolyl-ethyl)-carbamic acid tert-butyl ester [AA-42].



[AA-42]

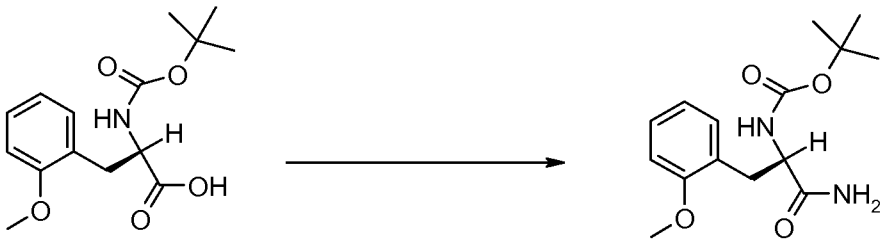
To a stirred solution of (S)-2-tert-butoxycarbonylamino-3-p-tolyl-propionic acid (560 mg, 2 mmol), pyridine (100 µl, 1.2 mmol) and di-tert-butyl dicarbonate (568 mg, 2.6 mmol) in dry dioxane (4 ml) was added ammonium carbonate (240 mg, 2.5 mmol). The mixture was stirred for 4 hours at room temperature. Ethylacetate was added and the mixture was washed with water and a solution of 5% H_2SO_4. The combined organic phases were dried with magnesium sulfate, filtered and evaporated to provide the title compound as a white solid. LCMS method: 2, RT: 3.69 min, MI: 279 [M+1].

[(S)-2-amino-1-(4-methyl-benzyl)-ethyl]-carbamic acid tert-butyl ester [AA-43]

[AA-42] [AA-43]

A 1M solution of BH_3 in THF (15 ml, 15mmol) was added dropwise to ((S)-1-carbamoyl-2-p-tolyl-ethyl)-carbamic acid tert-butyl ester [AA-42] (560 mg, 2mmol), the solution was stirred overnight at room temperature then subsequently hydrolysed by slow addition of excess of 10% acetic acid/MeOH (30 ml) and stirred at room temperature for a further 2 hours. The solvent was removed under reduced pressure the residue dissolved in methanol and passed through a SCX-2 cartridge and washed with methanol. The product was released from the cartridge using a solution of 2M ammonia / methanol. The solvent was evaporated to provide the title compound as a white solid. LCMS method: 2, RT: 2.42min, MI: 265 [M+1].

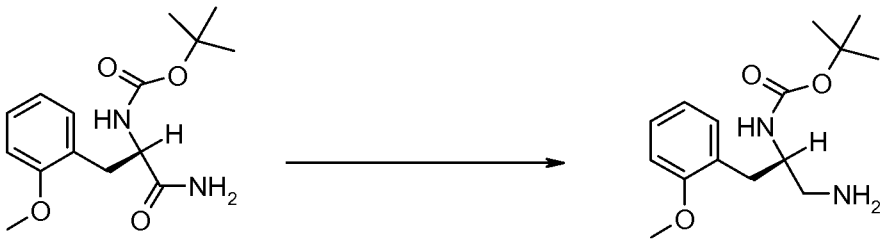
[(S)-1-carbamoyl-2-(2-methoxy-phenyl)-ethyl]-carbamic acid tert-butyl ester [AA-44]



[AA-44]

To a stirred solution of (S)-2-tert-butoxycarbonylamino-3-(2-methoxy-phenyl)-propionic acid (998 mg, 3.3 mmol), pyridine (300 µl, 3.6 mmol) and di-tert-butyl dicarbonate (1.16g, 5.32 mmol) in dry dioxane (10 ml) was added ammonium carbonate (512 mg, 5.32 mmol). The mixture was stirred for 4 hours at room temperature. Ethylacetate was added and after washings with water and a solution of 5% H_2SO_4. The combined organic phases were dried with magnesium sulfate, filtered and evaporated to provide the title compound as a white solid. LCMS method: 4, RT: 3.09 min, MI: 295 [M+1].

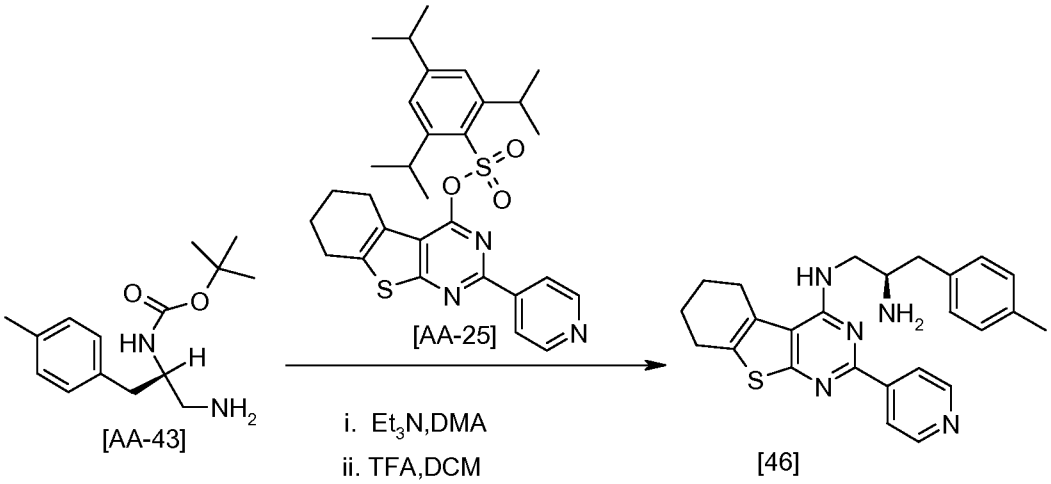
[(S)-2-amino-1-(2-methoxy-benzyl)-ethyl]-carbamic acid tert-butyl ester [AA-45]



[AA-44] [AA-45]

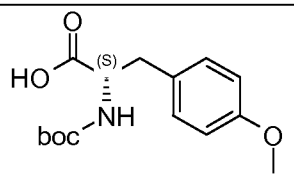
A 1M solution of BH_3 in THF (15 ml, 15mmol) was added dropwise to [(S)-1-carbamoyl-2-(2-methoxy-phenyl)-ethyl]-carbamic acid tert-butyl ester [AA-44] (980 mg, 3.32 mmol), the solution was stirred overnight at room temperature then subsequently hydrolysed by slow addition of excess of 10% acetic acid/MeOH (30 ml) and stirred at room temperature for a further 2 hours. The solvent was removed under reduced pressure the residue dissolved in methanol and passed through a SCX-2 cartridge and washed with methanol. The product was released from the cartridge using a solution of 2M ammonia / methanol. The solvent was evaporated to provide the title compound as a white solid. LCMS method: 2, RT: 2.40min, MI: 281 [M+1].

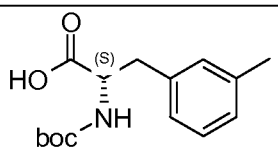
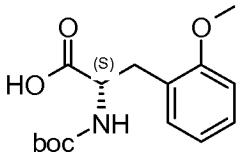
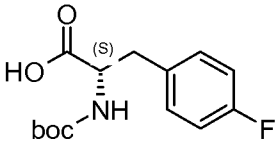
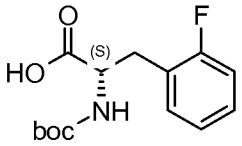
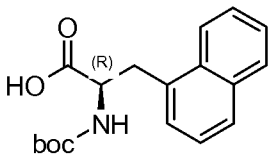
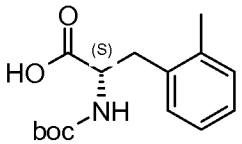
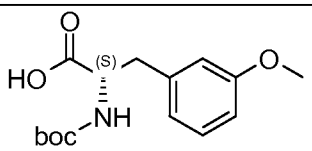
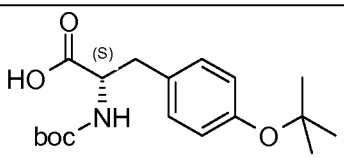
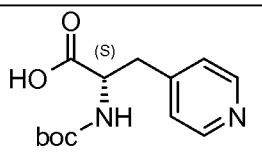
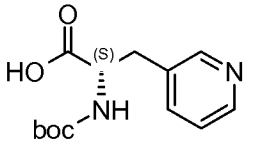
(S)-1-(4-methyl-benzyl)-3-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl)-propylamine [46]

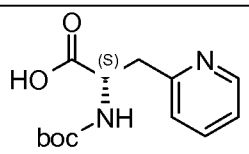
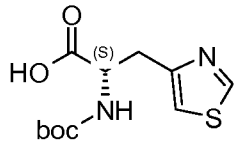
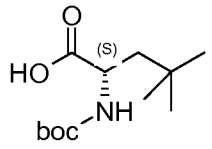
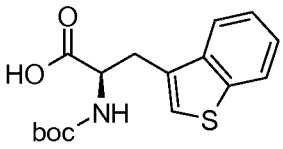
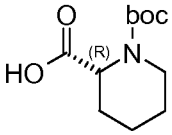
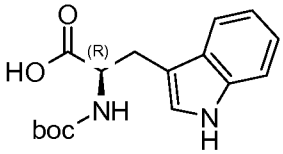
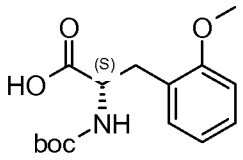


To a solution of 2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester (100 mg, 0.182 mmol) [AA-25] in DMA (2 ml) was added [(S)-2-amino-1-(4-methyl-benzyl)-ethyl]-carbamic acid tert-butyl ester [AA-43] (58 mg, 0.218 mmol) followed by Et_3N (76 µl, 0.546 mmol), the mixture was stirred at room temperature for 2 hours. Then the product was extracted with DCM (2 ml) and washed with brine (3 ml). To the organic phase was added TFA (2 ml) and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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 B) to yield to the title compound. LCMS method: 4, RT: 4.85 min, MI: 430 [M+1]. 1H NMR (300MHz, DMSO): 8.64 (d,2H), 7.99 (d,2H), 7.18 (m,4H), 3.89 (m,2H), 3.49 (m,2H), 2.98 (m,1H), 2.94 (m,2H), 2.78 (m,2H), 2.31 (s,3H), 1.83 (m,4H).

The following compounds were prepared according to the general synthesis shown in Scheme A7:

Ex	SM	Amino acid [F-14]	Characterisation
47	[AA-25]		method: 3, RT: 2.47 min, MI: 446 [M+1]

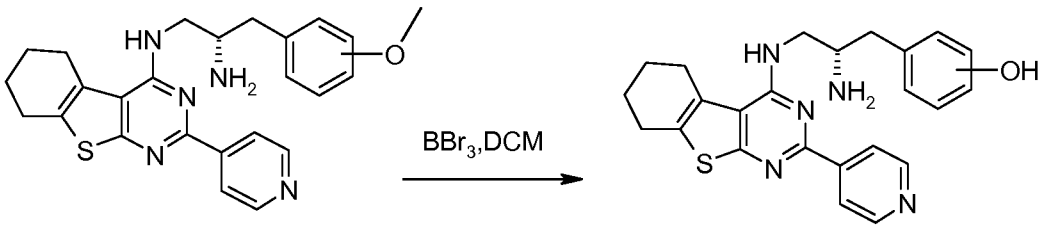
Ex	SM	Amino acid [F-14]	Characterisation
48	[AA-25]		method: 3, RT: 2.64 min, MI: 430 [M+1]
49	[AA-25]		method: 3, RT: 2.66 min, MI: 446 [M+1]
50	[AA-25]		method: 3, RT: 2.76 min, MI: 434 [M+1]
51	[AA-25]		method: 3, RT: 2.56 min, MI: 434 [M+1]
52	[AA-25]		method: 3, RT: 2.87 min, MI: 466 [M+1]
53	[AA-25]		method: 3, RT: 2.65 min, MI: 430 [M+1]
54	[AA-25]		method: 3, RT: 2.53 min, MI: 446 [M+1]
55	[AA-25]		method: 3, RT: 2.23 min, MI: 432 [M+1]
56	[AA-25]		method: 3, RT: 1.87 min, MI: 417 [M+1]
57	[AA-25]		method: 3, RT: 1.98 min, MI: 417 [M+1]

Ex	SM	Amino acid [F-14]	Characterisation
58	[AA-25]		method: 3, RT: 2.18 min, MI: 417 [M+1]
59	[AA-25]		method: 3, RT: 2.26 min, MI: 423 [M+1]
60	[AA-25]		method: 3, RT: 2.44 min, MI: 396 [M+1]
61	[AA-25]		method: 3, RT: 2.59 min, MI: 472 [M+1]
62	[AA-25]		method: 3, RT: 2.21 min, MI: 380 [M+1]
63	[AA-25]		method: 4, RT: 4.60 min, MI: 455 [M+1]
64	[AA-32]		method: 4, RT: 4.55 min, MI: 464 [M+1]

General synthesis of (S)-3-(2 or 3-hydroxy-phenyl)-N*1*-(2-pyridin-4-yl-5,6,7,8-tetra hy dro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl)-pro pane-1,2-diamine derivatives of general formula [F-18] (Scheme A8)

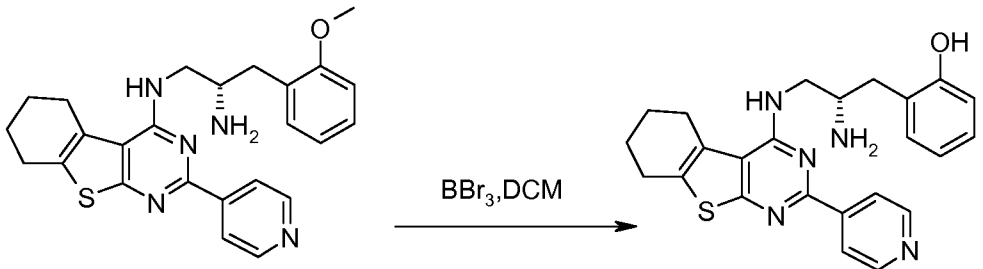
Compounds were synthesised starting from (S)-3-(2 or 3-methoxy-phenyl)-N*1*-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl)-propane-1,2-diamine derivatives of general formula [F-17] (described in scheme A7) by a de-methylation reaction with a Lewis acid such as BBr_3 or $AlCl_3$ in a chlorinated solvent such as DCM or DCE at low reaction temperature. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A8



[F-17] [F-18]

Synthesis of 2-[(S)-2-amino-3-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ylamino)-propyl]-phenol [65]



[49] [65]

To a solution of (S)-3-(2-methoxy-phenyl)-N*1*-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d] pyrimidin-4-yl)-propane-1,2-diamine [49] (30 mg, 0.06 mmol) in DCM (1 ml) at -30°C was added dropwise a solution of 1 M BBr_3 in DCM (180 µl, 0.180 mmol) under a nitrogen atmosphere. The reaction mixture was stirred at -30°C for 1 hour and then stirred overnight at room temperature. The crude reaction mixture was concentrated under reduced pressure and then purified by preparative HPLC (method A) to yield to the title compound. LCMS method: 3, RT: 2.28 min, MI: 432 [M+1].

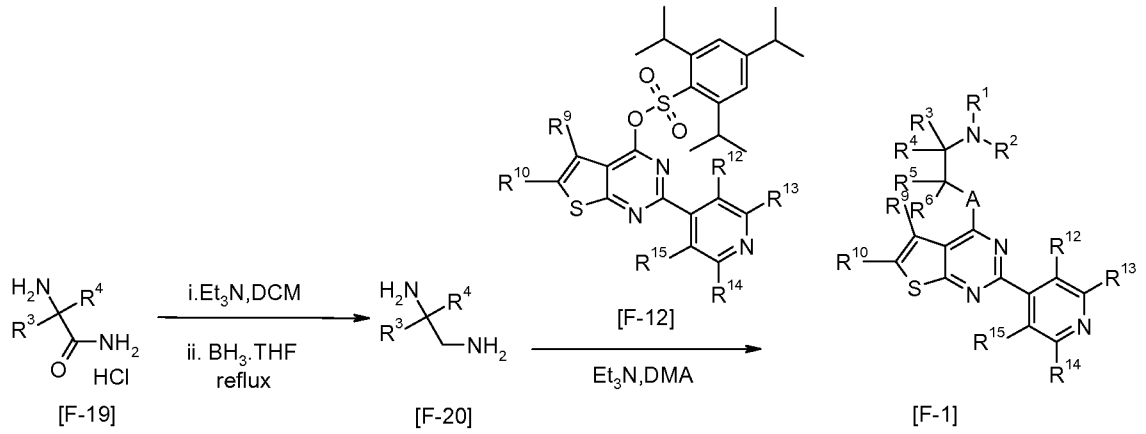
The following compounds were prepared according to the general synthesis shown in Scheme A8:

Example	SM	Characterisation
66	[54]	method: 3, RT: 2.34 min, MI: 432 [M+1]

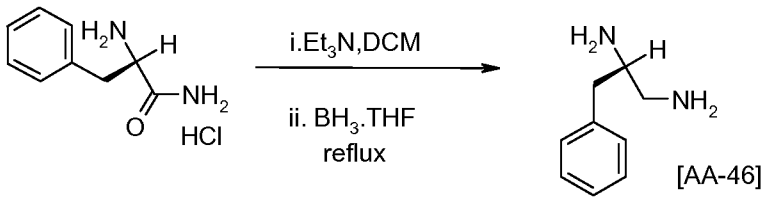
General synthesis of 5,6 substituted 4-amino-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-1] (Scheme A9)

Compounds were synthesised starting from the hydrochloride or hydrobromide salt of an α-amino acid carboxamide derivative of general formula [F-19] which was converted to the free base by reaction with a base such as Et_3N or DIPEA in a chlorinated solvent such as DCM or DCE. The resultant free base was then reduced to a diamino derivative of general formula [F-20] by reaction with a borane reducing agent such as BH_3.THF or $BH_3.SMe_2$ in an anhydrous solvent such as THF, dioxane or diethylether. The resultant diamino derivative [F-20] was then reacted with a 5,6-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester of general formula [F-12] [prepared in scheme A5] 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 crude reaction product was purified by reverse phase preparative HPLC.

Scheme A9



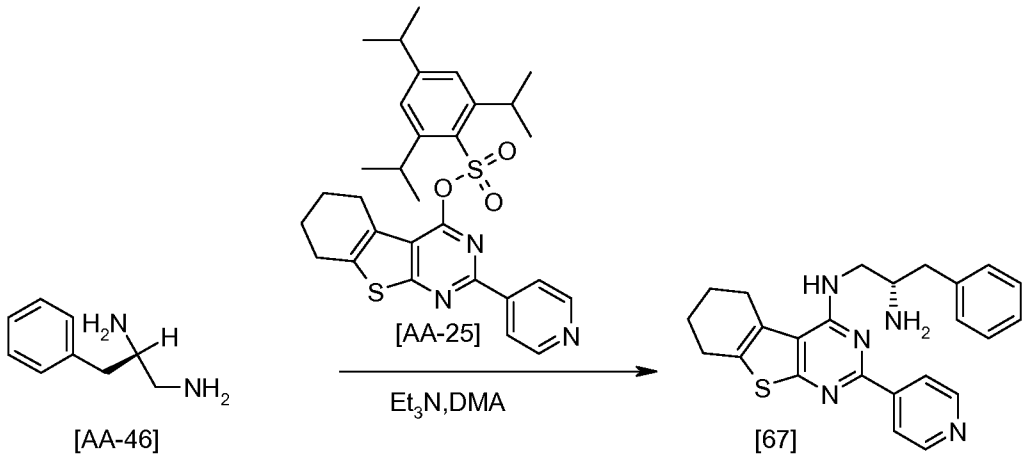
Synthesis of (S)-3-phenyl-propane-1,2-diamine [AA-46]



To a suspension of (S)-2-amino-3-phenyl-propionamide hydrochloride (540mg, 2.7 mmol) in DCM (5 ml) was added Et_3N (380µl, 2.7 mmol). The suspension was stirred for 2h at room temperature, the resulting solid was filtered and the filtrate was concentrated under reduced pressure to yield to a white solid to which was added dropwise a 1M solution of BH_3 in THF (20 ml, 20mmol) the solution was stirred overnight at reflux. After

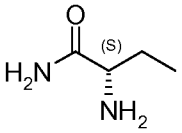
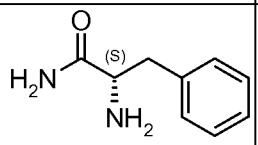
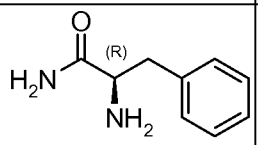
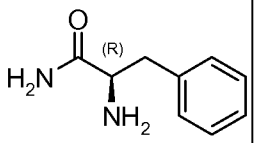
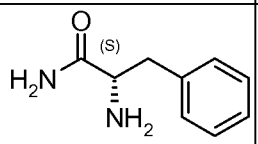
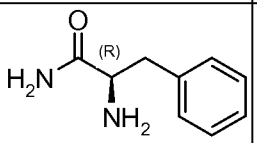
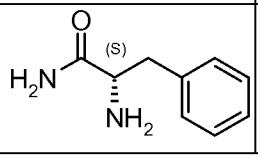
cooling the solution was hydrolysed by slow addition of excess of 10% acetic acid/MeOH (30ml) and refluxed for a further 2 hours. The solvent was removed under reduced pressure, the residue dissolved in methanol and passed through a SCX-2 cartridge and washed with methanol. The product was released from the cartridge using a solution of 2M ammonia / methanol. The solvent was evaporated to provide the title compound as a white solid. LCMS method: 1, RT: 0.36min, MI: 151 [M+1].

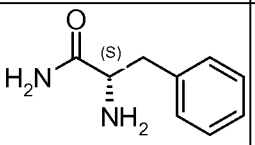
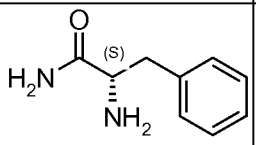
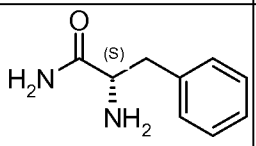
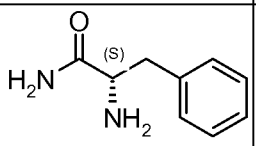
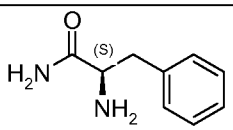
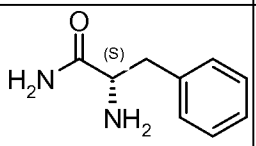
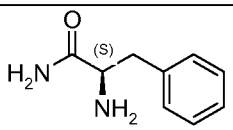
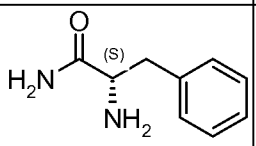
Synthesis of (S)-N*1*-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl)-butane-1,2-diamine [67]

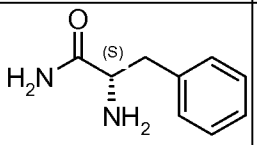


To a solution of 2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-25] (100 mg, 0.180 mmol) in DMA (2 ml) was added (S)-3-phenyl-propane-1,2-diamine [AA-46] (30 mg, 0.180 mmol) followed by Et_3N (50 µl, 0.36 mmol), the mixture was stirred at room temperature for 2 hours. After completion the mixture was loaded onto a SCX-2 cartridge 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: 4, RT: 2.51 min, MI: 416 [M+1]. 1H NMR (300MHz, DMSO): 8.64 (d,2H), 7.95 (d,2H), 7.36 (m,5H), 3.92 (m,2H), 3.46 (m,2H), 2.92 (m,1H), 2.91 (m,2H), 2.79 (m,2H), 1.83 (m,4H).

The following compounds were prepared according to the general synthesis shown in Scheme A9:

Ex	SM [F-12]	Carboxamide [F-19]	Characterisation	
68	[AA-25]		method: 2, RT: 2.16 min, MI: 354 [M+1]	1H NMR (300MHz, DMSO): 8.7(d,2H), 8.2 (d,2H), 3.9 (m,1H), 3.6 (m,1H), 3.3 (m,1H), 1.8 (m,4H), 1.6 (m,2H), 1 (t, 3H)
69	[AA-26]		method: 2, RT: 2.94 min, MI: 430 [M+1]	
70	[AA-28]		method: 2, RT: 2.72 min, MI: 430 [M+1]	
71	[AA-25]		method: 3, RT: 2.54 min, MI: 416 [M+1]	1H NMR (300MHz, DMSO): 8.67 (d,2H), 7.9 (d,2H), 7.3 (m,5H), 3.9 (m,2H), 3.53 (m,2H), 2.92 (m,1H), 2.91 (m,2H), 2.79 (m,2H), 1.83 (m,4H)
72	[AA-33]		method: 3, RT: 2.52 min, MI: 521 [M+1]	
73	[AA-33]		method: 3, RT: 2.53 min, MI: 521 [M+1]	
74	[AA-38]		method: 2, RT: 2.31 min, MI: 419	

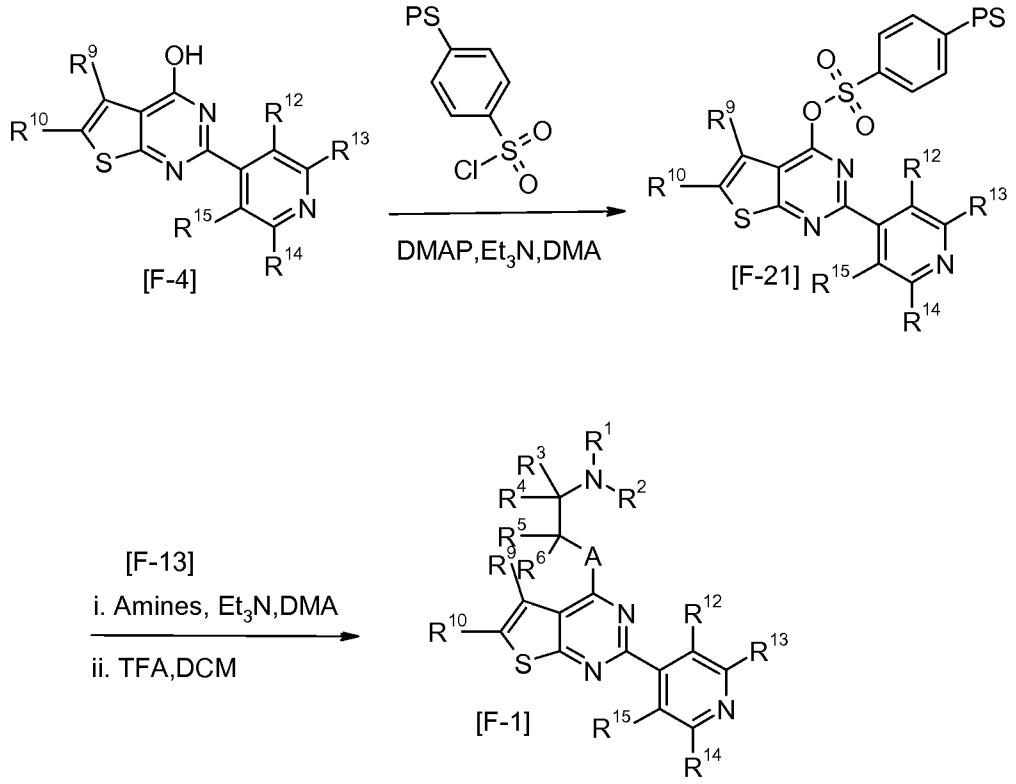
Ex	SM [F-12]	Carboxamide [F-19]	Characterisation	
			[M+1]	
75	[AA-39]		method: 2, RT: 2.56 min, MI: 404 [M+1]	
76	[AA-27]		method: 2, RT: 2.95 min, MI: 444 [M+1]	
77	[AA-30]		method: 3, RT: 2.77 min, MI: 444 [M+1]	
78	[AA-29]		method: 3, RT: 2.37 min, MI: 474 [M+1]	
79	[AA-29]		method: 3, RT: 2.37 min, MI: 474 [M+1]	
80	[AA-32]		method: 3, RT: 2.59 min, MI: 434 [M+1]	
81	[AA-32]		method: 3, RT: 2.60 min, MI: 434 [M+1]	
82	[AA-31]		method: 3, RT: 2.23 min, MI: 418 [M+1]	

Ex	SM [F-12]	Carboxamide [F-19]	Characterisation	
83	[AA-31]		method: 3, RT: 2.27 min, MI: 418 [M+1]	

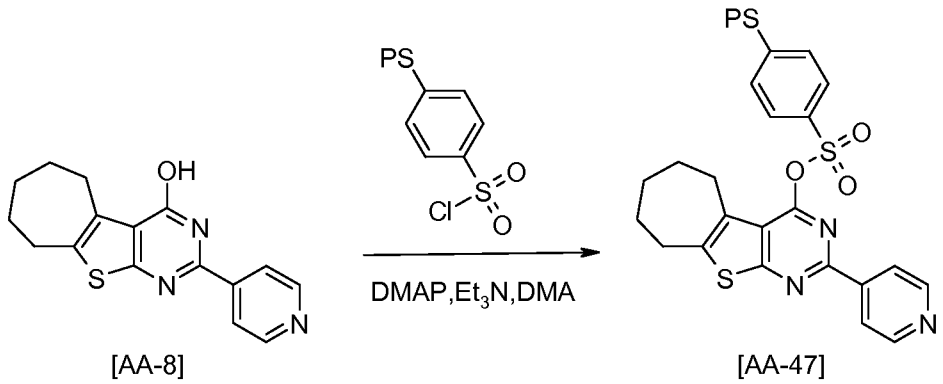
General synthesis of 5,6 substituted 4-amino-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-1] (Scheme A10)

5, 6-substituted 2-pyridin-4-yl-thieno [2, 3-d] pyrimidin-4-ol derivatives of general formula [F-4] [prepared in scheme A2] were subjected to a activation reaction by reaction with a solid supported sulfonyl chloride derivative such as benzenesulfonyl choride on polystyrene resin 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 with a catalytic amount of DMAP at ambient temperature. Excess reagents and reactants were removed by filtration and washing the polystyrene resin with solvents such as DCM, DMF, THF. The polymer supported reagent of general formula [F-21] was then reacted with an N-Boc protected diamino derivative of general formula [F-13] 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 resin was filtered through a PTFE frit and washed with a solvent such as DCM or ethylacetate, the filtrate was combined and 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 A10

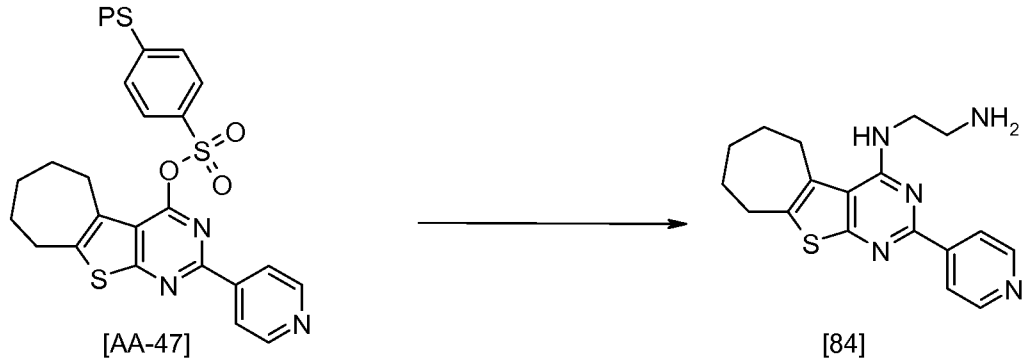


Synthesis of polystyrene supported benzenesulfonic acid 2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-yl ester [AA-47]



2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-ol [AA-8] (70mg, 0.241 mmol) and PS-TSCl (70mg, 0.241 mmol) were placed into sealed filter cartridge. DMA was added (2 ml) followed by Et_3N (100 µl, 0.723 mmol) and DMAP (1.5 mg, 0.001 mmol). The reaction mixture was shaken for 3 hours at room temperature and then the resin was filtered, through a PTFE frit. The resin was washed with DCM to yield to the polystyrene supported benzenesulfonic acid 2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-yl ester [AA-77] which was used in the next step without further purification.

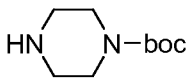
Synthesis of N*1*-(2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-yl)-ethane-1,2-diamine [84]

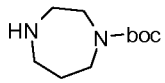
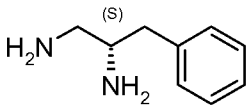
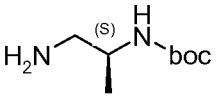
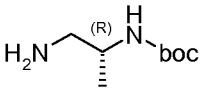
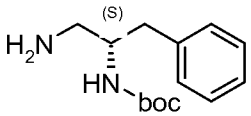
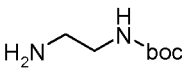
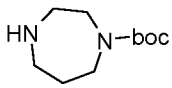
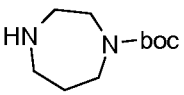


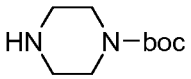
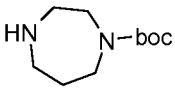
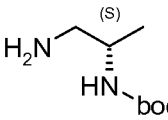
[AA-47] [84]

The polystyrene supported benzenesulfonic acid 2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-yl ester [AA-47] (70 mg, 0.24 mmol) was placed in a filter cartridge and DMA (2 ml) was added followed by Boc-ethylenediamine (39 mg, 0.241 mmol) and Et_3N (67 µl, 0.482 mmol). The reaction was shaken overnight at room temperature. The resin was filtered through a PTFE frit and washed with ethylacetate. The filtrate was concentrated under reduced pressure and the crude product was dissolved in DCM (2 ml) and TFA (2 ml) was added and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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: 2, RT: 3.22 min, MI: 340 [M+1].

The following compounds were prepared according to the general synthesis shown in Scheme A10:

Ex	SM	Amine [F-13]	Characterisation	
85	[AA-8]		method: 2, RT: 2.26 min, MI: 366 [M+1]	1H NMR (300MHz, DMSO): 8.72 (d,2H), 8.25 (d,2H), 3.62 (m,2H), 3.44 (m,4H), 3.06 (m,2H), 3.03 (m,4H), 1.88 (m,2H), 1.64 (m,4H)

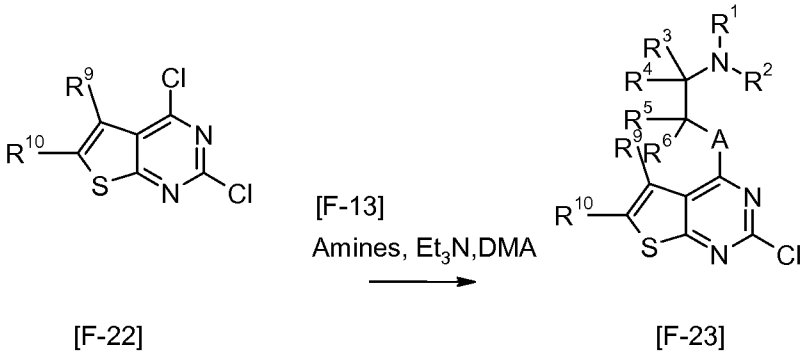
Ex	SM	Amine [F-13]	Characterisation	
86	[AA-8]		method: 2, RT: 2.27 min, MI: 380 [M+1]	
87	[AA-8]		method: 2, RT: 2.77 min, MI: 430 [M+1]	
88	[AA-8]		method: 2, RT: 2.25 min, MI: 354 [M+1]	
89	[AA-8]		method: 2, RT: 2.26 min, MI: 354 [M+1]	1H NMR (300MHz, DMSO): 8.71 (d,2H), 8.26 (d,2H), 3.83 (m,1H), 3.75 (m,1H), 3.62 (m,1H), 3.09 (m,2H), 2.98 (m,2H), 1.89 (m,2H), 1.66 (m,4H), 1.21 (d,3H)
90	[AA-11]		method: 2, RT: 2.63 min, MI: 517 [M+1]	
91	[AA-22]		method: 2, RT: 2.41 min, MI: 362 [M+1]	
92	[AA-22]		method: 2, RT: 2.41 min, MI: 402 [M+1]	
93	[AA-23]		method: 2, RT: 2.48 min, MI: 467 [M+1]	

Ex	SM	Amine [F-13]	Characterisation	
94	[AA-15]		method: 2, RT: 1.90 min, MI: 312 [M+1]	
95	[AA-15]		method: 2, RT: 1.91 min, MI: 326 [M+1]	
96	[AA-11]		method: 2, RT: 2.32 min, MI: 441 [M+1]	

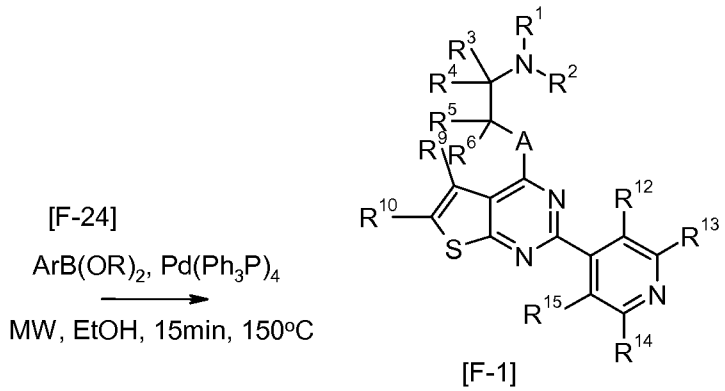
General synthesis of pyridyl substituted 4-amino-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-1] (Scheme A11)

A 2,4-dichloro-5,6,7,8-tetrahydro-enzo [4,5] thieno [2,3-d]pyrimidine derivative of general formula [F-21] was reacted with primary and secondary amino derivative of general formula [F-13] 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. Following reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the amino derivative of general formula [F-23] was reacted with pyridyl boronic acids or boronate esters of general formula [F-24] in the presence of 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. Following reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A11

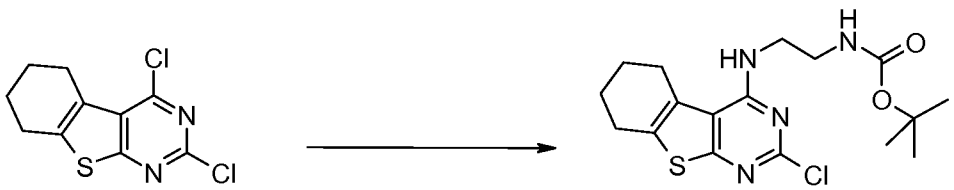


[F-22] [F-23]



[F-1]

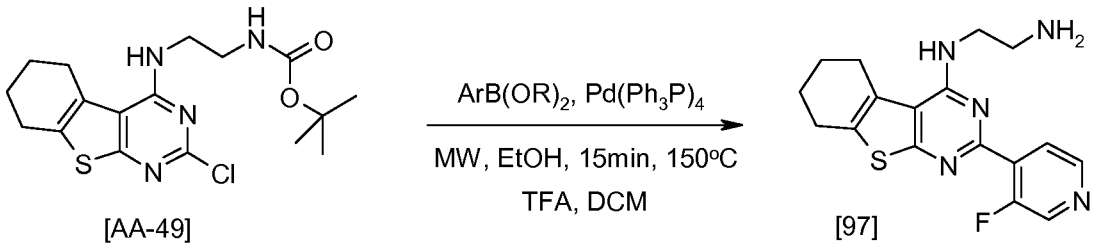
Synthesis of [2-(2-chloro-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yla mino)-ethyl]-carbamic acid tert-butyl ester [AA-49]



[AA-48] [AA-49]

To a solution of 2,4-dichloro-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [AA-48] (100mg, 0.387mmol) in DMA (5 ml) was added Boc-ethylenediamine (62 mg, 0.387mmol) followed by Et_3N (110 µl, 0.774 mmol), the mixture was stirred at room temperature for 2 hours. Then the product was extracted with DCM (2x10 ml) and washed with brine (2x10 ml). The combined organic phases were dried with magnesium sulfate, filtered and evaporated to provide a brown solid. The residue was used without further purification in the next step. LCMS method: 1, RT: 6.26 min, MI: 383 [M+1].

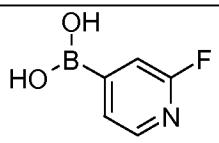
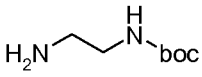
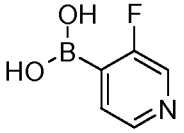
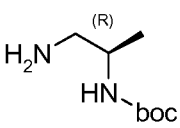
Synthesis of N*1*-[2-(3-fluoro-pyridin-4-yl)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl]-ethane-1,2-diamine [97]

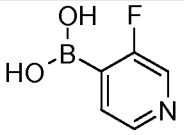
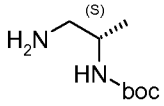
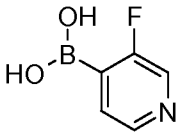
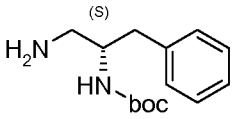
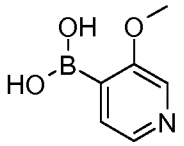
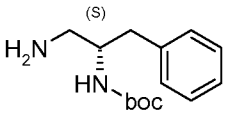


[AA-49] [97]

A microwave vial was charged with [2-(2-chloro-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [AA-49] (80mg, 0.210 mmol), 3-fluoropyridine-4-boronic acid hydrate (38mg, 0.24 mmol), tetrakis (triphenyl phosphine) palladium (12 mg, 0.01 mmol), Na_2CO_3 (2M in water, 300µl, 0.6 mmol) and EtOH (1ml). The reaction was heated to 150°C for 15 minutes under microwave irradiation. The mixture was then filtered through a plug of silica, washed with methanol and the filtrate was concentrated under reduced pressure. To a solution of the crude product in DCM (2 ml) was added TFA (2 ml) and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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: 2, RT: 2.41 min, MI: 344 [M+1].

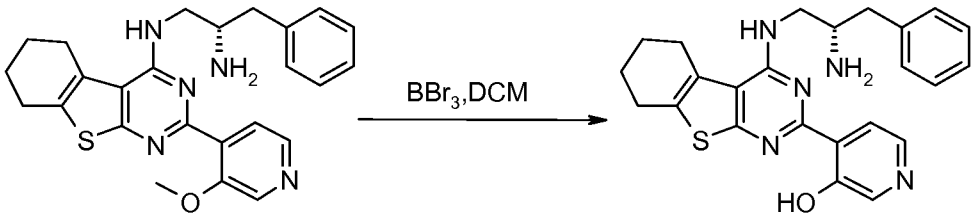
The following compounds were prepared according to the general synthesis shown in Scheme A11:

Ex	SM	Boronic acid [F24]	Amine [F-13]	Characterisation	
98	[AA-49]			method: 2, RT: 2.64 min, MI: 344 [M+1]	
99	[AA-49]			method: 2, RT: 2.56 min, MI: 358 [M+1]	1H NMR (300MHz, DMSO): 8.677 (d,1H), 8.26 (d,1H), 8.34 (s,1H), 3.83 (m,1H), 3.75 (m,1H), 3.62 (m,1H), 2.91 (m,2H), 2.79 (m,2H), 1.66

Ex	SM	Boronic acid [F24]	Amine [F-13]	Characterisation	
					(m,4H), 1.21 (d,3H)
100	[AA-49]			method: 2, RT: 2.52 min, MI: 358 [M+1]	
101	[AA-49]			method: 2, RT: 2.79 min, MI: 434 [M+1]	1H NMR (300MHz, DMSO): 8.64 (d,1H), 8.53 (d,1H), 7.83 (m,1H), 7.26 (m,5H), 3.92 (m,2H), 3.46 (m,2H), 2.92 (m,1H), 2.91 (m,2H), 2.79 (m,2H), 1.83 (m,4H)
102	[AA-49]			method: 4, RT: 4.22 min, MI: 446 [M+1]	

Synthesis of 4-[4-((S)-2-Amino-3-phenyl-propylamino)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-2-yl]-pyridin-3-ol [103] (Scheme A12)

Scheme A12



[102] [103]

To a solution of (S)-N*1*-[2-(3-methoxy-pyridin-4-yl)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine (prepared according to the general synthesis shown in scheme A11) [102] (30 mg, 0.06 mmol) in DCM (1 ml) cooled to -30°C was added dropwise a solution of 1 M BBr_3 in DCM (180 µl, 0.180 mmol) under nitrogen. The reaction mixture was stirred at -30°C for 1 hour and

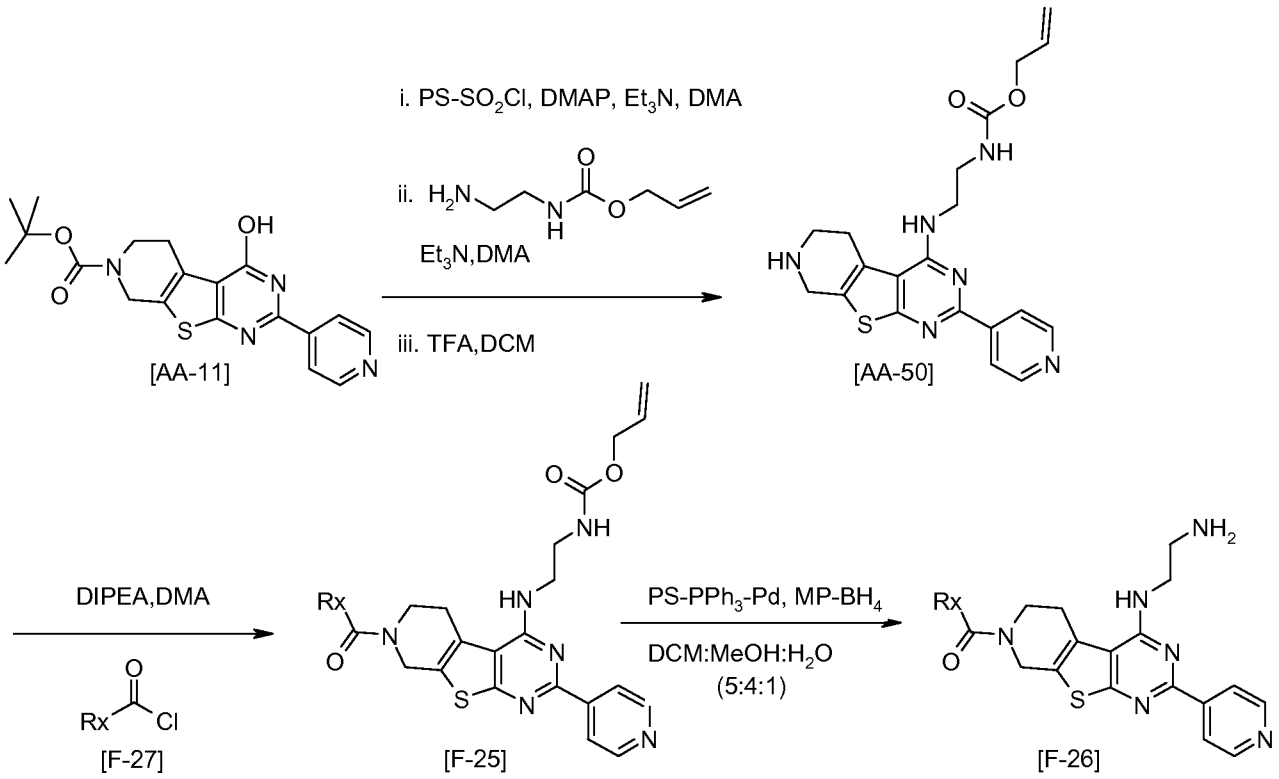
stirred overnight at room temperature. The residue was concentrated under reduced pressure and then dissolved in DMSO and purified by preparative HPLC (method B) to yield to the title compound. LCMS method: 4, RT: 4.43 min, MI: 432 [M+1]. 1H NMR (300MHz, DMSO): 8.30 (d,1H), 8.10 (d,1H), 7.81 d,1H), 7.28 (m,5H), 3.46 (m,2H), 3.40 (m,1H), 2.96 (m,2H), 2.79 (m,4H), 1.83 (m,4H).

General synthesis of 1-[4-(2-amino-ethylamino)-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-7-yl]-alkylanone derivatives of general formula [[F-26] (Scheme A13)

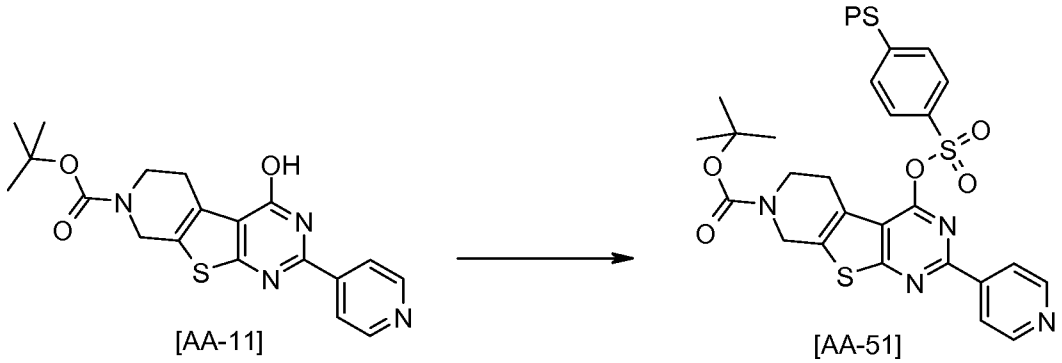
4-benzenesulfonyloxy-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5]thieno[2,3-d]pyrimidine-7-carboxylic acid tert-butyl ester [AA-11] (described in scheme A2) was subjected to an activation by reaction with a solid supported sulfonyl chloride derivative such as benzenesulfonyl choride on polystyrene 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 with a catalytic amount of DMAP at ambient temperature. Excess reagents and reactants were removed by filtration and washing the polystyrene resin with a solvent such as DCM, DMF, THF. The polymer supported reagent was then reacted with (2-amino-ethyl)-carbamic acid allyl ester 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 resin was fitred through a PTFE frit and washed with a solvent such as DCM or ethylacetate, the extracts were combined and after reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivative was 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 to give [2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-50]. Reaction of pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-50] with an acyl chloride derivative of general formula [F-27] 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 gave the N-acylated [F-25] derivative which was subjected to an N-allyl deprotection reaction with polymer supported palladium, polymer supported borohydride in DCM, MeOH and water to give the corresponding amino derivates [F-26] . Following reaction work up, typically by a liquid-liquid extraction or purification by

acidic ion exchange catch-release the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A13



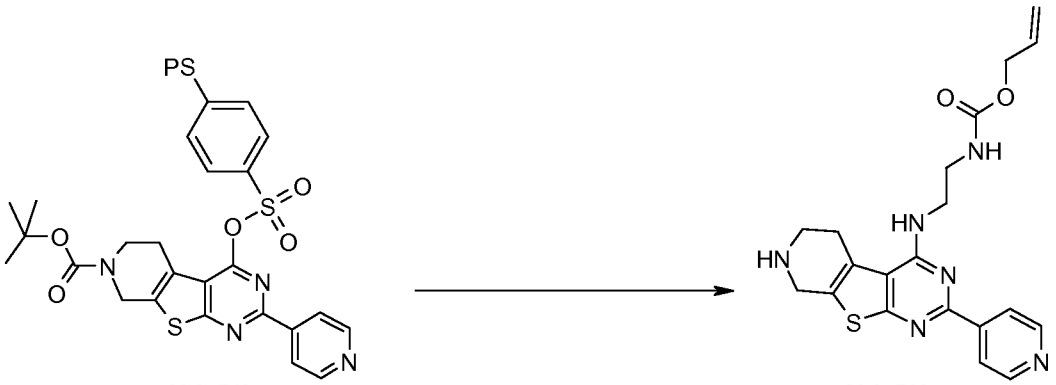
Synthesis of polystyrene supported 4-benzenesulfonyloxy-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5]thieno[2,3-d]pyrimidine-7-carboxylic acid tert-butyl ester [AA-51]



2-pyridin-4-yl-6,7,8,9-tetrahydro-5H-10-thia-1,3-diaza-benzo[a]azulen-4-ol [AA-11] (700mg, 1.83 mmol) and PS-TSCl (1.2 g, 2.92 mmol) were placed into filter cartridge closed with a stopper. DMA (10 ml) was added followed by Et_3N (510 µl, 3.66 mmol) and DMAP (11 mg, 0.09 mmol). The reaction was shaken for 3 hours at room temperature and then the resin was filtered through a PTFE frit. The resin was washed with DCM (6 ml) to

yield to the polystyrene supported 4-benzenesulfonyloxy-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5] thieno [2,3-d]pyrimidine-7-carboxylic acid tert-butyl ester [AA-51], which was used in the next step without further purification.

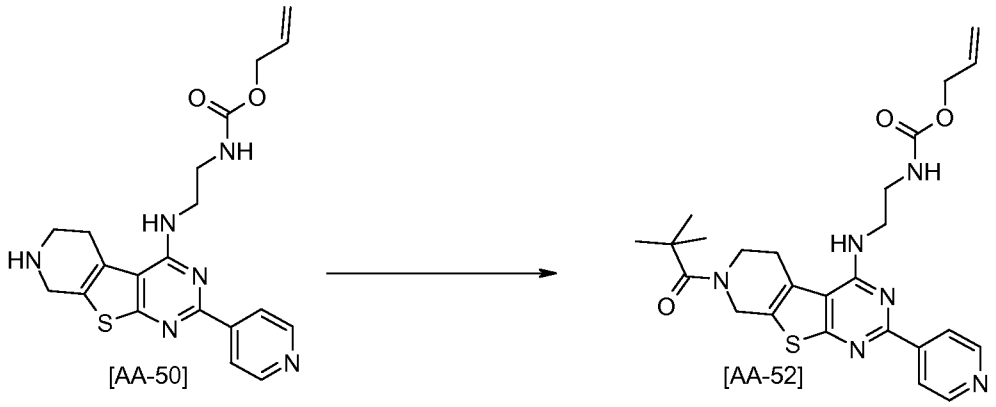
Synthesis of [2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-50]



[AA-51] [AA-50]

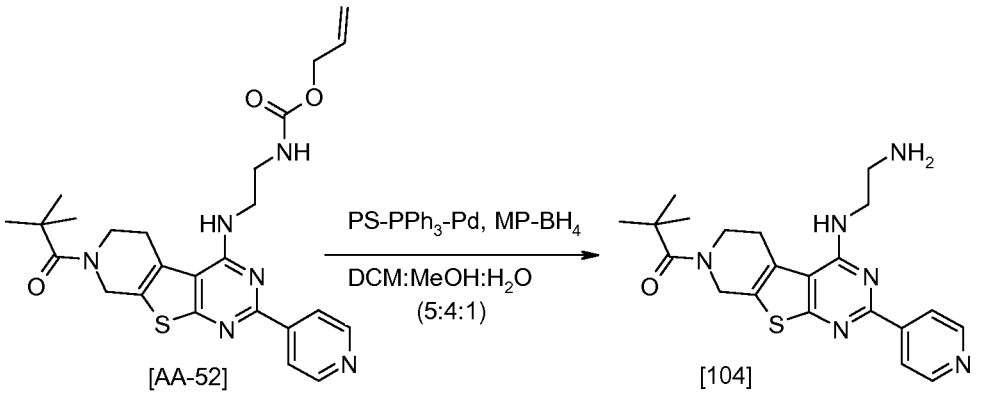
To the polystyrene supported 4-benzenesulfonyloxy-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5] thieno [2,3-d]pyrimidine-7-carboxylic acid tert-butyl ester [AA-51] placed into a filter cartridge was added DMA (2 ml) followed by allyl-N-(2-aminoethyl)carbamate hydrochloride (397 mg, 2.2 mmol) and Et_3N (510 µl, 3.66 mmol). The reaction was shaken overnight at room temperature. The resin was filtered through a PTFE frit and washed with ethylacetate (6 ml) followed by DCM (6 ml). The extracts were combined and evaporated under reduced pressure. The crude reaction product was dissolved in DCM (25 ml) and washed with sodium hydrogen carbonate (20 ml) then brine (20 ml), dried with magnesium sulfate, filtered and evaporated under reduced pressure to provide an orange solid. To a solution of the crude product in DCM (5 ml) was added TFA (5 ml) and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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 used without further purification in the next step. LCMS method: 1, RT: 4.23 min, MI: 411 [M+1].

Synthesis of {2-[7-(2,2-dimethyl-propionyl)-2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino]-ethyl}-carbamic acid allyl ester [AA-52]



To a solution of [2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-50] (50mg, 0.121 mmol) in DMA (1 ml) at -10°C were added trimethylacetyl chloride (16 µl, 0.133 mmol) and *N*,*N*,-di-isopropyethylamine (60 µl, 0.363 mmol). The mixture was stirred overnight. After completion the reaction mixture was treated with water (2 ml) and brine (2 ml) and extracted with DCM (3 ml). The organics were evaporated under vacuum and the crude product was used without further purification in the next step.

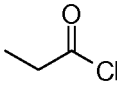
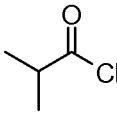
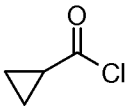
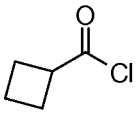
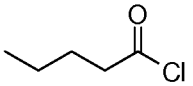
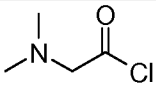
Synthesis of 1-[4-(2-amino-ethylamino)-2-pyridin-4-yl-5,8-dihydro-6H-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-7-yl]-2,2-dimethyl-propan-1-one [104]



To a solution of {2-[7-(2,2-dimethyl-propionyl)-2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5] thieno[2,3-d]pyrimidin-4-ylamino]-ethyl}-carbamic acid allyl ester [AA-52] (50mg, 0.121 mmol) in DCM:MeOH:H_2O (5:4:1) (2 ml) in a filter cartridge were added PS-PPh_3-Pd (18mg, 0.002 mmol) and MP-BH_4 (116mg, 0.363 mmol). The reaction was shaken for 2h after then the solution was filtered through Na_2SO_4 plug. The filtrate was concentrated under reduced pressure and the crude residue was purified by

preparative HPLC (method A) to yield to the title compound. LCMS method: 2, RT: 2.26 min, MI: 411 [M+1].

The following compounds were prepared according to the general synthesis shown in Scheme A13:

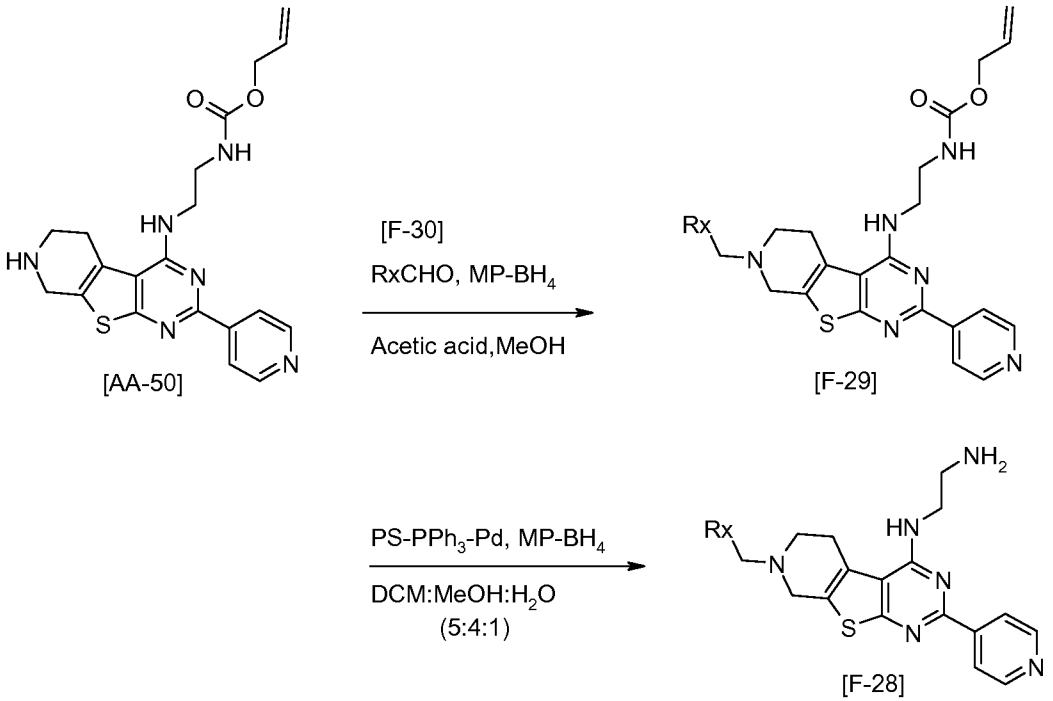
Ex	SM	Acid chloride [F-27]	Characterisation
105	[AA-52]		method: 2, RT: 1.83 min, MI: 369 [M+1]
106	[AA-52]		method: 2, RT: 1.97 min, MI: 383 [M+1]
107	[AA-52]		method: 2, RT: 2.02 min, MI: 397 [M+1]
108	[AA-52]		method: 2, RT: 2.01 min, MI: 395 [M+1]
109	[AA-52]		method: 2, RT: 2.13 min, MI: 409 [M+1]
110	[AA-52]		method: 2, RT: 2.32 min, MI: 411 [M+1]
111	[AA-52]		method: 2, RT: 1.66 min, MI: 412 [M+1]

General synthesis of N*1*-(7-alkyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-yl)-ethane-1,2-diamine derivatives of general formula [F-28] (Scheme A14)

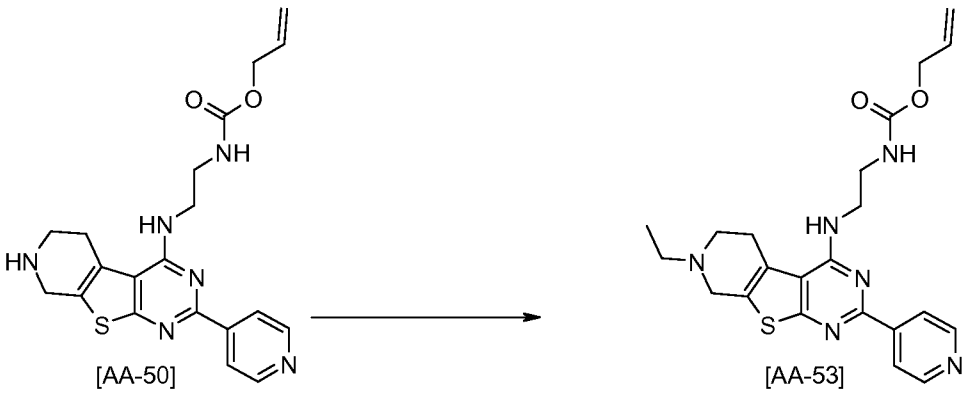
[2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-50] was reacted in reductive amination reaction with aldehyde derivative of general formula [F-30] and a solid supported borohydride reagent in acetic acid and a polar protic solvent such as MeOH or EtOH. The N-alkylated derivative of general formula [F-29] was subjected to an N-allyl deprotection reaction with polymer supported palladium, polymer supported borohydride in DCM, MeOH and water to provide the amino derivative [F-28]. Following reaction work up,

typically filtration through a PTFE frit followed by by a liquid-liquid extraction or purification by acidic ion exchange catch-release the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A14



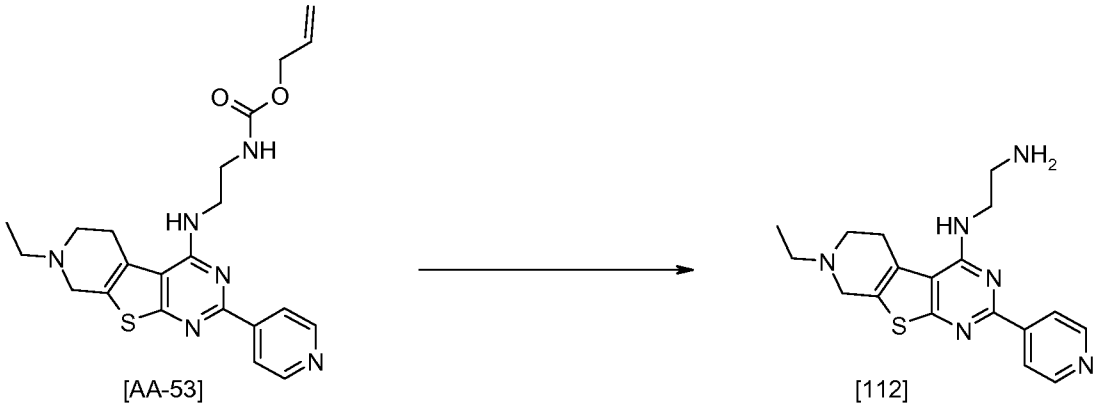
Synthesis of [2-(7-ethyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-53]



To a solution of [2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-50] (50mg, 0.121 mmol) in MeOH (1 ml) in a filter cartridge were added MP-BH_4 (144mg, 0.290 mmol) followed by acetaldehyde (4 µl, 0.075 mmol) and acetic acid (7 µl, 0.121 mmol). The reaction was shaken overnight at room temperature and then filtered through a PTFE frit. The filtrate was evaporated under reduced pressure and the resulting residue was dissolved in

methanol and the mixture was loaded onto a SCX-2 cartridge 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 to yield the title compound which was used without further purification in the next step.

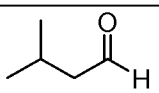
Synthesis of N*1*-(7-ethyl-2-pyridin-4-yl-5,6,7,8-tetrahydro-pyrido[4',3':4,5]thieno[2,3-d]pyrimidin-4-yl)-ethane-1,2-diamine [112]



[AA-53] [112]

To a solution of [2-(7-ethyl-2-pyridin-4-yl-5,6,7,8-tetrahydropyrido[4',3':4,5]-thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid allyl ester [AA-53] (50mg, 0.121 mmol) in DCM:MeOH:H2O (5:4:1) (2 ml) in a filter cartridge were added PS-PPh_3-Pd (18mg, 0.002 mmol) and MP-BH_4 (116mg, 0.363 mmol). The reaction was shaken for 2h after completion the solution was filtered through Na_2SO_4 plug. The filtrate was concentrated under reduced pressure and the residue purified by preparative HPLC (method A) to yield to the title compound. LCMS method: 2, RT: 1.89 min, MI: 355 [M+1].

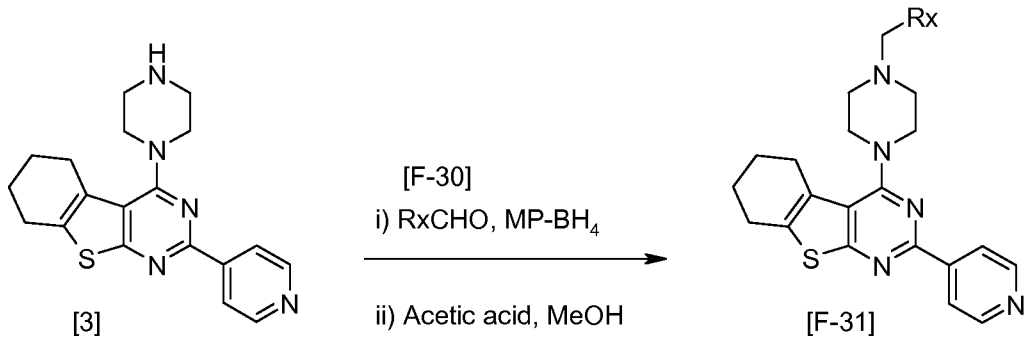
The following compounds were prepared according to the general synthesis shown in Scheme A14:

Ex	SM	Aldehyde [F-30]	Characterisation
113	[AA-50]		method: 2, RT: 1.96 min, MI: 341 [M+1]
114	[AA-50]		method: 2, RT: 1.61 min, MI: 383 [M+1]

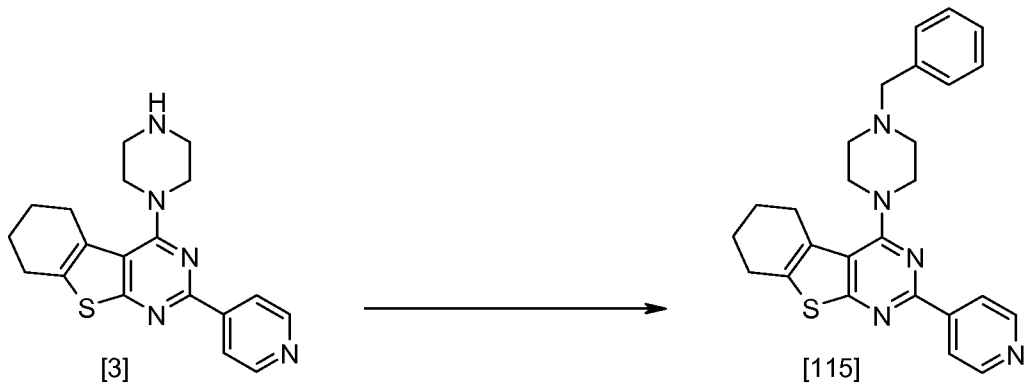
General synthesis of 4-(4-alkyl-piperazin-1-yl)-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine derivatives of general formula [F-31] (Scheme A15)

4-piperazin-1-yl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [3] was subjected to a reductive amination reaction with aldehyde derivatives of general formula [F-30] and a solid supported borohydride reagent in acetic acid and a polar protic solvent such as MeOH or EtOH to yield the alkylated derivative [F-27]. Following reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A15



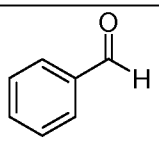
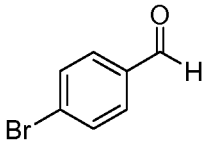
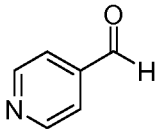
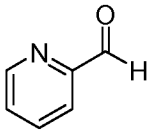
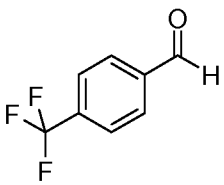
Synthesis of 4-(4-benzyl-piperazin-1-yl)-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [115]

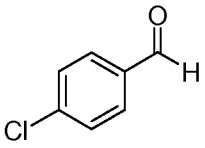
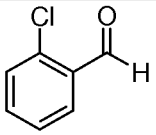
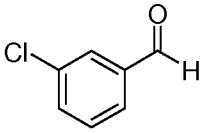
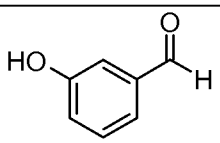
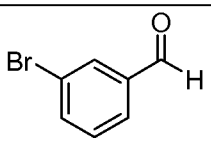
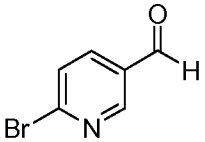
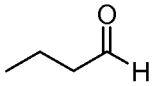
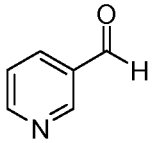


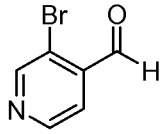
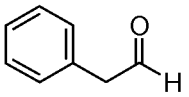
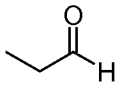
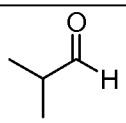
To a solution of 4-piperazin-1-yl-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [3] (50mg, 0.142 mmol) in MeOH (2 ml) in a filter cartridge were added MP-BH_4 (170mg, 0.341 mmol), p-anisaldehyde (11 µl, 0.09 mmol) and acetic acid (8 µl, 0.142 mmol). The reaction was shaken overnight at room temperature and then filtered through a PTFE frit. The filtrate was evaporated under

reduced pressure and the resulting residue was dissolved in methanol and the mixture was loaded onto a SCX-2 cartridge 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 purified by preparative HPLC (method A) to yield to the title compound. LCMS method: 2, RT: 2.61 min, MI: 456 [M+1]. 1H NMR (300MHz, DMSO): 8.70 (d,2H), 8.22 (d,2H), 7.21 (d,2H), 7.15 (d,2H), 3.47 (m,7H), 2.90 (m,5H), 2.54 (s,2H), 2.28 (s,3H), 1.87 (br s, 2H), 1.73 (br s, 2H).

The following compounds were prepared according to the general synthesis shown in Scheme A15:

Ex	SM	Aldehyde [F-30]	Characterisation	
116	[3]		method: 2, RT: 2.56 min, MI: 442 [M+1]	
117	[3]		method: 2, RT: 2.77 min, MI: 520 [M+1]	
118	[3]		method: 2, RT: 2.3 min, MI: 443 [M+1]	
119	[3]		method: 2, RT: 2.22 min, MI: 380 [M+1]	
120			method: 2, RT: 2.32 min, MI: 443 [M+1]	
121	[3]		method: 2, RT: 2.97 min, MI: 510 [M+1]	1H NMR (300MHz, DMSO): 8.72 (d,2H), 8.24 (d,2H), 8.17 (s,1H), 7,73 (d.2H), 7,58 (d.2H), 3,66 (s.2H), 3.51 (m,4H), 2.9 (m,4H), 2.61 (m,2H), 2.53 (m,2H), 1.87 (m,2H), 1.74 (m,2H)

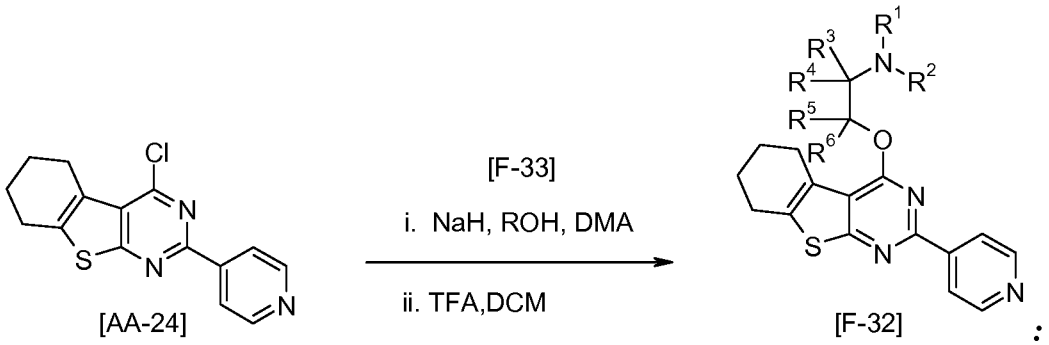
Ex	SM	Aldehyde [F-30]	Characterisation	
122	[3]		method: 2, RT: 2.72 min, MI: 476 [M+1]	
123	[3]		method: 2, RT: 2.78 min, MI: 476 [M+1]	
124	[3]		method: 2, RT: 2.76 min, MI: 476 [M+1]	1H NMR (300MHz, DMSO): 8.68 (d,2H), 8.22 (d,2H), 8.16 (s,1H), 7.34 (m,4H), 3.45 (s,2H), 3.48 (m,4H), 2.87 (m,4H), 2.57 (m,2H), 2.53 (m,2H), 1.87 (m,2H), 1.73 (m,2H)
125	[3]		method: 2, RT: 2.19 min, MI: 366 [M+1]	1H NMR (300MHz, DMSO): 8.68 (d,2H), 8.22 (d,2H), 3.48 (m,4H), 2.87 (m,4H), 2.57 (m,2H), 2.53 (m,2H), 2.28 (s,3H), 1.87 (d,2H), 1.72 (d,2H)
126	[3]		method: 2, RT: 2.41 min, MI: 458 [M+1]	
127	[3]		method: 2, RT: 2.83 min, MI: 520 [M+1]	
128	[3]		method: 2, RT: 2.57 min, MI: 520 [M+1]	
129	[3]		method: 2, RT: 2.32 min, MI: 408 [M+1]	
130	[3]		method: 2, RT: 2.23 min, MI: 443 [M+1]	1H NMR (300MHz, DMSO): 8.69 (d,2H), 8.53 (s,1H), 8.48 (m,1H), 8.23 (d,2H), 7.75 (m,1H), 7.35

Ex	SM	Aldehyde [F-30]	Characterisation	
				(m,1H), 3.58 (m,2H), 3.48 (m,4H), 2.88 (m,4H), 2.59 (m,2H), 2.53 (m,4H), 1.87 (m,2H), 1.73 (m,2H)
131	[3]		method: 2, RT: 3.28 min, MI: 520 [M+1]	
132	[3]		method: 2, RT: 2.57 min, MI: 456 [M+1]	
133	[3]		method: 2, RT: 2.30 min, MI: 394 [M+1]	
134	[3]		method: 2, RT: 2.32 min, MI: 408 [M+1]	

General synthesis of 5,6 substituted 4-alkoxy-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-32] (Scheme A16)

4-chloro-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [AA-24] was subjected to a nucleophilic substitution reaction with an amino alcohol or N-Boc protected amino alcohol of general formula [F-33] in the presence of a strong base such as NaH, KH or LDA in the presence of an anhydrous polar aprotic solvent such as DMA, DMF or NNP. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivative was 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 A16



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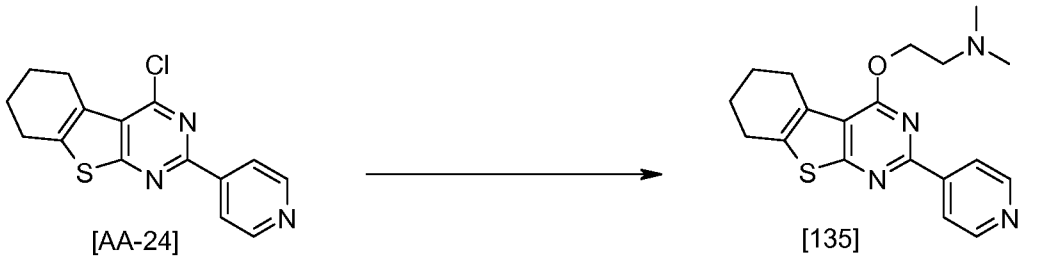
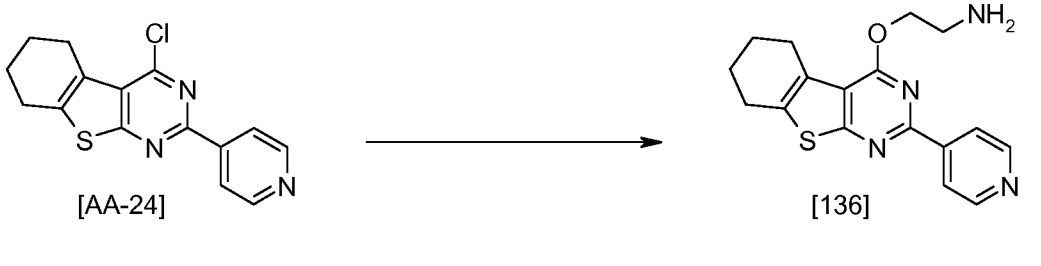
Synthesis of dimethyl-[2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yloxy)-ethyl]-amine [135]



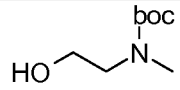
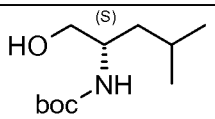
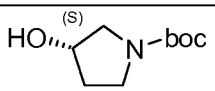
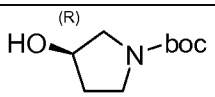
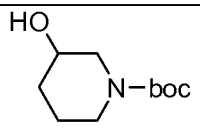
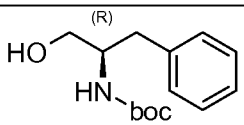
To a mixture of 4-chloro-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [AA-24] (80 mg, 0.280 mmol) and 2-dimethylaminoethanol (34 µl, 0.340 mmol) in DMA (1 ml) was added NaH (13 mg, 0.560 mmol). The reaction mixture was allowed to stir at room temperature for 2 hours and after completion the mixture was diluted with water and the product was extracted into DCM (2x2 ml). The combined organic phases were dried with magnesium sulfate, filtered and evaporated under reduced pressure and the crude product was purified by preparative HPLC (method A) to yield to the title compound. LCMS method: 2, RT: 2.20 min, MI: 355 [M+1]. 1H NMR (300MHz, DMSO): 8.70 (d,2H), 8.22 (d,2H), 3.1 (m,2H), 2.9 (m,2H), 2.75 (m,2H), 2.65 (m,2H), 2.34 (s,6H), 1.83 (m,4H).

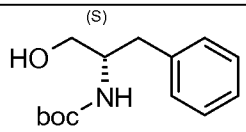
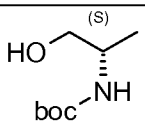
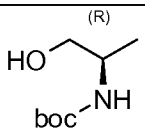
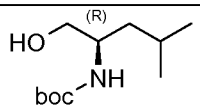
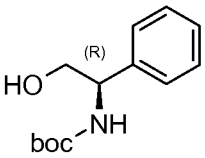
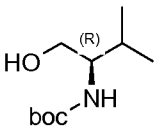
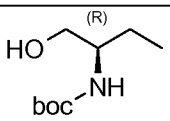
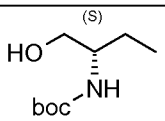
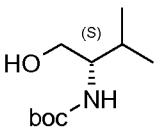
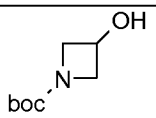
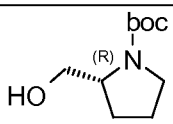
Synthesis of methyl-[2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yloxy)-ethyl]-amine [136]

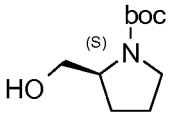
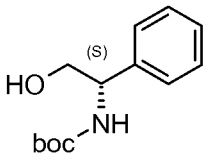


To a mixture of 4-chloro-2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [AA-24] (80 mg, 0.280 mmol) and tert-butyl-N-2-hydroxyethylcarbamate (53 µl, 0.340 mmol) in DMA (1 ml) was added NaH (13 mg, 0.560 mmol). The reaction mixture was allowed to stir at room temperature for 2 hours and after completion the mixture was diluted with water and the product was extracted into DCM (2x2 ml). The combined organic phases were dried with magnesium sulfate, filtered and evaporated under vacuum. To a solution of the crude product in DCM (1 ml) was added TFA (1 ml) and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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 product was purified by preparative HPLC (method A) to yield to the title compound. LCMS method: 2, RT: 2.16 min, MI: 327 [M+1]. 1H NMR (300MHz, DMSO): 8.70 (d,2H), 8.3 (d,2H), 2.96 (m,2H), 2.8 (m,2H), 2.56m,2H), 2.45(m,2H), 1.81 (m,4H).

The following compounds were prepared according to the general synthesis shown in Scheme A16:

Ex	SM	Alcohol [F-33]	Characterisation
137	[AA-24]		method: 2, RT: 2.83 min, MI: 341 [M+1]
138	[AA-24]		method: 2, RT: 2.45 min, MI: 383 [M+1]
139	[AA-24]		method: 2, RT: 2.20 min, MI: 353 [M+1]
140	[AA-24]		method: 2, RT: 2.20 min, MI: 353 [M+1]
141	[AA-24]		method: 2, RT: 2.29 min, MI: 367 [M+1]
142	[AA-24]		method: 2, RT: 2.60 min, MI: 417 [M+1]

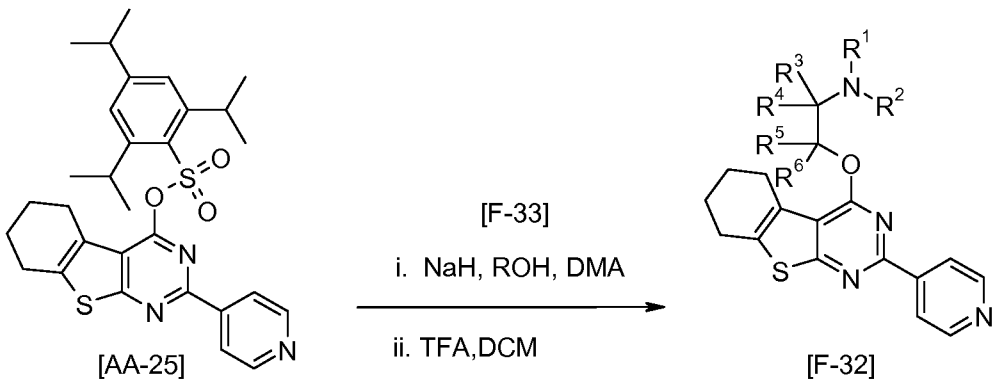
Ex	SM	Alcohol [F-33]	Characterisation
143	[AA-24]		method: 2, RT: 2.56 min, MI: 417 [M+1]
144	[AA-24]		method: 2, RT: 2.22 min, MI: 341 [M+1]
145	[AA-24]		method: 2, RT: 2.88 min, MI: 341 [M+1]
146	[AA-24]		method: 2, RT: 2.52 min, MI: 383 [M+1]
147	[AA-24]		method: 2, RT: 3.47 min, MI: 403 [M+1]
148	[AA-24]		method: 2, RT: 2.37 min, MI: 369 [M+1]
149	[AA-24]		method: 2, RT: 2.31 min, MI: 355 [M+1]
150	[AA-24]		method: 2, RT: 2.32 min, MI: 355 [M+1]
151	[AA-24]		method: 2, RT: 2.40 min, MI: 369 [M+1]
152	[AA-24]		method: 2, RT: 2.21 min, MI: 339 [M+1]
153	[AA-24]		method: 2, RT: 2.27 min, MI: 367 [M+1]

Ex	SM	Alcohol [F-33]	Characterisation
154	[AA-24]		method: 2, RT: 2.27 min, MI: 367 [M+1]
155	[AA-24]		method: 2, RT: 2.49 min, MI: 403 [M+1]

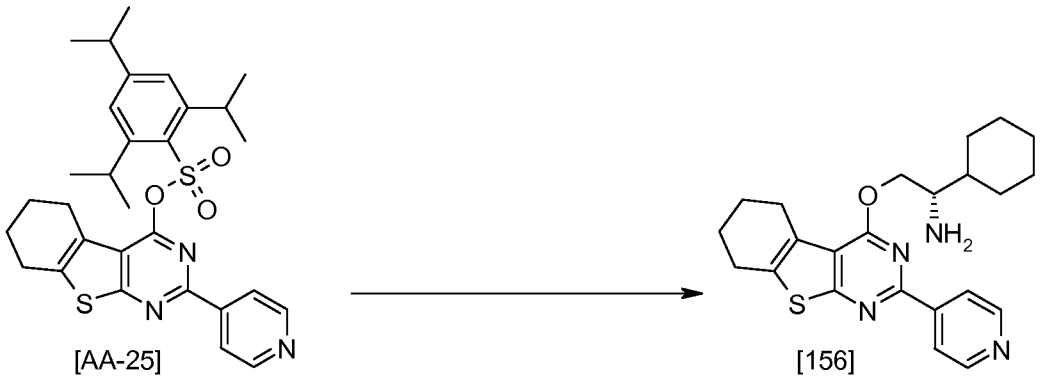
General synthesis of 5,6 substituted 4-alkoxy-2-pyridin-4-yl-thieno[2,3-d]pyrimidines [F-32] (Scheme A17)

2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-25] was subjected to a nucleophilic substitution reaction with a N-Boc protected amino alcohol of general formula F-33] in the presence of a strong base such as NaH, KH or LDA in the presence of an anhydrous polar aprotic solvent such as DMA, DMF or NNP. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivative was 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 and the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A17

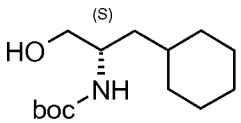


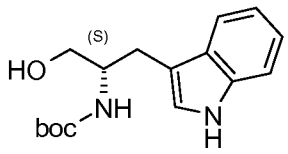
Synthesis of (S)-1-cyclohexyl-2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yloxy)-ethylamine [156]



To a mixture of 2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-25] (100 mg, 0.185 mmol) and N-Boc-L-cyclohexylglycinol (67 mg, 0.278 mmol) in DMA (1 ml) was added NaH (13 mg, 0.560 mmol). The reaction mixture was allowed to stir at room temperature for 2 hours and after completion the mixture was diluted with water and the product was extracted into DCM (2x2 ml). The combined organic phases were dried with magnesium sulfate, filtered and evaporated under reduced pressure. The crude product was dissolved in DCM (1 ml) and TFA (1 ml) was added and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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 product was purified by preparative HPLC (method A) to yield to the title compound. LCMS method: 2, RT: 2.62 min, MI: 409 [M+1]. 1H NMR (300MHz, DMSO): 8.7 (d,2H), 8.3 (d,2H), 4.7 (m,2H), 4.5 (m,2H), 3 (m,2H), 2.9 (m,2H), 1.81 (m,4H), 1.7 (m,3H), 1.6 (m,3H), 1.2 (m,4H).

The following compounds were prepared according to the general synthesis shown in Scheme A17:

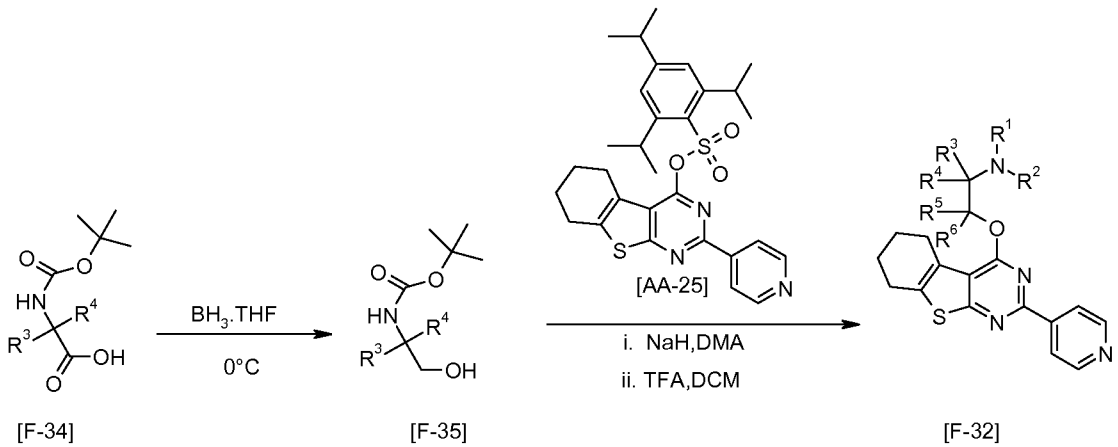
Ex	SM	Alcohol [F-33]	Characterisation	
157	[AA-25]		method: 2, RT: 2.82 min, MI: 423 [M+1]	1H NMR (300MHz, DMSO): 8.7 (d,2H), 8.3 (d,2H), 4.7 (m,2H), 4.5 (m,2H), 3.2 (m,2H), 2.8 (m,2H), 1.81 (m,4H), 1.7 (m,4H), 1.6 (m,2H), 1.4 (m,2H), 1.2 (m,2H), 0.9 (m,2H)

Ex	SM	Alcohol [F-33]	Characterisation	
158	[AA-25]		method: 2, RT: 2.82 min, MI: 456 [M+1]	

General synthesis of 5,6 substituted 4-alkoxy-2-pyridin-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-32] (Scheme A18)

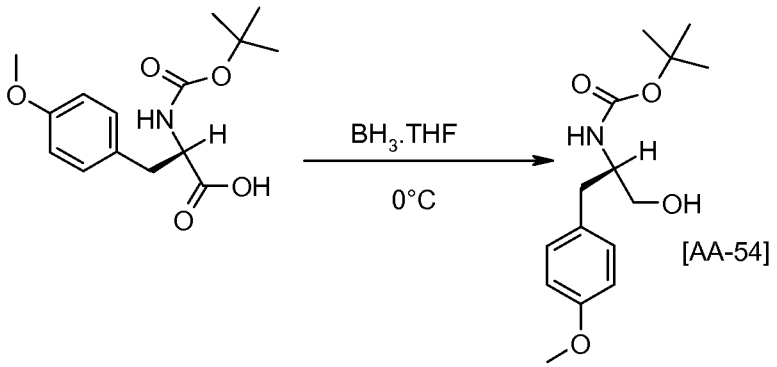
Compounds were synthesised starting from an N-Boc protected amino acid of general formula [F-34] which was converted to a primary alcohol derivative of general formula [F-35] by reduction with a borane reducing agent such as BH_3.THF or BH_3.SMe_2 in an anhydrous solvent such as THF, dioxane or diethylether. The resultant aminoalcohol derivative [F-35] was then reacted with a 5,6-substituted-(2,4,6-triisopropyl-benzenesulfonic acid)- 2-pyridin-4-yl-thieno[2,3-d]pyrimidin-4-yl ester [AA-25] [prepared in scheme A5] in the presence of a strong base such as NaH, KH or LDA in the presence of an anhydrous polar aprotic solvent such as DMA, DMF or NNP. After reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the N-Boc derivative was 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 the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A18



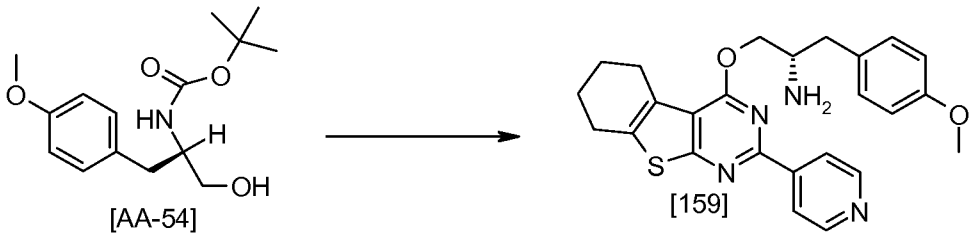
[F-34] [F-35] [F-32]

Synthesis of [(S)-2-hydroxy-1-(4-methoxy-benzyl)-ethyl]-carbamic acid tert-butyl ester [AA-54]



A 1M solution of BH_3 in THF (1.7 ml, 1.7 mmol) was added dropwise to a stirred solution of (S)-2-tert-butoxycarbonylamino-3-(4-methoxy-phenyl)-propionic acid (200 mg, 0.678 mmol) in dry THF (2.5 ml) at 0°C. The mixture was stirred for 2 hours at O°C then hydrolysed by slow addition of excess of 10% acetic acid/MeOH (5 ml) and stirred at room temperature for a further 2 hours. The solvent was removed under reduced pressure the residue was dissolved in ethylacetate (5 ml) and washed with saturated sodium bicarbonate (2x5 ml) and brine (2x5 ml). The combined organic phases were dried with magnesium sulfate, filtered and evaporated under reduced pressure to provide the title compound as a white solid which was used without further purification in the next step. LCMS method: 1, RT: 2.82 min, MI: 441 [M+1].

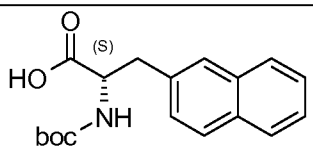
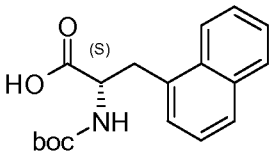
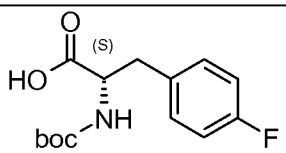
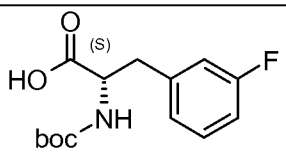
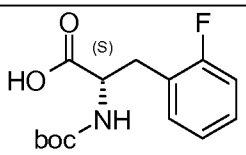
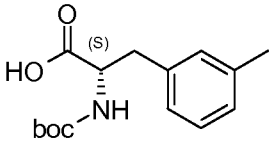
Synthesis of (S)-1-(4-methoxy-benzyl)-2-(2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo [4,5]thieno [2,3-d]pyrimidin-4-yloxy)-ethylamine [159]

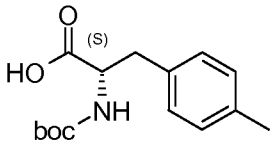
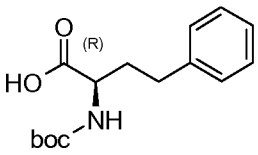
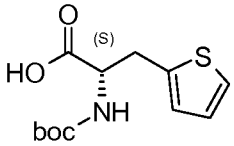
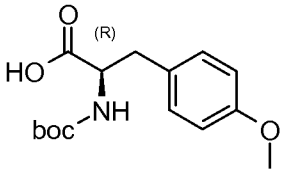
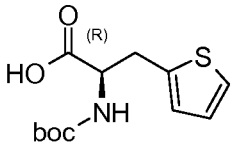
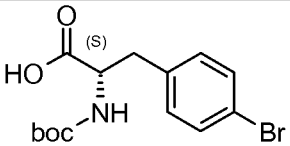
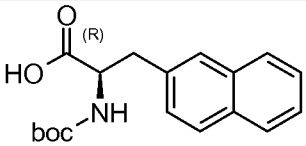
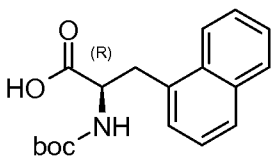
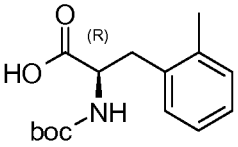


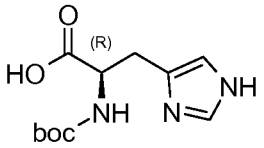
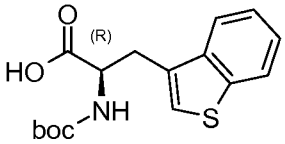
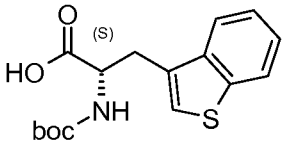
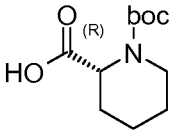
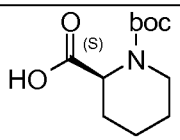
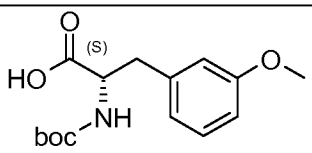
To a solution of 2,4,6-triisopropyl-benzenesulfonic acid 2-pyridin-4-yl-5,6,7,8-tetrahydro-benzo [4,5]thieno[2,3-d]pyrimidin-4-yl ester [AA-25] (50 mg, 0.091 mmol) in DMA (1 ml) was added [(S)-2-amino-1-(4-methyl-benzyl)-ethyl]-carbamic acid tert-butyl ester [AA-54] (31 mg, 0.110 mmol) followed by NaH (4 mg, 0.110 mmol), the mixture was stirred at room temperature for 2 hours. After completion the product was extracted with DCM (2 ml) and washed with brine (3 ml). To the organic phase was added TFA (2

ml) and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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: 2, RT: 2.61 min, MI: 447 [M+1]. 1H NMR (300MHz, DMSO): 8.7 (d,2H), 8.1 (d,2H), 7.2 (d,2H), 6.9 (d,2H), 4.7 (m,1H), 4.5 (m,1H), 3.8 (s,3H), 3.6 (m,2H), 2.9 (m,1H), 2.8 (m,2H), 2.7 (m,2H),1.81 (m,4H).

The following compounds were prepared according to the general synthesis shown in Scheme A18:

Ex	SM	Amino acid [F-34]	Characterisation
160	[AA-25]		method: 2, RT: 2.77 min, MI: 467 [M+1]
161	[AA-25]		method: 2, RT: 2.81 min, MI: 467 [M+1]
162	[AA-25]		method: 2, RT: 2.62 min, MI: 435 [M+1]
163	[AA-25]		method: 2, RT: 2.69 min, MI: 435 [M+1]
164	[AA-25]		method: 2, RT: 2.70 min, MI: 435 [M+1]
165	[AA-25]		method: 2, RT: 2.70 min, MI: 435 [M+1]

Ex	SM	Amino acid [F-34]	Characterisation
166	[AA-25]		method: 2, RT: 2.71 min, MI: 431 [M+1]
167	[AA-25]		method: 2, RT: 2.74min, MI: 431 [M+1]
168	[AA-25]		method: 2, RT: 2.71 min, MI: 423 [M+1]
169	[AA-25]		method: 2, RT: 2.71 min, MI: 447 [M+1]
170	[AA-25]		method: 2, RT: 2.58 min, MI: 423 [M+1]
171	[AA-25]		method: 2, RT: 2.76 min, MI: 495 [M+1]
172	[AA-25]		method: 2, RT: 3.04 min, MI: 467 [M+1]
173	[AA-25]		method: 2, RT: 2.81 min, MI: 467 [M+1]
174	[AA-25]		method: 2, RT: 2.76 min, MI: 431 [M+1]

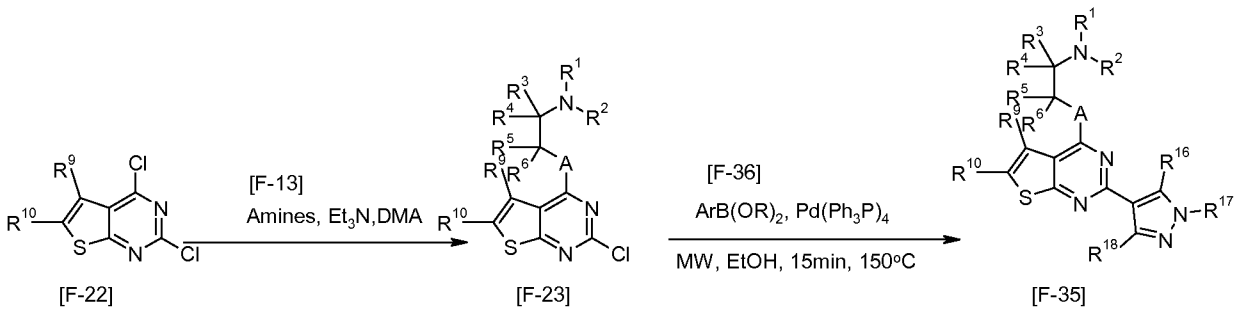
Ex	SM	Amino acid [F-34]	Characterisation
175	[AA-25]		method: 2, RT: 2.19 min, MI: 407 [M+1]
176	[AA-25]		method: 2, RT: 2.87 min, MI: 473 [M+1]
177	[AA-25]		method: 2, RT: 2.82 min, MI: 473 [M+1]
178	[AA-25]		method: 2, RT: 2.37 min, MI: 381 [M+1]
179	[AA-25]		method: 2, RT: 2.38 min, MI: 381 [M+1]
180	[AA-25]		method: 2, RT: 2.59 min, MI: 447 [M+1]

General synthesis of substituted 4-amino-2-pyrazolyl-4-yl-thieno[2,3-d]pyrimidine derivatives of general formula [F-35] (Scheme A19)

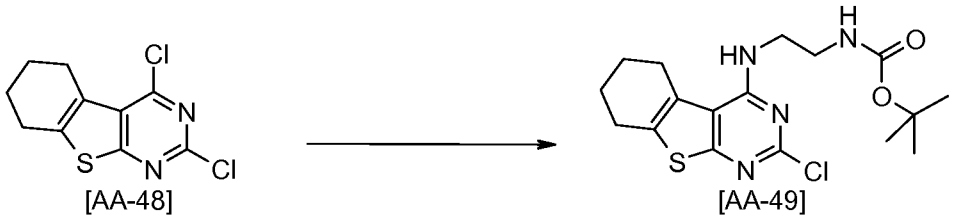
A 2,4-dichloro-5,6,7,8-tetrahydro-enzo [4,5] thieno [2,3-d]pyrimidine of general formula [F-21] was reacted with primary and secondary amino derivative of general formula [F-13] in a polar aprotic solvent such as DMA, DMF, NMP in the presence of a tertiary amine base such as Et_3N, DIPEA or NMM at ambient temperature. Following reaction work up, typically by a liquid-liquid extraction or purification by acidic ion exchange catch-release, the amino derivative of general formula [F-23] were reacted with pyrazolyl boronic acids or boronate esters of general formula [F-36] in the presence of 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 derivative was 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 the crude reaction product was purified by reverse phase preparative HPLC.

Scheme A19

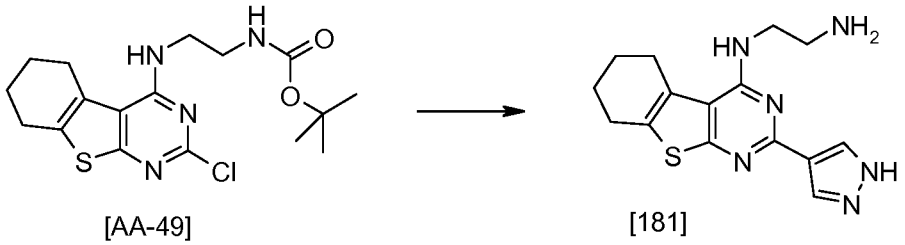


Synthesis of [2-(2-chloro-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yla mino)-ethyl]-carbamic acid tert-butyl ester [AA-49]



To a solution of 2,4-dichloro-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidine [AA-48] (100mg, 0.387mmol) in DMA (5 ml) was added Boc-ethylenediamine (62 mg, 0.387mmol) followed by Et_3N (110 µl, 0.774 mmol), the mixture was stirred at room temperature for 2 hours. Then the product was extracted with DCM (2x10 ml) and washed with brine (2x10 ml). The combined organic phases were dried with magnesium sulfate, filtered and evaporated under reduced pressure to provide a brown solid. The residue was used without further purification in the next step. LCMS method: 1, RT: 6.26 min, MI: 383 [M+1].

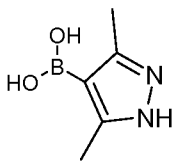
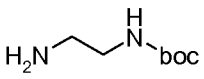
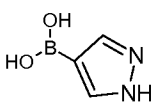
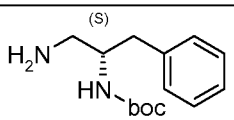
Synthesis of N*1*-[2-(1H-Pyrazol-4-yl)-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-yl]-ethane-1,2-diamine [181]

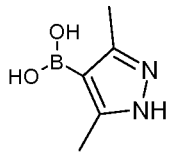
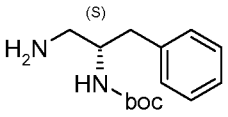
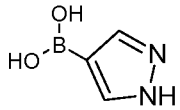
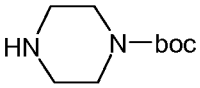
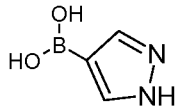
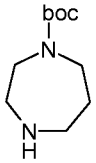
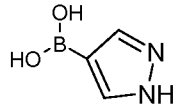
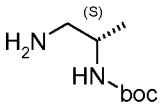
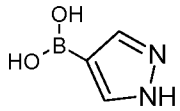
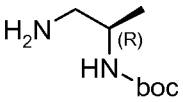
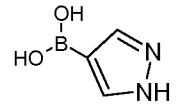
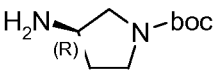
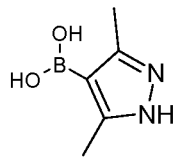
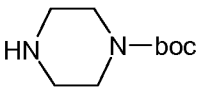
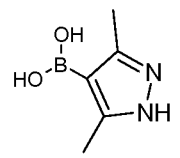
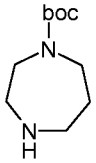


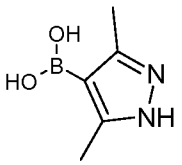
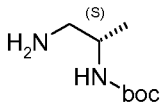
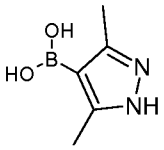
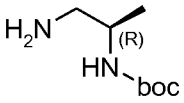
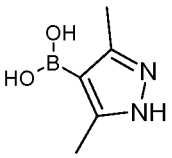
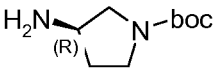
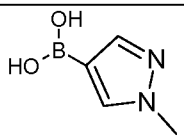
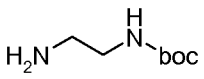
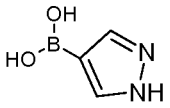
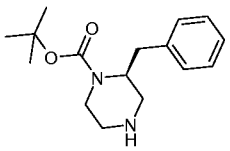
[AA-49] [181]

A microwave vial was charged with [2-(2-chloro-5,6,7,8-tetrahydro-benzo[4,5]thieno[2,3-d]pyrimidin-4-ylamino)-ethyl]-carbamic acid tert-butyl ester [AA-49] (40mg, 0.17 mmol), 1H-pyrazole-4-boronic acid (23 mg, 0.20 mmol), tetrakis (triphenyl phosphine) palladium (10 mg, 0.008 mmol), Na_2CO_3 (2M in water, 180µl, 0.6 mmol) and EtOH (1ml). The reaction was heated to 150°C for 15 minutes under microwave irradiation. The mixture was then filtered through a plug of silica, washed with methanol and the filtrate was concentrated under reduced pressure. To a solution of the crude product in DCM (2 ml) was added TFA (2 ml) and the mixture was stirred at room temperature for 1 hour. After completion the mixture was loaded onto a SCX-2 cartridge 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: 2, RT: 2.20 min, MI: 315 [M+1], ^{1}H NMR (300MHz, DMSO): 8,41 (s,1H), 8,20 (s,2H), 6.80 (t,1H), 3,74 (m,2H), 3,06 (m,2H), 2,94 (m,2H), 2,74 (s,2H), 2,53 (s,2H), 1,81 (s,4H).

The following compounds were prepared according to the general synthesis shown in Scheme A19:

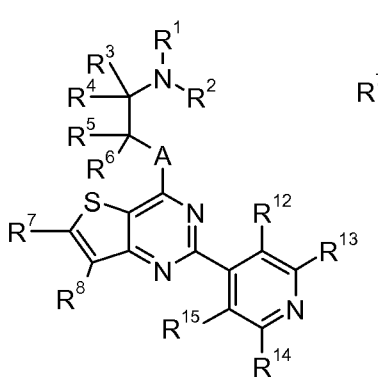
Ex	SM	Boronic acid [F36]	Amine [F-13]	Characterisation	
182	[AA-48]			method: 2, RT: 2.32 min, MI: 343 [M+1]	1H NMR (300MHz, DMSO): 8,37 (s,1H), 6,87 (t,1H), 3,73 (m,2H), 3,15 (m,2H), 3,03 (m,2H), 2,97 (s,2H), 2,74 (s,2H), 2,49 (s,6H), 1,84 (s,4H)
183	[AA-48]			method: 2, RT: 2.52 min, MI: 405 [M+1]	

Ex	SM	Boronic acid [F36]	Amine [F-13]	Characterisation	
184	[AA-48]			method: 2, RT: 2.65 min, MI: 433 [M+1]	
185	[AA-48]			method: 2, RT: 2.30 min, MI: 341 [M+1]	1H NMR (300MHz, DMSO): 8,20 (s,2H), 3,51 (m,4H), 3,19 (m,4H), 2,88 (m,4H), 1,87 (m,2H), 1,78 (m,2H)
186	[AA-48]			method: 2, RT: 2.31 min, MI: 355 [M+1]	1H NMR (300MHz, DMSO): 8,17 (s,2H), 3,87 (m,2H), 3,74 (m,2H), 3,38 (m,2H), 3,11 (m,2H), 2,84 (m,2H), 1,88 (m,2H), 1,77 (m,2H)
187	[AA-48]			method: 2, RT: 2.21 min, MI: 329 [M+1]	
188	[AA-49]			method: 2, RT: 2.26 min, MI: 329 [M+1]	
189	[AA-48]			method: 2, RT: 2.27 min, MI: 341 [M+1]	
190	[AA-48]			method: 2, RT: 2.49min, MI: 369[M+1]	1H NMR (300MHz, DMSO): 8,97 (s,1H), 3,51 (m,6H), 2,84 (m,6H), 1,88 (m,2H), 1,77 (m,2H)
191	[AA-48]			method: 2, RT: 2.48min, MI: 383[M+1]	

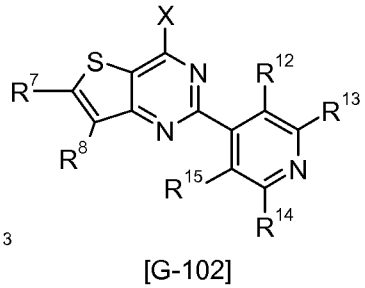
Ex	SM	Boronic acid [F36]	Amine [F-13]	Characterisation	
192	[AA-49]			method: 2, RT: 2.38min, MI: 357[M+1]	
193	[AA-48]			method: 2, RT: 2.37min, MI: 357[M+1]	
194	[AA-48]			method: 2, RT: 2.41min, MI: 369[M+1]	
195	[AA-48]			method: 2, RT: 2.27min, MI: 329[M+1]	
196	[AA-48]			method: 7, RT: 3.76min, MI: 431[M+1]	

4PT32P compounds

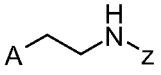
In one approach, compounds of formula [G-100] (where A = NH or N alkyl) are prepared by reacting a compound of formula [G-102] (where X is a halogen such as chlorine or a sulfonate) with a compound of formula [G-103] (where A is NH or NH_2 and Z on the terminal nitrogen is H, alkyl or a suitable nitrogen 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.



[G-100]



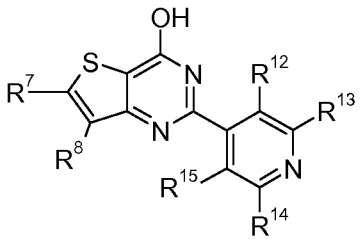
[G-102]



[G-103]

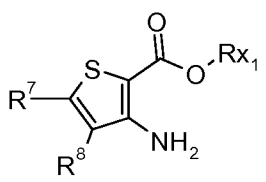
The reaction is suitably conducted at an elevated temperature for example 40 °C. Where Z is a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc, compounds of formula [G-100] are prepared by a suitable deprotection reaction. For example: where Z is a Boc protecting group reaction with 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 [G-100] (where A = O) are prepared by reacting a compound of formula [G-102] (where X is a halogen such as chlorine or sulfonate) with a compound of formula [G-103] (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 [G-100] 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 [G-102] (where X is a halogen such as chlorine) are prepared by reacting a compound of formula [G-104] with a suitable halogenating agent such as phosphorous oxychloride. The reaction is suitably conducted at elevated temperature such as 125 °C. Compounds of formula [G-102] (where X is a sulfonate) are prepared by reacting a compound of formula [G-104] 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.

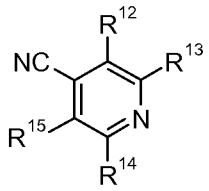


[G-104]

In one approach, compounds of formula [G-104] are prepared by reacting a compound of formula [G-105] (where R_{x1} is an alkyl group such as methyl or ethyl) with a compound of formula [G-106] in a suitable solvent such as dioxane with a suitable base such as potassium-tert-pentylate. The reaction is suitably conducted at ambient temperature.

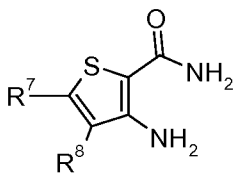


[G-105]

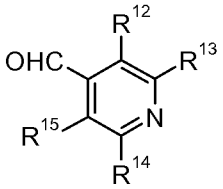


[G-106]

In another approach compounds of formula [G-104] are prepared by reacting a compound of [G-107] with a compound of formula [G-108] in a suitable solvent such as methanol with a suitable protic acid such as hydrogen chloride. The reaction is suitably conducted at elevated temperature. Full aromatisation to yield compounds of formula [G-104] is achieved by reaction with an oxidising agent such as 2,3-dichloro-5,6-dicyanobenzoquinone in a suitable solvent such as dichloromethane. The reaction is suitably conducted at ambient temperature.



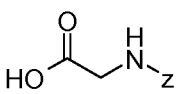
[G-107]



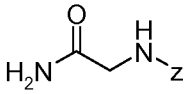
[G-108]

In one approach, compounds of formula [G-103] (where A is OH) are prepared by reacting a compound of formula [G-109] (where Z on the terminal nitrogen is H, alkyl or a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) with a reducing agent such as borane-THF complex in a suitable solvent such as THF. The reaction is suitably conducted at low temperature for example 0 °C. In one approach, compounds of formula [G-103] (where A is NH_2) are prepared by reacting a compound of formula [G-

110] (where Z on the terminal nitrogen is H, alkyl or a suitable nitrogen protecting group, such as Boc, Alloc, Cbz or Fmoc) with a reducing agent such as borane-THF complex in a suitable solvent such as THF. The reaction is suitably conducted at low temperature for example 0 °C. In one approach, compounds of formula [G-110] are prepared by reacting compounds of formula [G-109] with Boc anhydride in the presence of a suitable base such as pyridine, ammonium carbonate in a suitable solvent such as dioxane. The reaction is suitably conducted at ambient temperature.

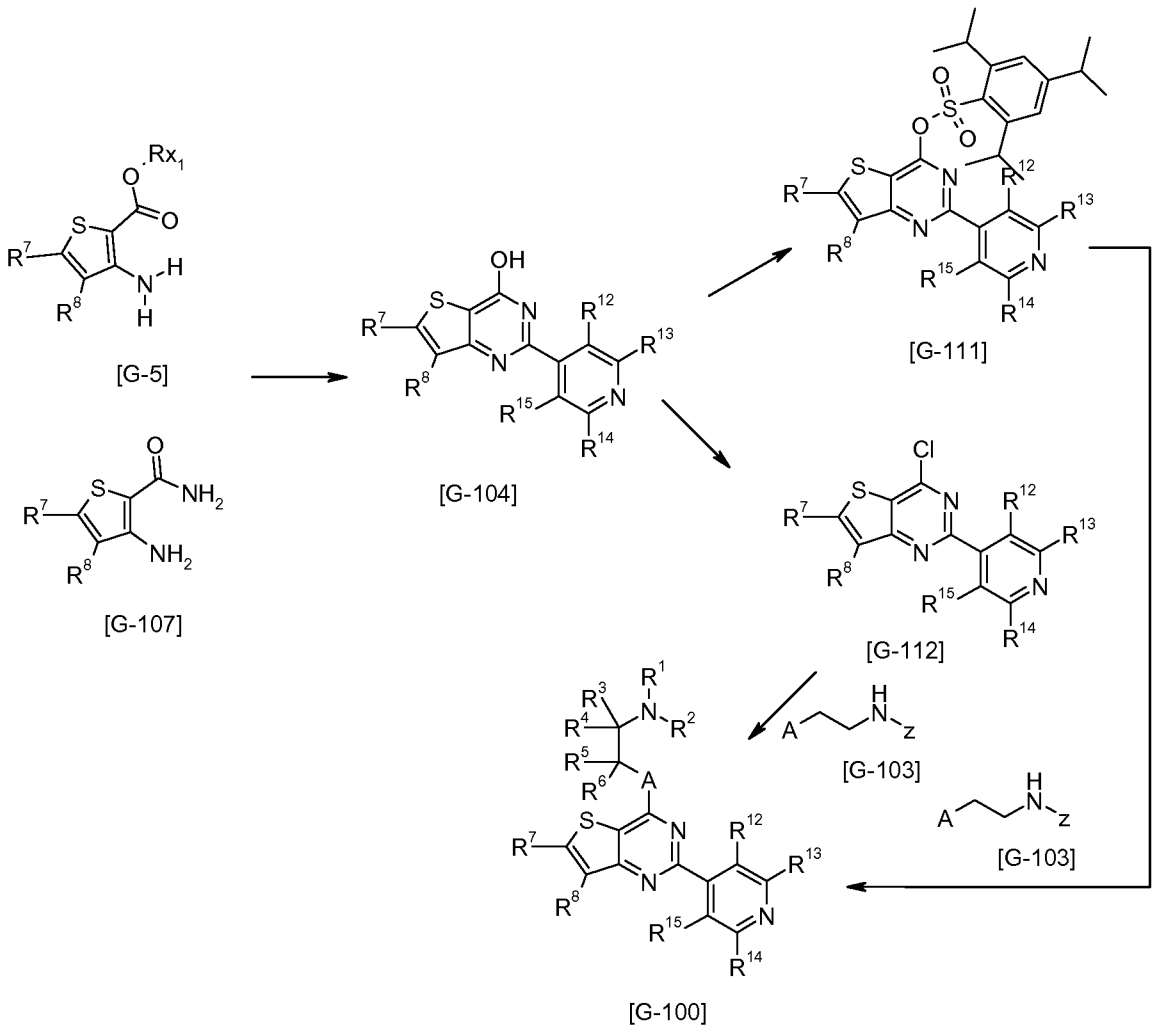


[G-109]



[G-110]

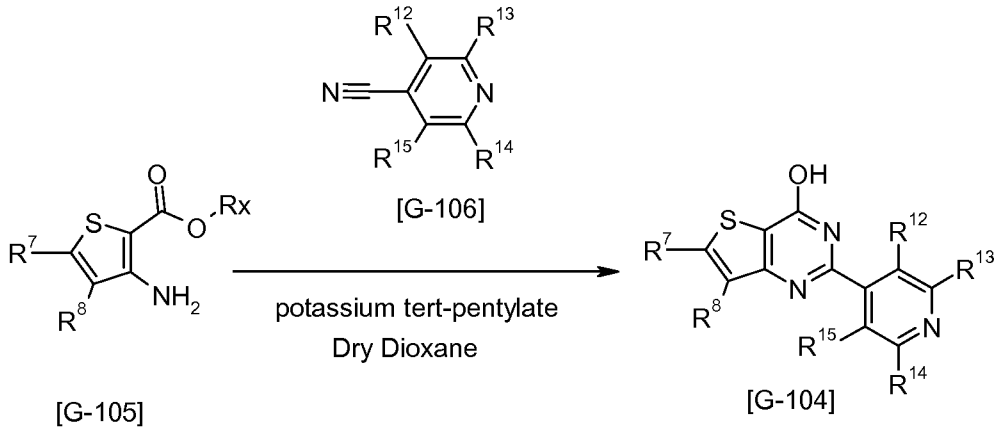
An example of a method as described above is illustrated in the following scheme.



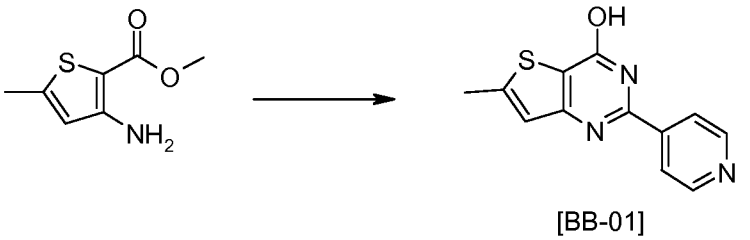
General synthesis of 6, 7 -substituted 2-pyridin-4-yl-thieno [3,2-d]pyrimidin-4-ol, of general formula [G-104] (Scheme B1)

A 4,5-substituted-3-Amino-thiophene-2-carboxylic acid alkyl ester derivative, of general formula [G-105] (wher Rx = alkyl such as methyl or ethyl) was subjected to a cyclisation reaction with a 4-cyanopyridine derivative of general formula [G-106] in the presence of a hindered alkoxide base such as potassium-tert-pentylate 1.7M in toluene or potassium-tert-butoxide in a dry non-aprotic solvent such as dioxane or THF at ambient temperature, to yield the 6, 7 -substituted 2-pyridin-4-yl-thieno [3,2-d]pyrimidin-4-ol derivative of formula [G-104].

Scheme B1



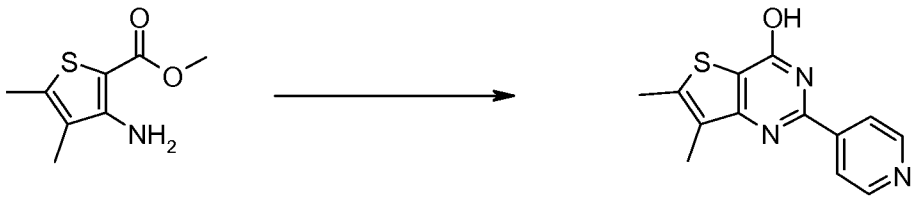
Synthesis of 6-methyl-2-pyridin-4-yl-thieno [3,2-d]pyrimidin-4-ol [BB-01]



To a solution of 4-cyanopyridine (552 mg, 5.3 mmol) in dry dioxane (10 ml) was added 3-amino-5-methyl-thiophene-2-carboxylic acid methyl ester (1 g, 5.84 mmol) followed by potassium-tert-pentylate 1.7M in toluene (6.9 ml, 11.7 mmol). The reaction mixture was stirred at room temperature overnight. After completion the precipitate formed was filtered and washed with diethyl ether. The residue was used without any

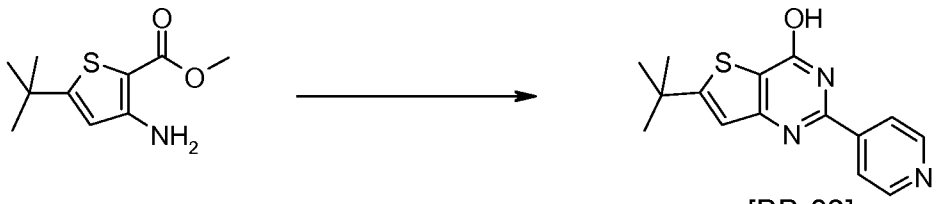
further purification in the next step. LCMS method: 3, RT: 2.44 min, MI: 244 [M+1]. 1H NMR (300MHz, DMSO): 2.60 (s,3H), 7.23 (d,1H), 8.05 (m,2H), 8.76 (m,2H).

The following compounds were prepared according to the general synthesis shown in scheme B1:



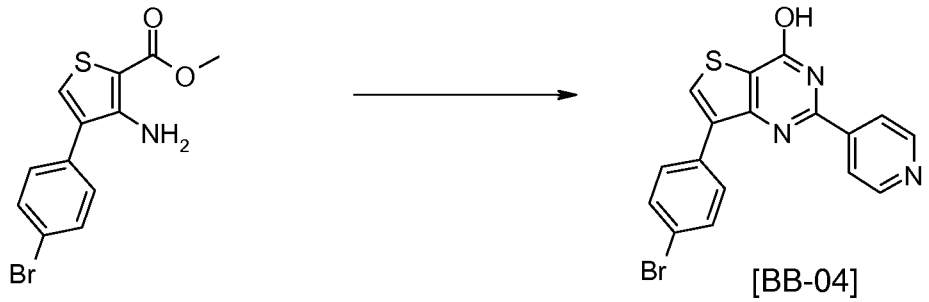
[BB-02]

6,7-Dimethyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-02] was prepared by reaction of 3-amino-4,5-dimethyl-thiophene-2-carboxylic acid methyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 3, RT: 3.05min, MI: 258 [M+1].



[BB-03]

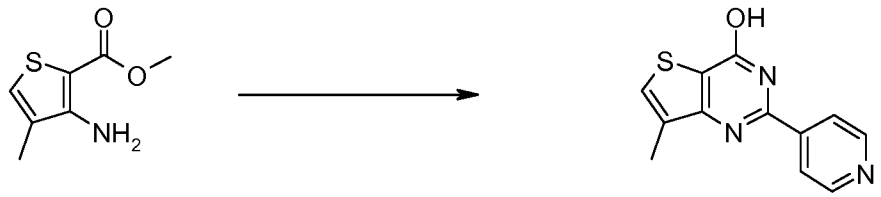
6-tert-butyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-03] was prepared by reaction of 3-amino-5-tert-butyl-thiophene-2-carboxylic acid methyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as an off-white solid. LCMS method: 3, RT: 3.02 min, MI: 286 [M+1].



[BB-04]

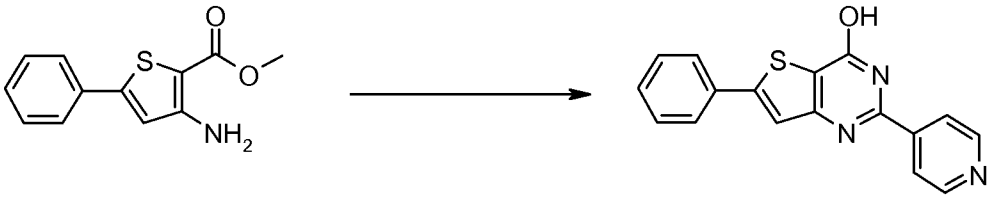
7-(4-bromo-phenyl)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-04] was prepared by reaction of 3-amino-4-(4-bromo-phenyl)-thiophene-2-carboxylic acid methyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room

temperature to give the title compound as a yellow solid. LCMS method: 3, RT: 4.11 min, MI: 384-386 [M+1].



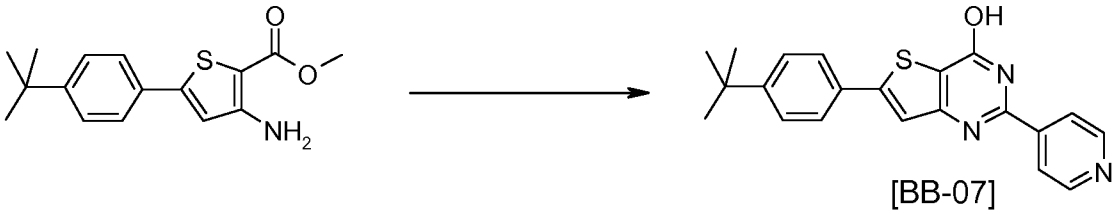
[BB-05]

7-methyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-05] was prepared by reaction of 3-amino-4-methyl-thiophene-2-carboxylic acid methyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as a yellow solid. LCMS method: 1, RT: 3.09 min, MI: 243 [M+1].



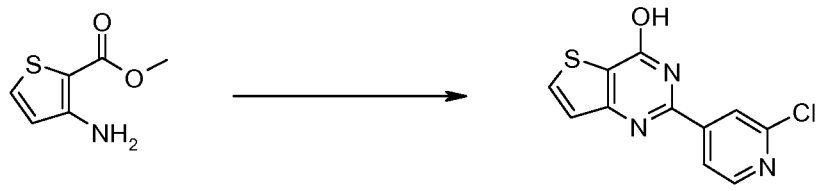
[BB-06]

6-phenyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-06] was prepared by reaction of 3-amino-5-phenyl-thiophene-2-carboxylic acid methyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as an off-white solid. LCMS method: 1, RT: 3.46 min, MI: 306 [M+1].



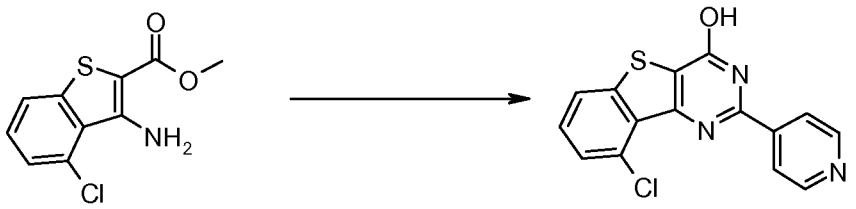
[BB-07]

6-(4-tert-butyl-phenyl)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-07] was prepared by reaction of 3-amino-5-(4-tert-butyl-phenyl)-thiophene-2-carboxylic acid methyl ester, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and dioxane at room temperature to give the title compound as an off-white solid. LCMS method: 1, RT: 4.78 min, MI: 362 [M+1].



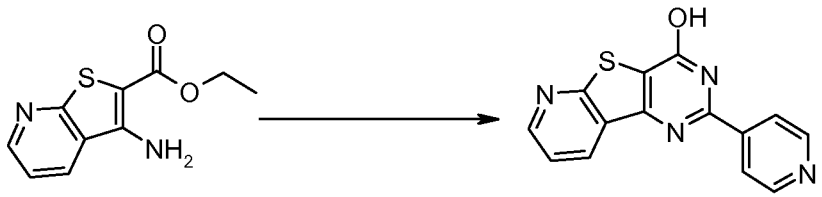
[BB-08]

2-(2-Chloro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-4-ol [BB-08] was prepared by reaction of methyl 3-amino-2-thiophene-carboxylate, 2-Chloro-4-pyridinecarbonitrile, potassium-tert-pentylate 1.7M in toluene and THF at room temperature to give the title compound as a pale yellow solid. LCMS method: 8, RT: 3.32 min, MI: 264 [M+1].



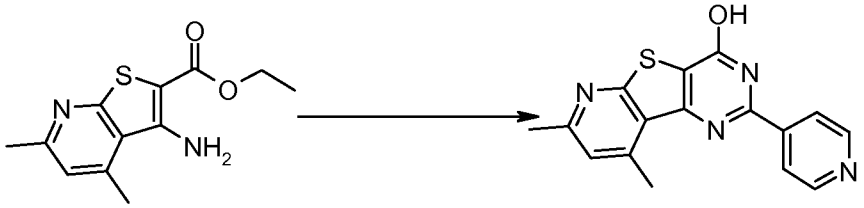
[BB-09]

9-Chloro-2-(2-chloro-pyridin-4-yl)-benzo[4,5]thieno[3,2-d]pyrimidin-4-ol [BB-09] was prepared by reaction of 3-Amino-4-chloro-benzo[b]thiophene-2-carboxylic acid methyl ester 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and THF at room temperature to give the title compound as an off-white solid. LCMS method: 2, RT: 3.6 min, MI: 314 [M+1].



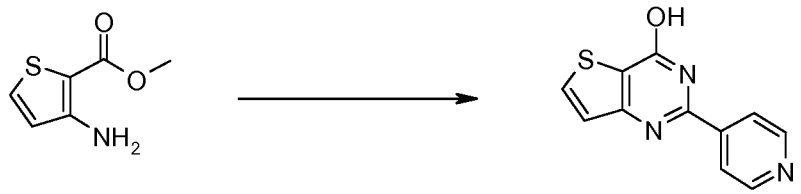
[BB-10]

2-Pyridin-4-yl-pyrido[3',2':4,5]thieno[3,2-d]pyrimidin-4-ol [BB-10] was prepared by reaction of ethyl 3-aminothieno[2,3-b]pyridine-2-carboxylate, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and THF at room temperature to give the title compound as an of-white solid. LCMS method: 2, RT: 2.57 min, MI: 281 [M+1].



[BB-11]

7,9-Dimethyl-2-pyridin-4-yl-pyrido[3',2':4,5]thieno[3,2-d]pyrimidin-4-ol [BB-11] was prepared by reaction of ethyl 3-amino-4,6-dimethylthieno[2,3-b]pyridine-2-carboxylate, 4-cyanopyridine, potassium-tert-pentylate 1.7M in toluene and THF at room temperature to give the title compound as an off-white solid. LCMS method: 2, RT: 3.07 min, MI: 309[M+1].



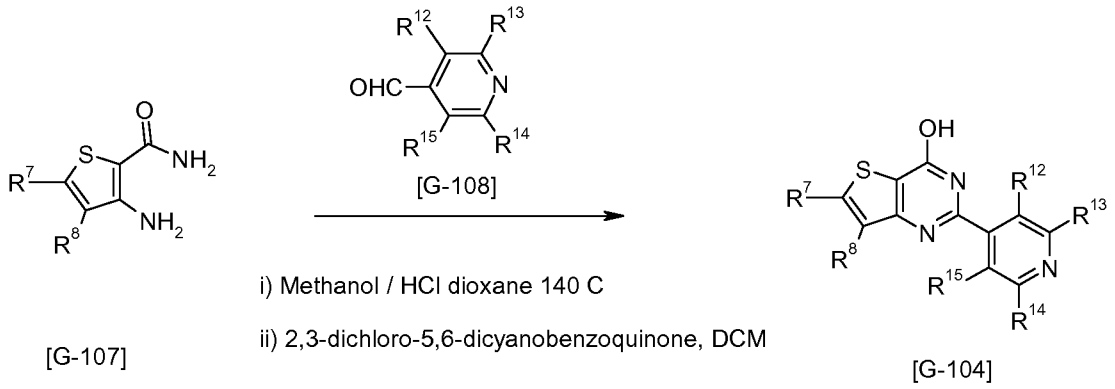
[BB-13]

2-Pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-13] was prepared by reaction of methyl 3-amino-2-thiophene-carboxylate, 4-pyridinecarbonitrile, potassium-tert-pentylate 1.7M in toluene and THF at room temperature to give the title compound as a pale yellow solid: LCMS method B: 1.98 min, 100%, 230.00 [M+H]

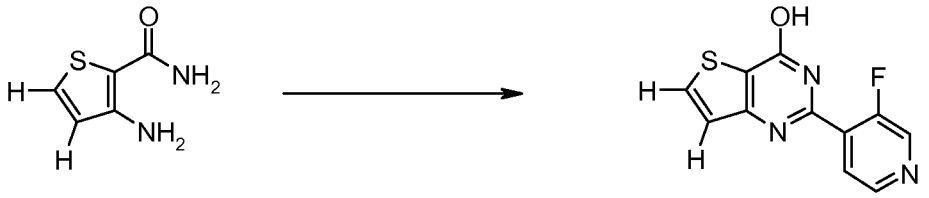
General synthesis of 6, 7 -substituted 2-pyridin-4-yl-thieno [3,2-d]pyrimidin-4-ol, of general formula [G-104] (Scheme B2)

An 4,5-substituted-3-amino-thiophene-2-carboxylic acid amide derivative of general formula [G-107] was subjected to a cyclisation reaction with an isonicotinaldehyde derivative of general formula [G-108] in the presence of 4M hydrogen chloride in dioxane in a suitable solvent such as methanol. The reaction is suitably conducted at an elevated temperature for example 140 °C in a microwave reactor for 20minutes. Full aromatisation is subsequently achieved with 2,3-dichloro-5,6-dicyanobenzoquinone in a suitable solvent such as dichloromethane at ambient temperature, to yield the 6, 7 -substituted 2-pyridin-4-yl-thieno [3,2-d]pyrimidin-4-ol, of general formula [G-104].

Scheme B2



Synthesis of 2-(3-Fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-4-ol [BB-14]

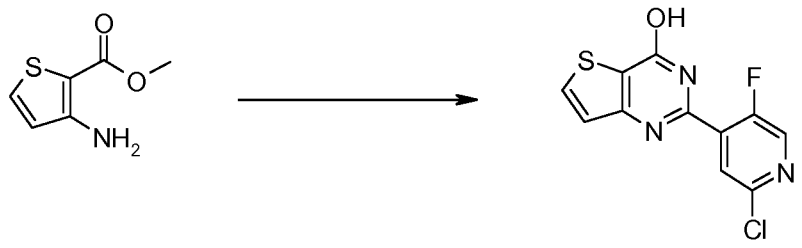


[B-14]

A microwave vial was charged with 3-amino-thiophene-2-carboxylic acid amide (2 g, 14.07 mmol), 3-fluoroisonicotinaldehyde (0.85 ml, 8.52 mmol), hydrogen chloride 4M in dioxane (0.7 ml, 2.81 mmol) and methanol (20 ml). The reaction mixture was heated to 140°C for 20 minutes under microwave irradiation. After completion, the mixture was concentrated under reduced pressure. To a solution of the crude product in dichloromethane (20 ml) was added 2,3-dichloro-5,6-dicyanobenzoquinone (3.2 g, 14.07). The mixture was stirred at room temperature for 18 hours. After completion, the precipitate formed was filtered and washed with methanol. The residue was used without any further purification in the next step. LCMS method: 5, RT: 3.39 min, MI: 248 [M+1]. NMR 1H (DMSO, 300MHz): 13.03 (s, 1H), 8.80 (d, 1H), 8.62 (dd, 1H), 8.27 (d,1H), 7.80 (t, 1H), 7.52 (d, 1H).

The following compounds were prepared according to the general synthesis shown in scheme B2:

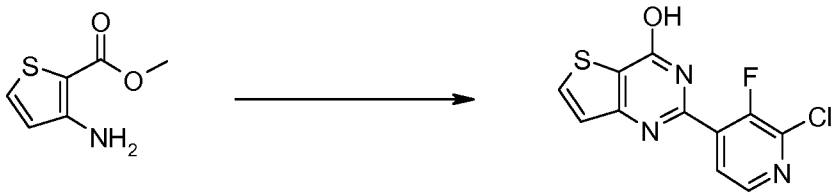
2-(2-Chloro-5-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-4-ol [BB-15]



[BB-15]

A microwave vial was charged with 3-amino-thiophene-2-carboxylic acid amide (1.3 g, 9.3 mmol), 2-Chloro-5-fluoro-4-formylpyridine (1g, 5.6 mmol), concentrated hydrogen chloride (1 drop) and methanol (10 ml). The reaction mixture was heated to 120 °C for 20 minutes under microwave irradiation. After completion, the mixture was concentrated under reduced pressure. To a solution of the crude product in dichloromethane (20 ml) was added 2,3-dichloro-5,6-dicyanobenzoquinone (2.3 g, 9.3 mmol). The mixture was stirred at room temperature for 18 hours. After completion, the precipitate formed was filtered and washed with methanol. The residue was used without any further purification in the next step. LCMS method: 8, RT: 3.20 min, MI: 281-283 [M+1]. 1H NMR (DMSO, 300MHz): 8.68 (1H, d), 8.27 (1H, d), 7.96 (1H, d), 7.51 (1H, d).

2-(2-Chloro-3-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-4-ol [BB-15a]

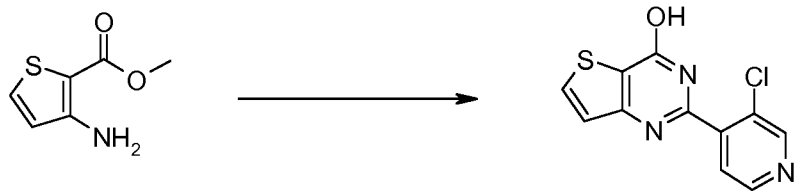


[BB-15a]

A microwave vial was charged with 3-amino-thiophene-2-carboxylic acid amide (0.5 g, 3.5 mmol), 2-Chloro-3-fluoro-4-formylpyridine (0.75 g, 2.12 mmol), 1.25 N hydrogen chloride (1 drop) and methanol (4 ml). The reaction mixture was heated to 120 °C for 20 minutes under microwave irradiation. After completion, the mixture was concentrated under reduced pressure. To a solution of the crude product in dichloromethane (5 ml) was added 2,3-dichloro-5,6-dicyanobenzoquinone (800 mg, 3.5 mmol). The mixture was stirred at room temperature for 18 hours. After completion, the precipitate formed was filtered and washed with methanol. The residue was used without any further purification in the next step. LCMS method: 8, RT: 3.21 min, MI: 281-283

[M+1]. ^{1}H NMR (DMSO) 13.09 (1H, s, br), 8.46 (1H, d), 8.29 (1H, d), 7.83 (1H, t), 7.51 (1H, d).

2-(3-Chloro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-4-ol [BB-15b]



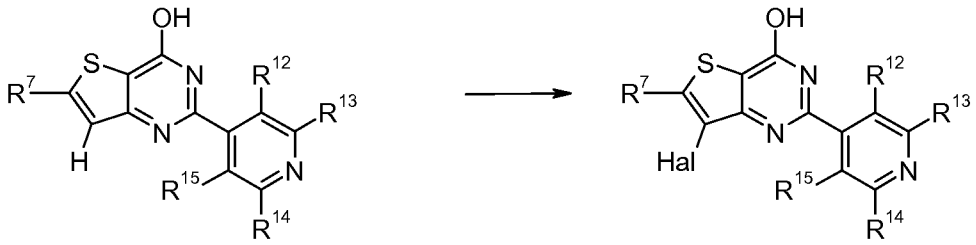
[BB-15b]

A microwave vial was charged with 3-amino-thiophene-2-carboxylic acid amide (1 g, 7.03 mmol), 3-Chloro-pyridine-4-carbaldehyde (0.6 g, 4.24 mmol), 2.5 N hydrogen chloride in ethanol (0.56 mL, 1.4 mmol) and ethanol (10 ml). The reaction mixture was heated to 140 °C for 20 minutes under microwave irradiation. After completion, the precipitate formed was filtered and washed with DCM then methanol. The residue was purified by flash column chromatography (SiO2, MeOH : DCM elution) to five the title compound (0.52g, 47% yield). LCMS method: 10, MI: 264 [M+1].

General synthesis of 7-halo substituted-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol of general formula [G-113] (Scheme B3a)

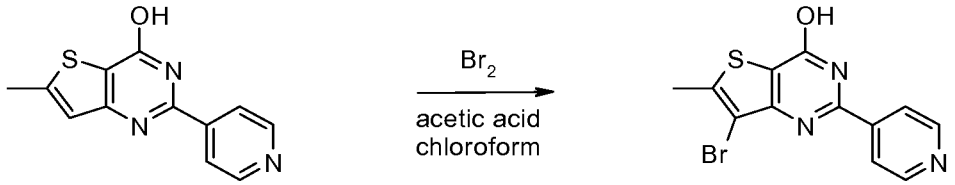
A 6 -substituted 2-pyridin-4-yl-thieno [3,2-d]pyrimidin-4-ol derivative of general formula [G-112] was brominated at the C7 position in the presence of a halogenating agent such as Br_2, *N*-Bromosuccinimide, Phosphorus(V) oxybromide, and an acidic reagent such as acetic acid. Or chlorinated at the C7 position in the presence of a halogenating agent such as N-chlorosuccinimide and an acidic reagent such as acetic acid to give the corresponding 7-halo substituted-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol derivative of general formula [G-113], Scheme B3a.

Scheme B3a



[G-112] [G-113]

Synthesis of 7-bromo-6-methyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-16]

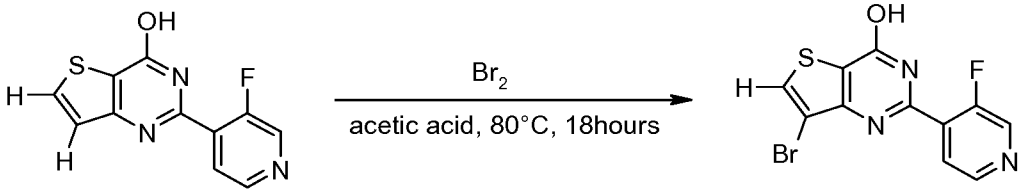


[BB-01] [BB-16]

A solution of bromine (1.2 ml, 23.2 mmol) in chloroform (10ml) was added to a stirring solution of 6-tert-butyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-01] (2.84 g, 11.6 mmol) in chloroform (15ml) acetic acid (15ml) at 0°C. The mixture was allowed to warm to room temperature and stirred over night. After completion the resulting solid was filtered and washed with chloroform and diethylether to yield the title compound as a yellow solid. LCMS method: 4, RT: 2.14 min, MI: 322-324 [M+1]. 1H NMR (300MHz, DMSO): 8.76 (m, 2H), 8.05 (m, 2H), 2.60 (s, 3H).

The following compounds were prepared according to the general synthesis shown in scheme B3a:

Synthesis of 7-Bromo-2-(3-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-4-ol [BB-17]

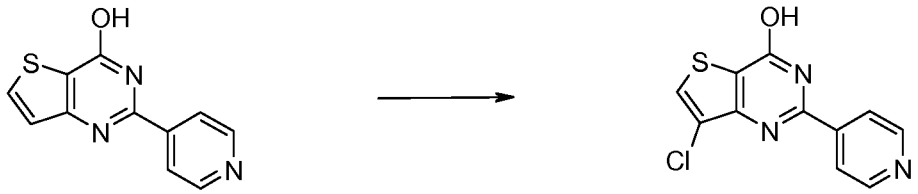


[BB-14] [BB-17]

Bromine (1.2 ml, 24.27 mmol) was added to a stirring solution of 2-(3-Fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-4-ol [BB-14] (2.00 g, 8.09 mmol) in acetic acid (20ml) at ambient temperature. The mixture was heated to 80°C and stirred over night under reflux conditions. After completion, 10% sodium thiosulphate solution (5ml) was

added and the resulting solid was filtered and washed with water and ethyl acetate to yield the title compound as a colourless solid. LCMS method: 6, RT: 4.33 min, MI: 326-238 [M+1]. NMR 1H (DMSO, 300MHz): 7.82 (dd, 1H), 8.47 (s, 1H), 8.63 (d, 1H), 8.81 (s, 1H), 13.28 (bs, 1H).

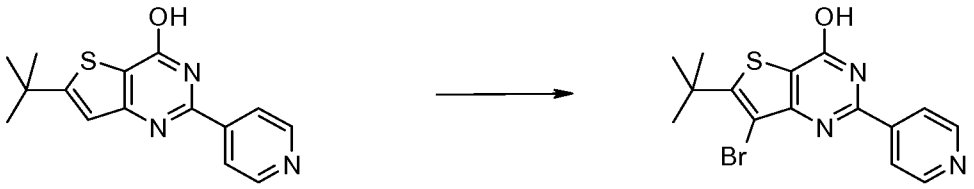
Synthesis of 7-Chloro-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-18]



[BB-13] [BB-18]

To a stirred suspension of 2-Pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-13] (0.5g, 2.18 mmol) in AcOH (10 ml) was added NCS (1.46g, 10.9 mmol) and the reaction heated to 80 °C. After 18hr further NCS (0.58g, 4.36 mmol) was added and the mixture was left to stir at 80 °C for a further another 24 hr. The reaction mixture was cooled and evapourated under reduced pressure and the resulting residue suspended in H_2O and the solid formed was collected by filtration, to give the title compound (0.4g, 70% yield) which was used without further purification: LCMS method B: 4.16 min, 64%, 263.95 [M+H]

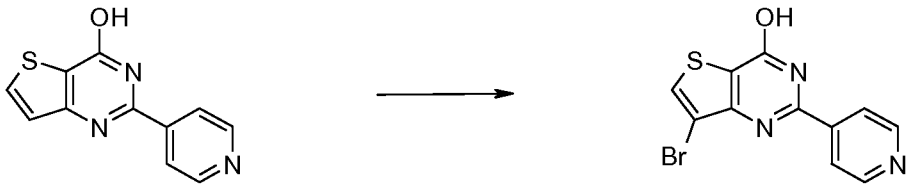
Synthesis of 7-Bromo-6-tert-butyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-19]



[BB-03] [BB-19]

A solution of bromine (60 µL, 1.17 mmol) in chloroform (1 ml) was added to a stirring solution of 6-tert-Butyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-03] (0.33g, 1.17 mmol) in chloroform (4 ml) and acetic acid (5 ml) at 0°C. The mixture was allowed to warm to room temperature and stirred over night. After completion the resulting solid was filtered and washed with chloroform and diethylether to yield the title compound as a yellow solid. LCMS method: 3, RT: 4.22 min, MI: 364-366 [M+1].

Synthesis of 7-Bromo-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-20]



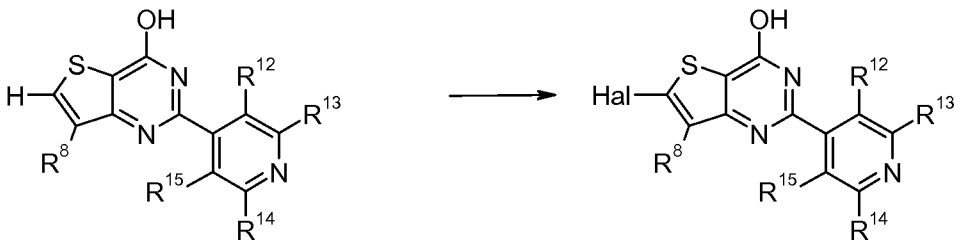
[BB-13] [BB-20]

To a stirred suspension of 2-Pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-13] (20g, 87.2 mmol) in AcOH (400 ml) was added Br_2 (20 ml). The mixture was left to stir 80 °C for 24 hr then an additional Br_2 (10ml) was added and the mixture was left to stir 80 °C for a further 24 hours. The reaction mixture was cooled and poured into H_2O-ice mixture, and the yellow precipitate was collected by filtration and washed with satutated sodium metabisulfite, then H_2O followed by Et_2O, to give the title compound as a pale yellow solid (24.1 g, 90% yield). LCMS method: 8, RT: 3.28 min, MI: 307-309 [M+1]. ^{1}H NMR (DMSO) 8.99 (2H, d), 8.49 (1H, s), 8.42 (2H, d).

General synthesis of 6-halo substituted-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol derivative of general formula [G-116] (Scheme B3b)

A 7 -substituted 2-pyridin-4-yl-thieno [3,2-d]pyrimidin-4-ol derivative of general formula [G-115] was brominated at the C6 position in the presence of a halogenating agent such as Br_2, *N*-Bromosuccinimide, Phosphorus(V) oxybromide, and an acidic reagent such as acetic acid. Or chlorinated at the C6 position in the presence of a halogenating agent such as *N*-chlorosuccinimide and an acidic reagenet such as acetic acid to give the corresponding 6-halo substituted-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol derivative of general formula [G-116], Scheme B3b.

Scheme B3b



[G-115] [G-116]

Synthesis of 6-Bromo-7-methyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-ol [BB-21]

DEMANDES OU BREVETS VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVETS COMPREND PLUS D'UN TOME.

CECI EST LE TOME __1___ DE __2___

NOTE: Pour les tomes additionels, veillez contacter le Bureau Canadien des Brevets.

JUMBO APPLICATIONS / PATENTS

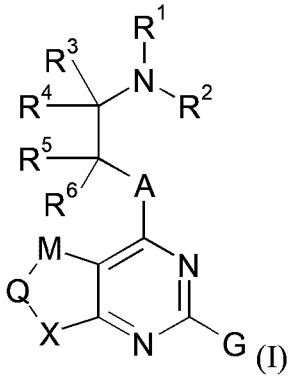
THIS SECTION OF THE APPLICATION / PATENT CONTAINS MORE THAN ONE VOLUME.

THIS IS VOLUME __1___ OF __2___

NOTE: For additional volumes please contact the Canadian Patent Office.

CLAIMS:

1. A compound of formula (I)

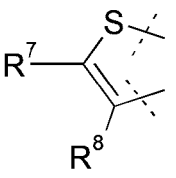
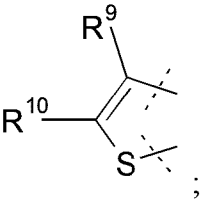


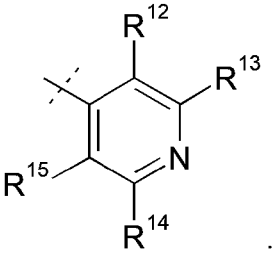
(I)

or a salt form thereof,

wherein

A is NR^{11}, wherein R^{11} is hydrogen;

M-Q-X is a group of formula  or  ;

G is a group of formula  ;

R^1 and R^2, are independently selected from the group consisting of 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-

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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}, and $-OR^{20}$;

R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{12}, R^{13}, R^{14} and R^{15} are independently selected from the group consisting of 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, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-C(=O)C(=O)R^{20}$, $-C(=NR^{25})R^{20}$, $-C(=NR^{25})NR^{22}R^{23}$, $-C(=NOH)NR^{22}R^{23}$, $-C(=NOR^{26})R^{20}$, $-C(=NNR^{22}R^{23})R^{20}$, $-C(=NNR^{24}C(=O)R^{21})R^{20}$, $-C(=NNR^{24}C(=O)OR^{21})R^{20}$, $-C(=S)NR^{22}R^{23}$, $-NC$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}NR^{22}R^{23}$, $-N=NR^{24}$, $-NR^{24}OR^{26}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)C(=O)R^{20}$, $-NR^{24}C(=O)OR^{21}$, $-NR^{24}C(=O)C(=O)OR^{21}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-NR^{24}C(=O)NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{24}C(=O)OR^{20}$, $-NR^{24}C(=NR^{25})NR^{22}R^{23}$, $-NR^{24}C(=O)C(=O)NR^{22}R^{23}$, $-NR^{24}C(=S)R^{20}$, $-NR^{24}C(=S)OR^{20}$, $-NR^{24}C(=S)NR^{22}R^{23}$, $-NR^{24}S(=O)_2R^{21}$, $-NR^{24}S(=O)_2NR^{22}R^{23}$, $-NR^{24}P(=O)R^{28}R^{28}$, $-NR^{24}P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-NR^{24}P(=O)(OR^{20})(OR^{20})$, $-NR^{24}P(=O)(SR^{20})(SR^{20})$, $-OR^{20}$, $-OCN$, $-OC(=O)R^{20}$, $-OC(=O)NR^{22}R^{23}$, $-OC(=O)OR^{20}$, $-OC(=NR^{25})NR^{22}R^{23}$, $-OS(=O)R^{20}$, $-OS(=O)_2R^{20}$, $-OS(=O)_2OR^{20}$, $-OS(=O)_2NR^{22}R^{23}$, $-OP(=O)R^{28}R^{28}$, $-OP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-OP(=O)(OR^{20})(OR^{20})$, $-OP(=O)(SR^{20})(SR^{20})$, $-Si(R^{24})_3$, $-SCN$, $-S(=O)_nR^{20}$, $-S(=O)_2OR^{20}$, $-SO_3R^{27}$, $-S(=O)_2NR^{22}R^{23}$, $-S(=O)NR^{22}R^{23}$, $-SP(=O)R^{28}R^{28}$, $-SP(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-SP(=O)(OR^{20})(OR^{20})$, $-SP(=O)(SR^{20})(SR^{20})$, $-P(=O)R^{28}R^{28}$, $-P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, $-P(=O)(OR^{20})(OR^{20})$, and $-P(=O)(SR^{20})(SR^{20})$; or

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any of R^1 and R^2, R^1 and R^3, and R^1 and R^5 can, together with the atoms linking them, form a 3-15 membered heterocycloalkyl optionally substituted by 1-28 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-15 R^{19}; or

any of R^3 and R^6, R^7 and R^8, R^9 and R^{10}, R^{12} and R^{13}, and R^{14} and R^{15} 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}; or

R^3 and R^5 or R^4 and R^6 can together form a double bond; or

any of R^3 and R^4, and R^5 and R^6 can together form =O, =NR^{20}, =NOR^{20}, or =S;

R^{19} at each occurrence is independently selected from the group consisting of 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)$R^{38}R^{38}$, –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)$NR^{32}R^{33}$,

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$-OC(=O)OR^{30}$, $-OC(=NR^{35})NR^{32}R^{33}$, $-OS(=O)R^{30}$, $-OS(=O)_2R^{30}$, $-OS(=O)_2OR^{30}$, $-OS(=O)_2NR^{32}R^{33}$, $-OP(=O)R^{38}R^{38}$, $-OP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-OP(=O)(OR^{30})(OR^{30})$, $-OP(=O)(SR^{30})(SR^{30})$, $-Si(R^{34})_3$, $-SCN$, $=S$, $-S(=O)_nR^{30}$, $-S(=O)_2OR^{30}$, $-SO_3R^{37}$, $-S(=O)_2NR^{32}R^{33}$, $-S(=O)NR^{32}R^{33}$, $-SP(=O)R^{38}R^{38}$, $-SP(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-SP(=O)(OR^{30})(OR^{30})$, $-SP(=O)(SR^{30})(SR^{30})$, $-P(=O)R^{38}R^{38}$, $-P(=O)(NR^{32}R^{33})(NR^{32}R^{33})$, $-P(=O)(OR^{30})(OR^{30})$, 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 selected from the group consisting of 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} and R^{38} at each occurrence is independently selected from the group consisting of 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^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently selected from the group consisting of 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

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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 selected from the group consisting of 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, $-CN$, $-C(=O)R^{70}$, $-C(=O)OR^{70}$, $-C(=O)NR^{72}R^{73}$, $-C(=O)C(=O)R^{70}$, $-C(=NR^{75})R^{70}$, $-C(=NR^{75})NR^{72}R^{73}$, $-C(=NOH)NR^{72}R^{73}$, $-C(=NOR^{76})R^{70}$, $-C(=NNR^{72}R^{73})R^{70}$, $-C(=NNR^{74}C(=O)R^{71})R^{70}$, $-C(=NNR^{74}C(=O)OR^{71})R^{70}$, $-C(=S)NR^{72}R^{73}$, $-NC$, $-NO_2$, $-NR^{72}R^{73}$, $-NR^{74}NR^{72}R^{73}$, $-N=NR^{74}$, $=NR^{70}$, $=NOR^{70}$, $-NR^{74}OR^{76}$, $-NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)C(=O)R^{70}$, $-NR^{74}C(=O)OR^{71}$, $-NR^{74}C(=O)C(=O)OR^{71}$, $-NR^{74}C(=O)NR^{72}R^{73}$, $-NR^{74}C(=O)NR^{74}C(=O)R^{70}$, $-NR^{74}C(=O)NR^{74}C(=O)OR^{70}$, $-NR^{74}C(=NR^{75})NR^{72}R^{73}$, $-NR^{74}C(=O)C(=O)NR^{72}R^{73}$, $-NR^{74}C(=S)R^{70}$, $-NR^{74}C(=S)OR^{70}$, $-NR^{74}C(=S)NR^{72}R^{73}$, $-NR^{74}S(=O)_2R^{71}$, $-NR^{74}S(=O)_2NR^{72}R^{73}$, $-NR^{74}P(=O)R^{78}R^{78}$, $-NR^{74}P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-NR^{74}P(=O)(OR^{70})(OR^{70})$, $-NR^{74}P(=O)(SR^{70})(SR^{70})$, $-OR^{70}$, $=O$, $-OCN$, $-OC(=O)R^{70}$, $-OC(=O)NR^{72}R^{73}$, $-OC(=O)OR^{70}$, $-OC(=NR^{75})NR^{72}R^{73}$, $-OS(=O)R^{70}$, $-OS(=O)_2R^{70}$, $-OS(=O)_2OR^{70}$,

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$-OS(=O)_2NR^{72}R^{73}$, $-OP(=O)R^{78}R^{78}$, $-OP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-OP(=O)(OR^{70})(OR^{70})$, $-OP(=O)(SR^{70})(SR^{70})$, $-Si(R^{74})_3$, $-SCN$, $=S$, $-S(=O)_nR^{70}$, $-S(=O)_2OR^{70}$, $-SO_3R^{77}$, $-S(=O)_2NR^{72}R^{73}$, $-S(=O)NR^{72}R^{73}$, $-SP(=O)R^{78}R^{78}$, $-SP(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-SP(=O)(OR^{70})(OR^{70})$, $-SP(=O)(SR^{70})(SR^{70})$, $-P(=O)R^{78}R^{78}$, $-P(=O)(NR^{72}R^{73})(NR^{72}R^{73})$, $-P(=O)(OR^{70})(OR^{70})$, 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 selected from the group consisting of 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 selected from the group consisting of 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 selected from the group consisting of C_{1-6} alkyl optionally substituted by 1-13 R^{89}, C_{2-6} alkenyl optionally substituted by 1-11 R^{89},

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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^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently selected from the group consisting of 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, $-CN$, $-C(=O)R^{110}$, $-C(=O)OR^{110}$, $-C(=O)NR^{110}R^{110}$, $-C(=O)C(=O)R^{110}$, $-C(=NR^{110})R^{110}$, $-C(=NR^{110})NR^{110}R^{110}$, $-C(=NOH)NR^{110}R^{110}$, $-C(=NOR^{110})R^{110}$, $-C(=NNR^{110}R^{110})R^{110}$, $-C(=NNR^{110}C(=O)R^{110})R^{110}$, $-C(=NNR^{110}C(=O)OR^{110})R^{110}$, $-C(=S)NR^{110}R^{110}$, $-NC$, $-NO_2$, $-NR^{110}R^{110}$, $-NR^{110}NR^{110}R^{110}$, $-N=NR^{110}$, $=NR^{110}$, $=NOR^{110}$, $-NR^{110}OR^{110}$, $-NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)C(=O)R^{110}$, $-NR^{110}C(=O)OR^{110}$, $-NR^{110}C(=O)C(=O)OR^{110}$, $-NR^{110}C(=O)NR^{110}R^{110}$, $-NR^{110}C(=O)NR^{110}C(=O)R^{110}$, $-NR^{110}C(=O)NR^{110}C(=O)OR^{110}$, $-NR^{110}C(=NR^{110})NR^{110}R^{110}$, $-NR^{110}C(=O)C(=O)NR^{110}R^{110}$, $-NR^{110}C(=S)R^{110}$, $-NR^{110}C(=S)OR^{110}$, $-NR^{110}C(=S)NR^{110}R^{110}$, $-NR^{110}S(=O)_2R^{110}$, $-NR^{110}S(=O)_2NR^{110}R^{110}$, $-NR^{110}P(=O)R^{111}R^{111}$, $-NR^{110}P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-NR^{110}P(=O)(OR^{110})(OR^{110})$, $-NR^{110}P(=O)(SR^{110})(SR^{110})$, $-OR^{110}$, $=O$, $-OCN$, $-OC(=O)R^{110}$, $-OC(=O)NR^{110}R^{110}$, $-OC(=O)OR^{110}$, $-OC(=NR^{110})NR^{110}R^{110}$, $-OS(=O)R^{110}$, $-OS(=O)_2R^{110}$, $-OS(=O)_2OR^{110}$, $-OS(=O)_2NR^{110}R^{110}$, $-OP(=O)R^{111}R^{111}$, $-OP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-OP(=O)(OR^{110})(OR^{110})$, $-OP(=O)(SR^{110})(SR^{110})$, $-Si(R^{110})_3$, $-SCN$, $=S$, $-S(=O)_nR^{110}$, $-S(=O)_2OR^{110}$, $-SO_3R^{110}$, $-S(=O)_2NR^{110}R^{110}$, $-S(=O)NR^{110}R^{110}$, $-SP(=O)R^{111}R^{111}$, $-SP(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-SP(=O)(OR^{110})(OR^{110})$, $-SP(=O)(SR^{110})(SR^{110})$,

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$-P(=O)R^{111}R^{111}$, $-P(=O)(NR^{110}R^{110})(NR^{110}R^{110})$, $-P(=O)(OR^{110})(OR^{110})$, and $-P(=O)(SR^{110})(SR^{110})$;

R^{110} at each occurrence is independently selected from the group consisting of H, C_{1-6} alkyl and C_{1-6} haloalkyl;

R^{111} at each occurrence is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl; and

n at each occurrence is independently selected from the group consisting of 0, 1, and 2.

2. A compound as defined in claim 1, or a salt form thereof, wherein R^1 and R^2 are independently selected from the group consisting of H and C_{1-6} alkyl optionally substituted by 1-3 R^{19}; R^3, R^4, R^5, and R^6 are independently selected from the group consisting of H, C_{1-6} alkyl optionally substituted by 1-3 R^{19}, halogen, $-CN$, $-C(=O)R^{20}$, $-C(=O)OR^{20}$, $-C(=O)NR^{22}R^{23}$, $-NO_2$, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}S(=O)_2R^{21}$,$-OR^{20}$, $-OC(=O)R^{20}$, $-S(=O)_nR^{20}$, and $-S(=O)_2NR^{22}R^{23}$; alternatively, R^3 and R^6 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}; alternatively R^3 and R^5 or R^4 and R^6 can together form a double bond; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5 can, together with the atoms linking them, form a 5-15 membered heterocycloalkyl optionally substituted by 1-3 R^{19} or a 5-15 membered heteroaryl optionally substituted by 1-3 R^{19}.

3. A compound as defined in claim 1, or a salt form thereof, wherein R^1, R^4, R^5, and R^6 are independently selected from the group consisting of H and C_{1-6} alkyl optionally substituted by 1-3 R^{19}; R^2 is selected from the group consisting of H, C_{1-6} alkyl optionally substituted by 1-3 R^{19}, C_{7-11} arylalkyl optionally substituted by 1-3 R^{19}, and 6-10 membered heteroarylalkyl optionally substituted by 1-3 R^{19}; R^3 is selected from the group consisting of H, C_{1-6} alkyl optionally substituted by 1-3 R^{19}, C_{7-11} arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7} cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19}; and alternatively any of R^1 and R^2, R^1 and R^3, R^1 and R^5 can,

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together with the atoms linking them, form a 3-7 membered heterocycloalkyl optionally substituted by 1-3 R^{19}.

4. A compound as defined in any one of claims 1-3, or a salt form thereof, wherein R^7, R^8, R^9, and R^{10} are independently selected from the group consisting of 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 $–S(=O)_2NR^{22}R^{23}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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}.

5. A compound as defined in any one of claims 1-3, or a salt form thereof, wherein R^7, R^8, R^9, and R^{10} are independently selected from the group consisting of 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}, 6-11 membered heteroarylalkyl optionally substituted by 1-3 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 $–OR^{20}$; alternatively, either or both of R^7 and R^8, and/or R^9 and R^{10}, 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}.

6. A compound as defined in any one of claims 1-5, or a salt form thereof, wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of 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

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membered heteroaryl optionally substituted by 1-3 R^{19}, halogen, –CN, $–C(=O)R^{20}$, $–C(=O)OR^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}C(=O)OR^{21}$, $–NR^{24}C(=O)NR^{22}R^{23}$, $–NR^{24}S(=O)_2R^{21}$, $–NR^{24}S(=O)_2NR^{22}R^{23}$, $–OR^{20}$, $–OC(=O)R^{20}$, $–OC(=O)NR^{22}R^{23}$, $–OC(=O)OR^{20}$, $–S(=O)_nR^{20}$, $–S(=O)_2OR^{20}$, $–SO_3R^{27}$, $–S(=O)_2NR^{22}R^{23}$, $–S(=O)NR^{22}R^{23}$, $–P(=O)R^{28}R^{28}$, $–P(=O)(NR^{22}R^{23})(NR^{22}R^{23})$, and $–P(=O)(OR^{20})(OR^{20})$; alternatively, 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}.

7. A compound as defined in any one of claims 1-5, or a salt form thereof, wherein R^{12}, R^{13}, and R^{14} are H; R^{15} is selected from the group consisting of 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, $–C(=O)R^{20}$, $–C(=O)NR^{22}R^{23}$, $–NO_2$, $–NR^{22}R^{23}$, $–NR^{24}C(=O)R^{20}$, $–NR^{24}S(=O)_2R^{21}$, $–OR^{20}$, $–S(=O)_nR^{20}$, and $–S(=O)_2NR^{22}R^{23}$.

8. A compound as defined in any one of claims 1 and 4-7, or a salt form thereof, wherein R^{17} is H; and R^{16} and R^{18} are independently selected from the group consisting of H and C_{1-6} alkyl.

9. A compound as defined in any one of claims 1-8, or a salt form thereof, wherein R^{19} at each occurrence is independently selected from the group consisting of 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 $–S(=O)_2NR^{32}R^{33}$.

10. A compound as defined in any one of claims 1-9, or a salt form thereof, 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

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selected from the group consisting of 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}.

11. A compound as defined in any one of claims 1-10, or a salt form thereof, wherein R^{22}, R^{23}, R^{32} and R^{33} at each occurrence is independently selected from the group consisting of H, C_{1-6} alkyl, C_{6-10} aryl, C_{7-11} arylalkyl, C_{3-10} cycloalkyl, 3-10 membered heterocycloalkyl, and 5-10 membered heteroaryl.

12. A compound as defined in any one of claims 1-11, or a salt form thereof, wherein R^{39}, R^{49}, R^{59} and R^{69} at each occurrence is independently selected from the group consisting of C_{1-6} alkyl optionally substituted by 1-3 R^{79}, C_{2-6} alkenyl optionally substituted by 1-3 R^{79}, C_{2-6} alkynyl 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, $–C(=O)R^{70}$, $–C(=O)OR^{70}$, $–C(=O)NR^{72}R^{73}$, $–NO_2$, $–NR^{72}R^{73}$, $–NR^{74}C(=O)R^{70}$, $–NR^{74}C(=O)NR^{72}R^{73}$, $–NR^{74}S(=O)_2R^{71}$, $–OR^{70}$, =O, $–S(=O)_nR^{70}$, and $–S(=O)_2NR^{72}R^{73}$.

13. A compound as defined in any one of claims 1-12, or a salt form thereof, wherein R^{70}, R^{71}, R^{74}, R^{75}, R^{76} and R^{77} at each occurrence is independently selected from the group consisting of H, 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}.

14. A compound as defined in any one of claims 1-12, or a salt form thereof, wherein R^{72} and R^{73} at each occurrence is independently selected from the group consisting of H, C_{1-6} alkyl, phenyl, benzyl, C_{5-6} cycloalkyl, 5-6 membered heterocycloalkyl, and 5-6 membered heteroaryl; alternatively, 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.

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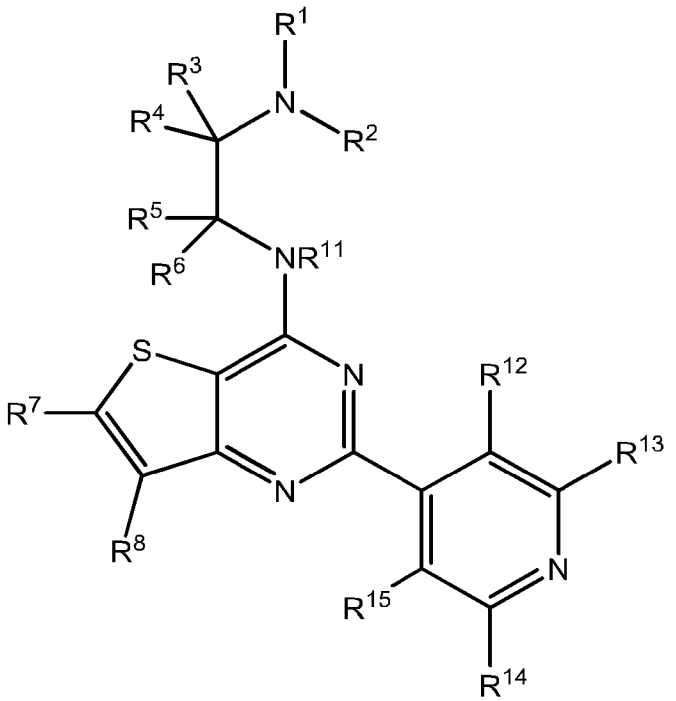
15. A compound as defined in any one of claims 1-14, or a salt form thereof, wherein R^{78} at each occurrence is independently selected from the group consisting of C_{1-6} alkyl, phenyl, benzyl, C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, and 5-6 membered heteroaryl.

16. A compound as defined in any one of claims 1-15, or a salt form thereof, wherein R^{79}, R^{89}, R^{99} and R^{109} at each occurrence is independently selected from the group consisting of 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, $–C(=O)R^{110}$, $–C(=O)OR^{110}$, $–C(=O)NR^{110}R^{110}$, $–NO_2$, $–NR^{110}R^{110}$, $–NR^{110}OR^{110}$, $–NR^{110}C(=O)R^{110}$, $–NR^{110}C(=O)NR^{110}R^{110}$, $–NR^{110}S(=O)_2R^{110}$, $–NR^{110}S(=O)_2NR^{110}R^{110}$, $–OR^{110}$, =O, –OCN, $–OC(=O)R^{110}$, $–S(=O)_nR^{110}$, $–S(=O)_2NR^{110}R^{110}$, and $–S(=O)NR^{110}R^{110}$.

17. A compound as defined in any one of claims 1-16, or a salt form thereof, wherein R^{110} at each occurrence is independently selected from the group consisting of H, C_{1-6} alkyl and C_{1-6} haloalkyl; and R^{111} at each occurrence is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl.

18. A compound, or a salt form thereof, according to claim 1 of Formula Ia:



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(Ia)

wherein,

R^1 and R^2 are independently selected from the group consisting of H and C_{1-6} alkyl optionally substituted by 1-13 R^{19};

R^{11} is H;

R^3 is selected from the group consisting of H, C_{1-6} alkyl optionally substituted by 1-13 R^{19}, C_{7-11} arylalkyl optionally substituted by 1-9 R^{19}, C_{6-7} cycloalkylalkyl optionally substituted by 1-6 R^{19}, and 6-11 membered heteroarylalkyl optionally substituted by 1-7 R^{19};

R^4, R^5, and R^6 are H;

R^7 is selected from the group consisting of H and C_{1-6} alkyl optionally substituted by 1-3 R^{19};

R^8 is selected from the group consisting of C_{2-6} alkynyl optionally substituted by 1-3 R^{19};

R^{12}, R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of H, C_{1-6} alkyl optionally substituted by 1-3 R^{19}, halogen, $-NR^{22}R^{23}$, $-NR^{24}C(=O)R^{20}$, $-NR^{24}C(=O)NR^{22}R^{23}$, $-OR^{20}$, and $-S(=O)_2NR^{22}R^{23}$;

R^{19} at each occurrence is independently selected from the group consisting of C_{1-6} alkyl, phenyl, C_{3-6} cycloalkyl, 3-6 membered heterocycloalkyl, halogen, $-C(=O)OR^{30}$ and $-OR^{30}$; and

R^{20}, R^{22}, R^{23} R^{24} and R^{30} at each occurrence are independently selected from the group consisting of H and C_{1-6}alkyl.

19. The compound, or a salt form thereof, according to claim 18 wherein R^1 and R^2 are H.

20. The compound, or a salt form thereof, according to any one of claims 18 and 19 wherein R^3 is selected from the group consisting of C_{1-6} alkyl optionally substituted by 1-13 R^{19} and C_{7-11} arylalkyl optionally substituted by 1-9 R^{19}.

21. The compound, or a salt form thereof, according to any one of claims 18 to 20 wherein R^7 is H.

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22. The compound, or a salt form thereof, according to any one of claims 18 to 21 wherein R^{19} at each occurrence is independently selected from the group consisting of C_{1-6} alkyl, phenyl, C_{3-6} cycloalkyl, halogen and $-OR^{30}$.

23. The compound, or a salt form thereof, according to any one of claims 18 to 22 wherein R^{12}, R^{13}, R^{14}, and R^{15} are independently selected from the group consisting of H and halogen.

24. The compound, or a salt form thereof, according to any one of claims 1 to 23 selected from the group consisting of:

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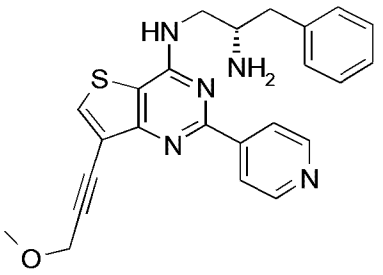
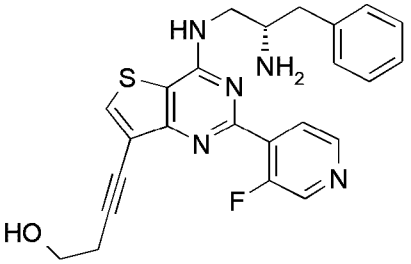
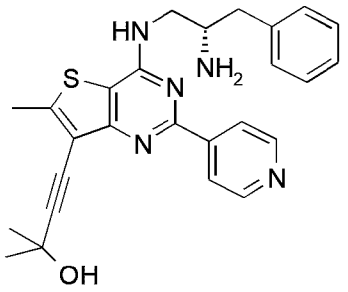
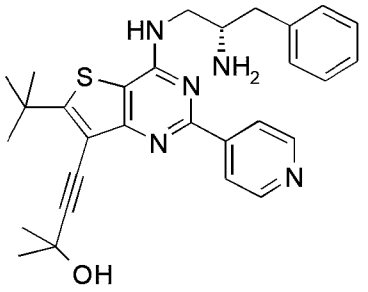
Structure	Name
	(S)-N*1*-[7-(3-Methoxy-prop-1-ynyl)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine
	4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-(3-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-7-yl]-but-3-yn-1-ol
	4-[4-((S)-2-Amino-3-phenyl-propylamino)-6-methyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-2-methyl-but-3-yn-2-ol
	4-[4-((S)-2-Amino-3-phenyl-propylamino)-6-tert-butyl-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-2-methyl-but-3-yn-2-ol

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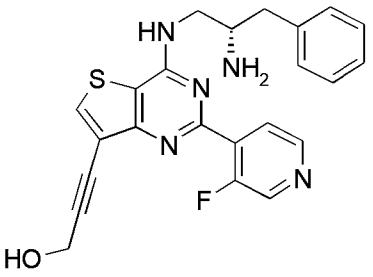
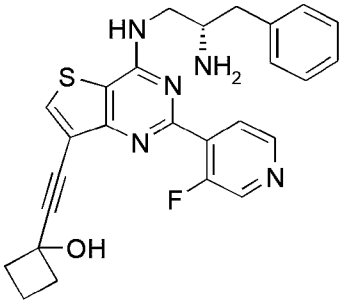
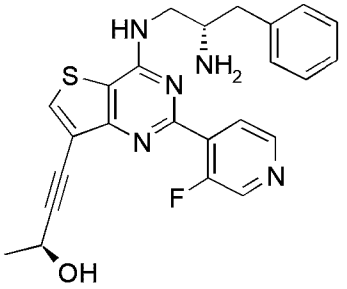
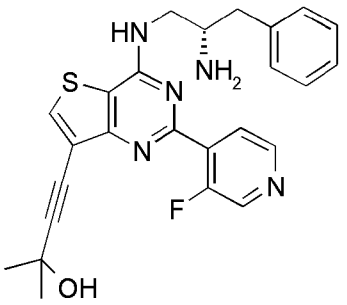
Structure	Name
	3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-(3-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-7-yl]-prop-2-yn-1-ol
	1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-(3-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-7-ylethynyl]-cyclobutanol
	(S)-4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-(3-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-7-yl]-but-3-yn-2-ol
	4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-(3-fluoro-pyridin-4-yl)-thieno[3,2-d]pyrimidin-7-yl]-2-methyl-but-3-yn-2-ol

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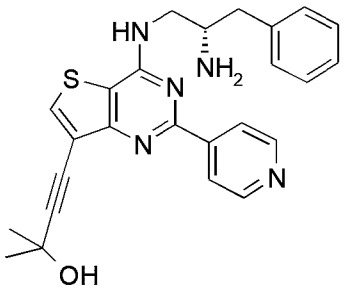
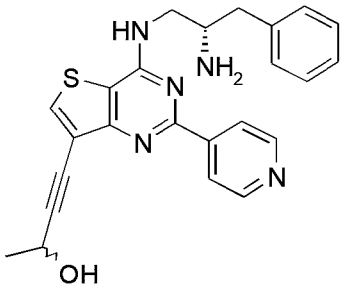
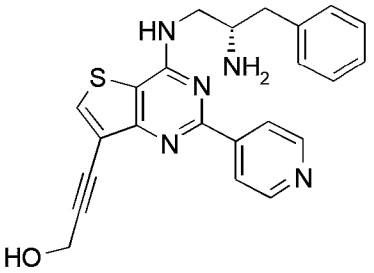
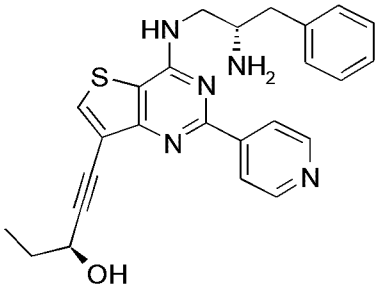
Structure	Name
	4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-2-methyl-but-3-yn-2-ol
	4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-but-3-yn-2-ol
	3-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-prop-2-yn-1-ol
	S)-1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-pent-1-yn-3-ol

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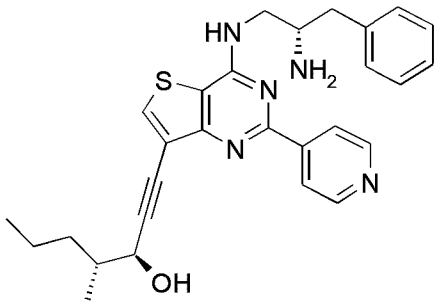
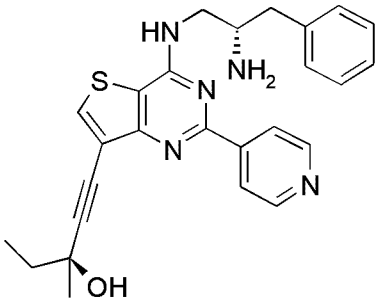
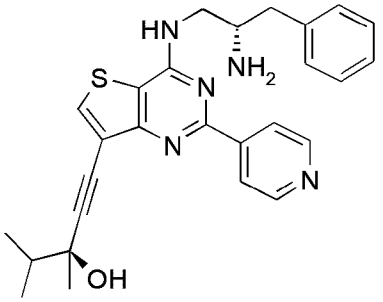
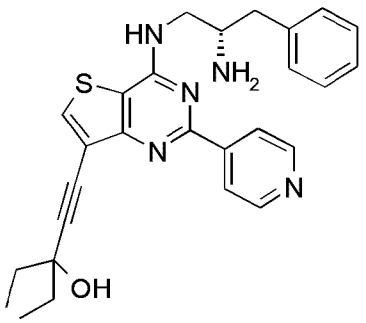
Structure	Name
	(S)-1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-4-methyl-hept-1-yn-3-ol
	(S)-1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-3-methyl-pent-1-yn-3-ol
	(S)-1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-3,4-dimethyl-pent-1-yn-3-ol
	1-[4-(2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-3-ethyl-pent-1-yn-3-ol

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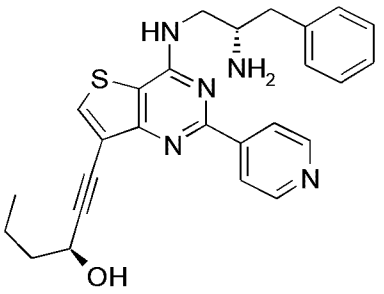
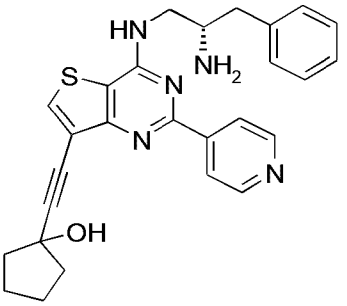
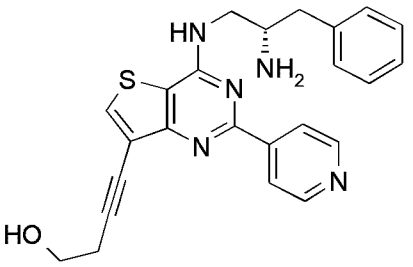
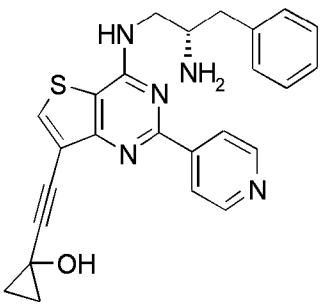
Structure	Name
	(S)-1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-hex-1-yn-3-ol
	1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-ylethynyl]-cyclopentanol
	4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-but-3-yn-1-ol
	1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-ylethynyl]-cyclopropanol

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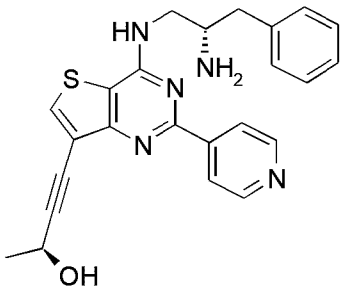
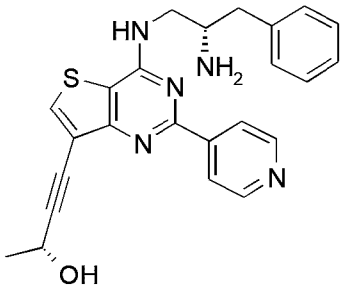
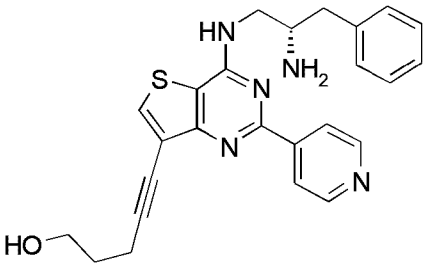
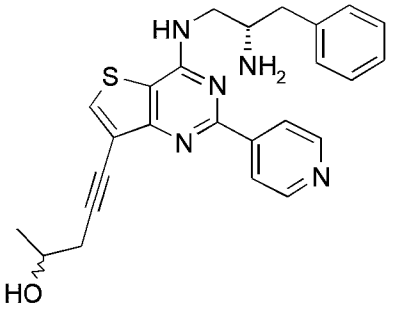
Structure	Name
	(S)-4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-but-3-yn-2-ol
	(R)-4-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-but-3-yn-2-ol
	5-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-pent-4-yn-1-ol
	5-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-pent-4-yn-2-ol

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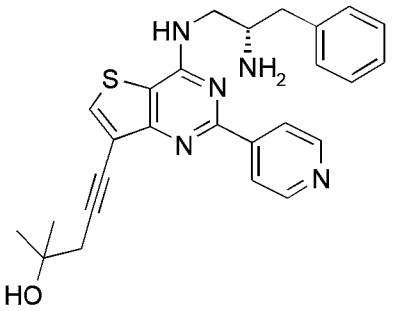
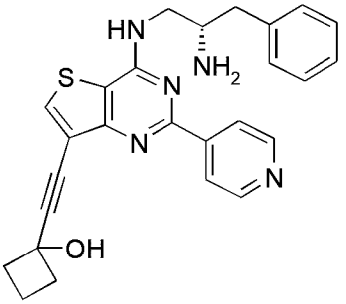
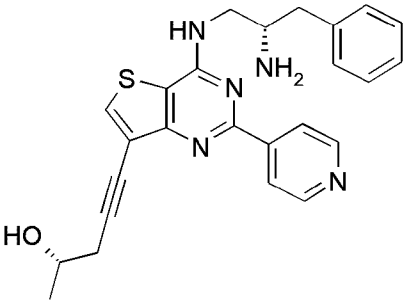
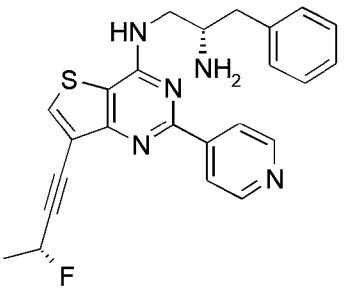
Structure	Name
	5-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-2-methyl-pent-4-yn-2-ol
	1-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-ylethynyl]-cyclobutanol
	(S)-5-[4-((S)-2-Amino-3-phenyl-propylamino)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-7-yl]-pent-4-yn-2-ol
	(S)-N*1*-[7-((R)-3-Fluoro-but-1-ynyl)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine

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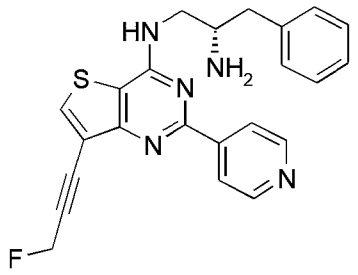
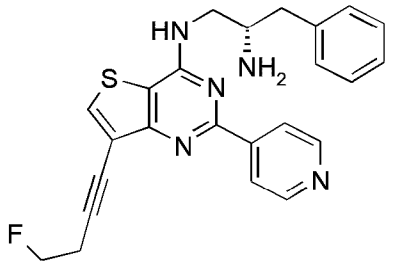
Structure	Name
	(S)-N*1*-[7-(3-Fluoro-prop-1-ynyl)-2-pyridin-4-yl-thieno[3,2-d]pyrimidin-4-yl]-3-phenyl-propane-1,2-diamine
and	
	(S)-N*1*-[7-(4-Fluoro-but-1-ynyl)-2-pyridin-4-yl-thieno[3,2-d]pyrimidine

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25. A pharmaceutical composition comprising a compound of any one of claims 1-24 or a salt form thereof and a pharmaceutically acceptable excipient, wherein the salt form is a pharmaceutically acceptable salt form.

26. Use of a compound of formula (I) or a salt form thereof as defined in any one of claims 1 to 24 in the manufacture of a medicament for treating cancer, wherein the salt form is a pharmaceutically acceptable salt form.

27. The use according to claim 26, wherein the cancer is selected from the group consisting of squamous cell carcinoma, leukemia, prostate cancer, non-Hodgkin's lymphoma, endometrial cancer, lung cancer and breast cancer.

28. The use according to claim 26 wherein the cancer is non-small cell lung cancer.

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29. The use according to claim 26 wherein the cancer is esophageal squamous cell carcinoma.

30. The use according to claim 26 wherein the cancer is follicular lymphoma.

31. A salt form of a compound according to any one of claims 1 to 24 wherein the salt form is a pharmaceutically acceptable salt form.

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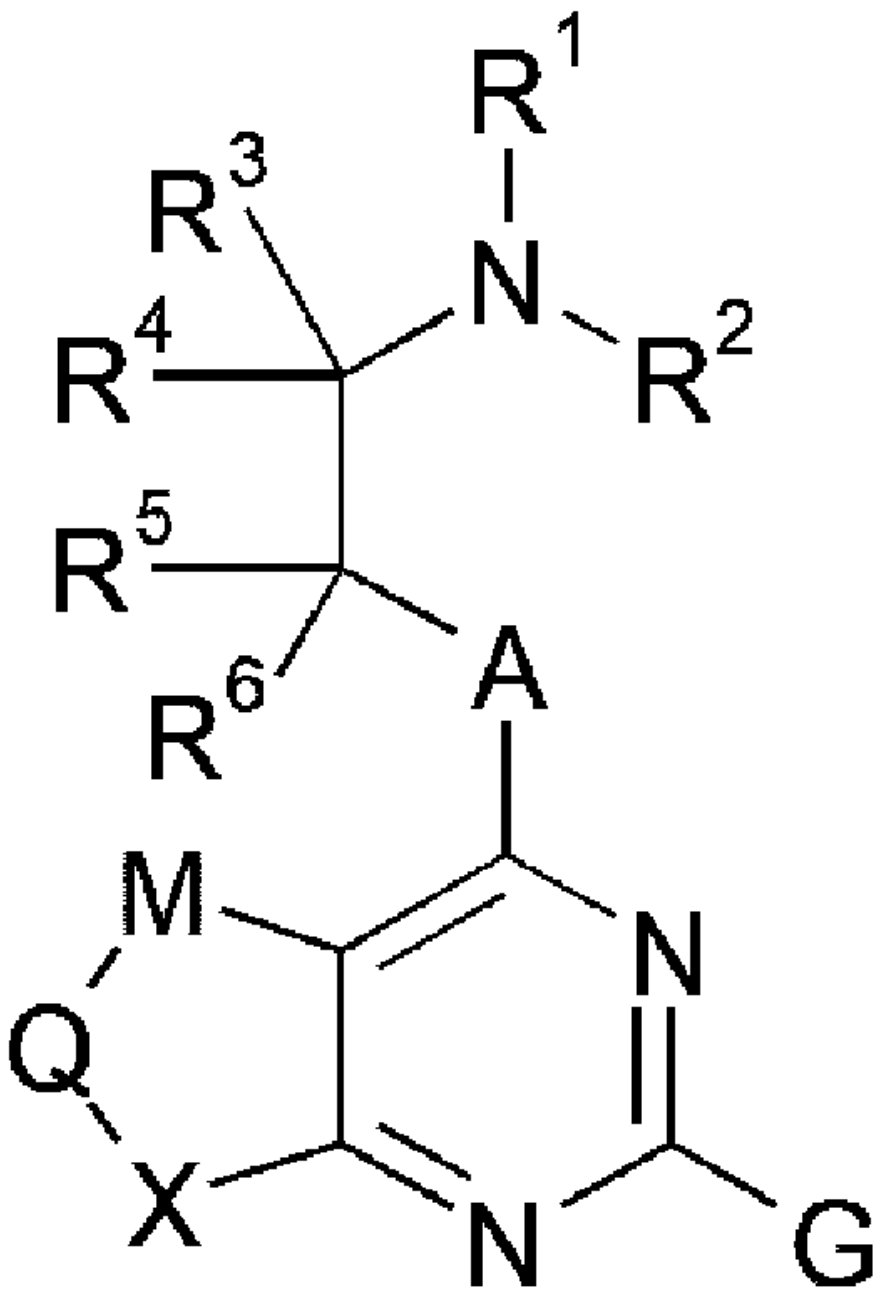

(I)