SUBSTITUTED IMIDAZOPYRIDINYL-AMINOPYRIDINE COMPOUNDS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to, and the benefit of, U.S. Provisional Application No. 61/290,923, filed December 30, 2009, ~~the contents of which are incorporated herein by reference in their entirety~~.

BACKGROUND OF THE INVENTION

[0002] Cancer is the second leading cause of death in the United States, exceeded only by heart disease. (*Cancer Facts and Figures 2004*, American Cancer Society, Inc.). Despite recent advances in cancer diagnosis and treatment, surgery and radiotherapy may be curative if a cancer is found early, but current drug therapies for metastatic disease are mostly palliative and seldom offer a long-term cure. Even with new chemotherapies entering the market, the need continues for new drugs effective in monotherapy or in combination with existing agents as first line therapy, and as second and third line therapies in treatment of resistant tumors.

[0003] Cancer cells are by definition heterogeneous. For example, within a single tissue or cell type, multiple mutational "mechanisms" may lead to the development of cancer. As such, heterogeneity frequently exists between cancer cells taken from tumors of the same tissue and same type that have originated in different individuals. Frequently observed mutational "mechanisms" associated with some cancers may differ between one tissue type and another (*e.g.*, frequently observed mutational "mechanisms" leading to colon cancer may differ from frequently observed "mechanisms" leading to leukemias). It is therefore often difficult to predict whether a particular cancer will respond to a particular chemotherapeutic agent (*Cancer Medicine*, 5th edition, Bast *et al.*, B. C. Decker Inc., Hamilton, Ontario).

[0004] Components of cellular signal transduction pathways that regulate the growth and differentiation of normal cells can, when dysregulated, lead to the development of cellular proliferative disorders and cancer. Mutations in cellular signaling proteins may cause such proteins to become expressed or activated at inappropriate levels or at inappropriate times during the cell cycle, which in turn may lead to uncontrolled cellular growth or changes in cell-cell attachment properties. For example, dysregulation of receptor tyrosine kinases by mutation, gene rearrangement, gene amplification, and overexpression of both receptor and ligand has been implicated in the development and progression of human cancers.

[0005] AKT protein family, which members are also called protein kinases B (PKB) plays an important role in mammalian cellular signaling. In humans, there are three genes in the AKT family: Akt1, Akt2, and Akt3. These genes code for enzymes that are members of the serine/threonine-specific protein kinase family. Akt1 is involved in cellular survival pathways, by inhibiting apoptotic processes. Akt1 is also able to induce protein synthesis pathways, and is therefore a key signaling protein in the cellular pathways that lead to skeletal muscle hypertrophy, and general tissue growth. Akt2 is an important signaling molecule in the Insulin signaling pathway and is required to induce glucose transport. The role of Akt3 is less clear, though it appears to be predominantly expressed in brain.

[0006] The AKT family regulates cellular survival and metabolism by binding and regulating many downstream effectors, e.g. Nuclear Factor-κB, Bcl-2 family proteins and murine double minute 2 (MDM2). Akt1 is known to play a role in the cell cycle. Moreover, activated Akt1 may enable proliferation and survival of cells that have sustained a potentially mutagenic impact and, therefore, may contribute to acquisition of mutations in other genes. Akt1 has also been implicated in angiogenesis and tumor development. Studies have shown that deficiency of Akt1 enhanced pathological angiogenesis and tumor growth associated with matrix abnormalities in skin and blood vessels. Since it can block apoptosis, and thereby promote cell survival, Akt1 is a major factor in many types of cancer.

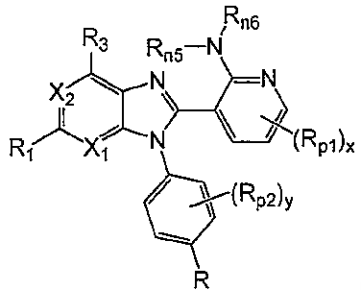
[0007] Accordingly, new compounds and methods for modulating AKT genes and treating proliferation disorders, including cancer, are needed. The present invention addresses these needs.

[0007a] WO 2005/011700 discloses novel 1 H-imidazo[4,5-c]pyridin-2-yl compounds, the use of such compounds as inhibitors of protein kinase B activity and in the treatment of cancer and arthritis.

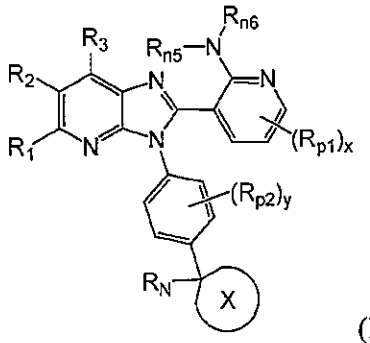
[0007b] WO 2007/111904 discloses compounds useful of inhibitors of protein kinases. It also provides processes for preparing the compounds of the invention, pharmaceutically acceptable compositions comprising the compounds of the invention, and methods of using the compositions in the treatment of various disorders.

SUMMARY OF THE INVENTION

[0008] The present invention provides, in part, substituted imidazopyridinyl-aminopyridine compounds of formula I, II, III or IV and methods of preparing the compounds of formula I, II, III or IV:



(I),



(II),

[00013] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods and materials are described below. ~~All publications, patent applications, patents, and other references mentioned herein are incorporated by reference.~~ The references cited herein are not admitted to be prior art to the claimed invention. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be limiting.

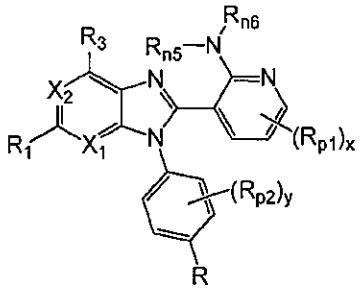
[00014] Other features and advantages of the invention will be apparent from the following detailed description and claims.

DETAILED DESCRIPTION OF THE INVENTION

1. Substituted Imidazopyridinyl-Aminopyridine Compounds

[00015] The present invention provides novel substituted imidazopyridinyl-aminopyridine compounds, synthetic methods for making the compounds, pharmaceutical compositions containing them and various uses of the disclosed compounds.

[00016] The present invention provides the compounds of Formula I:



(I),

wherein:

one of X_1 and X_2 is CR_x and the other is N;

R_x, R_1 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

[00027] For example, R_1 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[00028] For example, R_1 is unsubstituted methyl.

[00029] For example, R_1 is trifluoromethyl (*i.e.*, CF_3) or methyl substituted with dimethylamino.

[00030] For example, R_1 is unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[00031] For example, R_1 is unsubstituted or substituted methoxy.

[00032] For example, R_1 is unsubstituted amino.

[00033] For example, R_1 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

b) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

c) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl, each of which is optionally substituted with hydroxyl, nitro, amino, cyano, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*,

pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[00061] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[00062] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, morpholinyl, $C(O)OR_{17}$, and $C(O)R_{17}$, wherein R_{17} is H, methyl or trifluoromethyl.

[00063] For example, R_1 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[00064] For example, R_1 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[00065] For example, R_1 is piperidinyl.

[00066] For example, R_x is fluorine, chlorine, bromine or iodine.

[00067] For example, R_x is bromine.

[00068] For example, R_x is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[00069] For example, R_x is unsubstituted methyl.

[00070] For example, R_x is trifluoromethyl (*i.e.*, CF_3).

[00071] For example, R_x is unsubstituted amino.

[00072] For example, R_x is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[00087] For example, R_x is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[00088] For example, R_x is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, $C(O)OR_{17}$ wherein R_{17} is H or methyl.

[00089] For example, R_x is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[00090] For example, R_x is unsubstituted or substituted cyclopentyl.

[00091] For example, R_x is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[00092] For example, R_3 is fluorine, chlorine, bromine or iodine.

[00093] For example, R_3 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[00094] For example, R_3 is unsubstituted methyl.

[00095] For example, R_3 is unsubstituted amino.

[00096] For example, R_3 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

b) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

c) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl, each of which is optionally substituted with hydroxyl, nitro, amino, cyano, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*,

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy), and

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)).

[000101] For example, R_3 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000102] For example, R_3 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl,

imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000103] For example, R_3 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000104] For example, R_3 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000105] For example, x is 0.

[000106] For cxample, x is 1.

[000107] For example, each R_{p1} is independently fluorine, chlorine, bromine or iodine.

[000108] For example, each R_{p1} is independently chlorine.

[000109] For example, each R_{p1} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000110] For example, each R_{p1} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000111] For example, each R_{p1} is independently unsubstituted amino.

[000112] For example, each R_{p1} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000113] For example, y is 0.

[000114] For example, y is 1.

[000115] For example, each R_{p2} is independently fluorine, chlorine, bromine or iodine.

[000116] For example, each R_{p2} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000117] For example, each R_{p2} is independently methyl, ethyl, propyl, i-propyl or t-butyl.

[000118] For example, each R_{p2} is independently C_1-C_6 alkyl substituted with amino.

[000119] For example, each R_{p2} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000120] For example, each R_{p2} is independently unsubstituted amino.

[000121] For example, each R_{p2} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000122] For example, each R_{p2} is independently unsubstituted or substituted phenyl or naphthyl.

[000123] For example, each R_{p2} is independently heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000124] For example, each R_{p2} is independently oxazolyl.

[000125] For example, each R_{p2} is independently unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000126] For example, each R_{p2} is independently heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000127] For example, R_{n5} and R_{n6} are each H.

[000128] For example, R_{n5} is H and R_{n6} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000129] For example, R_{n5} and R_{n6} are each unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000130] For example, at least one of R_{n5} and R_{n6} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000131] For example, at least one of R_{n5} and R_{n6} is unsubstituted amino.

[000132] For example, at least one of R_{n5} and R_{n6} is amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000133] For example, at least one of R_{n5} and R_{n6} is $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000134] For example, at least one of R_{n5} and R_{n6} is $S(O)_2R_8$.

[000135] For example, R_8 is H.

[000136] For example, R_8 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000137] For example, R_8 is methyl.

[000138] For example, R_8 is unsubstituted or substituted phenyl or naphthyl.

[000139] For example, R_8 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl,

isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000140] For example, R_8 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000141] For example, R_8 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000142] For example, R is H.

[000143] For example, R is fluorine, chlorine, bromine or iodine.

[000144] For example, R is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000145] For example, R is C_1-C_6 alkyl and is optionally substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted amino,

c) unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)), which is optionally substituted with one or two groups selected from:

(1) unsubstituted or substituted C_6-C_{10} aryl,

(2) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S,

(3) unsubstituted or substituted C_3-C_{10} carbocycle,

(4) unsubstituted or substituted heterocycle comprising one or two 3-, 4-, 5-, 6- or 7-member rings and 1-4 heteroatoms selected from N, O and S,

d) NR_9R_{10}, $C(O)R_{11}$, wherein:

R_9 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, $S(O)R_{12}$, or $S(O)_2R_{12}$;

R_{11} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, OR_{14}, or $NR_{14}R_{15}$;

R_{10}, R_{12}, R_{13}, R_{14} and R_{15} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, and

c) a 3-, 4-, 5-, 6- or 7-member ring optionally comprising 1-4 heteroatoms selected from N, O and S, which is optionally substituted.

[000146] For example, R is C_1-C_6 alkyl substituted with C_1-C_6 alkylamino or di-C_1-C_6 alkylamino, which is optionally substituted with phenyl.

[000147] For example, R is methyl, ethyl, n-propyl, i-propyl, n-butyl, or t-butyl.

[000148] For example, R is methyl substituted with a 3-, 4-, 5-, 6-, or 7-member ring selected from unsubstituted or substituted C_3-C_7 carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cycloheptenyl.

[000149] For example, R is methyl substituted with a C_3-C_7 carbocycle and is optionally subsitued with one or more groups selected from hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), and unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000150] For example, R is methyl substituted with cyclobutyl.

[000151] For example, R is methyl substituted with a 3-, 4-, 5-, 6-, or 7-member ring selected from unsubstituted or substituted heterocycle selected from aziridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, diazetidinyl, dioxetanyl, dithietanyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, tetrahyrofuranyl, tetrahyrothiophenyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, oxepanyl, thiepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

[000152] For example, R is methyl substituted with a 3-, 4-, 5-, 6-, or 7-member heterocycle and is optionally subsitued with one or more groups selected from hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), and unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000153] For example, R is methyl substituted with oxetanyl.

[000154] For example, R is methyl substituted with NR_9R_{10}.

[000155] For example, R_9 and R_{10} are each H (*i.e.*, R_N is NH_2).

[000156] For example, R_9 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000157] For example, R_9 is unsubstituted or substituted phenyl or naphthyl.

[000158] For example, R_9 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000159] For example, R_9 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000160] For example, R_9 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000161] For example, R_9 is $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, or $S(O)_2R_{12}$.

[000162] For example, R_{12} is H.

[000163] For example, R_{12} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000164] For example, R_{12} is methyl, ethyl, or t-butyl.

[000165] For example, R_{12} is unsubstituted or substituted phenyl or naphthyl.

[000166] For example, R_{12} is unsubstituted phenyl.

[000167] For example, R_{12} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000168] For example, R_{12} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000169] For example, R_{12} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000170] For example, R_{13} is H.

[000171] For example, R_{13} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000172] For example, R_{13} is methyl, ethyl, or t-butyl.

[000173] For example, R_{13} is unsubstituted or substituted phenyl or naphthyl.

[000174] For example, R_{13} is unsubstituted phenyl.

[000175] For example, R_{13} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000176] For example, R_{13} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000177] For example, R_{13} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000178] For example, R_{10} is H.

[000179] For example, R_{10} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl,

i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000180] For example, R_{10} is unsubstituted or substituted phenyl or naphthyl.

[000181] For example, R_{10} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000182] For example, R_{10} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000183] For example, R_{10} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000184] For example, R is methyl substituted with $C(O)R_{11}$.

[000185] For example, R_{11} is H.

[000186] For example, R_{11} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000187] For example, R_{11} is unsubstituted or substituted phenyl or naphthyl.

[000188] For example, R_{11} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000189] For example, R_{11} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000190] For example, R_{11} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000191] For example, R_{11} is OR_{14} or $NR_{14}R_{15}$.

[000192] For example, R_{14} is H.

[000193] For example, R_{14} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with hydroxyl or halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000194] For example, R_{14} methyl or ethyl.

[000195] For example, R_{14} is C_1-C_6 alkyl substituted with hydroxyl.

[000196] For example, R_{14} is unsubstituted or substituted phenyl or naphthyl.

[000197] For example, R_{14} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000198] For example, R_{14} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000199] For example, R_{14} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000200] For example, R_{15} is H.

[000201] For example, R_{15} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000202] For example, R_{15} is unsubstituted or substituted phenyl or naphthyl.

[000203] For example, R_{15} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000204] For example, R_{15} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000205] For example, R_{15} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000206] For example, R is methyl substituted with both a 3-, 4-, 5-, 6- or 7-member ring optionally comprising 1-4 heteroatoms selected from N, O and S and NR_9R_{10}.

[000207] For example, R is methyl substituted with both cyclobutyl and NR_9R_{10}.

[000208] For example, R is methyl substituted with both oxetanyl and NR_9R_{10}.

[000209] For example, R is methyl substituted with both a 3-, 4-, 5-, 6- or 7-member ring optionally comprising 1-4 heteroatoms selected from N, O and S and $C(O)R_{11}$.

[000210] For example, R is methyl substituted with both cyclobutyl and $C(O)R_{11}$.

[000211] For example, R is methyl substituted with both oxetanyl and $C(O)R_{11}$.

[000212] For example, R is unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000213] For example, R is unsubstituted or substituted methoxy.

[000214] For example, R is unsubstituted amino.

[000215] For example, R is amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl)

[000216] For example, R is unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), or unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino).

[000217] For example, R is dimethylamino or diethylamino.

[000218] For example, R is unsubstituted or substituted phenyl or naphthyl.

[000219] For example, R is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000220] For example, R is pyrazolyl or triazolyl, and is optionally substituted.

[000221] For example, R is carbocycle selected from cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and

carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000222] For example, R is carbocycle substituted with NR_9R_{10}.

[000223] For example, R_9 and R_{10} are each H (*i.e.*, R_N is NH_2).

[000224] For example, R_9 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000225] For example, R_9 is unsubstituted or substituted phenyl or naphthyl.

[000226] For example, R_9 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000227] For example, R_9 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to, cyclopropyl,~~ cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000228] For example, R_9 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000229] For example, R_9 is $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, or $S(O)_2R_{12}$.

[000230] For example, R_{12} is H.

[000231] For example, R_{12} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000232] For example, R_{12} is methyl, ethyl, or t-butyl.

[000233] For example, R_{12} is unsubstituted or substituted phenyl or naphthyl.

[000234] For example, R_{12} is unsubstituted phenyl.

[000235] For example, R_{12} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl,

isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000236] For example, R_{12} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000237] For example, R_{12} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000238] For example, R_{13} is H.

[000239] For example, R_{13} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000240] For example, R_{13} is methyl, ethyl, or t-butyl.

[000241] For example, R_{13} is unsubstituted or substituted phenyl or naphthyl.

[000242] For example, R_{13} is unsubstituted phenyl.

[000243] For example, R_{13} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000244] For example, R_{13} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000245] For example, R_{13} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000246] For example, R_{10} is H.

[000247] For example, R_{10} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000248] For example, R_{10} is unsubstituted or substituted phenyl or naphthyl.

[000249] For example, R_{10} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl,

pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000250] For example, R_{10} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000251] For example, R_{10} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000252] For example, R is carbocycle substituted with $C(O)R_{11}$.

[000253] For example, R_{11} is H.

[000254] For example, R_{11} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000255] For example, R_{11} is unsubstituted or substituted phenyl or naphthyl.

[000256] For example, R_{11} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000257] For example, R_{11} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000258] For example, R_{11} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000259] For example, R_{11} is OR_{14} or $NR_{14}R_{15}$.

[000260] For example, R_{14} is H.

[000261] For example, R_{14} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with hydroxyl or halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000262] For example, R_{14} methyl or ethyl.

[000263] For example, R_{14} is C_1-C_6 alkyl substituted with hydroxyl.

[000264] For example, R_{14} is unsubstituted or substituted phenyl or naphthyl.

[000265] For example, R_{14} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000266] For example, R_{14} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000267] For example, R_{14} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, pipcrazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000268] For example, R_{15} is H.

[000269] For example, R_{15} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000270] For example, R_{15} is unsubstituted or substituted phenyl or naphthyl.

[000271] For example, R_{15} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000272] For example, R_{15} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000273] For example, R_{15} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000274] For example, R is cyclobutyl or cyclohexyl, and is optionally substituted.

[000275] For example, R is heterocycle selected from ziridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, diazetidinyl, dioxetanyl, dithietanyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, tetrahyrofuranyl, tetrahyrothiophenyl, imidazolidinyl,

pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, oxepanyl, thiepanyl, diazepanyl, oxazepanyl, thiazepanyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, morpholinyl, piperidinonyl, azetidinyl, azepanyl, oxazepanyl, and dioxoazaspirodecanyl, ~~and the like,~~ and is optionally substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino,

d) unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)), which is optionally substituted with one or two groups selected from:

(1) unsubstituted or substituted C_6-C_{10} aryl,

(2) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S,

(3) unsubstituted or substituted C_3-C_{10} carbocycle,

(4) unsubstituted or substituted heterocycle comprising one or two 3-, 4-, 5-, 6- or 7-member rings and 1-4 heteroatoms selected from N, O and S,

d) NR_9R_{10}, $C(O)R_{11}$, wherein:

R_9 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, $S(O)R_{12}$, or $S(O)_2R_{12}$;

R_{11} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted

heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, OR_{14}, or $NR_{14}R_{15}$;

R_{10}, R_{12}, R_{13}, R_{14} and R_{15} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000276] For example, R is heterocycle substituted with NR_9R_{10}.

[000277] For example, R_9 and R_{10} are each H (*i.e.*, R_N is NH_2).

[000278] For example, R_9 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000279] For example, R_9 is unsubstituted or substituted phenyl or naphthyl.

[000280] For example, R_9 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000281] For example, R_9 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000282] For example, R_9 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000283] For example, R_9 is $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, or $S(O)_2R_{12}$.

[000284] For example, R_{12} is H.

[000285] For example, R_{12} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000286] For example, R_{12} is methyl, ethyl, or t-butyl.

[000287] For example, R_{12} is unsubstituted or substituted phenyl or naphthyl.

[000288] For example, R_{12} is unsubstituted phenyl.

[000289] For example, R_{12} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000290] For example, R_{12} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000291] For example, R_{12} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000292] For example, R_{13} is H.

[000293] For example, R_{13} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000294] For example, R_{13} is methyl, ethyl, or t-butyl.

[000295] For example, R_{13} is unsubstituted or substituted phenyl or naphthyl.

[000296] For example, R_{13} is unsubstituted phenyl.

[000297] For example, R_{13} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000298] For example, R_{13} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000299] For example, R_{13} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000300] For example, R_{10} is H.

[000301] For example, R_{10} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl,

i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000302] For example, R_{10} is unsubstituted or substituted phenyl or naphthyl.

[000303] For example, R_{10} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000304] For example, R_{10} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000305] For example, R_{10} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000306] For example, R is heterocycle substituted with $C(O)R_{11}$.

[000307] For example, R_{11} is H.

[000308] For example, R_{11} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000309] For example, R_{11} is unsubstituted or substituted phenyl or naphthyl.

[000310] For example, R_{11} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000311] For example, R_{11} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000312] For example, R_{11} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000313] For example, R_{11} is OR_{14} or $NR_{14}R_{15}$.

[000314] For example, R_{14} is H.

[000315] For example, R_{14} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with hydroxyl or halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000316] For example, R_{14} methyl or ethyl.

[000317] For example, R_{14} is C_1-C_6 alkyl substituted with hydroxyl.

[000318] For example, R_{14} is unsubstituted or substituted phenyl or naphthyl.

[000319] For example, R_{14} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000320] For example, R_{14} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000321] For example, R_{14} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000322] For example, R_{15} is H.

[000323] For example, R_{15} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000324] For example, R_{15} is unsubstituted or substituted phenyl or naphthyl.

[000325] For example, R_{15} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000326] For example, R_{15} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000327] For example, R_{15} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000328] For example, R is oxetanyl, and is optionally substituted.

[000329] For example, R is Q-T.

[000330] For example, Q is a bond.

[000331] For example, Q is an unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl linker, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl linker.

[000332] For example, Q is a methyl linker.

[000333] For example, T is $NR_{n1}R_{n2}$.

[000334] For example, R_{n1} and R_{n2} are each H.

[000335] For example, R_{n1} is H.

[000336] For example, R_{n1} is H and R_{n2} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$.

[000337] For example, R_{n1} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000338] For example, R_{n1} is C_1-C_6 alkyl substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl,

thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl), and

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl).

[000339] For example, R_{n1} is C_1-C_6 alkyl substituted with phenyl.

[000340] For example, R_{n1} is methyl substituted with phenyl.

[000341] For example, R_{n1} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl and R_{n2} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$.

[000342] For example, R_{n1} is unsubstituted or substituted phenyl or naphthyl.

[000343] For example, R_{n1} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000344] For example, R_{n1} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000345] For example, R_{n1} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000346] For example, R_{n2} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000347] For example, R_{n2} is C_1-C_6 alkyl substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl), and

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl).

[000348] For example, R_{n2} is C_1-C_6 alkyl substituted with phenyl.

[000349] For example, R_{n2} is methyl substituted with phenyl.

[000350] For example, R_{n2} is unsubstituted or substituted phenyl or naphthyl.

[000351] For example, R_{n2} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl,

quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000352] For example, R_{n2} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000353] For example, R_{n2} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000354] For example, R_{n2} is $C(O)R_4$, $C(O)OR_4$, or $C(O)NR_4'R_4$.

[000355] For example, R_4' is H.

[000356] For example, R_4' is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000357] For example, R_4' is unsubstituted or substituted phenyl or naphthyl.

[000358] For example, R_4' is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000359] For example, R_4' is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000360] For example, R_4' is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000361] For example, R_4 is H.

[000362] For example, R_4 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, n-hexyl and 2-methylpropyl.

[000363] For example, R_4 is C_1-C_6 alkyl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

[000371] For example, R_4 is phenyl substituted with one, two or more groups independently selected from methyl, ethyl, i-propyl, t-butyl, trifluoromethyl, and benzyl.

[000372] For example, R_4 is phenyl substituted with one, two or more C_1-C_6 alkoxy, which is optionally substituted with one or more halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000373] For example, R_4 is phenyl substituted with one, two or more groups independently selected from methoxy, ethoxy, i-propyloxy, and trifluoromethoxy.

[000374] For example, R_4 is phenyl substituted with one, two or more groups independently selected from amino and dimethylamino.

[000375] For example, R_4 is phenyl substituted with phenyl.

[000376] For example, R_4 is phenyl substituted with heteroaryl, which is optionally substituted with unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000377] For example, R_4 is phenyl substituted with pyrazolyl or pyrazolonyl, each of which is optionally substituted with methyl.

[000378] For example, R_4 is phenyl substituted with $C(O)R_{19}$, $C(O)OR_{19}$, $NR_{19}'C(O)R_{19}$, and $NR_{19}'C(O)OR_{19}$.

[000379] For example, R_{19}' is H.

[000380] For example, R_{19} is H.

[000381] For example, R_{19} is methyl.

[000382] For example, R_{19} is phenyl and is optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000383] For example, R_{19} is phenyl substituted with halogen.

[000384] For example, R_4 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, indazolyl, and dihydrobenzofuranyl, ~~and the like;~~ and is optionally substituted.

[000385] For example, R_4 is heteroaryl optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000386] For example, R_4 is heteroaryl substituted with one or more groups selected from methyl and halogen.

[000387] For example, R_4 is pyridinyl, isoquinolinyl, isoxazolyl, thiophenyl, furanyl, indolyl, dihydrobenzofuranyl, pyrrolyl, benzothiophenyl, quinolinyl, pyrimidinyl, thiazolyl, or pyrazinyl, each of which is optionally substituted.

[000388] For example, R_4 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000389] For example, R_4 is cyclopentyl or cyclohexyl, each of which is optionally substituted.

[000390] For example, R_4 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000391] For example, R_{n2} is $S(O)R_5$ or $S(O)_2R_5$.

[000392] For example, R_5 is H.

[000393] For example, R_5 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, n-hexyl and 2-methylpropyl.

[000394] For example, R_5 is unsubstituted or substituted phenyl or naphthyl.

[000395] For example, R_5 is phenyl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

d) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino),

and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

e) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

f) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, pyrazolonyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

g) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

h) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

i) $C(O)R_{19}$, $C(O)OR_{19}$, $NR_{19}'C(O)R_{19}$, and $NR_{19}'C(O)OR_{19}$,

wherein:

R_{19} and R_{19}' are each independently H, unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), or unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl).

[000396] For example, R_5 is phenyl substituted with one, two or more groups, each of which is independently selected from methyl, methoxy, fluorine and chlorine.

[000397] For example, R_5 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, indazolyl, and dihydrobenzofuranyl, ~~and the like,~~ and is optionally substituted.

[000398] For example, R_5 is heteroaryl optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and

unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000399] For example, R_5 is heteroaryl substituted with one or more groups selected from methyl and halogen.

[000400] For example, R_5 is pyridinyl, isoxazolyl, thiophenyl, imidazolyl, pyrazolyl, dihydrobenzofuranyl, or quinolinyl, each of which is optionally substituted.

[000401] For example, R_5 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000402] For example, R_5 is cyclopropyl or cyclohexyl, each of which is optionally substituted.

[000403] For example, R_5 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000404] For example, R_5' is H.

[000405] For example, R_5' is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000406] For example, R_5' is unsubstituted or substituted phenyl or naphthyl.

[000407] For example, R_5' is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000408] For example, R_5' is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000409] For example, R_5' is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000410] For example, R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring selected from azetidinyl, diazetidinyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl,

hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

[000411] For example, R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring, which is optionally substituted with hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), or unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000412] For example, R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a morpholinyl or piperazinyl ring and is optionally substituted with methyl.

[000413] For example, T is $C(O)R_o$.

[000414] For example, R_o is H.

[000415] For example, R_o is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000416] For example, R_o is unsubstituted or substituted phenyl or naphthyl.

[000417] For example, R_o is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000418] For example, R_o is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000419] For example, R_o is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000420] For example, R_o is $NR_{o1}R_{o2}$.

[000421] For example, R_{o1} and R_{o2} are each H.

[000422] For example, at least one of R_{o1} and R_{o2} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000423] For example, at least one of R_{o1} and R_{o2} is C_1-C_6 alkyl substituted with one or more groups selected from:

[000428] For example, at least one of R_{o1} and R_{o2} is phenyl substituted with one, two or more groups, each of which is independently selected from cyano, halogen, methyl, t-butyl, methoxy and $NHC(O)R_{21}$ wherein R_{21} is methyl.

[000429] For example, at least one of R_{o1} and R_{o2} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, indazolyl and oxodihydrobenzofuranyl, ~~and the like,~~ and is optionally substituted.

[000430] For example, at least one of R_{o1} and R_{o2} is heteroaryl and is optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000431] For example, at least one of R_{o1} and R_{o2} is heteroaryl substituted with one or more groups selected from methyl and halogen.

[000432] For example, at least one of R_{o1} and R_{o2} is pyridinyl, benzothiazolyl, benzoimidazolyl, quinolinyl, or oxodihydrobenzofuranyl, each of which is optionally substituted.

[000433] For example, at least one of R_{o1} and R_{o2} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000434] For example, at least one of R_{o1} and R_{o2} is cyclopentyl.

[000435] For example, at least one of R_{o1} and R_{o2} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000436] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring selected from azetidinyl, diazetidinyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl,

hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

[000437] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring, which is optionally substituted with one or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, pyrazolonyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzoimidazolonyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl), and

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl).

[000438] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a piperidinyl ring and is optionally substituted with benzoimidazolonyl.

[000439] For example, R_o is OR_{o3}.

[000440] For example, R_{o3} is H.

[000441] For example, R_{o3} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, n-hexyl and 2-methylpropyl.

[000442] For example, R_{o3} is unsubstituted or substituted phenyl or naphthyl.

[000443] For example, R_{o3} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl,

pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000444] For example, R_{o3} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000445] For example, R_{o3} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000446] For example, T is $S(O)R_s$ or $S(O)_2R_s$.

[000447] For example, R_s is H.

[000448] For example, R_s is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000449] For example, R_s is unsubstituted or substituted phenyl or naphthyl.

[000450] For example, R_s is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000451] For example, R_s is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000452]

[000453] For example, R_s is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000454] For example, R_s is $NR_{s1}R_{s2}$.

[000455] For example, R_{s1} and R_{s2} are each H.

[000456] For example, at least one of R_{s1} and R_{s2} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000457] For example, at least one of R_{s1} and R_{s2} is methyl

[000458] For example, at least one of R_{s1} and R_{s2} is unsubstituted or substituted phenyl or naphthyl.

[000459] For example, at least one of R_{o1} and R_{o2} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

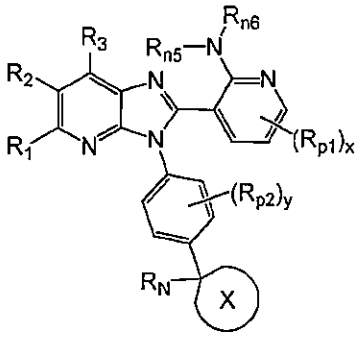
[000460] For example, at least one of R_{o1} and R_{o2} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000461] For example, at least one of R_{o1} and R_{o2} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000462] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring selected from azetidinyl, diazetidinyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

[000463] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a piperidinyl ring and is optionally substituted.

[000464] The present invention also provides the compounds of Formula II:



(II),

wherein:

unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000472] For example, R_1 is fluorine, chlorine, bromine or iodine.

[000473] For example, R_1 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000474] For example, R_1 is unsubstituted methyl.

[000475] For example, R_1 is trifluoromethyl (*i.e.*, CF_3) or methyl substituted with dimethylamino.

[000476] For example, R_1 is unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000477] For example, R_1 is unsubstituted or substituted methoxy.

[000478] For example, R_1 is unsubstituted amino.

[000479] For example, R_1 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

b) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

[000506] For example, R_1 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000507] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000508] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, morpholinyl, $C(O)OR_{17}$, and $C(O)R_{17}$, wherein R_{17} is H, methyl or trifluoromethyl.

[000509] For example, R_1 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000510] For example, R_1 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000511] For example, R_1 is piperidinyl.

[000512] For example, R_2 is fluorine, chlorine, bromine or iodine.

[000513] For example, R_2 is bromine.

[000514] For example, R_2 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000515] For example, R_2 is unsubstituted methyl.

[000516] For example, R_2 is trifluoromethyl (*i.e.*, CF_3).

[000517] For example, R_2 is unsubstituted amino.

[000518] For example, R_2 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000533] For example, R_2 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000534] For example, R_2 is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, $C(O)OR_{17}$ wherein R_{17} is H or methyl.

[000535] For example, R_2 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000536] For example, R_2 is unsubstituted or substituted cyclopentyl.

[000537] For example, R_2 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000538] For example, R_3 is fluorine, chlorine, bromine or iodine.

[000539] For example, R_3 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000540] For example, R_3 is unsubstituted methyl.

[000541] For example, R_3 is unsubstituted amino.

[000542] For example, R_3 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

b) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

c) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl, each of which is optionally substituted with hydroxyl, nitro, amino, cyano, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*,

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy), and

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)).

[000547] For example, R_3 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000548] For example, R_3 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl,

imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000549] For example, R_3 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000550] For example, R_3 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000551] For example, x is 0.

[000552] For example, x is 1.

[000553] For example, each R_{p1} is independently fluorine, chlorine, bromine or iodine.

[000554] For example, each R_{p1} is independently chlorine.

[000555] For example, each R_{p1} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000556] For example, each R_{p1} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000557] For example, each R_{p1} is independently unsubstituted amino.

[000558] For example, each R_{p1} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000559] For example, y is 0.

[000560] For example, y is 1.

[000561] For example, each R_{p2} is independently fluorine, chlorine, bromine or iodine.

[000562] For example, each R_{p2} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000563] For example, each R_{p2} is independently methyl, ethyl, propyl, i-propyl or t-butyl.

[000564] For example, each R_{p2} is independently C_1-C_6 alkyl substituted with amino.

[000565] For example, each R_{p2} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000566] For example, each R_{p2} is independently unsubstituted amino.

[000567] For example, each R_{p2} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000568] For example, each R_{p2} is independently unsubstituted or substituted phenyl or naphthyl.

[000569] For example, each R_{p2} is independently heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000570] For example, each R_{p2} is independently oxazolyl.

[000571] For example, each R_{p2} is independently unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000572] For example, each R_{p2} is independently heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000573] For example, R_{n5} and R_{n6} are each H.

[000574] For example, R_{n5} is H and R_{n6} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000575] For example, R_{n5} and R_{n6} are each unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000576] For example, at least one of R_{n5} and R_{n6} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000577] For example, at least one of R_{n5} and R_{n6} is unsubstituted amino.

[000578] For example, at least one of R_{n5} and R_{n6} is amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000579] For example, at least one of R_{n5} and R_{n6} is $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000580] For example, at least one of R_{n5} and R_{n6} is $S(O)_2R_8$.

[000581] For example, R_8 is H.

[000582] For example, R_8 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000583] For example, R_8 is methyl.

[000584] For example, R_8 is unsubstituted or substituted phenyl or naphthyl.

[000585] For example, R_8 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl,

isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000586] For example, R_8 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000587] For example, R_8 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000588] For example, R_N is NR_9R_{10}.

[000589] For example, R_9 and R_{10} are each H (*i.e.*, R_N is NH_2).

[000590] For example, R_9 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000591] For example, R_9 is unsubstituted or substituted phenyl or naphthyl.

[000592] For example, R_9 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000593] For example, R_9 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000594] For example, R_9 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000595] For example, R_9 is $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, or $S(O)_2R_{12}$.

[000596] For example, R_{12} is H.

[000597] For example, R_{12} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000598] For example, R_{12} is methyl, ethyl, or t-butyl.

[000599] For example, R_{12} is unsubstituted or substituted phenyl or naphthyl.

[000600] For example, R_{12} is unsubstituted phenyl.

[000601] For example, R_{12} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000602] For example, R_{12} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000603] For example, R_{12} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000604] For example, R_{13} is H.

[000605] For example, R_{13} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000606] For example, R_{13} is methyl, ethyl, or t-butyl.

[000607] For example, R_{13} is unsubstituted or substituted phenyl or naphthyl.

[000608] For example, R_{13} is unsubstituted phenyl.

[000609] For example, R_{13} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000610] For example, R_{13} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000611] For example, R_{13} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000612] For example, R_{10} is H.

[000613] For example, R_{10} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl,

i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000614] For example, R_{10} is unsubstituted or substituted phenyl or naphthyl.

[000615] For example, R_{10} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000616] For example, R_{10} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000617] For example, R_{10} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000618] For example, R_N is $C(O)R_{11}$.

[000619] For example, R_{11} is H.

[000620] For example, R_{11} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000621] For example, R_{11} is unsubstituted or substituted phenyl or naphthyl.

[000622] For example, R_{11} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000623] For example, R_{11} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000624] For example, R_{11} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000625] For example, R_{11} is OR_{14} or $NR_{14}R_{15}$.

[000626] For example, R_{14} is H.

[000627] For example, R_{14} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with hydroxyl or halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000628] For example, R_{14} methyl or ethyl.

[000629] For example, R_{14} is C_1-C_6 alkyl substituted with hydroxyl.

[000630] For example, R_{14} is unsubstituted or substituted phenyl or naphthyl.

[000631] For example, R_{14} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substitutcd.

[000632] For example, R_{14} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000633] For example, R_{14} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000634] For example, R_{15} is H.

[000635] For example, R_{15} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000636] For example, R_{15} is unsubstituted or substituted phenyl or naphthyl.

[000637] For example, R_{15} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000638] For example, R_{15} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

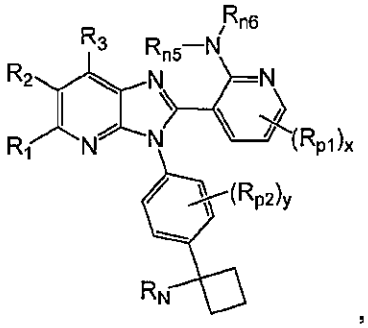
[000639] For example, R_{15} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000640] For example,  is a 3-, 4-, 5-, 6-, or 7-member carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cycloheptenyl.

[000641] For example,  is a 3-, 4-, 5-, 6-, or 7-member carbocycle and is optionally subsitued with one or more groups selected from hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), and unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000642] For example,  is cyclobutyl.

[000643] For example, the compounds of the present invention have the following formula:



wherein each of substituent groups is defined according to Formula II.

[000644] For example,  is a 3-, 4-, 5-, 6-, or 7-member heterocycle selected from aziridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, diazetidinyl, dioxetanyl, dithietanyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, tetrahyrofuranyl, tetrahyrothiophenyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, oxepanyl, thiepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

any two adjacent R_{p3}, together with the carbon atoms to which they attach, form a 4-, 5-, 6- or 7-member ring optionally comprising 1-4 heteroatoms selected from N, O and S;

R_{16} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S; and

R_{16}' is H or unsubstituted or substituted C_1-C_6 alkyl.

[000649] For example, z is 0.

[000650] For example, z is 1 or 2.

[000651] For example, each R_{p3} is independently fluorine, chlorine, bromine or iodine.

[000652] For example, each R_{p3} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl

[000653] For example, each R_{p3} is independently C_1-C_6 alkyl, which is optionally substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, t-butoxy, methylenedioxy, and ethylenedioxy), and

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)).

[000654] For example, each R_{p3} is independently methyl, which is optionally substituted.

[000655] For example, each R_{p3} is independently methyl, which is optionally substituted with hydroxyl, amino, or dimethylamino.

[000656] For example, each R_{p3} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, t-butoxy, methylenedioxy, and ethylenedioxy, each of which is optionally substituted with halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000657] For example, each R_{p3} is independently methoxy, trifluoromethoxy, ethoxy, propyloxy, or ethylenedioxy.

[000658] For example, each R_{p3} is independently unsubstituted amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), or unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino).

[000659] For example, each R_{p3} is independently unsubstituted amino, dimethylamino or diethylamino.

[000660] For example, each R_{p3} is independently unsubstituted or substituted phenyl or naphthyl.

[000661] For example, each R_{p3} is independently heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000662] For example, each R_{p3} is independently pyrazolyl.

[000663] For example, each R_{p3} is independently carbocycle selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl, and is optionally substituted.

[000664] For example, each R_{p3} is independently heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, morpholinyl, piperidinonyl, azetidinyl, azepanyl, oxazepanyl, and dioxoazaspirodecanyl, ~~and the like,~~ and is optionally substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl)

c) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

d) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)), and

e) $C(O)R_{18}$, $C(O)OR_{18}$, wherein:

R_{18} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000665] For example, each R_{p3} is independently heterocycle, which is optionally substituted with hydroxyl, halogen, methyl, dimethylamino, and $C(O)R_{18}$ wherein R_{18} is methyl.

[000666] For example, each R_{p3} is independently $C(O)R_{16}$, $C(O)OR_{16}$, $C(O)NR_{16}R_{16}$', NR_{16}'$C(O)R_{16}$, NR_{16}'$C(O)OR_{16}$, NR_{16}'$S(O)_2R_{16}$, $S(O)R_{16}$, or $S(O)_2R_{16}$.

[000667] For example, R_{16} is H.

[000668] For example, R_{16} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000669] For example, R_{16} is C_1-C_6 alkyl optionally substituted with one or more groups selected from hydroxyl and halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000670] For example, R_{16} is methyl, ethyl, propyl, i-propyl.

[000671] For example, R_{16} is unsubstituted amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), or unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino).

[000672] For example, R_{16} is dimethylamino.

[000673] For example, R_{16} is unsubstituted or substituted phenyl or naphthyl.

[000674] For example, R_{16} is phenyl substituted with one or more groups selected from hydroxyl, cyano, nitro, amino, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), and unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000675] For example, R_{16} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000676] For example, R_{16} is carbocycle selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl, and is optionally substituted.

[000677] For example, R_{16} is cyclopropyl.

[000678] For example, R_{16} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000679] For example, R_{16} is morpholinyl.

[000680] For example, R_{16}' is H.

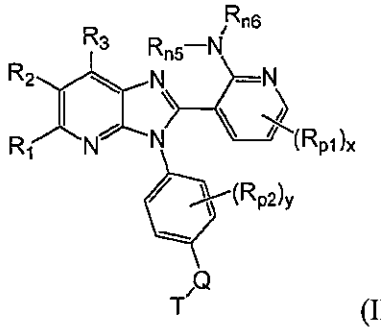
[000681] For example, R_{16}' is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000682] For example, R_{16}' is methyl or ethyl.

[000683] For example, any two adjacent R_{p3}, together with the carbon atoms to which they attach, form a carbocycle ring (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl) or a heterocycle ring (*e.g.*, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, morpholinyl, and morpholinonyl), each of which is optionally susbstituted.

[000684] For example, any two adjacent R_{p3}, together with the carbon atoms to which they attach, form a morpholinyl or morpholinonyl ring, each of which is optionally susbsituted with unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000685] The present invention also provides the compounds of Formula III:



(III),

wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

[000686] For example, Q is a bond.

[000687] For example, Q is an unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl linker, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl linker.

[000688] For example, Q is a methyl linker.

[000689] For example, T is $NR_{n1}R_{n2}$.

[000690] For example, R_{n1} and R_{n2} are each H.

[000691] For example, R_{n1} is H.

[000692] For example, R_{n1} is H and R_{n2} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$.

[000693] For example, R_{n1} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000694] For example, R_{n1} is C_1-C_6 alkyl substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl), and

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl).

[000695] For example, R_{n1} is C_1-C_6 alkyl substituted with phenyl.

[000696] For example, R_{n1} is methyl substituted with phenyl.

[000697] For example, R_{n1} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl and R_{n2} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$.

[000698] For example, R_{n1} is unsubstituted or substituted phenyl or naphthyl.

[000699] For example, R_{n1} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000700] For example, R_{n1} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000701] For example, R_{n1} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000702] For example, R_{n2} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000703] For example, R_{n2} is C_1-C_6 alkyl substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl), and

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl).

[000704] For example, R_{n2} is C_1-C_6 alkyl substituted with phenyl.

[000705] For example, R_{n2} is methyl substituted with phenyl.

[000706] For example, R_{n2} is unsubstituted or substituted phenyl or naphthyl.

[000707] For example, R_{n2} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000708] For example, R_{n2} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000709] For example, R_{n2} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000710] For example, R_{n2} is $C(O)R_4$, $C(O)OR_4$, or $C(O)NR_4'R_4$.

[000711] For example, R_4' is H.

[000712] For example, R_4' is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000713] For example, R_4' is unsubstituted or substituted phenyl or naphthyl.

[000714] For example, R_4' is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000715] For example, R_4' is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000716] For example, R_4' is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000717] For example, R_4 is H.

[000718] For example, R_4 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, n-hexyl and 2-methylpropyl.

[000719] For example, R_4 is C_1-C_6 alkyl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

[000728] For example, R_4 is phenyl substituted with one, two or more C_1-C_6 alkoxy, which is optionally substituted with one or more halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000729] For example, R_4 is phenyl substituted with one, two or more groups independently selected from methoxy, ethoxy, i-propyloxy, and trifluoromethoxy.

[000730] For example, R_4 is phenyl substituted with one, two or more groups independently selected from amino and dimethylamino.

[000731] For example, R_4 is phenyl substituted with phenyl.

[000732] For example, R_4 is phenyl substituted with heteroaryl, which is optionally substituted with unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000733] For example, R_4 is phenyl substituted with pyrazolyl or pyrazolonyl, each of which is optionally substituted with methyl.

[000734] For example, R_4 is phenyl substituted with $C(O)R_{19}$, $C(O)OR_{19}$, $NR_{19}'C(O)R_{19}$, and $NR_{19}'C(O)OR_{19}$.

[000735] For example, R_{19}' is H.

[000736] For example, R_{19} is H.

[000737] For example, R_{19} is methyl.

[000738] For example, R_{19} is phenyl and is optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000739] For example, R_{19} is phenyl substituted with halogen.

[000740] For example, R_4 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, indazolyl, and dihydrobenzofuranyl, ~~and the like,~~ and is optionally substituted.

[000741] For example, R_4 is heteroaryl optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl,

n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000742] For example, R_4 is heteroaryl substituted with one or more groups selected from methyl and halogen.

[000743] For example, R_4 is pyridinyl, isoquinolinyl, isoxazolyl, thiophenyl, furanyl, indolyl, dihydrobenzofuranyl, pyrrolyl, benzothiophenyl, quinolinyl, pyrimidinyl, thiazolyl, or pyrazinyl, each of which is optionally substituted.

[000744] For example, R_4 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000745] For example, R_4 is cyclopentyl or cyclohexyl, each of which is optionally substituted.

[000746] For example, R_4 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000747] For example, R_{n2} is $S(O)R_5$ or $S(O)_2R_5$.

[000748] For example, R_5 is H.

[000749] For example, R_5 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, n-hexyl and 2-methylpropyl.

[000750] For example, R_5 is unsubstituted or substituted phenyl or naphthyl.

[000751] For example, R_5 is phenyl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

d) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

e) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

f) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, pyrazolonyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

g) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

h) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

i) $C(O)R_{19}$, $C(O)OR_{19}$, $NR_{19}'C(O)R_{19}$, and $NR_{19}'C(O)OR_{19}$,

wherein:

R_{19} and R_{19}' are each independently H, unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), or unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl).

[000752] For example, R_5 is phenyl substituted with one, two or more groups, each of which is independently selected from methyl, methoxy, fluorine and chlorine.

[000753] For example, R_5 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, indazolyl, and dihydrobenzofuranyl, ~~and the like,~~ and is optionally substituted.

[000754] For example, R_5 is heteroaryl optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000755] For example, R_5 is heteroaryl substituted with one or more groups selected from methyl and halogen.

[000756] For example, R_5 is pyridinyl, isoxazolyl, thiophenyl, imidazolyl, pyrazolyl, dihydrobenzofuranyl, or quinolinyl, each of which is optionally substituted.

[000757] For example, R_5 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000758] For example, R_5 is cyclopropyl or cyclohexyl, each of which is optionally substituted.

[000759] For example, R_5 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000760] For example, R_5' is H.

[000761] For example, R_5' is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000762] For example, R_5' is unsubstituted or substituted phenyl or naphthyl.

[000763] For example, R_5' is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000764] For example, R_5' is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000765] For example, R_5' is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000766] For example, R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring selected from azetidinyl, diazetidinyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

[000767] For example, R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring, which is optionally substituted with hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), or unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000768] For example, R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a morpholinyl or piperazinyl ring and is optionally substituted with methyl.

[000769] For example, T is $C(O)R_o$.

[000770] For example, R_o is H.

[000771] For example, R_o is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000772] For example, R_o is unsubstituted or substituted phenyl or naphthyl.

[000773] For example, R_o is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000774] For example, R_o is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000775] For example, R_o is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000776] For example, R_o is $NR_{o1}R_{o2}$.

[000777] For example, R_{o1} and R_{o2} are each H.

[000778] For example, at least one of R_{o1} and R_{o2} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000779] For example, at least one of R_{o1} and R_{o2} is C_1-C_6 alkyl substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

[000785] For example, at least one of R_{o1} and R_{o2} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, indazolyl and oxodihydrobenzofuranyl, ~~and the like,~~ and is optionally substituted.

[000786] For example, at least one of R_{o1} and R_{o2} is heteroaryl and is optionally substituted with one or more groups, each of which is independently selected from hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000787] For example, at least one of R_{o1} and R_{o2} is heteroaryl substituted with one or more groups selected from methyl and halogen.

[000788] For example, at least one of R_{o1} and R_{o2} is pyridinyl, benzothiazolyl, benzoimidazolyl, quinolinyl, or oxodihydrobenzofuranyl, each of which is optionally substituted.

[000789] For example, at least one of R_{o1} and R_{o2} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000790] For example, at least one of R_{o1} and R_{o2} is cyclopentyl.

[000791] For example, at least one of R_{o1} and R_{o2} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000792] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring selected from azetidinyl, diazetidinyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

[000793] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring, which is optionally substituted with one or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, pyrazolonyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzoimidazolonyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl), and

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl).

[000794] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a piperidinyl ring and is optionally substituted with benzoimidazolonyl.

[000795] For example, R_o is OR_{o3}.

[000796] For example, R_{o3} is H.

[000797] For example, R_{o3} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, n-hexyl and 2-methylpropyl.

[000798] For example, R_{o3} is unsubstituted or substituted phenyl or naphthyl.

[000799] For example, R_{o3} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl,

isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000800] For example, R_{o3} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000801] For example, R_{o3} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000802] For example, T is $S(O)R_s$ or $S(O)_2R_s$.

[000803] For example, R_s is H.

[000804] For example, R_s is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000805] For example, R_s is unsubstituted or substituted phenyl or naphthyl.

[000806] For example, R_s is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000807] For example, R_s is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000808]

[000809] For example, R_s is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000810] For example, R_s is $NR_{s1}R_{s2}$.

[000811] For example, R_{s1} and R_{s2} are each H.

[000812] For example, at least one of R_{s1} and R_{s2} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000813] For example, at least one of R_{s1} and R_{s2} is methyl

[000814] For example, at least one of R_{s1} and R_{s2} is unsubstituted or substituted phenyl or naphthyl.

[000815] For example, at least one of R_{o1} and R_{o2} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, and indazolyl, ~~and the like,~~ and is optionally substituted.

[000816] For example, at least one of R_{o1} and R_{o2} is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000817] For example, at least one of R_{o1} and R_{o2} is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substitutcd.

[000818] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring selected from azetidinyl, diazetidinyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, diazepanyl, oxazepanyl, and thiazepanyl, ~~and the like,~~ and is optionally substituted.

[000819] For example, R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a piperidinyl ring and is optionally substituted.

[000820] For example, R_1, R_2 and R_3 are each H.

[000821] For example, R_1 and R_2 are each H.

[000822] For example, R_2 and R_3 are each H.

[000823] For example, R_1 and R_3 are each H.

[000824] For example, only R_1 is H, and R_2 and R_3 are each independently H, halogen, hydroxyl, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000825] For example, only R_2 is H, and R_1 and R_3 are each independently H, halogen, hydroxyl, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted

C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000826] For example, only R_3 is H, and R_1 and R_2 are each independently H, halogen, hydroxyl, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000827] For example, R_1 is fluorine, chlorine, bromine or iodine.

[000828] For example, R_1 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000829] For example, R_1 is unsubstituted methyl.

[000830] For example, R_1 is trifluoromethyl (*i.e.*, CF_3) or methyl substituted with dimethylamino.

[000831] For example, R_1 is unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, morpholinyl, and morpholinonyl), each of which is optionally susbstituted.

[000860] For example, R_1 is phenyl substituted with two or more groups and any two adjacent substituent groups, together with the carbon atoms to which they attach, form a morpholinyl or morpholinonyl ring, each of which is optionally susbsituted with unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000861] For example, R_1 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000862] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000863] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, morpholinyl, $C(O)OR_{17}$, and $C(O)R_{17}$, wherein R_{17} is H, methyl or trifluoromethyl.

[000864] For example, R_1 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000865] For example, R_1 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000866] For example, R_1 is piperidinyl.

[000867] For example, R_2 is fluorine, chlorine, bromine or iodine.

[000868] For example, R_2 is bromine.

[000869] For example, R_2 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10}

[000885] For example, R_{16} is C_1-C_6 alkyl optionally substituted with one or more groups selected from hydroxyl and halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[000886] For example, R_{16} is methyl, ethyl, propyl, i-propyl.

[000887] For example, R_2 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000888] For example, R_2 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000889] For example, R_2 is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, $C(O)OR_{17}$ wherein R_{17} is H or methyl.

[000890] For example, R_2 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000891] For example, R_2 is unsubstituted or substituted cyclopentyl.

[000892] For example, R_2 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000893] For example, R_3 is fluorine, chlorine, bromine or iodine.

[000894] For example, R_3 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000895] For example, R_3 is unsubstituted methyl.

[000896] For example, R_3 is unsubstituted amino.

[000897] For example, R_3 is amino substituted with one or two groups, each of which is independently selected from:

H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000900] For example, R_3 is phenyl substituted with two or more groups, and any two adjacent substituent groups, together with the carbon atoms to which they attach, form a 4-, 5-, 6- or 7-member ring optionally comprising 1-4 heteroatoms selected from N, O and S.

[000901] For example, R_3 is phenyl substituted with C_1-C_6 alkyl, which is optionally substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy), and

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)).

[000902] For example, R_3 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[000903] For example, R_3 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl,

thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000904] For example, R_3 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000905] For example, R_3 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000906] For example, x is 0.

[000907] For example, x is 1.

[000908] For example, each R_{p1} is independently fluorine, chlorine, bromine or iodine.

[000909] For example, each R_{p1} is independently chlorine.

[000910] For example, each R_{p1} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000911] For example, each R_{p1} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000912] For example, each R_{p1} is independently unsubstituted amino.

[000913] For example, each R_{p1} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl

(*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000914] For example, y is 0.

[000915] For example, y is 1.

[000916] For example, each R_{p2} is independently fluorine, chlorine, bromine or iodine.

[000917] For example, each R_{p2} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000918] For example, each R_{p2} is independently methyl, ethyl, propyl, i-propyl or t-butyl.

[000919] For example, each R_{p2} is independently C_1-C_6 alkyl substituted with amino.

[000920] For example, each R_{p2} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000921] For example, each R_{p2} is independently unsubstituted amino.

[000922] For example, each R_{p2} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000923] For example, each R_{p2} is independently unsubstituted or substituted phenyl or naphthyl.

[000924] For example, each R_{p2} is independently heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000925] For example, each R_{p2} is independently oxazolyl.

[000926] For example, each R_{p2} is independently unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000927] For example, each R_{p2} is independently heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000928] For example, R_{n5} and R_{n6} are each H.

[000929] For example, R_{n5} is H and R_{n6} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000930] For example, R_{n5} and R_{n6} are each unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000931] For example, at least one of R_{n5} and R_{n6} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000932] For example, at least one of R_{n5} and R_{n6} is unsubstituted amino.

[000933] For example, at least one of R_{n5} and R_{n6} is amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000934] For example, at least one of R_{n5} and R_{n6} is $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[000935] For example, at least one of R_{n5} and R_{n6} is $S(O)_2R_8$.

[000936] For example, R_8 is H.

[000937] For example, R_8 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl,

i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[000938] For example, R_8 is methyl.

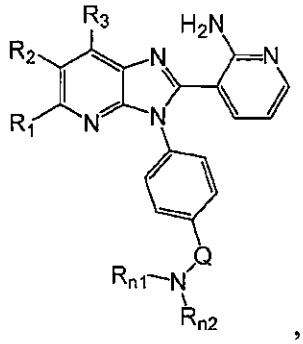
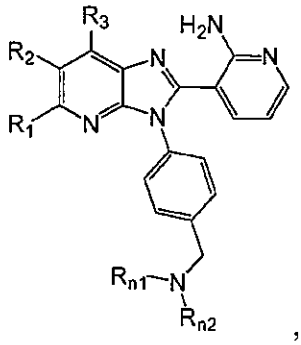
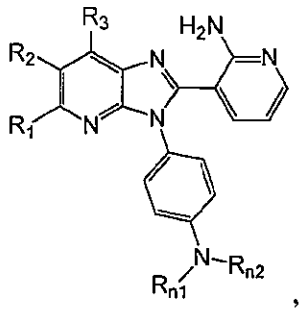
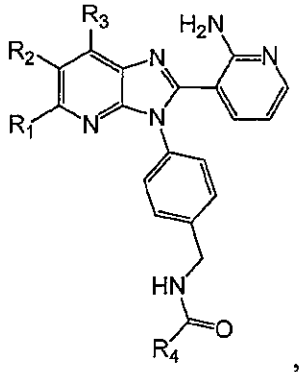
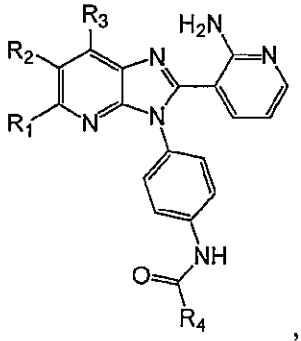
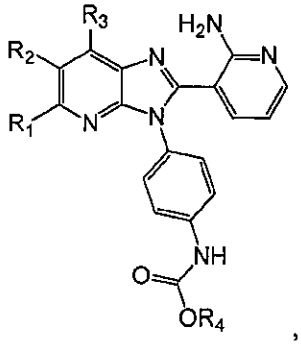
[000939] For example, R_8 is unsubstituted or substituted phenyl or naphthyl.

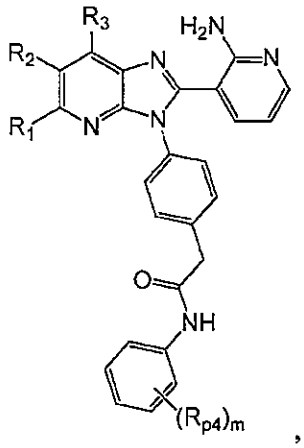
[000940] For example, R_8 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000941] For example, R_8 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

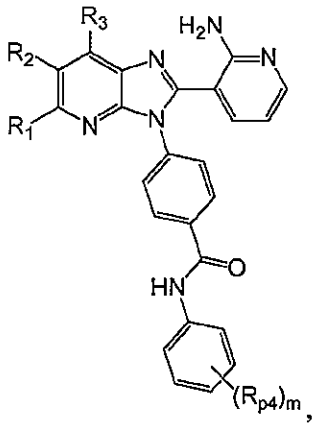
[000942] For example, R_8 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000943] The present invention also provides the compounds of the following formula:


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, or



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wherein:

R_1, R_2, R_3, R_4, R_5, R_{n1}, R_{n2}, R_o, R_{o1}, R_{o2}, R_{o3}, R_{s1} and R_{s2} are defined according to Formula III;

m is 0, 1, 2, 3, 4 or 5;

each R_{p4} is independently hydroxyl, cyano, nitro, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_{22}$, $C(O)OR_{22}$, $NR_{22}'C(O)R_{22}$, and $NR_{22}'C(O)OR_{22}$; and

R_{22} and R_{22}' are each independently H, unsubstituted or substituted C_1-C_6 alkyl or unsubstituted or substituted C_6-C_{10} aryl.

[000944] For example, m is 0.

[000945] For example, m is 1, 2 or 3.

[000946] For example, each R_{p4} is independently fluorine, chlorine, bromine or iodine.

[000947] For example, each R_{p4} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000948] For example, each R_{p4} is independently C_1-C_6 alkyl, which is optionally substituted with one or more groups selected from:

a) hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)), and

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl).

[000949] For example, each R_{p4} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy

[000950] For example, each R_{p4} is independently unsubstituted amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), or unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino).

[000951] For example, each R_{p4} is independently unsubstituted or substituted phenyl and naphthyl.

[000952] For example, each R_{p4} is independently heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000953] For example, each R_{p4} is independently heteroaryl substituted with unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[000954] For example, each R_{p4} is independently unsubstituted or substituted carbocycle selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[000955] For example, each R_{p4} is independently heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[000956] For example, each R_{p4} is independently $C(O)R_{22}$, $C(O)OR_{22}$, $NR_{22}'C(O)R_{22}$, and $NR_{22}'C(O)OR_{22}$.

[000957] For example, R_{22} is H.

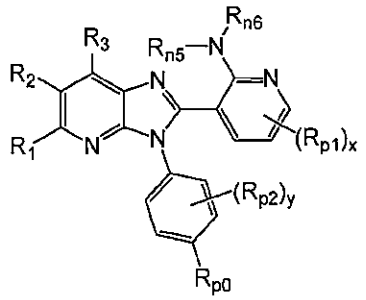
[000958] For example, R_{22} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000959] For example, R_{22} is phenyl and is optionally substituted with hydroxyl, cyano, nitro, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), and unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, n-propyloxy, i-propyloxy, n-butoxy, and t-butoxy).

[000960] For example, R_{22}' is H.

[000961] For example, R_{22}' is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000962] The present invention also provides the compounds of Formula IV:



(IV),

wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

R_{p0} is H, hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$; and

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000963] For example, R_{p0} is H.

[000964] For example, R_{p0} is fluorine, chlorine, bromine or iodine.

[000965] For example, R_{p0} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl.

[000966] For example, R_{p0} is C_1-C_6 alkyl and is optionally substituted with

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted amino,

c) unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), or unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)), which is optionally substituted with one or two groups selected from:

(1) unsubstituted or substituted C_6-C_{10} aryl,

(2) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S,

(3) unsubstituted or substituted C_3-C_{10} carbocycle, and

(4) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000967] For example, R_{p0} is C_1-C_6 alkyl substituted with C_1-C_6 alkylamino or di-C_1-C_6 alkylamino, which is optionally substituted with phenyl.

[000968] For example, R_{p0} is methyl, ethyl, n-propyl, i-propyl, n-butyl, or t-butyl.

[000969] For example, R_{p0} is unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000970] For example, R_{p0} is unsubstituted or substituted methoxy.

[000971] For example, R_{p0} is unsubstituted amino.

[000972] For example, R_{p0} is amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl)

[000973] For example, R_{p0} is unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), or unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino).

[000974] For example, R_{p0} is dimethylamino or diethylamino.

[000975] For example, R_{p0} is unsubstituted or substituted phenyl or naphthyl.

[000976] For example, R_{p0} is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[000977] For example, R_{p0} is pyrazolyl or triazolyl, and is optionally substituted.

[000978] For example, R_{p0} is carbocycle selected from cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cycloheptenyl, and is optionally substituted.

[000979] For example, R_{p0} is cyclobutyl or cyclohexyl, and is optionally substituted.

[000980] For example, R_{p0} is heterocycle selected from ziridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, diazetidinyl, dioxetanyl, dithietanyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, tetrahyrofuranyl, tetrahyrothiophenyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, oxepanyl, thiepanyl, diazepanyl, oxazepanyl, thiazepanyl, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl,

triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, morpholinyl, piperidinonyl, azetidinyl, azepanyl, oxazepanyl, and dioxoazaspirodecanyl, ~~and the like,~~ and is optionally substituted.

[000981] For example, R_{p0} is oxetanyl, and is optionally substituted.

[000982] For example, R_1, R_2 and R_3 are each H.

[000983] For example, R_1 and R_2 are each H.

[000984] For example, R_2 and R_3 are each H.

[000985] For example, R_1 and R_3 are each H.

[000986] For example, only R_1 is H, and R_2 and R_3 are each independently H, halogen, hydroxyl, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000987] For example, only R_2 is H, and R_1 and R_3 are each independently H, halogen, hydroxyl, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000988] For example, only R_3 is H, and R_1 and R_2 are each independently H, halogen, hydroxyl, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000989] For example, R_1 is fluorine, chlorine, bromine or iodine.

[000990] For example, R_1 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[000991] For example, R_1 is unsubstituted methyl.

[000992] For example, R_1 is trifluoromethyl (*i.e.*, CF_3) or methyl substituted with dimethylamino.

[000993] For example, R_1 is unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[000994] For example, R_1 is unsubstituted or substituted methoxy.

[000995] For example, R_1 is unsubstituted amino.

[000996] For example, R_1 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

b) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

c) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl, each of which is optionally substituted with hydroxyl, nitro, amino, cyano, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), or unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy)), and

[0001011] For example, R_1 is phenyl substituted with $C(O)R_{16}$, $C(O)OR_{16}$, $C(O)NR_{16}R_{16}'$, $NR_{16}'C(O)R_{16}$, $NR_{16}'C(O)OR_{16}$, $NR_{16}'S(O)_2R_{16}$, $S(O)R_{16}$, or $S(O)_2R_{16}$.

[0001012] For example, R_{16} is H.

[0001013] For example, R_{16} is C_1-C_6 alkyl optionally substituted with one or more groups selected from hydroxyl and halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[0001014] For example, R_{16} is methyl, ethyl, propyl, i-propyl.

[0001015] For example, R_{16} is dimethylamino.

[0001016] For example, R_{16} is phenyl and is optionally substituted with one or more groups selected from hydroxyl, cyano, nitro, amino, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), and unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001017] For example, R_{16} is cyclopropyl.

[0001018] For cxamplc, R_{16} is morpholinyl.

[0001019] For example, R_{16}' is H.

[0001020] For example, R_{16}' is methyl or ethyl.

[0001021] For example, R_1 is phenyl substituted with two or more groups and any two adjacent substituent groups, together with the carbon atoms to which they attach, form a carbocycle ring (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl) or a heterocycle ring (*e.g.*, pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, morpholinyl, and morpholinonyl), each of which is optionally susbstituted.

[0001022] For example, R_1 is phenyl substituted with two or more groups and any two adjacent substituent groups, together with the carbon atoms to which they attach, form a morpholinyl or morpholinonyl ring, each of which is optionally susbsituted with unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001023] For example, R_1 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[0001024] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001025] For example, R_1 is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, morpholinyl, $C(O)OR_{17}$, and $C(O)R_{17}$, wherein R_{17} is H, methyl or trifluoromethyl.

[0001026] For example, R_1 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0001027] For example, R_1 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[0001028] For example, R_1 is piperidinyl.

[0001029] For example, R_2 is fluorine, chlorine, bromine or iodine.

[0001030] For example, R_2 is bromine.

[0001031] For example, R_2 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[0001032] For example, R_2 is unsubstituted methyl.

[0001033] For example, R_2 is trifluoromethyl (*i.e.*, CF_3).

[0001034] For example, R_2 is unsubstituted amino.

[0001035] For example, R_2 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

b) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

[0001039] For example, R_2 is phenyl substituted with C_1-C_6 alkyl, which is optionally substituted with one or more groups selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy), and

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)).

[0001040] For example, R_2 is phenyl substituted with methyl, which is optionally substituted.

[0001041] For example, R_2 is phenyl substituted with methyl, which is optionally substituted with hydroxyl.

[0001042] For example, R_2 is phenyl substituted with C_1-C_6 alkoxy, which is optionally substituted with halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[0001043] For example, R_2 is phenyl substituted with methoxy or ethoxy.

[0001044] For example, R_2 is phenyl substituted with unsubstituted amino.

[0001045] For example, R_2 is phenyl substituted with $C(O)R_{16}$, $C(O)OR_{16}$, $C(O)NR_{16}R_{16}'$, $NR_{16}'C(O)R_{16}$, $NR_{16}'C(O)OR_{16}$, $NR_{16}'S(O)_2R_{16}$, $S(O)R_{16}$, or $S(O)_2R_{16}$.

[0001046] For example, R_{16} is H.

[0001047] For example, R_{16} is C_1-C_6 alkyl optionally substituted with one or more groups selected from hydroxyl and halogen (*e.g.*, fluorine, chlorine, bromine and iodine).

[0001048] For example, R_{16} is methyl, ethyl, propyl, i-propyl.

[0001049] For example, R_2 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[0001050] For example, R_2 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001051] For example, R_2 is heteroaryl substituted with one, two or more groups, each of which is independently selected from methyl, hydroxyl, halogen, unsubstituted amino, $C(O)OR_{17}$ wherein R_{17} is H or methyl.

[0001052] For example, R_2 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0001053] For example, R_2 is unsubstituted or substituted cyclopentyl.

[0001054] For example, R_2 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[0001055] For example, R_3 is fluorine, chlorine, bromine or iodine.

[0001056] For example, R_3 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[0001057] For example, R_3 is unsubstituted methyl.

[0001058] For example, R_3 is unsubstituted amino.

[0001059] For example, R_3 is amino substituted with one or two groups, each of which is independently selected from:

a) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

b) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

c) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl, each of which is optionally substituted with hydroxyl, nitro, amino, cyano, halogen (*e.g.*, fluorine, chlorine, bromine and iodine), unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl), or unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy)), and

d) unsubstituted or substituted C_6-C_{10} aryl-C_1-C_6 alkyl (*e.g.*, benzyl, phenylethyl, and naphthylmethyl).

[0001064] For example, R_3 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, quinoxalinyl, dioxotetrahydropyrimidinyl, indazolyl, and pyrrolopyridinyl, ~~and the like,~~ and is optionally substituted.

[0001065] For example, R_3 is heteroaryl substituted with one, two or more groups, each of which is independently selected from:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino), and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl),

e) unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (*e.g.*, pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl),

f) unsubstituted or substituted C_3-C_{10} carbocycle (*e.g.*, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl),

g) unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S (pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl),

h) $C(O)R_{17}$, and $C(O)OR_{17}$, wherein:

R_{17} is H or unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001066] For example, R_3 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0001067] For example, R_3 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[0001068] For example, x is 0.

[0001069] For example, x is 1.

[0001070] For example, each R_{p1} is independently fluorine, chlorine, bromine or iodine.

[0001071] For example, each R_{p1} is independently chlorine.

[0001072] For example, each R_{p1} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[0001073] For example, each R_{p1} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[0001074] For example, each R_{p1} is independently unsubstituted amino.

[0001075] For example, each R_{p1} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001076] For example, y is 0.

[0001077] For example, y is 1.

[0001078] For example, each R_{p2} is independently fluorine, chlorine, bromine or iodine.

[0001079] For example, each R_{p2} is independently unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted with:

a) hydroxyl, halogen (*e.g.*, fluorine, chlorine, bromine and iodine),

b) unsubstituted or substituted C_1-C_6 alkoxy (*e.g.*, methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy),

c) unsubstituted or substituted amino (*e.g.*, amino, unsubstituted or substituted C_1-C_6 alkylamino (*e.g.*, methylamino, ethylamino, propylamino, and i-propylamino),

and unsubstituted or substituted di-C_1-C_6 alkylamino (*e.g.*, dimethylamino, diethylamino, dipropylamino, and di-i-propylamino)),

d) unsubstituted or substituted C_6-C_{10} aryl (*e.g.*, phenyl and naphthyl), unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

[0001080] For example, each R_{p2} is independently methyl, ethyl, propyl, i-propyl or t-butyl.

[0001081] For example, each R_{p2} is independently C_1-C_6 alkyl substituted with amino.

[0001082] For example, each R_{p2} is independently unsubstituted or substituted C_1-C_6 alkoxy, including ~~but not limited to,~~ methoxy, ethoxy, propyloxy, i-propyloxy, butoxy, and t-butoxy.

[0001083] For example, each R_{p2} is independently unsubstituted amino.

[0001084] For example, each R_{p2} is independently amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001085] For example, each R_{p2} is independently unsubstituted or substituted phenyl or naphthyl.

[0001086] For example, each R_{p2} is independently heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[0001087] For example, each R_{p2} is independently oxazolyl.

[0001088] For example, each R_{p2} is independently unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0001089] For example, each R_{p2} is independently heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[0001090] For example, R_{n5} and R_{n6} are each H.

[0001091] For example, R_{n5} is H and R_{n6} is unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[0001092] For example, R_{n5} and R_{n6} are each unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[0001093] For example, at least one of R_{n5} and R_{n6} is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[0001094] For example, at least one of R_{n5} and R_{n6} is unsubstituted amino.

[0001095] For example, at least one of R_{n5} and R_{n6} is amino substituted with one or two groups, each of which is independently selected from unsubstituted or substituted C_1-C_6 alkyl (*e.g.*, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl).

[0001096] For example, at least one of R_{n5} and R_{n6} is $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$.

[0001097] For example, at least one of R_{n5} and R_{n6} is $S(O)_2R_8$.

[0001098] For example, R_8 is H.

[0001099] For example, R_8 is unsubstituted or substituted, straight chain C_1-C_6 alkyl or branched C_3-C_6 alkyl, including ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl, and n-hexyl, each of which is optionally substituted.

[0001100] For example, R_8 is methyl.

[0001101] For example, R_8 is unsubstituted or substituted phenyl or naphthyl.

[0001102] For example, R_8 is heteroaryl selected from pyrrolyl, furanyl, thiophenyl, thiazolyl, isothiazolyl, imidazolyl, triazolyl, tetrazolyl, pyrazolyl, oxazolyl, isoxazolyl, pyridinyl, pyrazinyl, pyridazinyl, pyrimidinyl, benzoxazolyl, benzodioxazolyl, benzothiazolyl, benzoimidazolyl, benzothiophenyl, methylenedioxyphenyl, quinolinyl, isoquinolinyl, naphthrydinyl, indolyl, indolonyl, benzofuranyl, purinyl, indolizinyl, and quinoxalinyl, ~~and the like,~~ and is optionally substituted.

[0001103] For example, R_8 is unsubstituted or substituted C_3-C_{10} carbocycle, including ~~but not limited to,~~ cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0001104] For example, R_8 is heterocycle selected from pyrrolidinyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, triazolidinyl, tetrahyrofuranyl, piperidinyl, piperazinyl, and morpholinyl, ~~and the like,~~ and is optionally substituted.

[0001106] As used herein, "alkyl", "C_1, C_2, C_3, C_4, C_5 or C_6 alkyl" or "C_1-C_6 alkyl" is intended to include C_1, C_2, C_3, C_4, C_5 or C_6 straight chain (linear) saturated aliphatic hydrocarbon groups and C_3, C_4, C_5 or C_6 branched saturated aliphatic hydrocarbon groups. For example, C_1-C_6 alkyl is intended to include C_1, C_2, C_3, C_4, C_5 and C_6 alkyl groups. Examples of alkyl include, moieties having from one to six carbon atoms, such as, ~~but not limited to,~~ methyl, ethyl, n-propyl, i-propyl, n-butyl, s-butyl, t-butyl, n-pentyl, s-pentyl or n-hexyl.

[0001107] In certain embodiments, a straight chain or branched alkyl has six or fewer carbon atoms (*e.g.*, C_1-C_6 for straight chain, C_3-C_6 for branched chain), and in another embodiment, a straight chain or branched alkyl has four or fewer carbon atoms.

[0001108] "Heteroalkyl" groups are alkyl groups, as defined above, that have an oxygen, nitrogen, sulfur or phosphorous atom replacing one or more hydrocarbon backbone carbon atoms.

[0001109] As used herein, the term "cycloalkyl", "C_3, C_4, C_5, C_6, C_7 or C_8 cycloalkyl" or "C_3-C_8 cycloalkyl" is intended to include hydrocarbon rings having from three to eight carbon atoms in their ring structure. In one embodiment, a cycloalkyl group has five or six carbons in the ring structure.

[0001110] The term "substituted alkyl" refers to alkyl moieties having substituents replacing one or more hydrogen atoms on one or more carbons of the hydrocarbon backbone. Such substituents can include, for example, alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety. Cycloalkyls can be further substituted, *e.g.*, with the substituents described above. An "alkylaryl" or an "aralkyl" moiety is an alkyl substituted with an aryl (*e.g.*, phenylmethyl (benzyl)).

[0001111] Unless the number of carbons is otherwise specified, "lower alkyl" includes an alkyl group, as defined above, having from one to six, or in another embodiment from one to four, carbon atoms in its backbone structure. "Lower alkenyl" and "lower alkynyl" have chain lengths of, for example, two to six or of two to four carbon atoms.

[0001112] As used herein, "alkyl linker" is intended to include C_1, C_2, C_3, C_4, C_5 or C_6 straight chain (linear) saturated aliphatic hydrocarbon groups and C_3, C_4, C_5 or C_6 branched saturated aliphatic hydrocarbon groups. For example, C_1-C_6 alkyl linker is intended to include C_1, C_2, C_3, C_4, C_5 and C_6 alkyl linker groups. Examples of alkyl linker include, moieties having from one to six carbon atoms, such as, ~~but not limited to,~~ methyl (-CH_2-), ethyl (-CH_2CH_2-), n-propyl (-$CH_2CH_2CH_2$-), i-propyl (-$CHCH_3CH_2$-), n-butyl (-$CH_2CH_2CH_2CH_2$-), s-butyl (-$CHCH_3CH_2CH_2$-), i-butyl (-$C(CH_3)_2CH_2$-), n-pentyl (-$CH_2CH_2CH_2CH_2CH_2$-), s-pentyl (-$CHCH_3CH_2CH_2CH_2$-) or n-hexyl (-$CH_2CH_2CH_2CH_2CH_2CH_2$-).

[0001113] "Alkenyl" includes unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but that contain at least one double bond. For example, the term "alkenyl" includes straight chain alkenyl groups (*e.g.*, ethenyl, propenyl, butenyl, pentenyl, hexenyl, heptenyl, octenyl, nonenyl, decenyl), branched alkenyl groups, cycloalkenyl (*e.g.*, alicyclic) groups (*e.g.*, cyclopropenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl), alkyl or alkenyl substituted cycloalkenyl groups, and cycloalkyl or cycloalkenyl substituted alkenyl groups. In certain embodiments, a straight chain or branched alkenyl group has six or fewer carbon atoms in its backbone (*e.g.*, C_2-C_6 for straight chain, C_3-C_6 for branched chain). Likewise, cycloalkenyl groups may have from five to eight carbon atoms in their ring structure, and in one embodiment, cycloalkenyl groups have five or six carbons in the ring structure. The term "C_2-C_6" includes alkenyl groups containing two to six carbon atoms. The term "C_3-C_6" includes alkenyl groups containing three to six carbon atoms.

[0001114] "Heteroalkenyl" includes alkenyl groups, as defined herein, having an oxygen, nitrogen, sulfur or phosphorous atom replacing one or more hydrocarbon backbone carbons.

[0001115] The term "substituted alkenyl" refers to alkenyl moieties having substituents replacing one or more hydrogen atoms on one or more hydrocarbon backbone carbon atoms. Such substituents can include, for example, alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl,

sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

[0001116] "Alkynyl" includes unsaturated aliphatic groups analogous in length and possible substitution to the alkyls described above, but which contain at least one triple bond. For example, "alkynyl" includes straight chain alkynyl groups (*e.g.*, ethynyl, propynyl, butynyl, pentynyl, hexynyl, heptynyl, octynyl, nonynyl, decynyl), branched alkynyl groups, and cycloalkyl or cycloalkenyl substituted alkynyl groups. In certain embodiments, a straight chain or branched alkynyl group has six or fewer carbon atoms in its backbone (*e.g.*, C_2-C_6 for straight chain, C_3-C_6 for branched chain). The term "C_2-C_6" includes alkynyl groups containing two to six carbon atoms. The term "C_3-C_6" includes alkynyl groups containing three to six carbon atoms.

[0001117] "Heteroalkynyl" includes alkynyl groups, as defined herein, having an oxygen, nitrogen, sulfur or phosphorous atom replacing one or more hydrocarbon backbone carbons.

[0001118] The term "substituted alkynyl" refers to alkynyl moieties having substituents replacing one or more hydrogen atoms on one or more hydrocarbon backbone carbon atoms. Such substituents can include, for example, alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

[0001119] "Aryl" includes groups with aromaticity, including "conjugated", or multicyclic, systems with at least one aromatic ring. Examples include phenyl, benzyl, ~~etc.~~

[0001120] "Heteroaryl" groups are aryl groups, as defined above, having from one to four heteroatoms in the ring structure, and may also be referred to as "aryl heterocycles" or "heteroaromatics". As used herein, the term "heteroaryl" is intended to include a stable 5-, 6-, or 7-membered monocyclic or 7-, 8-, 9-, 10-, 11- or 12-membered bicyclic aromatic heterocyclic ring which consists of carbon atoms and one or more heteroatoms, *e.g.*, 1 or 1-2 or 1-3 or 1-4 or 1-5 or 1-6 heteroatoms, independently selected from the group consisting of nitrogen, oxygen and sulfur. The nitrogen atom may be substituted or unsubstituted (*i.e.*, N

or NR wherein R is H or other substituents, as defined). The nitrogen and sulfur heteroatoms may optionally be oxidized (*i.e.*, N→O and $S(O)_p$, where p = 1 or 2). It is to be noted that total number of S and O atoms in the aromatic heterocycle is not more than 1.

[0001121] Examples of heteroaryl groups include pyrrole, furan, thiophene, thiazole, isothiazole, imidazole, triazole, tetrazole, pyrazole, oxazole, isoxazole, pyridine, pyrazine, pyridazine, pyrimidine, ~~and the like~~.

[0001122] Furthermore, the terms "aryl" and "heteroaryl" include multicyclic aryl and heteroaryl groups, *e.g.*, tricyclic, bicyclic, *e.g.*, naphthalene, benzoxazole, benzodioxazole, benzothiazole, benzoimidazole, benzothiophene, methylenedioxyphenyl, quinoline, isoquinoline, naphthridine, indole, benzofuran, purine, benzofuran, deazapurine, indolizine.

[0001123] In the case of multicyclic aromatic rings, only one of the rings needs to be aromatic (*e.g.*, 2,3-dihydroindole), although all of the rings may be aromatic (*e.g.*, quinoline). The second ring can also be fused or bridged.

[0001124] The aryl or heteroaryl aromatic ring can be substituted at one or more ring positions with such substituents as described above, for example, alkyl, alkenyl, akynyl, halogen, hydroxyl, alkoxy, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, alkylaminocarbonyl, aralkylaminocarbonyl, alkenylaminocarbonyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, alkenylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety. Aryl groups can also be fused or bridged with alicyclic or heterocyclic rings, which are not aromatic so as to form a multicyclic system (*e.g.*, tetralin, methylenedioxyphenyl).

[0001125] As used herein, "carbocycle" or "carbocyclic ring" is intended to include any stable monocyclic, bicyclic or tricyclic ring having the specified number of carbons, any of which may be saturated, unsaturated, or aromatic. For example, a C_3-C_{14} carbocycle is intended to include a monocyclic, bicyclic or tricyclic ring having 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 carbon atoms. Examples of carbocycles include, ~~but are not limited to,~~ cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cycloheptenyl, cycloheptyl, cycloheptenyl, adamantyl, cyclooctyl, cyclooctenyl, cyclooctadienyl, fluorenyl, phenyl, naphthyl, indanyl, adamantyl and tetrahydronaphthyl.

Bridged rings are also included in the definition of carbocycle, including, for example, [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane and [2.2.2]bicyclooctane. A bridged ring occurs when one or more carbon atoms link two non-adjacent carbon atoms. In one embodiment, bridge rings are one or two carbon atoms. It is noted that a bridge always converts a monocyclic ring into a tricyclic ring. When a ring is bridged, the substituents recited for the ring may also be present on the bridge. Fused (*e.g.*, naphthyl, tetrahydronaphthyl) and spiro rings are also included.

[0001126] As used herein, "heterocycle" includes any ring structure (saturated or partially unsaturated) which contains at least one ring heteroatom (*e.g.*, N, O or S). Examples of heterocycles include, ~~but are not limited to,~~ morpholine, pyrrolidine, tetrahydrothiophene, piperidine, piperazine and tetrahydrofuran.

[0001127] Examples of heterocyclic groups include, ~~but are not limited to,~~ acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl, benzoxazolinyl, benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazolinyl, carbazolyl, 4a*H*-carbazolyl, carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, 3H-indolyl, isatinoyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl, isothiazolyl, isoxazolyl, methylenedioxyphenyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,4-oxadiazol5(4H)-one, oxazolidinyl, oxazolyl, oxindolyl, pyrimidinyl, phenanthridinyl, phenanthrolinyl, phenazinyl, phenothiazinyl, phenoxathinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidinyl, pyrrolinyl, 2H-pyrrolyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydroquinolinyl, tetrazolyl, 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl and xanthenyl.

[0001128] The term "substituted", as used herein, means that any one or more hydrogen atmos on the designated atom is replaced with a selection from the indicated groups, provided that the designated atom's normal valency is not exceeded, and that the substitution results in

a stable compound. When a substituent is keto (*i.e.*, =O), then 2 hydrogen atoms on the atom are replaced. Keto substituents are not present on aromatic moieties. Ring double bonds, as used herein, are double bonds that are formed between two adjacent ring atoms (*e.g.*, C=C, C=N or N=N). "Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

[0001129] When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom in the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such formula. Combinations of substituents and/or variables are permissible, but only if such combinations result in stable compounds.

[0001130] When any variable (*e.g.*, R_1) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 R_1 moieties, then the group may optionally be substituted with up to two R_1 moieties and R_1 at each occurrence is selected independently from the definition of R_1. Also, combinations of substituents and/or variables are permissible, but only if such combinations result in stable compounds.

[0001131] The term "hydroxy" or "hydroxyl" includes groups with an -OH or $-O^-$.

[0001132] As used herein, "halo" or "halogen" refers to fluoro, chloro, bromo and iodo. The term "perhalogenated" generally refers to a moiety wherein all hydrogen atoms are replaced by halogen atoms.

[0001133] The term "carbonyl" or "carboxy" includes compounds and moieties which contain a carbon connected with a double bond to an oxygen atom. Examples of moieties containing a carbonyl include, ~~but are not limited to,~~ aldehydes, ketones, carboxylic acids, amides, esters, anhydrides, ~~etc.~~

[0001134] "Acyl" includes moieties that contain the acyl radical (-C(O)-) or a carbonyl group. "Substituted acyl" includes acyl groups where one or more of the hydrogen atoms are replaced by, for example, alkyl groups, alkynyl groups, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including

alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moiety.

[0001135] "Aroyl" includes moieties with an aryl or heteroaromatic moiety bound to a carbonyl group. Examples of aroyl groups include phenylcarboxy, naphthyl carboxy, ~~etc~~.

[0001136] "Alkoxyalkyl", "alkylaminoalkyl" and "thioalkoxyalkyl" include alkyl groups, as described above, wherein oxygen, nitrogen or sulfur atoms replace one or more hydrocarbon backbone carbon atoms.

[0001137] The term "alkoxy" or "alkoxyl" includes substituted and unsubstituted alkyl, alkenyl and alkynyl groups covalently linked to an oxygen atom. Examples of alkoxy groups or alkoxyl radicals include, ~~but are not limited to,~~ methoxy, ethoxy, isopropyloxy, propoxy, butoxy and pentoxy groups. Examples of substituted alkoxy groups include halogenated alkoxy groups. The alkoxy groups can be substituted with groups such as alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, phosphate, phosphonato, phosphinato, amino (including alkylamino, dialkylamino, arylamino, diarylamino, and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moieties. Examples of halogen substituted alkoxy groups include, ~~but are not limited to,~~ fluoromethoxy, difluoromethoxy, trifluoromethoxy, chloromethoxy, dichloromethoxy and trichloromethoxy.

[0001138] The term "ether" or "alkoxy" includes compounds or moieties which contain an oxygen bonded to two carbon atoms or heteroatoms. For example, the term includes "alkoxyalkyl", which refers to an alkyl, alkenyl, or alkynyl group covalently bonded to an oxygen atom which is covalently bonded to an alkyl group.

[0001139] The term "ester" includes compounds or moieties which contain a carbon or a heteroatom bound to an oxygen atom which is bonded to the carbon of a carbonyl group. The term "ester" includes alkoxycarboxy groups such as methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, pentoxycarbonyl, ~~etc~~.

[0001140] The term "thioalkyl" includes compounds or moieties which contain an alkyl group connected with a sulfur atom. The thioalkyl groups can be substituted with groups such as alkyl, alkenyl, alkynyl, halogen, hydroxyl, alkylcarbonyloxy, arylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, carboxylate, carboxyacid, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, alkylthiocarbonyl, alkoxyl, amino (including alkylamino, dialkylamino, arylamino, diarylamino and alkylarylamino), acylamino (including alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido), amidino, imino, sulfhydryl, alkylthio, arylthio, thiocarboxylate, sulfates, alkylsulfinyl, sulfonato, sulfamoyl, sulfonamido, nitro, trifluoromethyl, cyano, azido, heterocyclyl, alkylaryl, or an aromatic or heteroaromatic moieties.

[0001141] The term "thiocarbonyl" or "thiocarboxy" includes compounds and moieties which contain a carbon connected with a double bond to a sulfur atom.

[0001142] The term "thioether" includes moieties which contain a sulfur atom bonded to two carbon atoms or heteroatoms. Examples of thioethers include~~, but are not limited to~~ alkthioalkyls, alkthioalkenyls and alkthioalkynyls. The term "alkthioalkyls" include moieties with an alkyl, alkenyl or alkynyl group bonded to a sulfur atom which is bonded to an alkyl group. Similarly, the term "alkthioalkenyls" refers to moieties wherein an alkyl, alkenyl or alkynyl group is bonded to a sulfur atom which is covalently bonded to an alkenyl group; and alkthioalkynyls" refers to moieties wherein an alkyl, alkenyl or alkynyl group is bonded to a sulfur atom which is covalently bonded to an alkynyl group.

[0001143] As used herein, "amine" or "amino" includes moieties where a nitrogen atom is covalently bonded to at least one carbon or heteroatom. "Alkylamino" includes groups of compounds wherein nitrogen is bound to at least one alkyl group. Examples of alkylamino groups include benzylamino, methylamino, ethylamino, phenethylamino~~, etc~~. "Dialkylamino" includes groups wherein the nitrogen atom is bound to at least two additional alkyl groups. Examples of dialkylamino groups include, ~~but are not limited to,~~ dimethylamino and diethylamino. "Arylamino" and "diarylamino" include groups wherein the nitrogen is bound to at least one or two aryl groups, respectively. "Alkylarylamino", "alkylaminoaryl" or "arylaminoalkyl" refers to an amino group which is bound to at least one alkyl group and at least one aryl group. "Alkaminoalkyl" refers to an alkyl, alkenyl, or alkynyl group bound to a nitrogen atom which is also bound to an alkyl group. "Acylamino" includes groups wherein nitrogen is bound to an acyl group. Examples of acylamino include, ~~but are not limited to,~~ alkylcarbonylamino, arylcarbonylamino, carbamoyl and ureido groups.

[0001144] The term "amide" or "aminocarboxy" includes compounds or moieties that contain a nitrogen atom that is bound to the carbon of a carbonyl or a thiocarbonyl group. The term includes "alkaminocarboxy" groups that include alkyl, alkenyl or alkynyl groups bound to an amino group which is bound to the carbon of a carbonyl or thiocarbonyl group. It also includes "arylaminocarboxy" groups that include aryl or heteroaryl moieties bound to an amino group that is bound to the carbon of a carbonyl or thiocarbonyl group. The terms "alkylaminocarboxy", "alkenylaminocarboxy", "alkynylaminocarboxy" and "arylaminocarboxy" include moieties wherein alkyl, alkenyl, alkynyl and aryl moieties, respectively, are bound to a nitrogen atom which is in turn bound to the carbon of a carbonyl group. Amides can be substituted with substituents such as straight chain alkyl, branched alkyl, cycloalkyl, aryl, heteroaryl or heterocycle. Substituents on amide groups may be further substituted.

[0001145] Compounds of the present invention that contain nitrogens can be converted to N-oxides by treatment with an oxidizing agent (*e.g.*, 3-chloroperoxybenzoic acid (*m*-CPBA) and/or hydrogen peroxides) to afford other compounds of the present invention. Thus, all shown and claimed nitrogen-containing compounds are considered, when allowed by valency and structure, to include both the compound as shown and its N-oxide derivative (which can be designated as N→O or N^+-O^-). Furthermore, in other instances, the nitrogens in the compounds of the present invention can be converted to N-hydroxy or N-alkoxy compounds. For example, N-hydroxy compounds can be prepared by oxidation of the parent amine by an oxidizing agent such as *m*-CPBA. All shown and claimed nitrogen-containing compounds are also considered, when allowed by valency and structure, to cover both the compound as shown and its N-hydroxy (*i.e.*, N-OH) and N-alkoxy (*i.e.*, N-OR, wherein R is substituted or unsubstituted C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, 3-14-membered carbocycle or 3-14-membered heterocycle) derivatives.

[0001146] In the present specification, the structural formula of the compound represents a certain isomer for convenience in some cases, but the present invention includes all isomers, such as geometrical isomers, optical isomers based on an asymmetrical carbon, stereoisomers, tautomers, ~~and the like.~~ In addition, a crystal polymorphism may be present for the compounds represented by the formula. It is noted that any crystal form, crystal form mixture, or anhydride or hydrate thereof is included in the scope of the present invention. Furthermore, so-called metabolite which is produced by degradation of the present compound *in vivo* is included in the scope of the present invention.

one tautomer predominates. In solutions where tautomerization is possible, a chemical equilibrium of the tautomers will be reached. The exact ratio of the tautomers depends on several factors, including temperature, solvent and pH. The concept of tautomers that are interconvertable by tautomerizations is called tautomerism.

[0001153] Of the various types of tautomerism that are possible, two are commonly observed. In keto-enol tautomerism a simultaneous shift of electrons and a hydrogen atom occurs. Ring-chain tautomerism arises as a result of the aldehyde group (-CHO) in a sugar chain molecule reacting with one of the hydroxy groups (-OH) in the same molecule to give it a cyclic (ring-shaped) form as exhibited by glucose.

[0001154] Common tautomeric pairs are: ketone-enol, amide-nitrile, lactam-lactim, amide-imidic acid tautomerism in heterocyclic rings (*e.g.*, in nucleobases such as guanine, thymine and cytosine), amine-enamine and enamine-enamine.

[0001155] It is to be understood that the compounds of the present invention may be depicted as different tautomers. It should also be understood that when compounds have tautomeric forms, all tautomeric forms are intended to be included in the scope of the present invention, and the naming of the compounds does not exclude any tautomer form.

[0001156] The term "crystal polymorphs", "polymorphs" or "crystal forms" means crystal structures in which a compound (or a salt or solvate thereof) can crystallize in different crystal packing arrangements, all of which have the same elemental composition. Different crystal forms usually have different X-ray diffraction patterns, infrared spectral, melting points, density hardness, crystal shape, optical and electrical properties, stability and solubility. Recrystallization solvent, rate of crystallization, storage temperature, and other factors may cause one crystal form to dominate. Crystal polymorphs of the compounds can be prepared by crystallization under different conditions.

[0001157] Additionally, the compounds of the present invention, for example, the salts of the compounds, can exist in either hydrated or unhydrated (the anhydrous) for or as solvates with other solvent molecules. ~~Nonlimiting e~~Examples of hydrates include monohydrates~~,~~ and dihydrates~~, etc~~. ~~Nonlimiting e~~Examples of solvates include ethanol solvates~~,~~ and acetone solvates~~, etc~~.

[0001158] "Solvate" means solvent addition forms that contain either stoichiometric or non stoichiometric amounts of solvent. Some compounds have a tendency to trap a fixed molar ratio of solvent molecules in the crystalline solid state, thus forming a solvate. If the solvent is water the solvate formed is a hydrate; and if the solvent is alcohol, the solvate formed is an alcoholate. Hydrates are formed by the combination of one or more molecules of

water with one molecule of the substance in which the water retains its molecular state as H_2O.

[0001159] As used herein, the term "analog" refers to a chemical compound that is structurally similar to another but differs slightly in composition (as in the replacement of one atom by an atom of a different element or in the presence of a particular functional group, or the replacement of one functional group by another functional group). Thus, an analog is a compound that is similar or comparable in function and appearance, but not in structure or origin to the reference compound.

[0001160] As defined herein, the term "derivative" refers to compounds that have a common core structure, and are substituted with various groups as described herein. For example, all of the compounds represented by Formula I are imidazopyridinyl-aminopyridine derivatives, and have Formula I as a common core.

[0001161] The term "bioisostere" refers to a compound resulting from the exchange of an atom or of a group of atoms with another, broadly similar, atom or group of atoms. The objective of a bioisosteric replacement is to create a new compound with similar biological properties to the parent compound. The bioisosteric replacement may be physicochemically or topologically based. Examples of carboxylic acid bioisosteres include, ~~but are not limited to,~~ acyl sulfonimides, tetrazoles, sulfonates and phosphonates. See, *e.g.*, Patani and LaVoie, *Chem. Rev.* 96, 3147-3176, 1996.

[0001162] The present invention is intended to include all isotopes of atoms occurring in the present compounds. Isotopes include those atoms having the same atomic number but different mass numbers. ~~By way of general example and without limitation~~For example, isotopes of hydrogen include tritium and deuterium, and isotopes of carbon include C-13 and C-14.

2. Synthesis of Substituted Imidazopyridinyl-Aminopyridine Compounds

[0001163] The present invention provides methods for the synthesis of the compounds of each of the formulae described herein. The present invention also provides detailed methods for the synthesis of various disclosed compounds of the present invention according to the following schemes as shown in the examples.

[0001164] Throughout the description, where compositions are described as having, including, or comprising specific components, it is contemplated that compositions also consist essentially of, or consist of, the recited components. Similarly, where methods or processes are described as having, including, or comprising specific process steps, the processes also consist essentially of, or consist of, the recited processing steps. Further, it

should be understood that the order of steps or order for performing certain actions is immaterial so long as the invention remains operable. Moreover, two or more steps or actions can be conducted simultaneously.

[0001165] The synthetic processes of the invention can tolerate a wide variety of functional groups, therefore various substituted starting materials can be used. The processes generally provide the desired final compound at or near the end of the overall process, although it may be desirable in certain instances to further convert the compound to a pharmaceutically acceptable salt, ester or prodrug thereof.

[0001166] Compounds of the present invention can be prepared in a variety of ways using commercially available starting materials, compounds known in the literature, or from readily prepared intermediates, by employing standard synthetic methods and procedures either known to those skilled in the art, or which will be apparent to the skilled artisan in light of the teachings herein. Standard synthetic methods and procedures for the preparation of organic molecules and functional group transformations and manipulations can be obtained from the relevant scientific literature or from standard textbooks in the field. Although not limited to any one or several sources, classic texts such as Smith, M. B., March, J., *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th edition, John Wiley & Sons: New York, 2001; and Greene, T.W., Wuts, P.G. M., *Protective Groups in Organic Synthesis*, 3rd edition, John Wiley & Sons: New York, 1999, ~~incorporated by reference herein,~~ are useful and recognized reference textbooks of organic synthesis known to those in the art. The following descriptions of synthetic methods are designed to illustrate~~, but not to limit,~~ general procedures for the preparation of compounds of the present invention.

[0001167] Compounds of the present invention can be conveniently prepared by a variety of methods familiar to those skilled in the art. The compounds each of the formulae described herein may be prepared according to the following procedures from commercially available starting materials or starting materials which can be prepared using literature procedures. These procedures show the preparation of representative compounds of this invention.

General Procedure A

[0001168] One general procedure for imidazo-pyridine formation is described below in Scheme 1-1: Imidazo-pyridine formation

[0001194] The present invention provides methods for the treatment of a cell proliferative disorder in a subject in need thereof by administering to a subject in need of such treatment, a therapeutically effective amount of a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof. The cell proliferative disorder can be cancer or a precancerous condition. The present invention further provides the use of a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, for the preparation of a medicament useful for the treatment of a cell proliferative disorder.

[0001195] The present invention also provides methods of protecting against a cell proliferative disorder in a subject in need thereof by administering a therapeutically effective amount of compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, to a subject in need of such treatment. The cell proliferative disorder can be cancer or a precancerous condition. The present invention also provides the use of compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, for the preparation of a medicament useful for the prevention of a cell proliferative disorder.

[0001196] As used herein, a "subject in need thereof" is a subject having a cell proliferative disorder, or a subject having an increased risk of developing a cell proliferative disorder relative to the population at large. A subject in need thereof can have a precancerous condition. Preferably, a subject in need thereof has cancer. A "subject" includes a mammal. The mammal can be *e.g.*, any mammal, *e.g.*, a human, primate, bird, mouse, rat, fowl, dog, cat, cow, horse, goat, camel, sheep or a pig. Preferably, the mammal is a human.

[0001197] As used herein, the term "cell proliferative disorder" refers to conditions in which unregulated or abnormal growth, or both, of cells can lead to the development of an unwanted condition or disease, which may or may not be cancerous. Exemplary cell proliferative disorders of the invention encompass a variety of conditions wherein cell division is deregulated. Exemplary cell proliferative disorder include~~, but are not limited to,~~ neoplasms, benign tumors, malignant tumors, pre-cancerous conditions, *in situ* tumors, encapsulated tumors, metastatic tumors, liquid tumors, solid tumors, immunological tumors, hematological tumors, cancers, carcinomas, leukemias, lymphomas, sarcomas, and rapidly dividing cells. The term "rapidly dividing cell" as used herein is defined as any cell that divides at a rate that exceeds or is greater than what is expected or observed among neighboring or juxtaposed cells within the same tissue. A cell proliferative disorder includes a precancer or a precancerous condition. A cell proliferative disorder includes cancer.

Preferably, the methods provided herein are used to treat or alleviate a symptom of cancer. The term "cancer" includes solid tumors, as well as, hematologic tumors and/or malignancies. A "precancer cell" or "precancerous cell" is a cell manifesting a cell proliferative disorder that is a precancer or a precancerous condition. A "cancer cell" or "cancerous cell" is a cell manifesting a cell proliferative disorder that is a cancer. Any reproducible means of measurement may be used to identify cancer cells or precancerous cells. Cancer cells or precancerous cells can be identified by histological typing or grading of a tissue sample (*e.g.*, a biopsy sample). Cancer cells or precancerous cells can be identified through the use of appropriate molecular markers.

[0001198] Exemplary non-cancerous conditions or disorders include, ~~but are not limited to,~~ rheumatoid arthritis; inflammation; autoimmune disease; lymphoproliferative conditions; acromegaly; rheumatoid spondylitis; osteoarthritis; gout, other arthritic conditions; sepsis; septic shock; endotoxic shock; gram-negative sepsis; toxic shock syndrome; asthma; adult respiratory distress syndrome; chronic obstructive pulmonary disease; chronic pulmonary inflammation; inflammatory bowel disease; Crohn's disease; psoriasis; eczema; ulcerative colitis; pancreatic fibrosis; hepatic fibrosis; acute and chronic renal disease; irritable bowel syndrome; pyresis; restenosis; cerebral malaria; stroke and ischemic injury; neural trauma; Alzheimer's disease; Huntington's disease; Parkinson's disease; acute and chronic pain; allergic rhinitis; allergic conjunctivitis; chronic heart failure; acute coronary syndrome; cachexia; malaria; leprosy; leishmaniasis; Lyme disease; Reiter's syndrome; acute synovitis; muscle degeneration, bursitis; tendonitis; tenosynovitis; herniated, ruptures, or prolapsed intervertebral disk syndrome; osteopetrosis; thrombosis; restenosis; silicosis; pulmonary sarcosis; bone resorption diseases, such as osteoporosis; graft-versus-host reaction; Multiple Sclerosis; lupus; fibromyalgia; AIDS and other viral diseases such as Herpes Zoster, Herpes Simplex I or II, influenza virus and cytomegalovirus; and diabetes mellitus.

[0001199] Exemplary cancers include, ~~but are not limited to,~~ adrenocortical carcinoma, AIDS-related cancers, AIDS-related lymphoma, anal cancer, anorectal cancer, cancer of the anal canal, appendix cancer, childhood cerebellar astrocytoma, childhood cerebral astrocytoma, basal cell carcinoma, skin cancer (non-melanoma), biliary cancer, extrahepatic bile duct cancer, intrahepatic bile duct cancer, bladder cancer, uringary bladder cancer, bone and joint cancer, osteosarcoma and malignant fibrous histiocytoma, brain cancer, brain tumor, brain stem glioma, cerebellar astrocytoma, cerebral astrocytoma/malignant glioma, ependymoma, medulloblastoma, supratentorial primitive neuroectodeimal tumors, visual pathway and hypothalamic glioma, breast cancer, bronchial adenomas/carcinoids, carcinoid tumor,

having one or more chromosomes that are abnormal in appearance. A cancer that is to be treated can be classified as being aneuploid, triploid, tetraploid, or as having an altered ploidy. A cancer that is to be treated can be classified as having a chromosomal translocation, or a deletion or duplication of an entire chromosome, or a region of deletion, duplication or amplification of a portion of a chromosome.

[0001219] A cancer that is to be treated can be evaluated by DNA cytometry, flow cytometry, or image cytometry. A cancer that is to be treated can be typed as having 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of cells in the synthesis stage of cell division (*e.g.,* in S phase of cell division). A cancer that is to be treated can be typed as having a low S-phase fraction or a high S-phase fraction.

[0001220] As used herein, a "normal cell" is a cell that cannot be classified as part of a "cell proliferative disorder". A normal cell lacks unregulated or abnormal growth, or both, that can lead to the development of an unwanted condition or disease. Preferably, a normal cell possesses normally functioning cell cycle checkpoint control mechanisms.

[0001221] As used herein, "contacting a cell" refers to a condition in which a compound or other composition of matter is in direct contact with a cell, or is close enough to induce a desired biological effect in a cell.

[0001222] As used herein, "candidate compound" refers to a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, that has been or will be tested in one or more *in vitro* or *in vivo* biological assays, in order to determine if that compound is likely to elicit a desired biological or medical response in a cell, tissue, system, animal or human that is being sought by a researcher or clinician. A candidate compound is a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof. The biological or medical response can be the treatment of cancer. The biological or medical response can be treatment or prevention of a cell proliferative disorder. *In vitro* or *in vivo* biological assays can include, ~~but are not limited to,~~ enzymatic activity assays, electrophoretic mobility shift assays, reporter gene assays, *in vitro* cell viability assays, and the assays described herein.

[0001223] As used herein, "monotherapy" refers to the administration of a single active or therapeutic compound to a subject in need thereof. Preferably, monotherapy will involve administration of a therapeutically effective amount of an active compound. For example, cancer monotherapy with one of the compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, analog or derivative thereof, to a subject in need of treatment of cancer. Monotherapy may be contrasted with combination

thereof, can be measured in the disclosed assays. The change in enzymatic activity can be characterized by the change in the extent of phosphorylation of certain substrates. As used herein, "phosphorylation" refers to the addition of phosphate groups to a substrate, including proteins and organic molecules; and, plays an important role in regulating the biological activities of proteins. Preferably, the phosphorylation assayed and measured involves the addition of phosphate groups to tyrosine residues. The substrate can be a peptide or protein.

[0001270] In some assays, immunological reagents, *e.g.*, antibodies and antigens, are employed. Fluorescence can be utilized in the measurement of enzymatic activity in some assays. As used herein, "fluorescence" refers to a process through which a molecule emits a photon as a result of absorbing an incoming photon of higher energy by the same molecule. Specific methods for assessing the biological activity of the disclosed compounds are described in the examples.

[0001271] As used herein, an activity of c-Met refers to any biological function or activity that is carried out by c-Met. For example, a function of c-Met includes phosphorylation of downstream target proteins. Other functions of c-Met include autophosphorylation, binding of adaptor proteins such as Gab-1, Grb-2, Shc, SHP2 and c-Cbl, and activation of signal transducers such as Ras, Src, PI3K, PLC-γ, STATs, ERK1 and 2 and FAK.

[0001272] Administering a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, to a cell or a subject in need thereof results in modulation (*i.e.*, stimulation or inhibition) of an activity of an intracellular target (*e.g.*, substrate). Several intracellular targets can be modulated with the compounds of the present invention, including, ~~but not limited to,~~ adaptor proteins such as Gab-1, Grb-2, Shc, SHP2 and c-Cbl, and signal transducers such as Ras, Src, PI3K, PLC-γ, STATs, ERK1 and 2 and FAK.

[0001273] Activating refers to placing a composition of matter (*e.g.*, protein or nucleic acid) in a state suitable for carrying out a desired biological function. A composition of matter capable of being activated also has an unactivated state. An activated composition of matter may have an inhibitory or stimulatory biological function, or both.

[0001274] Elevation refers to an increase in a desired biological activity of a composition of matter (*e.g.*, a protein or a nucleic acid). Elevation may occur through an increase in concentration of a composition of matter.

[0001275] As used herein, "a cell cycle checkpoint pathway" refers to a biochemical pathway that is involved in modulation of a cell cycle checkpoint. A cell cycle checkpoint

cancer cells. Contacting a cell with a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, can induce cell death selectively in one or more cells affected by a cell proliferative disorder. Preferably, administering to a subject in need thereof a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, induces cell death selectively in one or more cells affected by a cell proliferative disorder.

[0001280] The present invention relates to a method of treating or preventing cancer by administering a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, to a subject in need thereof, where administration of the compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, results in one or more of the following: accumulation of cells in G1 and/or S phase of the cell cycle, cytotoxicity via cell death in cancer cells without a significant amount of cell death in normal cells, antitumor activity in animals with a therapeutic index of at least 2, and activation of a cell cycle checkpoint. As used herein, "therapeutic index" is the maximum tolerated dose divided by the efficacious dose.

[0001281] One skilled in the art may refer to general reference texts for detailed descriptions of known techniques discussed herein or equivalent techniques. These texts include Ausubel *et al., Current Protocols in Molecular Biology*, John Wiley and Sons, Inc. (2005); Sambrook *et al.*, *Molecular Cloning, A Laboratory Manual* (3rd edition), Cold Spring Harbor Press, Cold Spring Harbor, New York (2000); Coligan *et al.*, *Current Protocols in Immunology*, John Wiley & Sons, N.Y.; Enna *et al.*, *Current Protocols in Pharmacology*, John Wiley & Sons, N.Y.; Fingl *et al.*, *The Pharmacological Basis of Therapeutics* (1975), *Remington's Pharmaceutical Sciences*, Mack Publishing Co., Easton, PA, 18th edition (1990). These texts can, of course, also be referred to in making or using an aspect of the invention

[0001282] As used herein, "combination therapy" or "co-therapy" includes the administration of a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, and at least a second agent as part of a specific treatment regimen intended to provide the beneficial effect from the co-action of these therapeutic agents. The beneficial effect of the combination includes, ~~but is not limited to,~~ pharmacokinetic or pharmacodynamic co-action resulting from the combination of therapeutic agents. Administration of these therapeutic agents in combination typically is carried out over a defined time period (usually minutes, hours, days or weeks depending upon the combination selected). "Combination therapy" may be, but generally is not, intended to

encompass the administration of two or more of these therapeutic agents as part of separate monotherapy regimens that incidentally and arbitrarily result in the combinations of the present invention.

[0001283] "Combination therapy" is intended to embrace administration of these therapeutic agents in a sequential manner, wherein each therapeutic agent is administered at a different time, as well as administration of these therapeutic agents, or at least two of the therapeutic agents, in a substantially simultaneous manner. Substantially simultaneous administration can be accomplished, for example, by administering to the subject a single capsule having a fixed ratio of each therapeutic agent or in multiple, single capsules for each of the therapeutic agents. Sequential or substantially simultaneous administration of each therapeutic agent can be effected by any appropriate route including, ~~but not limited to,~~ oral routes, intravenous routes, intramuscular routes, and direct absorption through mucous membrane tissues. The therapeutic agents can be administered by the same route or by different routes. For example, a first therapeutic agent of the combination selected may be administered by intravenous injection while the other therapeutic agents of the combination may be administered orally. Alternatively, for example, all therapeutic agents may be administered orally or all therapeutic agents may be administered by intravenous injection. The sequence in which the therapeutic agents are administered is not narrowly critical.

[0001284] "Combination therapy" also embraces the administration of the therapeutic agents as described above in further combination with other biologically active ingredients and non-drug therapies (*e.g.*, surgery or radiation treatment). Where the combination therapy further comprises a non-drug treatment, the non-drug treatment may be conducted at any suitable time so long as a beneficial effect from the co-action of the combination of the therapeutic agents and non-drug treatment is achieved. For example, in appropriate cases, the beneficial effect is still achieved when the non-drug treatment is temporally removed from the administration of the therapeutic agents, perhaps by days or even weeks.

[0001285] A compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, analog or derivative thereof, may be administered in combination with a second chemotherapeutic agent. The second chemotherapeutic agent (also referred to as an anti-neoplastic agent or anti-proliferative agent) can be an alkylating agent; an antibiotic; an anti-metabolite; a detoxifying agent; an interferon; a polyclonal or monoclonal antibody; an EGFR inhibitor; a HER2 inhibitor; a histone deacetylase inhibitor; a hormone; a mitotic inhibitor; an MTOR inhibitor; a multi-kinase inhibitor; a serine/threonine kinase inhibitor; a tyrosine kinase inhibitors; a VEGF/VEGFR inhibitor; a taxane or taxane derivative, an

aromatase inhibitor, an anthracycline, a microtubule targeting drug, a topoisomerase poison drug, an inhibitor of a molecular target or enzyme (*e.g.*, a kinase inhibitor), a cytidine analogue drug or any chemotherapeutic, anti-neoplastic or anti-proliferative agent listed in www.cancer.org/docroot/cdg/cdg_0.asp.

[0001286] Exemplary alkylating agents include, ~~but are not limited to,~~ cyclophosphamide (Cytoxan; Neosar); chlorambucil (Leukeran); melphalan (Alkeran); carmustine (BiCNU); busulfan (Busulfex); lomustine (CeeNU); dacarbazine (DTIC-Dome); oxaliplatin (Eloxatin); carmustine (Gliadel); ifosfamide (Ifex); mechlorethamine (Mustargen); busulfan (Myleran); carboplatin (Paraplatin); cisplatin (CDDP; Platinol); temozolomide (Temodar); thiotepa (Thioplex); bendamustine (Treanda); or streptozocin (Zanosar).

[0001287] Exemplary antibiotics include, ~~but are not limited to,~~ doxorubicin (Adriamycin); doxorubicin liposomal (Doxil); mitoxantrone (Novantrone); bleomycin (Blenoxane); daunorubicin (Cerubidine); daunorubicin liposomal (DaunoXome); dactinomycin (Cosmegen); epirubicin (Ellence); idarubicin (Idamycin); plicamycin (Mithracin); mitomycin (Mutamycin); pentostatin (Nipent); or valrubicin (Valstar).

[0001288] Exemplary anti-metabolites include, ~~but are not limited to,~~ fluorouracil (Adrucil); capecitabine (Xeloda); hydroxyurea (Hydrea); mercaptopurine (Purinethol); pemetrexed (Alimta); fludarabine (Fludara); nelarabine (Arranon); cladribine (Cladribine Novaplus); clofarabine (Clolar); cytarabine (Cytosar-U); decitabine (Dacogen); cytarabine liposomal (DepoCyt); hydroxyurea (Droxia); pralatrexate (Folotyn); floxuridine (FUDR); gemcitabine (Gemzar); cladribine (Leustatin); fludarabine (Oforta); methotrexate (MTX; Rheumatrex); methotrexate (Trexall); thioguanine (Tabloid); TS-1 or cytarabine (Tarabine PFS).

[0001289] Exemplary detoxifying agents include, ~~but are not limited to,~~ amifostine (Ethyol) or mesna (Mesnex).

[0001290] Exemplary interferons include, ~~but are not limited to,~~ interferon alfa-2b (Intron A) or interferon alfa-2a (Roferon-A).

[0001291] Exemplary polyclonal or monoclonal antibodies include, ~~but are not limited to,~~ trastuzumab (Herceptin); ofatumumab (Arzerra); bevacizumab (Avastin); rituximab (Rituxan); cetuximab (Erbitux); panitumumab (Vectibix); tositumomab/iodine^{131} tositumomab (Bexxar); alemtuzumab (Campath); ibritumomab (Zevalin; In-111; Y-90 Zevalin); gemtuzumab (Mylotarg); eculizumab (Soliris) ordenosumab.

[0001292] Exemplary EGFR inhibitors include, ~~but are not limited to,~~ gefitinib (Iressa); lapatinib (Tykerb); cetuximab (Erbitux); erlotinib (Tarceva); panitumumab (Vectibix); PKI-166; canertinib (CI-1033); matuzumab (Emd7200) or EKB-569.

[0001293] Exemplary HER2 inhibitors include, ~~but are not limited to,~~ trastuzumab (Herceptin); lapatinib (Tykerb) or AC-480.

[0001294] Histone Deacetylase Inhibitors include, ~~but are not limited to,~~ vorinostat (Zolinza).

[0001295] Exemplary hormones include, ~~but are not limited to,~~ tamoxifen (Soltamox; Nolvadex); raloxifene (Evista); megestrol (Megace); leuprolide (Lupron; Lupron Depot; Eligard; Viadur) ; fulvestrant (Faslodex); letrozole (Femara); triptorelin (Trelstar LA; Trelstar Depot) ; exemestane (Aromasin) ; goserelin (Zoladex) ; bicalutamide (Casodex); anastrozole (Arimidex); fluoxymesterone (Androxy; Halotestin); medroxyprogesterone (Provera; Depo-Provera); estramustine (Emcyt); flutamide (Eulexin); toremifene (Fareston); degarelix (Firmagon); nilutamide (Nilandron); abarelix (Plenaxis); or testolactone (Teslac).

[0001296] Exemplary mitotic inhibitors include, ~~but are not limited to,~~ paclitaxel (Taxol; Onxol; Abraxane); docetaxel (Taxotere); vincristine (Oncovin; Vincasar PFS); vinblastine (Velban); etoposide (Toposar; Etopophos; VePesid); teniposide (Vumon); ixabepilone (Ixempra); nocodazole; epothilone; vinorelbine (Navelbine); camptothecin (CPT); irinotecan (Camptosar); topotecan (Hycamtin); amsacrine or lamellarin D (LAM-D).

[0001297] Exemplary MTOR inhibitors include, ~~but are not limited to,~~ everolimus (Afinitor) or temsirolimus (Torisel); rapamune, ridaforolimus; or AP23573.

[0001298] Exemplary multi-kinase inhibitors include, ~~but are not limited to,~~ sorafenib (Nexavar); sunitinib (Sutent); BIBW 2992; E7080; Zd6474; PKC-412; motesanib; or AP24534.

[0001299] Exemplary serine/threonine kinase inhibitors include, ~~but are not limited to,~~ ruboxistaurin; eril/easudil hydrochloride; flavopiridol; seliciclib (CYC202; Roscovitrine); SNS-032 (BMS-387032); Pkc412; bryostatin; KAI-9803;SF1126; VX-680; Azd1152; Arry-142886 (AZD-6244); SCIO-469; GW681323; CC-401; CEP-1347 or PD 332991.

[0001300] Exemplary tyrosine kinase inhibitors include, ~~but are not limited to,~~ erlotinib (Tarceva); gefitinib (Iressa); imatinib (Gleevec); sorafenib (Nexavar); sunitinib (Sutent); trastuzumab (Herceptin); bevacizumab (Avastin); rituximab (Rituxan); lapatinib (Tykerb); cetuximab (Erbitux); panitumumab (Vectibix); everolimus (Afinitor); alemtuzumab (Campath); gemtuzumab (Mylotarg); temsirolimus (Torisel); pazopanib (Votrient); dasatinib (Sprycel); nilotinib (Tasigna); vatalanib (Ptk787; ZK222584); CEP-701; SU5614; MLN518;

XL999; VX-322; Azd0530; BMS-354825; SKI-606 CP-690; AG-490; WHI-P154; WHI-P131; AC-220; or AMG888.

[0001301] Exemplary VEGF/VEGFR inhibitors include, ~~but are not limited to,~~ bevacizumab (Avastin); sorafenib (Nexavar); sunitinib (Sutent); ranibizumab; pegaptanib; or vandetinib.

[0001302] Exemplary microtubule targeting drugs include, ~~but are not limited to,~~ paclitaxel, docetaxel, vincristin, vinblastin, nocodazole, epothilones and navelbine.

[0001303] Exemplary topoisomerase poison drugs include, ~~but are not limited to,~~ teniposide, etoposide, adriamycin, camptothecin, daunorubicin, dactinomycin, mitoxantrone, amsacrine, epirubicin and idarubicin.

[0001304] Exemplary taxanes or taxane derivatives include, ~~but are not limited to,~~ paclitaxel and docetaxol.

[0001305] Exemplary general chemotherapeutic, anti-neoplastic, anti-proliferative agents include, but are not limited to, altretamine (Hexalen); isotretinoin (Accutane; Amnesteem; Claravis; Sotret); tretinoin (Vesanoid); azacitidine (Vidaza); bortezomib (Velcade) asparaginase (Elspar); levamisole (Ergamisol); mitotane (Lysodren); procarbazine (Matulane); pegaspargase (Oncaspar); denileukin diftitox (Ontak); porfimer (Photofrin); aldesleukin (Proleukin); lenalidomide (Revlimid); bexarotene (Targretin); thalidomide (Thalomid); temsirolimus (Torisel); arsenic trioxide (Trisenox); verteporfin (Visudyne); mimosine (Leucenol); (1M tegafur - 0.4 M 5-chloro-2,4-dihydroxypyrimidine - 1 M potassium oxonate) or lovastatin.

[0001306] In another aspect, the second chemotherapeutic agent can be a cytokine such as G-CSF (granulocyte colony stimulating factor). In another aspect, a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, analog or derivative thereof, may be administered in combination with radiation therapy. Radiation therapy can also be administered in combination with a compound of the present invention and another chemotherapeutic agent described herein as part of a multiple agent therapy. In yet another aspect, a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, analog or derivative thereof, may be administered in combination with standard chemotherapy combinations such as, ~~but not restricted to,~~ CMF (cyclophosphamide, methotrexate and 5-fluorouracil), CAF (cyclophosphamide, adriamycin and 5-fluorouracil), AC (adriamycin and cyclophosphamide), FEC (5-fluorouracil, epirubicin, and cyclophosphamide), ACT or ATC (adriamycin, cyclophosphamide, and paclitaxel), rituximab, Xeloda (capecitabine), Cisplatin (CDDP), Carboplatin, TS-1 (tegafur, gimestat and

otastat potassium at a molar ratio of 1:0.4:1), Camptothecin-11 (CPT-11, Irinotecan or Camptosar™) or CMFP (cyclophosphamide, methotrexate, 5-fluorouracil and prednisone).

[0001307] In preferred embodiments, a compound of the present invention, or a pharmaceutically acceptable salt, prodrug, metabolite, polymorph or solvate thereof, may be administered with an inhibitor of an enzyme, such as a receptor or non-receptor kinase. Receptor and non-receptor kinases of the invention are, for example, tyrosine kinases or serine/threonine kinases. Kinase inhibitors of the invention are small molecules, polynucleic acids, polypeptides, or antibodies.

[0001308] Exemplary kinase inhibitors include, ~~but are not limited to,~~ Bevacizumab (targets VEGF), BIBW 2992 (targets EGFR and Erb2), Cetuximab/Erbitux (targets Erb1), Imatinib/Gleevic (targets Bcr-Abl), Trastuzumab (targets Erb2), Gefitinib/Iressa (targets EGFR), Ranibizumab (targets VEGF), Pegaptanib (targets VEGF), Erlotinib/Tarceva (targets Erb1), Nilotinib (targets Bcr-Abl), Lapatinib (targets Erb1 and Erb2/Her2), GW-572016/lapatinib ditosylate (targets HER2/Erb2), Panitumumab/Vectibix (targets EGFR), Vandetinib (targets RET/VEGFR), E7080 (multiple targets including RET and VEGFR), Herceptin (targets HER2/Erb2), PKI-166 (targets EGFR), Canertinib/CI-1033 (targets EGFR), Sunitinib/SU-11464/Sutent (targets EGFR and FLT3), Matuzumab/Emd7200 (targets EGFR), EKB-569 (targets EGFR), Zd6474 (targets EGFR and VEGFR), PKC-412 (targets VEGR and FLT3), Vatalanib/Ptk787/ZK222584 (targets VEGR), CEP-701 (targets FLT3), SU5614 (targets FLT3), MLN518 (targets FLT3), XL999 (targets FLT3), VX-322 (targets FLT3), Azd0530 (targets SRC), BMS-354825 (targets SRC), SKI-606 (targets SRC), CP-690 (targets JAK), AG-490 (targets JAK), WHI-P154 (targets JAK), WHI-P131 (targets JAK), sorafenib/Nexavar (targets RAF kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR- ß, KIT, FLT-3, and RET), Dasatinib/Sprycel (BCR/ABL and Src), AC-220 (targets Flt3), AC-480 (targets all HER proteins, "panHER"), Motesanib diphosphate (targets VEGF1-3, PDGFR, and c-kit), Denosumab (targets RANKL, inhibits SRC), AMG888 (targets HER3), and AP24534 (multiple targets including Flt3).

[0001309] Exemplary serine/threonine kinase inhibitors include, ~~but are not limited to,~~ Rapamune (targets mTOR/FRAP1), Deforolimus (targets mTOR), Certican/Everolimus (targets mTOR/FRAP1), AP23573 (targets mTOR/FRAP1), Eril/Fasudil hydrochloride (targets RHO), Flavopiridol (targets CDK), Seliciclib/CYC202/Roscovitrine (targets CDK), SNS-032/BMS-387032 (targets CDK), Ruboxistaurin (targets PKC), Pkc412 (targets PKC), Bryostatin (targets PKC), KAI-9803 (targets PKC), SF1126 (targets PI3K), VX-680 (targets Aurora kinase), Azd1152 (targets Aurora kinase), Arry-142886/AZD-6244 (targets

MAP/MEK), SCIO-469 (targets MAP/MEK), GW681323 (targets MAP/MEK), CC-401 (targets JNK), CEP-1347 (targets JNK), and PD 332991 (targets CDK).

4. Pharmaceutical Compositions

[0001310] The present invention also provides pharmaceutical compositions comprising a compound of each of the formulae described herein in combination with at least one pharmaceutically acceptable excipient or carrier.

[0001311] A "pharmaceutical composition" is a formulation containing the compounds of the present invention in a form suitable for administration to a subject. In one embodiment, the pharmaceutical composition is in bulk or in unit dosage form. The unit dosage form is any of a variety of forms, including, for example, a capsule, an IV bag, a tablet, a single pump on an aerosol inhaler or a vial. The quantity of active ingredient (*e.g.*, a formulation of the disclosed compound or salt, hydrate, solvate or isomer thereof) in a unit dose of composition is an effective amount and is varied according to the particular treatment involved. One skilled in the art will appreciate that it is sometimes necessary to make routine variations to the dosage depending on the age and condition of the patient. The dosage will also depend on the route of administration. A variety of routes are contemplated, including oral, pulmonary, rectal, parenteral, transdermal, subcutaneous, intravenous, intramuscular, intraperitoneal, inhalational, buccal, sublingual, intrapleural, intrathecal, intranasal, ~~and the like~~. Dosage forms for the topical or transdermal administration of a compound of this invention include powders, sprays, ointments, pastes, creams, lotions, gels, solutions, patches and inhalants. In one embodiment, the active compound is mixed under sterile conditions with a pharmaceutically acceptable carrier, and with any preservatives, buffers or propellants that are required.

[0001312] As used herein, the phrase "pharmaceutically acceptable" refers to those compounds, materials, compositions, carriers, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

[0001313] "Pharmaceutically acceptable excipient" means an excipient that is useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable, and includes excipient that is acceptable for veterinary use as well as human pharmaceutical use. A "pharmaceutically acceptable

excipient" as used in the specification and claims includes both one and more than one such excipient.

[0001314] A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, *e.g.,* intravenous, intradermal, subcutaneous, oral (*e.g.*, inhalation), transdermal (topical), and transmucosal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates, and agents for the adjustment of tonicity such as sodium chloride or dextrose. The pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.

[0001315] A compound or pharmaceutical composition of the invention can be administered to a subject in many of the well-known methods currently used for chemotherapeutic treatment. For example, for treatment of cancers, a compound of the invention may be injected directly into tumors, injected into the blood stream or body cavities or taken orally or applied through the skin with patches. The dose chosen should be sufficient to constitute effective treatment but not as high as to cause unacceptable side effects. The state of the disease condition (*e.g.*, cancer, precancer, ~~and the like~~) and the health of the patient should preferably be closely monitored during and for a reasonable period after treatment.

[0001316] The term "therapeutically effective amount", as used herein, refers to an amount of a pharmaceutical agent to treat, ameliorate, or prevent an identified disease or condition, or to exhibit a detectable therapeutic or inhibitory effect. The effect can be detected by any assay method known in the art. The precise effective amount for a subject will depend upon the subject's body weight, size, and health; the nature and extent of the condition; and the therapeutic or combination of therapeutics selected for administration. Therapeutically effective amounts for a given situation can be determined by routine experimentation that is within the skill and judgment of the clinician. In a preferred aspect, the disease or condition to be treated is cancer. In another aspect, the disease or condition to be treated is a cell proliferative disorder.

the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, ~~and the like~~), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, ~~and the like~~. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as manitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

[0001321] Sterile injectable solutions can be prepared by incorporating the active compound in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle that contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, methods of preparation are vacuum drying and freeze-drying that yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

[0001322] Oral compositions generally include an inert diluent or an edible pharmaceutically acceptable carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches ~~and the like~~ can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

growth of the tumors and also preferably causing complete regression of the cancer. Dosages can range from about 0.01 mg/kg per day to about 5000 mg/kg per day. In preferred aspects, dosages can range from about 1 mg/kg per day to about 1000 mg/kg per day. In an aspect, the dose will be in the range of about 0.1 mg/day to about 50 g/day; about 0.1 mg/day to about 25 g/day; about 0.1 mg/day to about 10 g/day; about 0.1 mg to about 3 g/day; or about 0.1 mg to about 1 g/day, in single, divided, or continuous doses (which dose may be adjusted for the patient's weight in kg, body surface area in m^2, and age in years). An effective amount of a pharmaceutical agent is that which provides an objectively identifiable improvement as noted by the clinician or other qualified observer. For example, regression of a tumor in a patient may be measured with reference to the diameter of a tumor. Decrease in the diameter of a tumor indicates regression. Regression is also indicated by failure of tumors to reoccur after treatment has stopped. As used herein, the term "dosage effective manner" refers to amount of an active compound to produce the desired biological effect in a subject or cell.

[0001328] The pharmaceutical compositions can be included in a container, pack, or dispenser together with instructions for administration.

[0001329] The compounds of the present invention are capable of further forming salts. All of these forms are also contemplated within the scope of the claimed invention.

[0001330] As used herein, "pharmaceutically acceptable salts" refer to derivatives of the compounds of the present invention wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, ~~but are not limited to,~~ mineral or organic acid salts of basic residues such as amines, alkali or organic salts of acidic residues such as carboxylic acids, ~~and the like~~. The pharmaceutically acceptable salts include the conventional non-toxic salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include, ~~but are not limited to,~~ those derived from inorganic and organic acids selected from 2-acetoxybenzoic, 2-hydroxyethane sulfonic, acetic, ascorbic, benzene sulfonic, benzoic, bicarbonic, carbonic, citric, edetic, ethane disulfonic, 1,2-ethane sulfonic, fumaric, glucoheptonic, gluconic, glutamic, glycolic, glycollyarsanilic, hexylresorcinic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxymaleic, hydroxynaphthoic, isethionic, lactic, lactobionic, lauryl sulfonic, maleic, malic, mandelic, methane sulfonic, napsylic, nitric, oxalic, pamoic, pantothenic, phenylacetic, phosphoric, polygalacturonic, propionic, salicyclic, stearic, subacetic, succinic, sulfamic,

sulfanilic, sulfuric, tannic, tartaric, toluene sulfonic, and the commonly occurring amine acids, *e.g.*, glycine, alanine, phenylalanine, arginine, ~~etc~~.

[0001331] Other examples of pharmaceutically acceptable salts include hexanoic acid, cyclopentane propionic acid, pyruvic acid, malonic acid, 3-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphorsulfonic acid, 4-methylbicyclo-[2.2.2]-oct-2-ene-1-carboxylic acid, 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, muconic acid, ~~and the like~~. The present invention also encompasses salts formed when an acidic proton present in the parent compound either is replaced by a metal ion, *e.g.*, an alkali metal ion, an alkaline earth ion, or an aluminum ion; or coordinates with an organic base such as ethanolamine, diethanolamine, triethanolamine, tromethamine, N-methylglucamine, ~~and the like~~.

[0001332] It should be understood that all references to pharmaceutically acceptable salts include solvent addition forms (solvates) or crystal forms (polymorphs) as defined herein, of the same salt.

[0001333] The compounds of the present invention can also be prepared as esters, for example, pharmaceutically acceptable esters. For example, a carboxylic acid function group in a compound can be converted to its corresponding ester, *e.g.*, a methyl, ethyl or other ester. Also, an alcohol group in a compound can be converted to its corresponding ester, *e.g.*, an acetate, propionate or other ester.

[0001334] The compounds of the present invention can also be prepared as prodrugs, for example, pharmaceutically acceptable prodrugs. The terms "pro-drug" and "prodrug" are used interchangeably herein and refer to any compound which releases an active parent drug *in vivo*. Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (*e.g.*, solubility, bioavailability, manufacturing, etc.), the compounds of the present invention can be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same and compositions containing the same. "Prodrugs" are intended to include any covalently bonded carriers that release an active parent drug of the present invention *in vivo* when such prodrug is administered to a subject. Prodrugs in the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, sulfhydryl, carboxy or carbonyl group is bonded to any group that may be cleaved *in vivo* to form a free hydroxyl, free amino, free sulfhydryl, free carboxy or free carbonyl group, respectively.

[0001335] Examples of prodrugs include, ~~but are not limited to,~~ esters (*e.g.*, acetate, dialkylaminoacetates, formates, phosphates, sulfates and benzoate derivatives) and carbamates (*e.g.*, N,N-dimethylaminocarbonyl) of hydroxy functional groups, esters (*e.g.*, ethyl esters, morpholinoethanol esters) of carboxyl functional groups, N-acyl derivatives (*e.g.*, N-acetyl) N-Mannich bases, Schiff bases and enaminones of amino functional groups, oximes, acetals, ketals and enol esters of ketone and aldehyde functional groups in compounds of the invention, ~~and the like~~, See Bundegaard, H., *Design of Prodrugs*, p1-92, Elesevier, New York-Oxford (1985).

[0001336] The compounds, or pharmaceutically acceptable salts, esters or prodrugs thereof, are administered orally, nasally, transdermally, pulmonary, inhalationally, buccally, sublingually, intraperintoneally, subcutaneously, intramuscularly, intravenously, rectally, intrapleurally, intrathecally and parenterally. In one embodiment, the compound is administered orally. One skilled in the art will recognize the advantages of certain routes of administration.

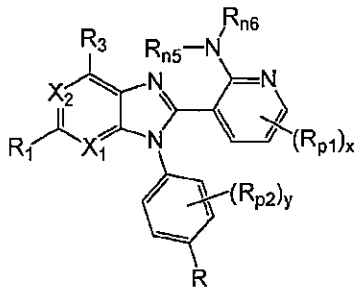
[0001337] The dosage regimen utilizing the compounds is selected in accordance with a variety of factors including type, species, age, weight, sex and medical condition of the patient; the severity of the condition to be treated; the route of administration; the renal and hepatic function of the patient; and the particular compound or salt thereof employed. An ordinarily skilled physician or veterinarian can readily determine and prescribe the effective amount of the drug required to prevent, counter or arrest the progress of the condition.

[0001338] Techniques for formulation and administration of the disclosed compounds of the invention can be found in *Remington: the Science and Practice of Pharmacy*, 19th edition, Mack Publishing Co., Easton, PA (1995). In an embodiment, the compounds described herein, and the pharmaceutically acceptable salts thereof, are used in pharmaceutical preparations in combination with a pharmaceutically acceptable carrier or diluent. Suitable pharmaceutically acceptable carriers include inert solid fillers or diluents and sterile aqueous or organic solutions. The compounds will be present in such pharmaceutical compositions in amounts sufficient to provide the desired dosage amount in the range described herein.

[0001339] All percentages and ratios used herein, unless otherwise indicated, are by weight. Other features and advantages of the present invention are apparent from the different examples. The provided examples illustrate different components and methodology useful in practicing the present invention. ~~The examples do not limit the claimed invention.~~ Based on the present disclosure the skilled artisan can identify and employ other components and methodology useful for practicing the present invention.

CLAIMS

1. A compound having formula I:



(I),

or a pharmaceutically acceptable salt or ester thereof, wherein:

one of X_1 and X_2 is CR_x and the other is N;

R_x, R_1 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$;

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or

unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R is H, hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 3-, 4-, 5-, 6- or 7-member rings and 1-4 heteroatoms selected from N, O and S, or Q-T;

Q is a bond or unsubstituted or substituted C_1-C_6 alkyl linker;

T is $NR_{n1}R_{n2}$, $C(O)R_o$, $S(O)R_s$ or $S(O)_2R_s$;

R_{n1} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n2} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$, or R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_4, R_4', R_5 and R_5' are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_o is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $NR_{o1}R_{o2}$, or OR_{o3};

R_s is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or $NR_{s1}R_{s2}$;

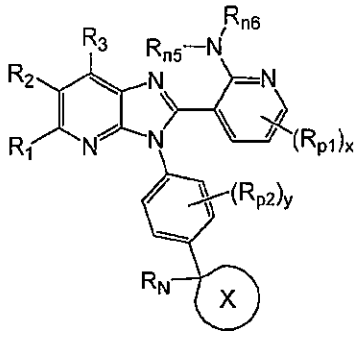
R_{o1} and R_{o2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_{o3} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S; and

R_{s1} and R_{s2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{s1} and R_{s2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S.

2. The compound of claim 1, wherein X_1 is N and X_2 is CR_x.

3. The compound of claim 1, having formula II:



(II),

or a pharmaceutically acceptable salt or ester thereof, wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$,

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_N is NR_9R_{10} or $C(O)R_{11}$;

R_9 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, $S(O)R_{12}$, or $S(O)_2R_{12}$;

R_{11} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, OR_{14}, or $NR_{14}R_{15}$;

R_{10}, R_{12}, R_{13}, R_{14} and R_{15} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S; and



is a 3-, 4-, 5-, 6- or 7-member carbocycle or heterocycle comprising 1-4 heteroatoms selected from N, O and S and is optionally substituted.

4. The compound of claim 3, wherein x is 0 and y is 0.

5. The compound of claim 3, wherein R_1 is unsubstituted or substituted phenyl.

6. The compound of claim 3, wherein 

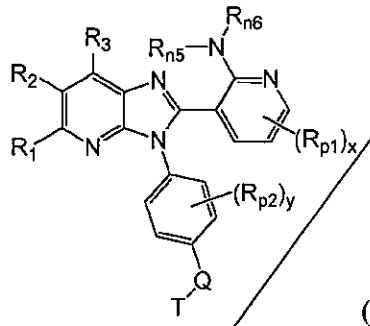
is unsubstituted or substituted carbocycle selected from cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cycloheptenyl, or a heterocycle selected from aziridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, diazetidinyl, dioxetanyl, dithietanyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, tetrahyrofuranyl, tetrahyrothiophenyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl, oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl,

piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, oxepanyl, thiepanyl, diazepanyl, oxazepanyl, and thiazepanyl.

7. The compound of claim 6, wherein  is unsubstituted or substituted cyclobutyl or unsubstituted or substituted oxetanyl

8. The compound of claim 3, wherein R_N is NH_2.

9. The compound of claim 1, having formula III:



(III),

or a pharmaceutically acceptable salt or ester thereof, wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$;

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

Q is a bond or unsubstituted or substituted C_1-C_6 alkyl linker;

T is $NR_{n1}R_{n2}$, $C(O)R_o$, $S(O)R_s$ or $S(O)_2R_s$;

R_{n1} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n2} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$, or R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_4, R_4', R_5 and R_5' are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_o is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $NR_{o1}R_{o2}$, or OR_{o3};

R_s is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and

1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or $NR_{s1}R_{s2}$;

R_{o1} and R_{o2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_{o3} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S; and

R_{s1} and R_{s2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{s1} and R_{s2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S.

10. The compound of claim 9, wherein x is 0 and y is 0.

11. The compound of claim 9, wherein Q is a bond.

12. The compound of claim 9, wherein Q is a methyl linker.

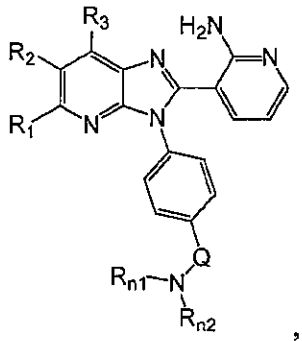
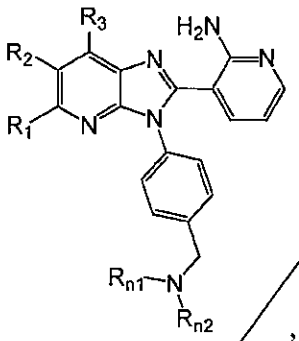
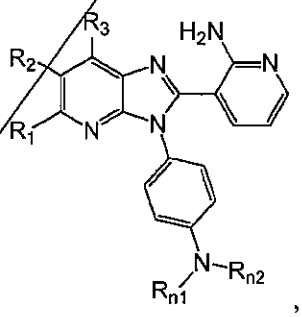
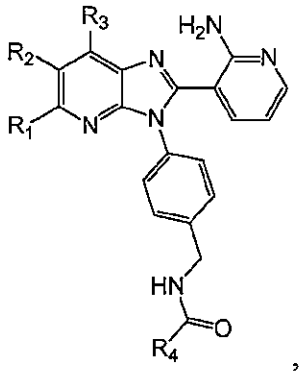
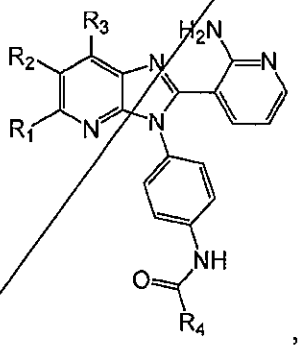
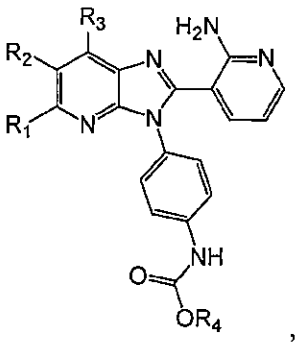
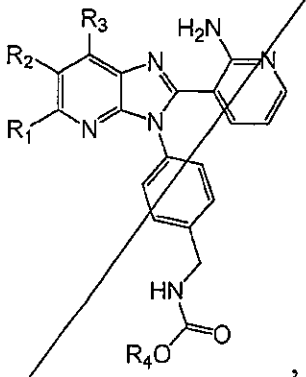
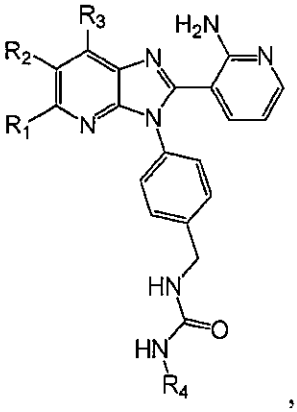
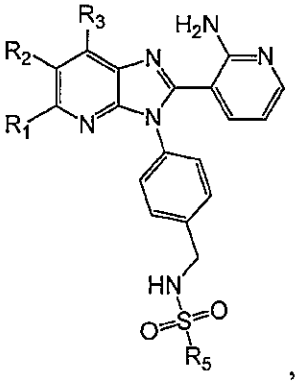
13. The compound of claim 9, wherein T is $NR_{n1}R_{n2}$.

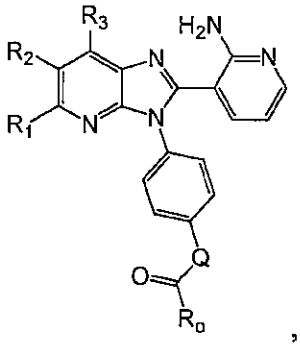
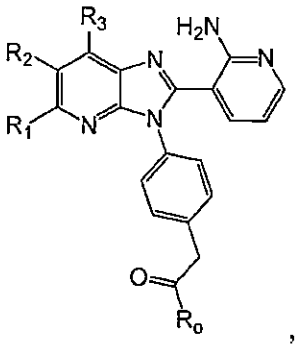
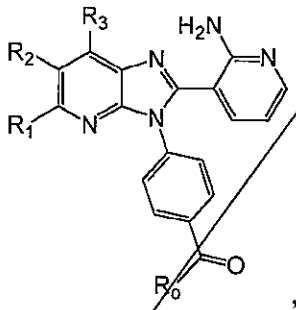
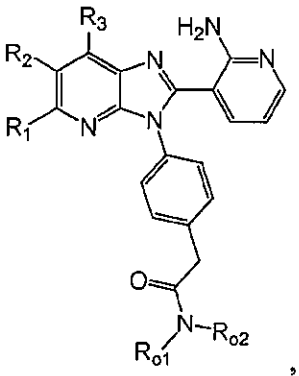
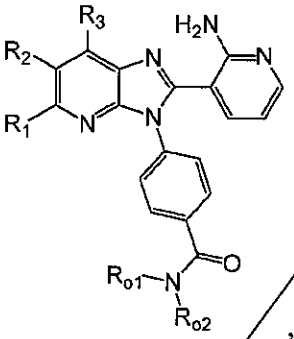
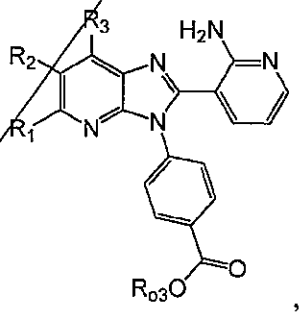
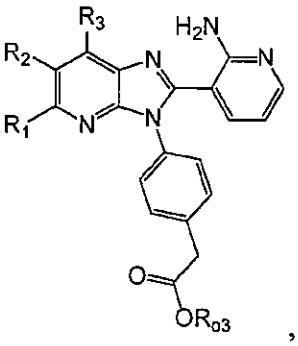
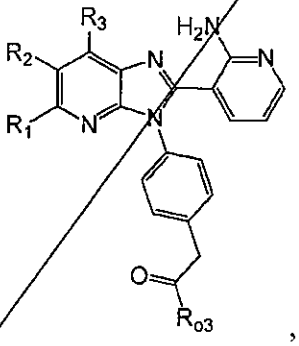
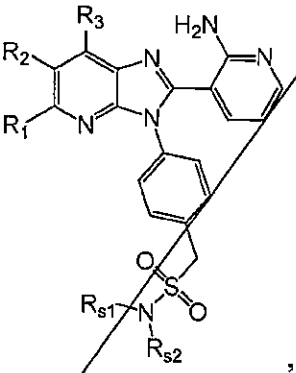
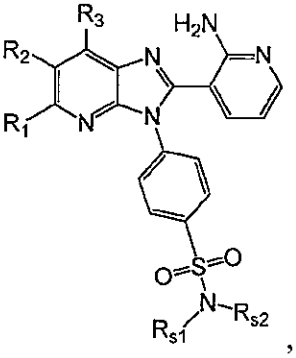
14. The compound of claim 13, wherein R_{n1} is $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, or $S(O)_2R_5$.

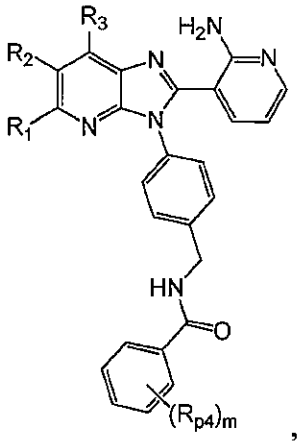
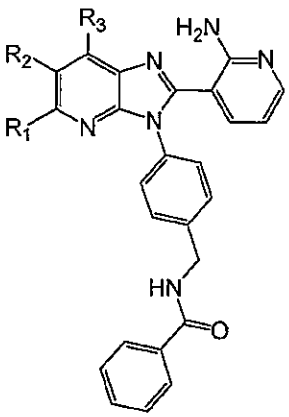
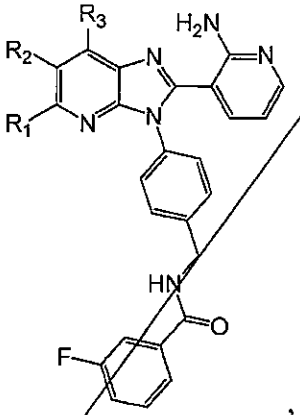
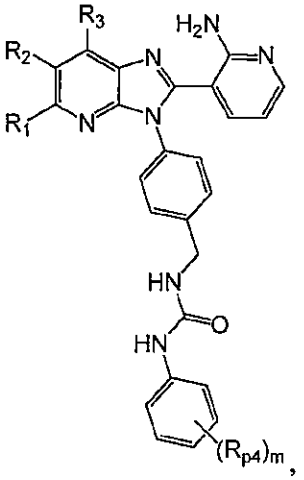
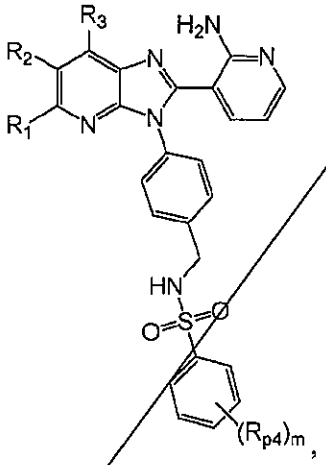
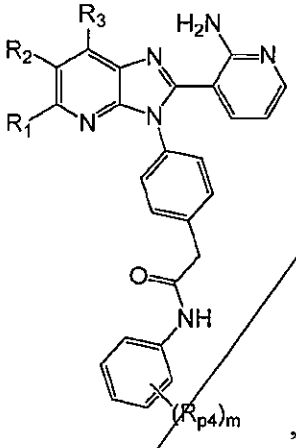
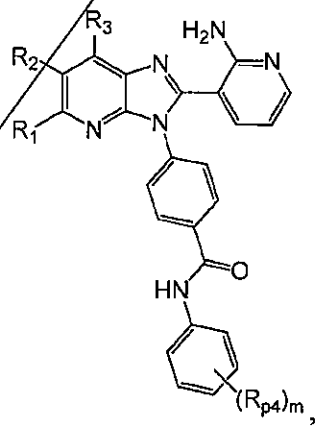
15. The compound of claim 9, wherein T is $C(O)R_o$.

16. The compound of claim 15, wherein R_o is $NR_{o1}R_{o2}$.

17. The compound of claim 9, having one of the following formulae:


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wherein:

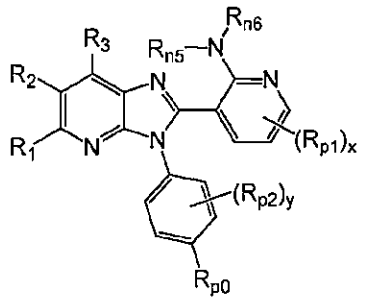
m is 0, 1, 2, 3, 4 or 5;

each R_{p4} is independently hydroxyl, cyano, nitro, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S,

unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_{22}$, $C(O)OR_{22}$, $NR_{22}'C(O)R_{22}$, and $NR_{22}'C(O)OR_{22}$; and

R_{22} and R_{22}' are each independently H, unsubstituted or substituted C_1-C_6 alkyl or unsubstituted or substituted C_6-C_{10} aryl.

18. The compound of claim 1, having formula IV:



(IV),

or a pharmaceutically acceptable salt or ester thereof, wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

R_{p0} is H, hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

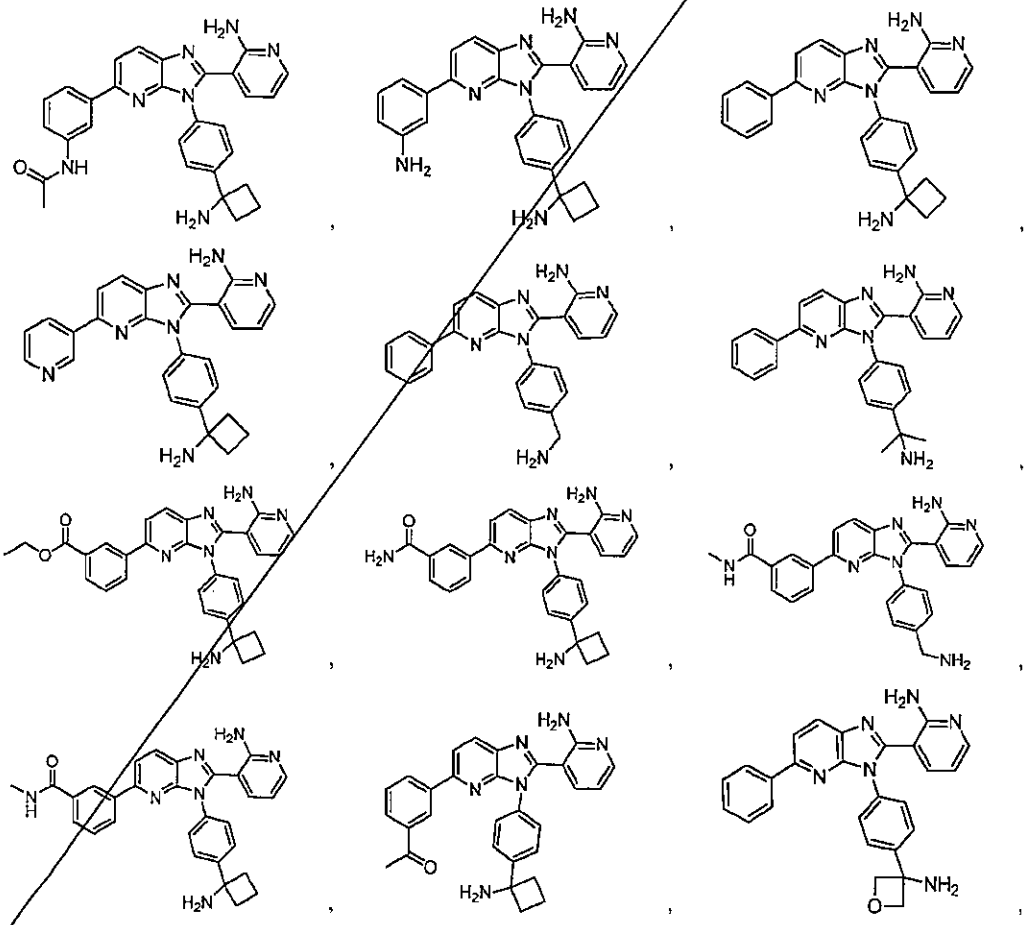
each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising

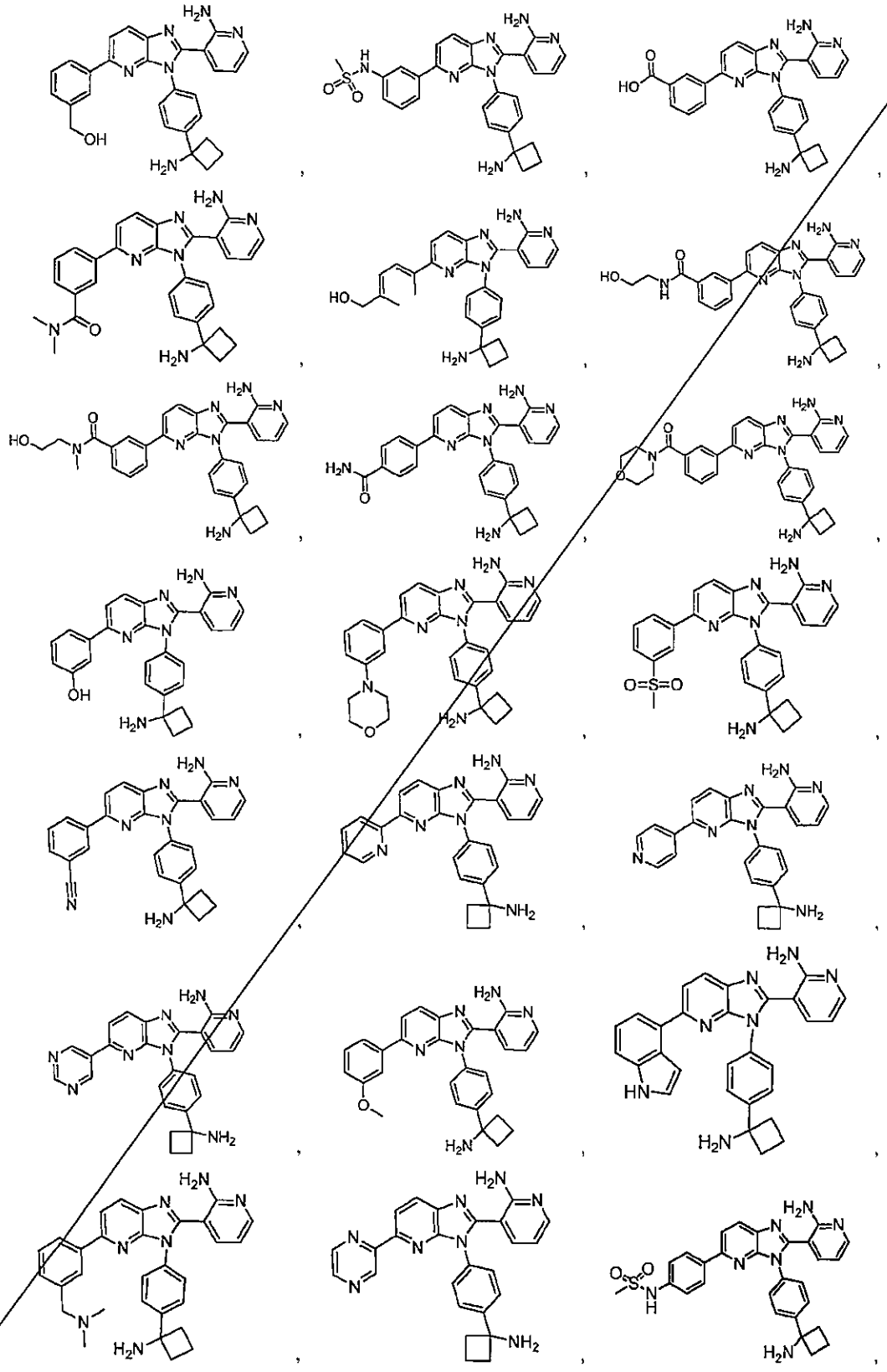
one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

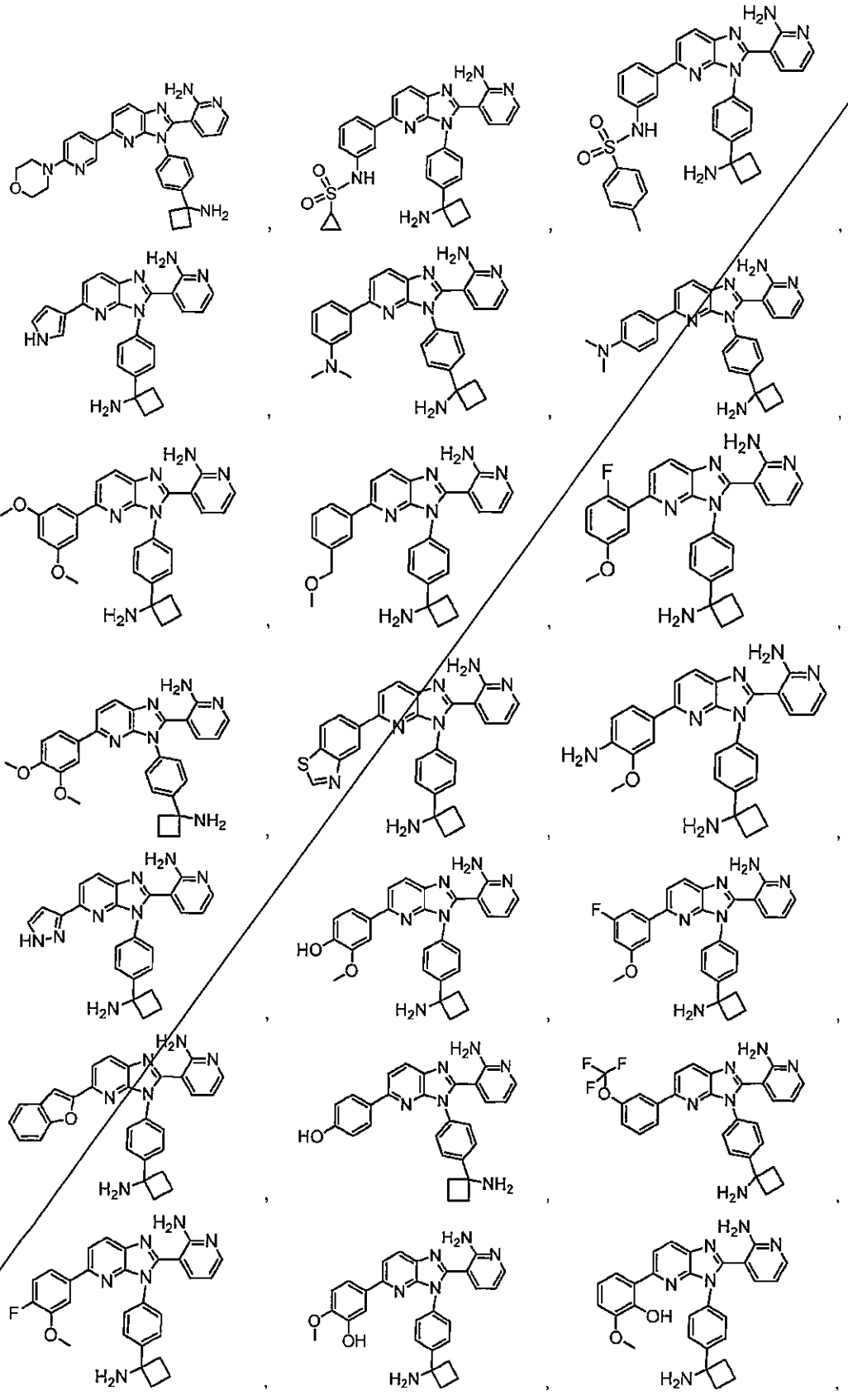
R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$; and

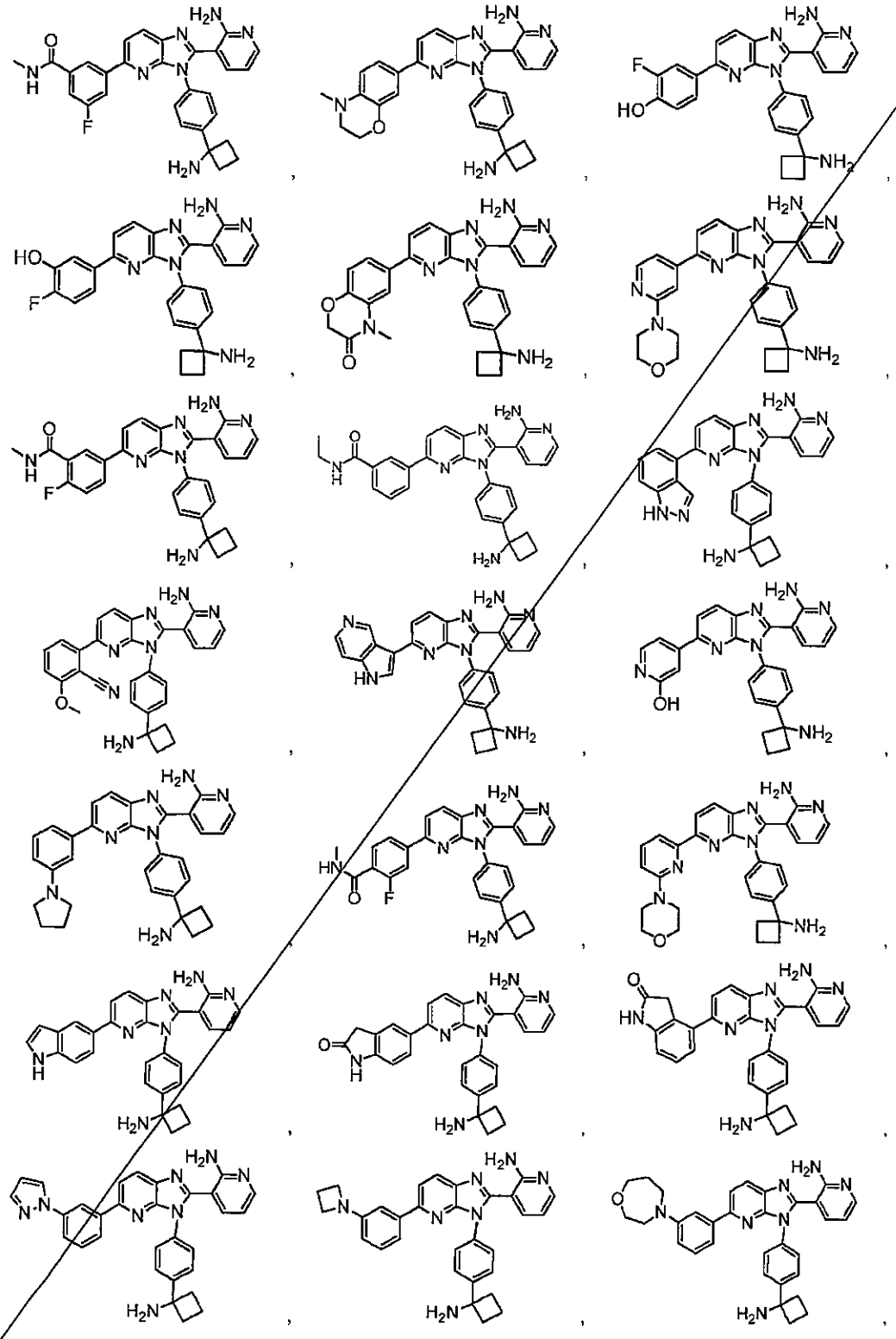
R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

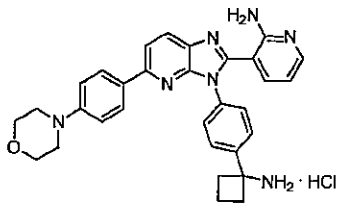
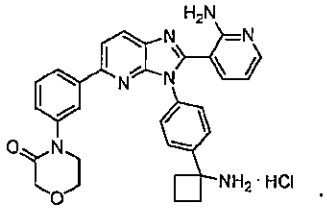
19. The compound of claim 1, selected from the group consisting of:



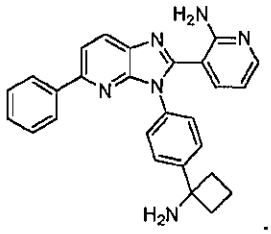






20. The compound of claim 19, wherein said compound is:



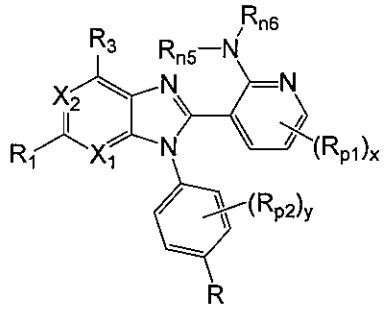
21. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1, or a salt, solvate, hydrate or prodrug thereof, and a pharmaceutically acceptable carrier or excipient.

22. A method of treating a cell proliferative disorder by administering to a subject in need thereof, a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt, prodrug, metabolite, analog or derivative thereof, in combination with a pharmaceutically acceptable carrier, such that the disorder is treated.

23. The method of claim 22, further comprising administering to the subject in need thereof, a second anti-proliferative agent.

CLAIMS

1. A compound having formula I:



(I),

or a pharmaceutically acceptable salt or ester thereof, wherein:

X_1 is N and X_2 is CR_x;

R_x, R_1 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$;

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4

heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R is H, hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 3-, 4-, 5-, 6- or 7-member rings and 1-4 heteroatoms selected from N, O and S, or Q-T;

Q is a bond or unsubstituted or substituted C_1-C_6 alkyl linker;

T is $NR_{n1}R_{n2}$, $C(O)R_o$, $S(O)R_s$ or $S(O)_2R_s$;

R_{n1} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n2} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$, or R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_4, R_4', R_5 and R_5' are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_o is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4

heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $NR_{o1}R_{o2}$, or OR_{o3};

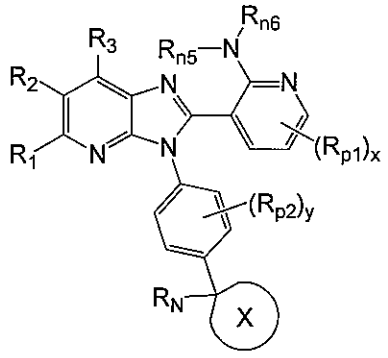
R_s is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or $NR_{s1}R_{s2}$;

R_{o1} and R_{o2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_{o3} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S; and

R_{s1} and R_{s2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{s1} and R_{s2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S.

2. The compound of claim 1, having formula II:



(II),

or a pharmaceutically acceptable salt or ester thereof, wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$,

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_N is NR_9R_{10} or $C(O)R_{11}$;

R_9 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{12}R_{13}$, $S(O)R_{12}$, or $S(O)_2R_{12}$;

R_{11} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, OR_{14}, or $NR_{14}R_{15}$;

R_{10}, R_{12}, R_{13}, R_{14} and R_{15} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S; and



is a 3-, 4-, 5-, 6- or 7-member carbocycle or heterocycle comprising 1-4 heteroatoms selected from N, O and S.

3. The compound of claim 2, wherein x is 0 and y is 0.

4. The compound of claim 2, wherein R_1 is unsubstituted or substituted phenyl.

5. The compound of claim 2, wherein 

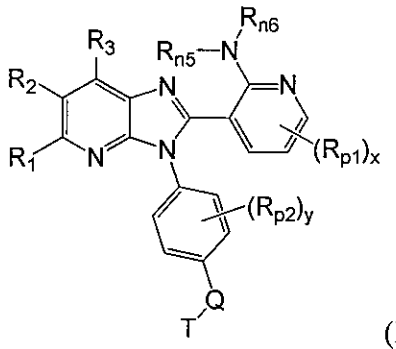
is unsubstituted or substituted carbocycle selected from cyclopropyl, cyclobutyl, cyclobutenyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, and cycloheptenyl, or a heterocycle selected from aziridinyl, oxiranyl, thiiranyl, azetidinyl, oxetanyl, thietanyl, diazetidinyl, dioxetanyl, dithietanyl, oxazetidinyl, thiazetidinyl, pyrrolidinyl, tetrahyrofuranyl, tetrahyrothiophenyl, imidazolidinyl, pyrazolidinyl, oxazolidinyl, isoxazolidinyl, thiazolidinyl, isothiazolidinyl, triazolidinyl,

oxadiazolidinyl, thiadiazolidinyl, piperidinyl, hexahydropyrimidinyl, piperazinyl, morpholinyl, oxazinanyl, thiazinanyl, azepanyl, oxepanyl, thiepanyl, diazepanyl, oxazepanyl, and thiazepanyl.

6. The compound of claim 5, wherein  is unsubstituted or substituted cyclobutyl or unsubstituted or substituted oxetanyl

7. The compound of claim 2, wherein R_N is NH_2.

8. The compound of claim 1, having formula III:



(III),

or a pharmaceutically acceptable salt or ester thereof, wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or

substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$;

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

Q is a bond or unsubstituted or substituted C_1-C_6 alkyl linker;

T is $NR_{n1}R_{n2}$, $C(O)R_o$, $S(O)R_s$ or $S(O)_2R_s$;

R_{n1} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n2} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, $S(O)R_5$, $S(O)_2R_5$, $S(O)NR_5'R_5$, or $S(O)_2NR_5'R_5$, or R_{n1} and R_{n2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_4, R_4', R_5 and R_5' are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_o is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4

heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $NR_{o1}R_{o2}$, or OR_{o3};

R_s is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or $NR_{s1}R_{s2}$;

R_{o1} and R_{o2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{o1} and R_{o2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S;

R_{o3} is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S; and

R_{s1} and R_{s2} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, or R_{s1} and R_{s2}, together with the nitrogen atom to which they attach, form a 4-, 5-, 6- or 7-member ring which optionally comprises 1-3 additional heteroatoms selected from N, O and S.

9. The compound of claim 8, wherein x is 0 and y is 0.

10. The compound of claim 8, wherein Q is a bond.

11. The compound of claim 8, wherein Q is a methyl linker.

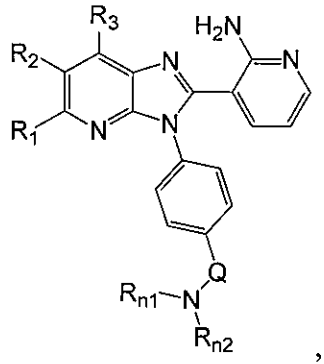
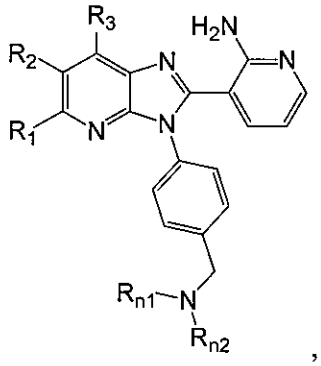
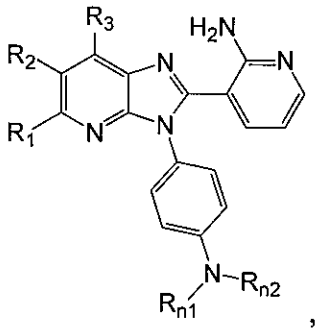
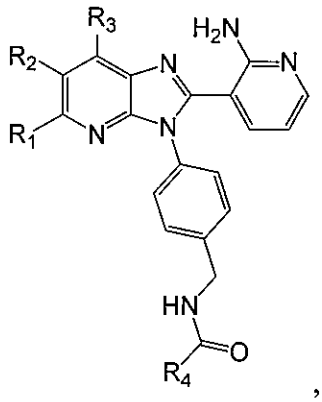
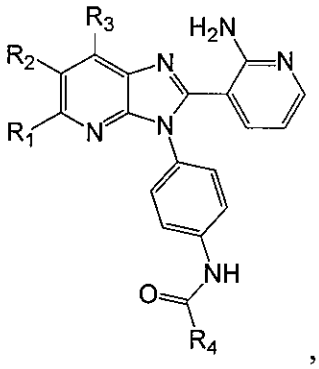
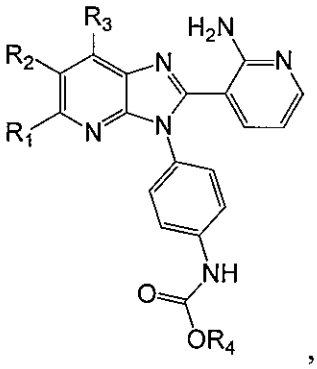
12. The compound of claim 8, wherein T is $NR_{n1}R_{n2}$.

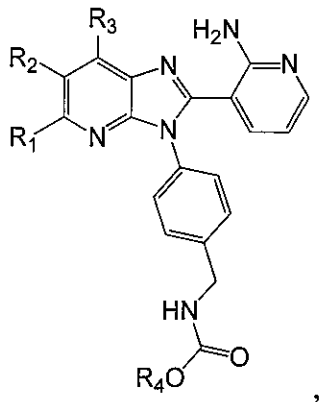
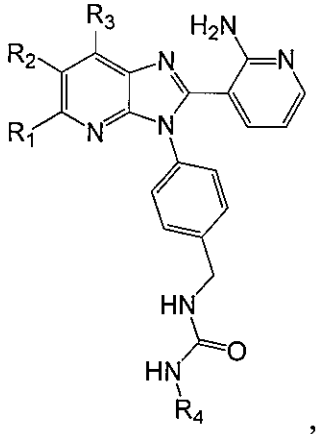
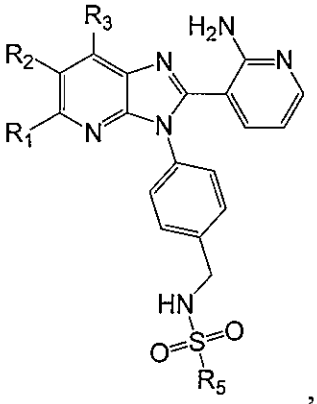
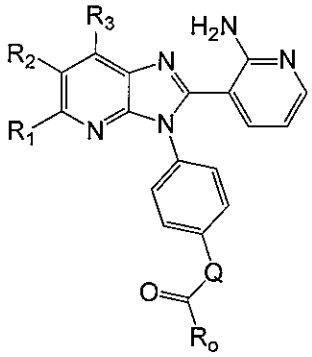
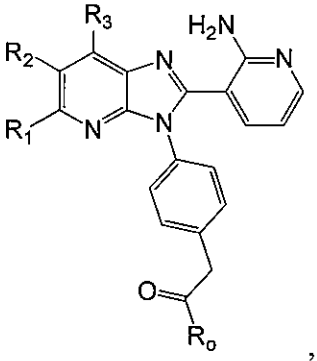
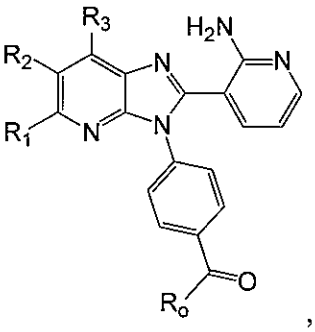
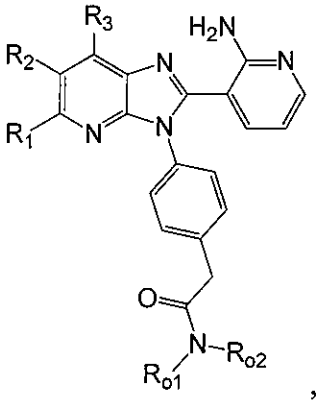
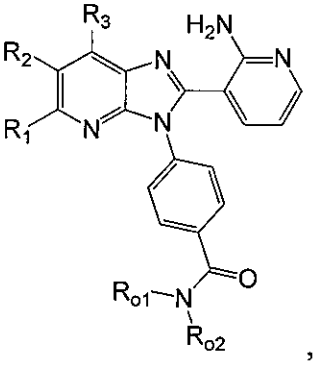
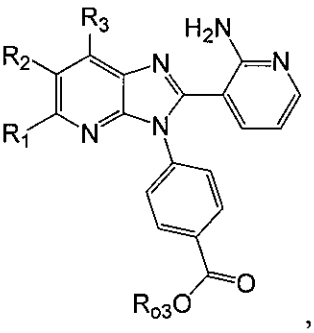
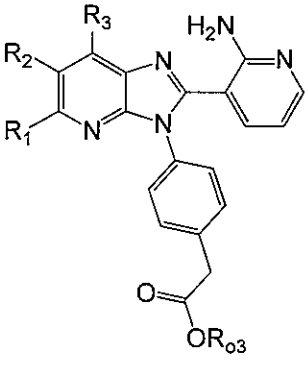
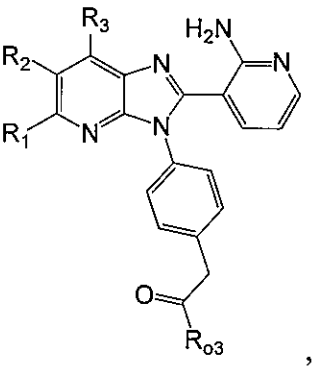
13. The compound of claim 12, wherein R_{n1} is $C(O)R_4$, $C(O)OR_4$, $C(O)NR_4'R_4$, or $S(O)_2R_5$.

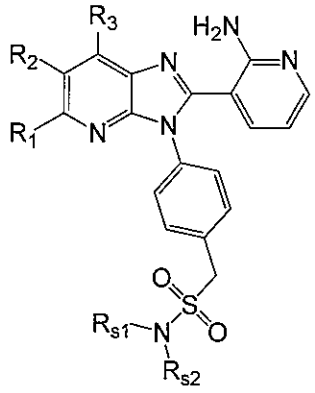
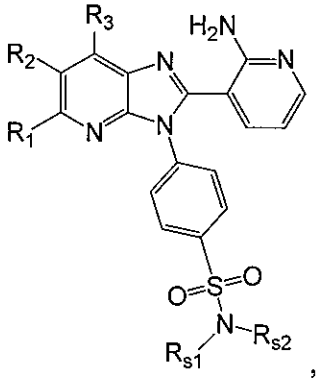
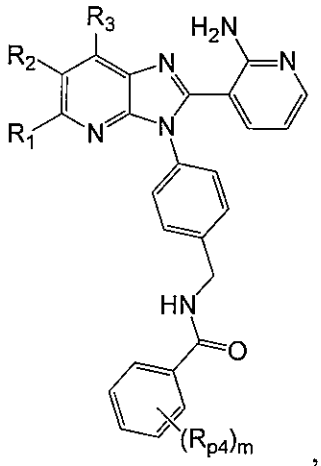
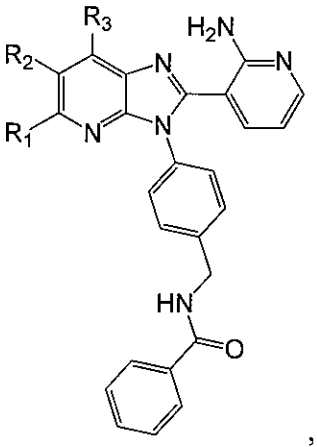
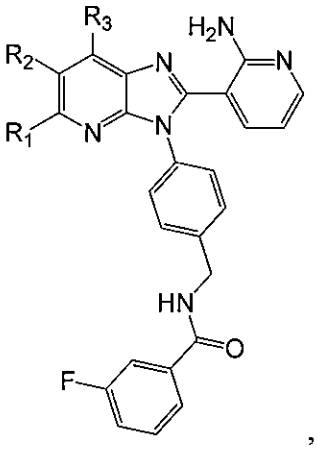
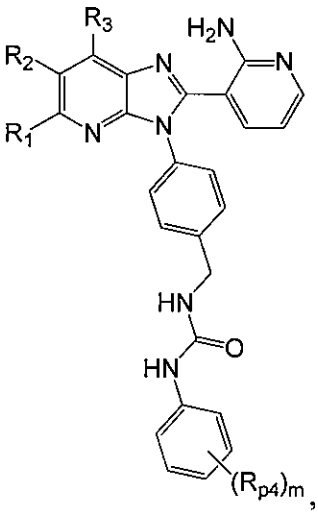
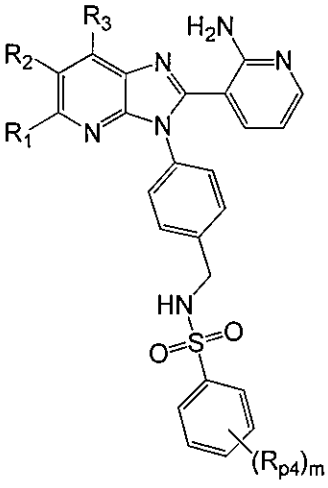
14. The compound of claim 8, wherein T is $C(O)R_o$.

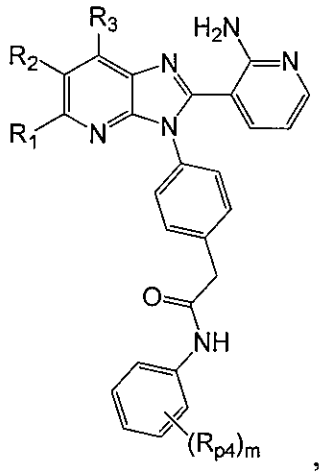
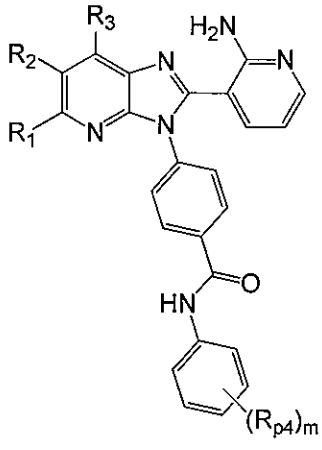
15. The compound of claim 4, wherein R_o is $NR_{o1}R_{o2}$.

16. The compound of claim 8, having one of the following formulae:


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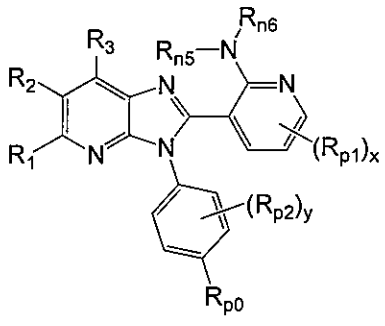
wherein:

m is 0, 1, 2, 3, 4 or 5;

each R_{p4} is independently hydroxyl, cyano, nitro, halogen, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, $C(O)R_{22}$, $C(O)OR_{22}$, $NR_{22}'C(O)R_{22}$, and $NR_{22}'C(O)OR_{22}$; and

R_{22} and R_{22}' are each independently H, unsubstituted or substituted C_1-C_6 alkyl or unsubstituted or substituted C_6-C_{10} aryl.

17. The compound of claim 1, having formula IV:



(IV),

or a pharmaceutically acceptable salt or ester thereof, wherein:

R_1, R_2 and R_3 are each independently H, hydroxyl, halogen, cyano, nitro, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted

amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

x is 0, 1, 2 or 3;

y is 0, 1, 2, 3 or 4;

R_{p0} is H, hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

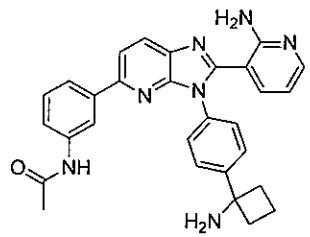
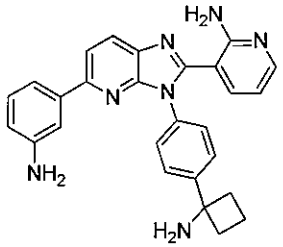
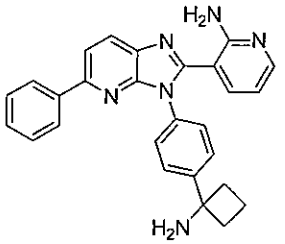
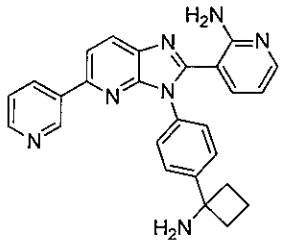
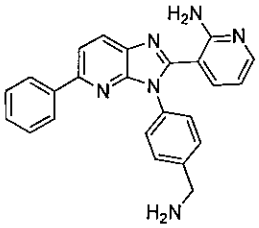
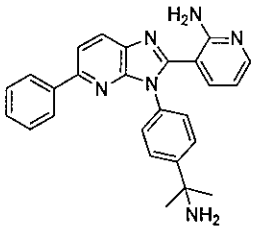
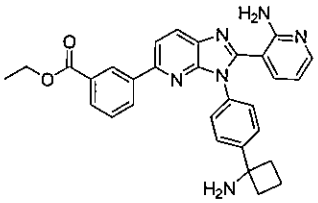
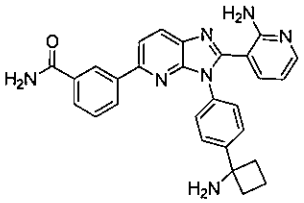
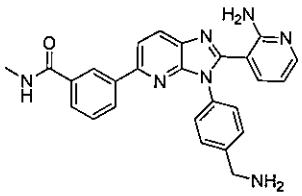
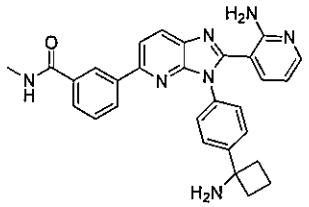
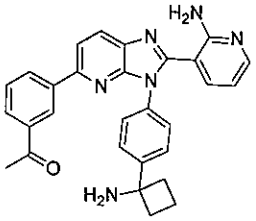
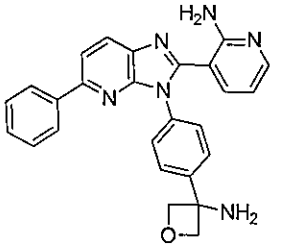
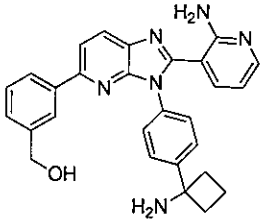
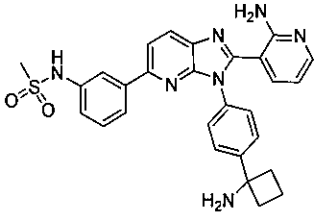
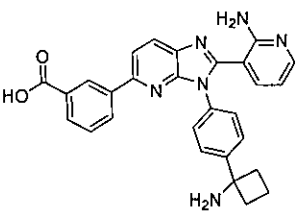
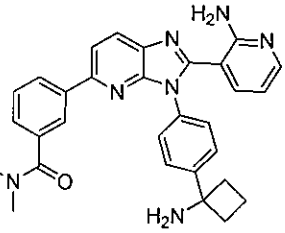
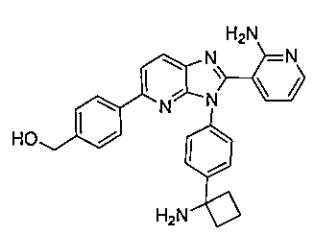
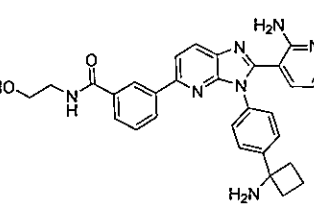
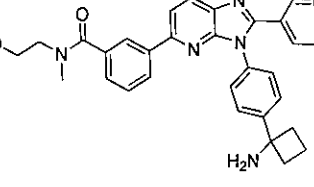
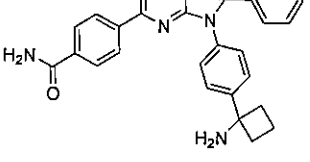
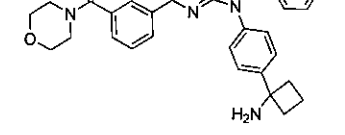
each R_{p1} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, or unsubstituted or substituted amino;

each R_{p2} is independently hydroxyl, halogen, nitro, cyano, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_1-C_6 alkoxy, unsubstituted or substituted amino, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S;

R_{n5} and R_{n6} are each independently H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted amino, $C(O)R_8$, $C(O)OR_8$, $S(O)R_8$, or $S(O)_2R_8$; and

R_8 is H, unsubstituted or substituted C_1-C_6 alkyl, unsubstituted or substituted C_6-C_{10} aryl, unsubstituted or substituted heteroaryl comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S, unsubstituted or substituted C_3-C_{10} carbocycle, or unsubstituted or substituted heterocycle comprising one or two 5- or 6-member rings and 1-4 heteroatoms selected from N, O and S.

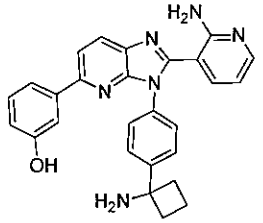
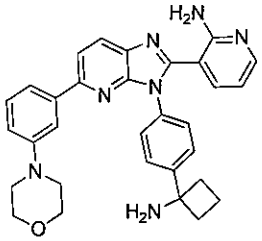
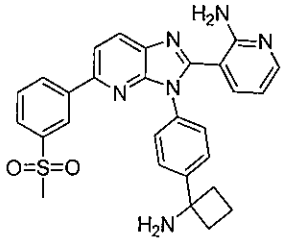
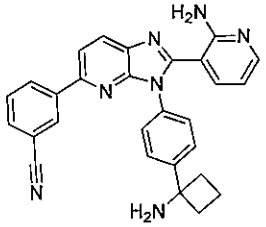
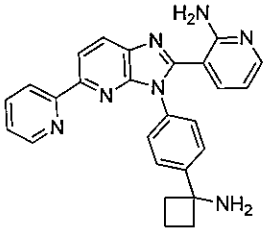
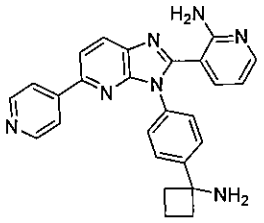
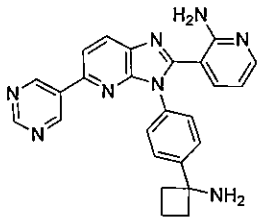
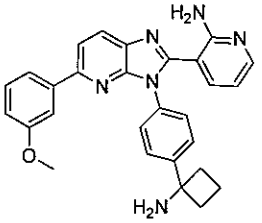
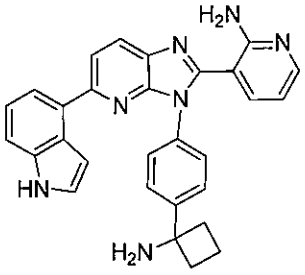
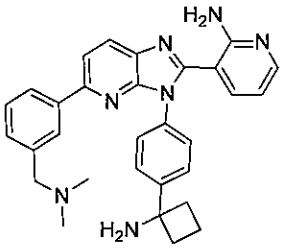
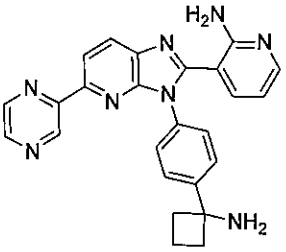
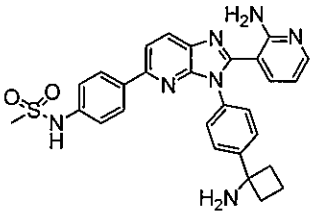
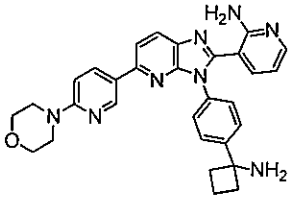
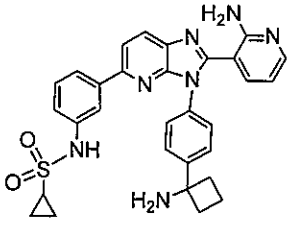
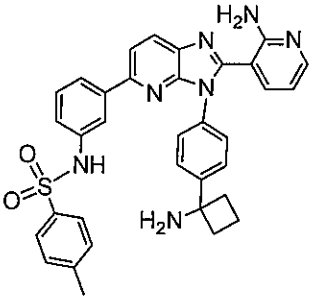
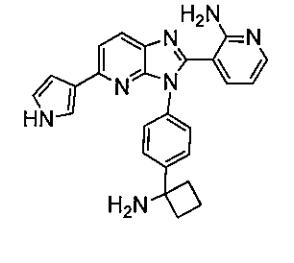
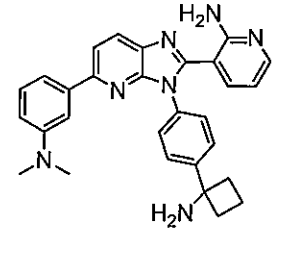
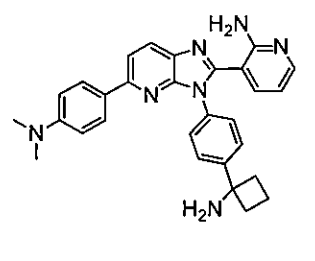
18. The compound of claim 1, selected from the group consisting of:

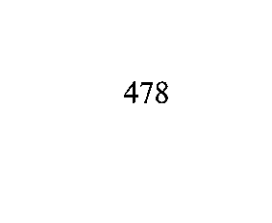

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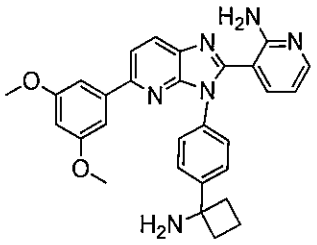
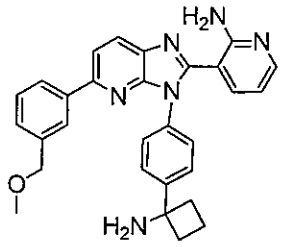
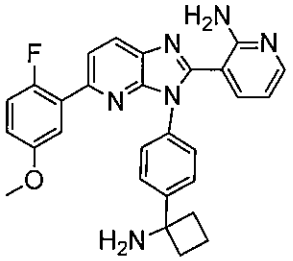
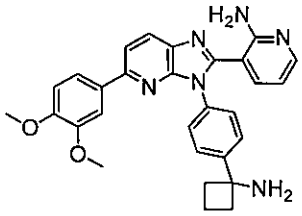
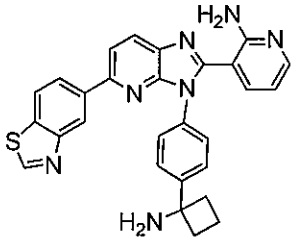
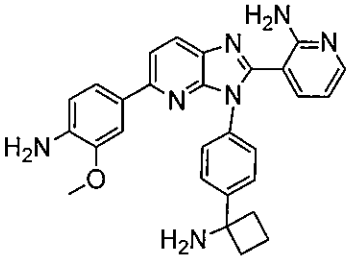
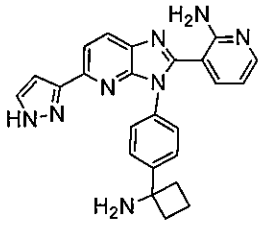
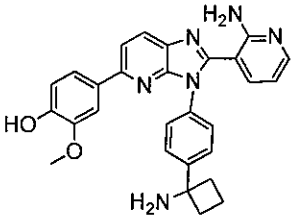
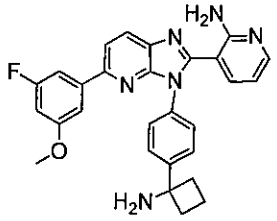
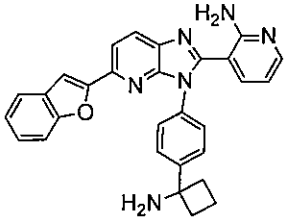
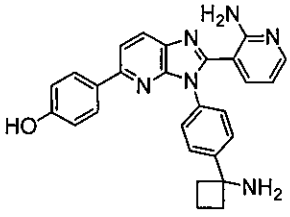
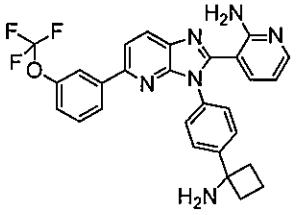
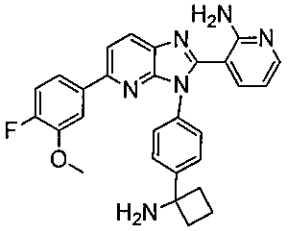
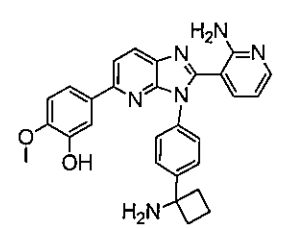
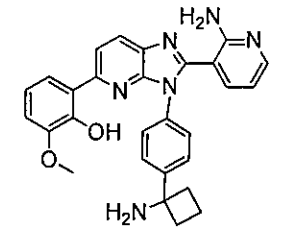
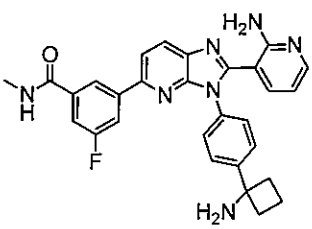
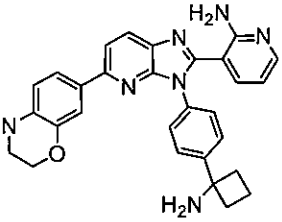
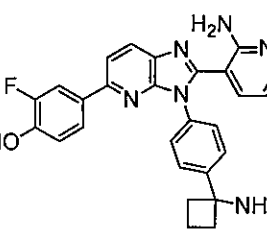
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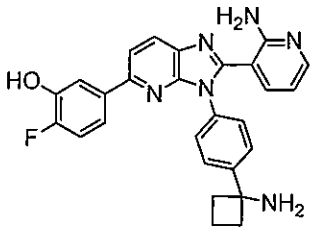
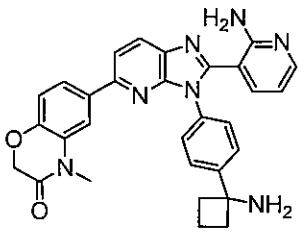
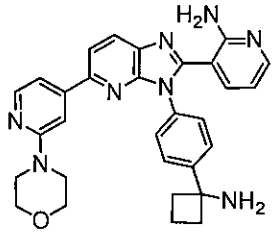
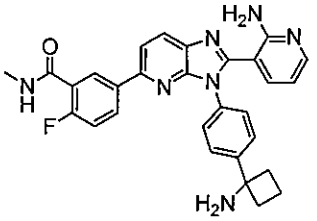
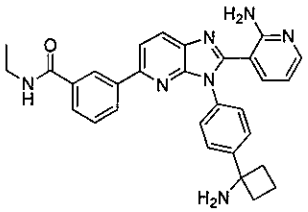
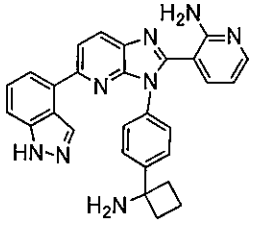
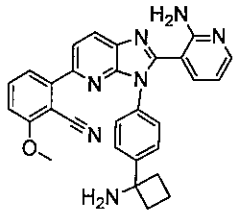
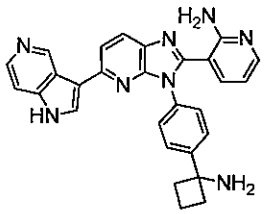
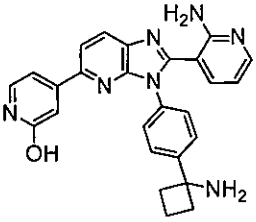
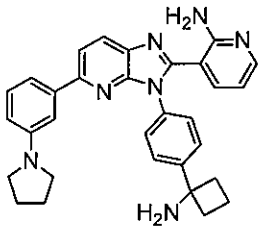
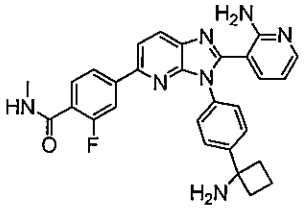
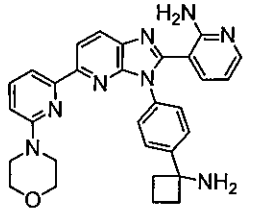
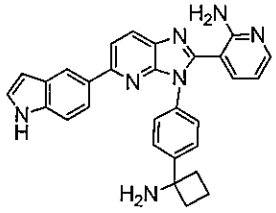
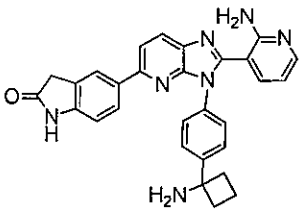
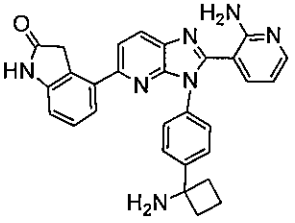
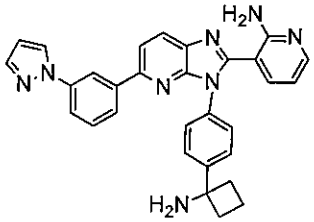
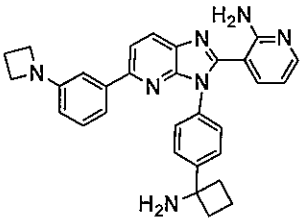
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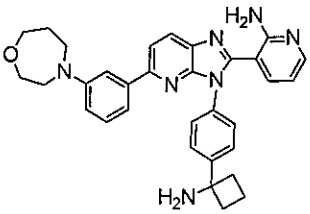
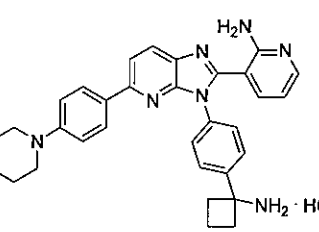
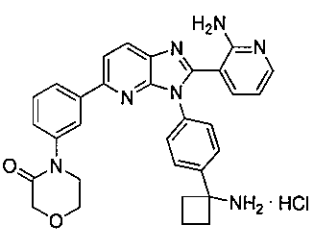
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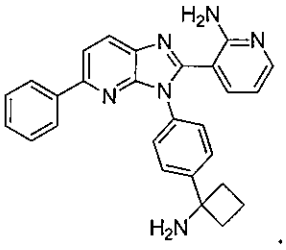
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19. The compound of claim 18, wherein said compound is:



20. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1 or a salt thereof, and a pharmaceutically acceptable carrier or excipient.

21. A method of treating a cell proliferative disorder by administering to a subject in need thereof, a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, such that the disorder is treated.

22. The method of claim 21, further comprising administering to the subject in need thereof, a second anti-proliferative agent.