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(54) Title: COMBINATION THERAPIES WITH SETD2 INHIBITORS

(57) Abstract: The present disclosure provides SETD2 protein inhibitors, and methods, uses, compositions, and kits for treating diseases, disorders, or conditions in a subject with a SETD2 protein inhibitor and a Second Therapeutic Agent, wherein the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

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COMBINATION THERAPIES WITH SETD2 INHIBITORS

BACKGROUND OF THE INVENTION

Field of the Invention

[0001] The present disclosure provides SETD2 protein inhibitors, and methods, uses, compositions, and kits for treating diseases, disorders, or conditions in a subject with a SETD2 protein inhibitor in combination with a Second Therapeutic Agent, wherein the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

Background

[0002] The selective addition of methyl groups to specific amino acid sites on histones is controlled by the action of a family of enzymes known as histone methyltransferases (HMTs). The level of expression of a particular gene is influenced by the presence or absence of one or more methyl groups at a relevant histone site. The specific effect of a methyl group at a particular histone site persists until the methyl group is removed by a histone demethylase, or until the modified histone is replaced through nucleosome turnover. In a like manner, other enzyme classes can decorate DNA and histones with other chemical species, and still other enzymes can remove these species to provide control of gene expression.

[0003] SETD2 is a human histone methyltransferase located at the cytogenic band p21.31 of chromosome 3 (3p21.31). The acronym "SETD2" stands for Suppressor of variegation, Enhancer of zeste, and Trithorax domain containing 2. The SETD2 protein comprises three conserved functional domains: (1) the triplicate AWS-SET-PostSET domain; (2) a WW domain; and (3) a Set2-Rbp1 interacting ("SRI") domain. These three functional domains define the biological function of SETD2. *See*, Li, J. *et al.*, *Oncotarget* *7*:50719-50734 (2016). SETD2 is believed to be the single human gene responsible for

the trimethylation of lysine 36 (Lys-36) of histone H3 (H3K36me3) using dimethylated Lys-36 (H3K36me2) as substrate. Edmunds, J.W. *et al., The EMBO Journal 27*:406–420 (2008).

[0004] Human SETD2 has been shown to have tumor suppressor functionality. Li, J. *et al.*, *Oncotarget 7*:50719-50734 (2016). For example, inactivation of human SETD2 has been reported in renal cell carcinoma (RCC). Larkin, J., *et al., Nature Reviews 9*:147-155 (2012). Also, expression levels of SETD2 in breast cancer samples have been reported as significantly lower than in adjacent non-cancerous tissue (ANCT) samples. Newbold, R.F. and Mokbel, K., *Anticancer Research 30*: 3309-3311 (2010). Additionally, biallelic mutations and loss-of-function point mutations in SETD2 were reported in patients with acute leukemia. Zhu, X. *et al.*, *Nature Genetics 46*: 287-293 (2014). Mutations in SETD2 have also been reported in pediatric high-grade gliomas. Fontebasso, A.M. *et al.*, *Acta Neuropathol. 125*: 659-669 (2013).

BRIEF SUMMARY OF THE INVENTION

[0005] The present disclosure generally provides SETD2 protein inhibitors, and methods, uses, compositions, and kits for treating diseases, disorders, or conditions in a subject with a SETD2 protein inhibitor and a Second Therapeutic Agent, wherein the second therapeutic agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

[0006] In one aspect, the present disclosure provides methods of treating diseases, disorders, or conditions, e.g., cancer, in a subject in need thereof with:

[0007] (1) a therapeutically effective amount of a substituted indole represented by any one of Formulae **I**, **II**, **II-A**, **III**, **III-A**, **IV**, **IV-A**, **IV-B**, **IV-C**, **IV-D**, **V**, **V-A**, **V-B**, **VI**, **VII**, **VII-A**, **VII-B**, **VII-C**, **VII-D**, **VII-E**, **VII-F**, **VII-G**, **VII-H**, **VIII**, **VIII-A**, or **VIII-B**, or a compound of Table 1, or a compound of Table 1B, below, and the

pharmaceutically acceptable salts and solvates thereof, collectively referred to herein as a "Compounds of the Disclosure;" and

[0008] (2) a therapeutically effective amount of a Second Therapeutic Agent,

[0009] wherein the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

[0010] In another aspect, the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, or one or more CARM1 inhibitors, or a combination thereof.

[0011] In another aspect, the present disclosure provides methods of treating diseases, disorders, or conditions, e.g., cancer, in a subject in need thereof with:

[0012] (1) a therapeutically effective amount of a Compound of the Disclosure;

[0013] (2) a therapeutically effective amount of a Second Therapeutic Agent; and

[0014] (3) a therapeutically effective amount of a Third Therapeutic Agent.

[0015] wherein the Third Therapeutic Agent comprises one or more glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

[0016] In another aspect, the present disclosure provides a Compound of the Disclosure for use in treating cancer, e.g., multiple myeloma, in a subject in need thereof, wherein the Compound of the Disclosure is to be administered to the subject in combination with a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent.

[0017] In another aspect, the present disclosure provides a Compound of the Disclosure for use in the manufacture of a medicament for treating cancer in a mammal, wherein the

Compound of the Disclosure is to be administered to the subject in combination with a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent.

[0018] In another aspect, the present disclosure provides a kit comprising a Compound of the Disclosure and a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent

[0019] In another aspect, the present disclosure provides a pharmaceutical composition comprising a Compound of the Disclosure and a pharmaceutically acceptable carrier, for use in treating a disease, disorder, or condition in a subject in combination with a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent.

[0020] Additional embodiments and advantages of the disclosure will be set forth, in part, in the description that follows, and will flow from the description, or can be learned by practice of the disclosure. The embodiments and advantages of the disclosure will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

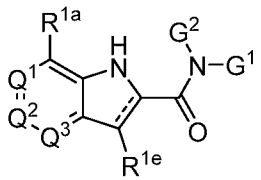
[0021] It is to be understood that both the foregoing summary and the following detailed description are exemplary and explanatory only, and are not restrictive of the invention as claimed.

DETAILED DESCRIPTION OF THE INVENTION

I. Compounds of the Disclosure

[0022] Certain Compounds of the Disclosure are disclosed in WO 2020/037079 and WO 2021/168313 as SETD2 inhibitors. WO 2020/037079 and WO 2021/168313 are fully incorporated by reference herein in its entirety.

[0023] In one embodiment, Compounds of the Disclosure are compounds having Formula **I**:



I,

wherein:

[0024] R^{1a} is selected from the group consisting of halogen, alkyl, alkoxy, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

[0025] Q^1 is selected from the group consisting of -C(R^{1b})= and –N=;

[0026] Q^2 is selected from the group consisting of -C(R^{1c})= and –N=;

[0027] Q^3 is selected from the group consisting of -C(R^{1d})= and –N=;

[0028] provided that at least one of Q^1, Q^2, or Q^3 is -C(R^{1b})=, -C(R^{1c})=, or -C(R^{1d})=, respectively;

[0029] R^{1b}, R^{1c}, and R^{1d} are each independently selected from the group consisting of hydrogen, halogen, alkyl, alkenyl, (hydroxy)alkyl, and alkoxy;

[0030] R^{1e} is selected from the group consisting of hydrogen, halogen, alkyl, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

[0031] ---- is a single or double bond;

[0032] G^1 is selected from the group consisting of optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, optionally substituted cycloalkyl, (aryl)alkyl, (heteroaryl)alkyl, (heterocyclo)alkyl, (amino)(aryl)alkyl, (heteroaryl)(aryl)alkyl, (heteroaryl)(heterocyclo)alkyl, (heteroaryl)(carboxamido)alkyl, (heteroaryl)(cycloalkyl)alkyl, (aryl)(alkoxycarbonyl)alkyl, (cycloalkyl)alkyl, (heteroaryl)(amino)alkyl, (cycloalkyl)(alkoxycarbonyl)alkyl, (heteroaryl)(alkoxycarbonyl)alkyl, (heterocyclo)(cycloalkyl)alkyl, (aryl)(cycloalkyl)alkyl, (aryl)(hydroxy)alkyl, (cycloalkyl)(hydroxy)alkyl, (hydroxy)alkyl, optionally substituted alkyl, (aryl)(haloalkyl)alkyl, (cycloalkyl)(haloalkyl)alkyl, (hydroxy)(haloalkyl)alkyl, and (alkoxycarbonyl)(haloalkyl)alkyl; and

[0033] G^2 is selected from the group consisting of hydrogen and alkyl; or

[0034] G^1 and G^2 taken together with the nitrogen atom to which they are attached form an optionally substituted heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

[0035] In another embodiment, the compound having Formula **I** is not N-(1-(1-(L-alanyl)piperidin-4-yl)ethyl)-7-methyl-1H-indole-2-carboxamide, N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-7-methyl-1H-indole-2-carboxamide, or N-((1r,4r)-4-aminocyclohexyl)-7-methyl-1H-indole-2-carboxamide.

[0036] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein:

[0037] R^{1a} is selected from the group consisting of halogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_3-C_8 cycloalkyl, (hydroxy)C_{1-6} alkyl, and (C_3-C_6 cycloalkyl)C_{1-6} alkyl;

[0038] R^{1b}, R^{1c}, and R^{1d} are each independently selected from the group consisting of hydrogen, halogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, (hydroxy)C_1-C_6 alkyl, and C_1-C_6 alkoxy;

[0039] R^{1e} is selected from the group consisting of hydrogen and C_1-C_6 alkyl;

[0040] G^1 is selected from the group consisting of optionally substituted C_6-C_{10} aryl, optionally substituted 5- to 10-membered heteroaryl, optionally substituted 3- to 10-membered heterocyclo, optionally substituted C_3-C_8 cycloalkyl, (C_6-C_{10} aryl)C_1-C_6 alkyl, (5- to 10-membered heteroaryl)C_1-C_6 alkyl, (3- to 10-membered heterocyclo)C_1-C_6 alkyl, (amino)(C_6-C_{10} aryl)C_1-C_6 alkyl, (5- to 14-membered heteroaryl)(C_6-C_{10} aryl)C_1-C_6 alkyl, (5- to 10-membered heteroaryl)(3- to 10-membered heterocyclo)C_1-C_6 alkyl, (5- to 10-membered heteroaryl)(carboxamido)C_1-C_6 alkyl, (5- to 10-membered heteroaryl)(C_3-C_6 cycloalkyl)C_1-C_6 alkyl, (C_6-C_{10} aryl)(alkoxycarbonyl)C_1-C_6 alkyl, (C_3-C_6 cycloalkyl)C_1-C_6 alkyl, (5- to 10-membered heteroaryl)(amino)C_1-C_6 alkyl, (C_3-C_6 cycloalkyl)(alkoxycarbonyl)C_1-C_6 alkyl, (5- to 14-membered heteroaryl)(alkoxycarbonyl)C_1-C_6 alkyl, (3- to 14-membered heterocyclo)(C_3-C_8 cycloalkyl)C_1-C_6 alkyl, (C_{6-10} aryl)(C_3-C_8 cycloalkyl)C_1-C_6 alkyl, (C_6-C_{10} aryl)(hydroxy)C_1-C_6 alkyl, (C_3-C_6 cycloalkyl)(hydroxy)C_1-C_6 alkyl, (hydroxy)C_1-C_6 alkyl, optionally substituted C_1-C_6 alkyl, (C_6-C_{10} aryl)(C_1-C_6 haloalkyl)C_1-C_6 alkyl, (C_3-C_6 cycloalkyl)(C_1-C_6 haloalkyl)C_1-C_6 alkyl, (hydroxy)(C_1-C_6 haloalkyl)C_1-C_6 alkyl; and (alkoxycarbonyl)(C_1-C_6 haloalkyl)C_1-C_6 alkyl; and

[0041] G^2 is selected from the group consisting of hydrogen and C_1-C_6 alkyl; or

[0042] G^1 and G^2 taken together with the nitrogen atom to which they are attached form a 5- to 10-membered optionally substituted heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

[0043] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein:

[0044] R^{1a} is selected from the group consisting of halogen, C_1-C_3 alkyl, C_1-C_3 alkoxy, C_3-C_6 cycloalkyl, (hydroxy)C_{1-4} alkyl, and (C_3-C_6 cycloalkyl)C_{1-4} alkyl;

[0045] R^{1b}, R^{1c}, and R^{1d} are each independently selected from the group consisting of hydrogen, halogen, C_1-C_3 alkyl, C_2-C_4 alkenyl, (hydroxy)C_1-C_4 alkyl, and C_1-C_3 alkoxy;

[0046] R^{1e} is selected from the group consisting of hydrogen and C_1-C_3 alkyl;

[0047] G^1 is selected from the group consisting of optionally substituted C_6-C_{10} aryl, optionally substituted 5- to 10-membered heteroaryl, optionally substituted 3- to 10-membered heterocyclo, optionally substituted C_3-C_8 cycloalkyl, (C_6-C_{10} aryl)C_1-C_4

alkyl, (5- to 10-membered heteroaryl)C_1-C_6 alkyl, (3- to 10-membered heterocyclo)C_1-C_4 alkyl, (amino)(C_6-C_{10} aryl)C_1-C_6 alkyl, (5- to 14-membered heteroaryl)(C_6-C_{10} aryl)C_1-C_4 alkyl, (5- to 10-membered heteroaryl)(3- to 10-membered heterocyclo)C_1-C_4 alkyl, (5- to 10-membered heteroaryl)(carboxamido)C_1-C_4 alkyl, (5- to 10-membered heteroaryl)(C_3-C_6 cycloalkyl)C_1-C_4 alkyl, (C_6-C_{10} aryl)(alkoxycarbonyl)C_1-C_4 alkyl, (C_3-C_6 cycloalkyl)C_1-C_4 alkyl, (5- to 10-membered heteroaryl)(amino)C_1-C_4 alkyl, (C_3-C_6 cycloalkyl)(alkoxycarbonyl)C_1-C_4 alkyl, (5- to 14-membered heteroaryl)(alkoxycarbonyl)C_1-C_4 alkyl, (3- to 14-membered heterocyclo)(C_3-C_6 cycloalkyl)C_1-C_4 alkyl, (C_{6-10} aryl)(C_3-C_6 cycloalkyl)C_1-C_4 alkyl, (C_6-C_{10} aryl)(hydroxy)C_1-C_4 alkyl, (C_3-C_6 cycloalkyl)(hydroxy)C_1-C_4 alkyl, (hydroxy)C_1-C_4 alkyl, optionally substituted C_1-C_4 alkyl, (C_6-C_{10} aryl)(C_1-C_4 haloalkyl)C_1-C_4 alkyl, (C_3-C_6 cycloalkyl)(C_1-C_4 haloalkyl)C_1-C_4 alkyl, (hydroxy)(C_1-C_4 haloalkyl)C_1-C_4 alkyl, and (alkoxycarbonyl)(C_1-C_4 haloalkyl)C_1-C_4 alkyl; and

[0048] G^2 is selected from the group consisting of hydrogen and C_1-C_4 alkyl; or

[0049] G^1 and G^2 taken together with the nitrogen atom to which they are attached form a 5- to 10-membered optionally substituted heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

[0050] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein ---- is a double bond, or a pharmaceutically acceptable salt or solvate thereof.

[0051] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein Q^1 and Q^2 are -C(H)=, or a pharmaceutically acceptable salt or solvate thereof.

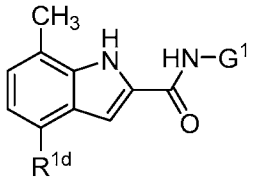
[0052] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein Q^3 is -C(R^{1d})=; and R^{1d} is selected from the group consisting of hydrogen and halo, or a pharmaceutically acceptable salt or solvate thereof.

[0053] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein R^{1e} is hydrogen, or a pharmaceutically acceptable salt or solvate thereof.

[0054] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein R^{1a} is C_1-C_3 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0055] In another embodiment, Compounds of the Disclosure are compounds having Formula **I**, wherein G^2 is hydrogen, or a pharmaceutically acceptable salt or solvate thereof.

[0056] In another embodiment, Compounds of the Disclosure are compounds having Formula **II**:

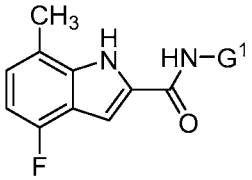


II,

or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1d} and G^1 are as defined in connection with Formula **I**.

[0057] In another embodiment, Compounds of the Disclosure are compounds having Formulae **I** or **II**, wherein R^{1d} is selected from the group consisting of hydrogen and fluoro, or a pharmaceutically acceptable salt or solvate thereof.

[0058] In another embodiment, Compounds of the Disclosure are compounds having Formula **II-A**:

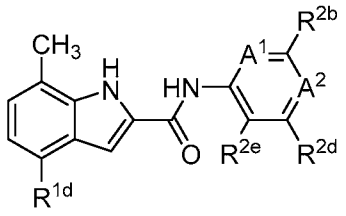


II-A,

or a pharmaceutically acceptable salt or solvate thereof, wherein G^1 is as defined in connection with Formula **II**.

[0059] In another embodiment, Compounds of the Disclosure are compounds having Formulae **I**, **II**, or **II-A**, wherein G^1 is selected from the group consisting of optionally substituted C_6-C_{10} aryl, optionally substituted 5- to 9-membered heteroaryl, optionally substituted 3- to 10-membered heterocyclo, optionally substituted C_6-C_8 cycloalkyl, (5- to 9-membered heteroaryl)C_1-C_6 alkyl, (5- to 9-membered heteroaryl)(C_{6-10} aryl)C_1-C_4 alkyl, (5- to 9-membered heteroaryl heteroaryl)(C_3-C_6 cycloalkyl)C_1-C_4 alkyl, and (C_3-C_6 cycloalkyl)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0060] In another embodiment, Compounds of the Disclosure are compounds having Formula **III**:



III,

wherein:

[0061] A^1 is selected from the group consisting of -N= and -C(R^{2a})=;

[0062] R^{2a} is selected from the group consisting of hydrogen, alkyl, halogen, and haloalkyl;

[0063] R^{2b} is selected from the group consisting of optionally substituted alkyl, optionally substituted heterocyclo, optionally substituted cycloalkyl, optionally substituted heteroaryl, optionally substituted aryl, (carboxamido)alkyl, -OR^{10c}, amino, (heterocyclo)alkyl, (amino)alkyl, (hydroxy)alkyl, carboxamido, (heteroaryl)alkyl, -S(=O)R^{9b}, -S(=O)$_2R^{9b}$, and -C(=O)R^{9c};

[0064] A^2 is selected from the group consisting of -N= and -C(R^{2c})=;

[0065] R^{2c} is selected from the group consisting of hydrogen, alkyl, halogen, and haloalkyl;

[0066] R^{2d} is selected from the group consisting of hydrogen, alkyl, halogen, cyano, and haloalkyl;

[0067] R^{2e} is selected from the group consisting of hydrogen, alkyl, halogen, and haloalkyl;

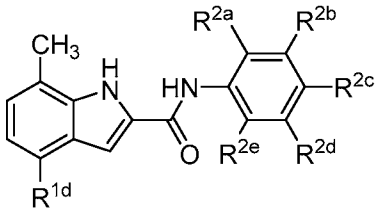
[0068] R^{9b} is selected from the group consisting of amino, alkyl, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocyclo, and optionally substituted heteroaryl;

[0069] R^{9c} is selected from the group consisting of amino, alkyl, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocyclo, and optionally substituted heteroaryl; and

[0070] R^{10c} is selected from the group consisting of alkyl, (hydroxy)alkyl, and (amino)alkyl; and

[0071] R^{1d} is as defined in connection with Formula **I**, or a pharmaceutically acceptable salt or solvate thereof.

[0072] In another embodiment, Compounds of the Disclosure are compounds having Formula **III-A**:



III-A,

wherein R^{1d}, R^{2a}, R^{2b}, R^{2c}, R^{2d}, and R^{2e} are as defined in connection with Formula **III**, or a pharmaceutically acceptable salt or solvate thereof.

[0073] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein:

[0074] R^{2a} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, halogen, and C_1-C_4 haloalkyl;

[0075] R^{2b} is selected from the group consisting of:

[0076] (A) unsubstituted 4- to 10-membered heterocyclo;

[0077] (B) substituted 4- to 10-membered heterocyclo having one, two, three, or four substituents independently selected from the group consisting of (i) $-N(R^{3a})C(=O)R^{4a}$; (ii) $-NR^{5a}R^{5b}$; (iii) unsubstituted 4- to 10-membered heterocyclo; (iv) substituted 4- to 10-membered heterocyclo having one, two, or three substituents independently selected from the group consisting of hydroxy, $-NR^{5c}R^{5d}$, C_1-C_4 alkyl, C_1-C_6 alkoxy, $-C(R^{6a})(R^{6b})C(=O)NR^{5e}R^{5f}$, $-C(=O)R^{4b}$, (hydroxy)C_1-C_4 alkyl, and halo; (v) unsubstituted C_3-C_6 cycloalkyl; (vi) (hydroxy)C_1-C_4 alkyl; (vii) C_1-C_6 alkyl; (viii) $-C(=O)NR^{5g}R^{5h}$; (ix) halo; (x) $-C(=O)R^{4c}$; (xi) C_1-C_6 haloalkyl; (xii) hydroxy; (xiii) (amino)C_1-C_4 alkyl; (xiv) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (xv) $-S(=O)_2R^{9a}$; (xvi) (3- to 8-membered heterocyclo)C_1-C_4 alkyl; (xvii) C_1-C_6 alkoxy; (xviii) (C_3-C_6 cycloalkyl)C_{1-4} alkyl; (xix) (C_{6-10} aryl)C_1-C_4 alkyl; and (xxii) $-OR^{10b}$;

[0078] (C) unsubstituted C_3-C_8 cycloalkyl;

[0079] (D) substituted C_3-C_8 cycloalkyl having one, two, three, or four substituents independently selected from the group consisting of (i)unsubstituted 4- to 10-membered heterocyclo; (ii) substituted 4- to 10-membered heterocyclo having one or two substituents, independently selected from the group consisting of amino and C_1-C_4 alkyl; (iii) unsubstituted 5- or 6-membered heteroaryl; (iv) substituted 5- or 6-membered heteroaryl having one, two, or three substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, (3- to 8-membered heterocyclo)alkyl, hydroxy, and

amino; (v) $-NR^{5i}R^{5j}$; (vi) cyano; (vii) $-N(R^{3d})C(=O)R^{4f}$; (viii) hydroxy; and (ix) C_1-C_4 alkyl;

[0080] (E) unsubstituted 5- to 10-membered heteroaryl;

[0081] (F) substituted 5- to 10-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of (i) halo; (ii) C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (hydroxy)C_1-C_4 alkyl; C_3-C_6 cycloalkyl; (amino)C_1-C_4 alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one, two, three, or four substituents independently selected from the group consisting of $-NR^{5g}R^{5h}$; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; $-NR^{5q}R^{5r}$; and (ix) (3- to 8-membered heterocyclo)C_1-C_4 alkyl;

[0082] (G) unsubstituted C_6-C_{10} aryl;

[0083] (H) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of (i) halo; (ii) C_1-C_4 alkyl; (iii) $-CH_2N(H)S(=O)_2R^8$; (iv) (5- to 9-membered heteroaryl)C_1-C_4 alkyl; (v) $-OR^{10a}$; (vi) $-N(R^{3b})C(=O)R^{4b}$; (vii) (amino)C_1-C_4 alkyl; and (viii) (hydroxy)C_1-C_4 alkyl;

[0084] (I) (carboxamido)C_1-C_4 alkyl;

[0085] (J) $-OR^{10c}$;

[0086] (K) $-NR^{5o}R^{5p}$;

[0087] (L) (3- to 8-membered heterocyclo)C_1-C_4 alkyl;

[0088] (M) (amino)C_1-C_4 alkyl;

[0089] (N) (hydroxy)C_1-C_4 alkyl;

[0090] (O) $-C(=O)NR^{5s}R^{5t}$;

[0091] (P) (5- to 9-membered heteroaryl)C_1-C_4 alkyl; and

[0092] (Q) $-S(=O)_2R^{9b}$;

[0093] R^{2c} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, halogen, and C_1-C_4 haloalkyl;

[0094] R^{2d} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, halogen, cyano, and C_1-C_4 haloalkyl;

[0095] R^{2e} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, halogen, and C_1-C_4 haloalkyl;

[0096] R^{3a}, R^{3b}, R^{3c}, and R^{3d} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, optionally substituted C_3-C_6 cycloalkyl, and optionally substituted 4- to 14-membered heterocyclo;

[0097] R^{4a}, R^{4b}, R^{4c}, R^{4d}, R^{4e}, and R^{4f} are each independently selected from the group consisting of C_1-C_6 alkyl; C_1-C_6 haloalkyl; C_3-C_6 cycloalkyl; C_1-C_6 alkoxy; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (C_{6-10} aryl)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (hydroxy)C_1-C_4 alkyl; (cyano)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted C_6-C_{10} aryl; substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; and substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo and C_1-C_4 alkyl;

[0098] R^{5a} and R^{5b} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl;

[0099] R^{5c} and R^{5d} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; or

[0100] R^{5c} and R^{5d} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0101] R^{5e} and R^{5f} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; or

[0102] R^{5e} and R^{5f} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0103] R^{5g} and R^{5h} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; or

[0104] R^{5g} and R^{5h} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0105] R^{5i} and R^{5j} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; or

[0106] R^{5i} and R^{5j} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0107] R^{5k} and R^{5l} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or

6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; or

[0108] R^{5k} and R^{5l} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0109] R^{5m} and R^{5n} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; or

[0110] R^{5m} and R^{5n} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0111] R^{5o} and R^{5p} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; or

[0112] R^{5o} and R^{5p} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0113] R^{5q} and R^{5r} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered

heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl;

[0114] R^{5s} and R^{5t} are independently selected from the group consisting of hydrogen; C_1-C_4 alkyl; C_1-C_4 haloalkyl; (hydroxy)C_1-C_4 alkyl; (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl;

[0115] R^{6a}, R^{6b}, R^{6c}, and R^{6d} are each independently selected from the group consisting of hydrogen and C_1-C_4 alkyl;

[0116] R^8 is C_1-C_6 alkyl;

[0117] R^{9a} is selected from the group consisting of C_1-C_6 alkyl; unsubstituted C_3-C_8 cycloalkyl; and substituted C_3-C_8 cycloalkyl having one or two substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl;

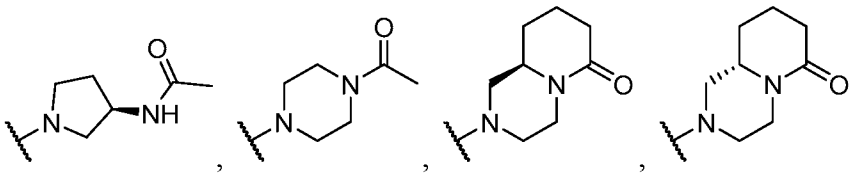
[0118] R^{9b} is selected from the group consisting of C_1-C_6 alkyl and amino;

[0119] R^{10a} is selected from the group consisting of alkyl, (hydroxy)C_1-C_4 alkyl, and (amino)C_1-C_4 alkyl;

[0120] R^{10b} is (amino)C_1-C_4 alkyl; and

[0121] R^{10c} is (amino)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

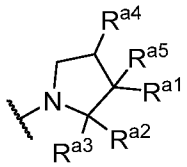
[0122] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is an optionally substituted 3- to 10-membered heterocycle linked to the rest of the molecule through a nitrogen atom, e.g., R^{2b} is:



and the like.

[0123] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein:

[0124] R^{2b} is selected from the group consisting of: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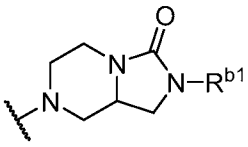
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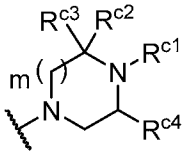
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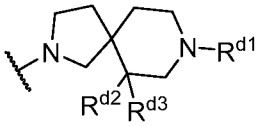
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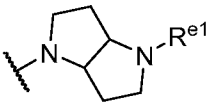
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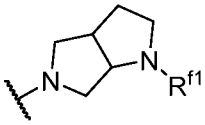
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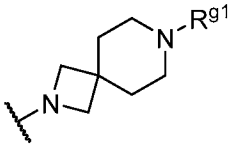
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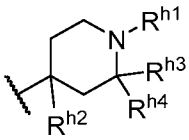
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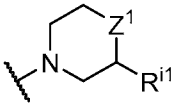
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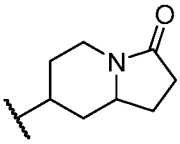
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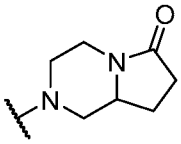
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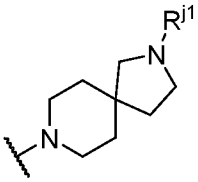
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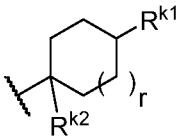
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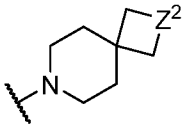
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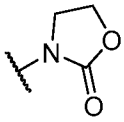
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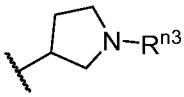
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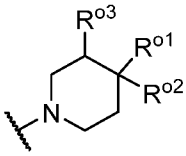
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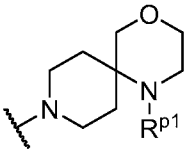
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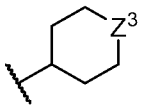
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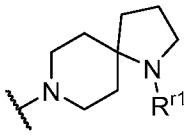
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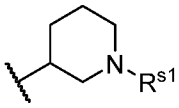
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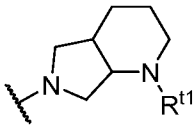
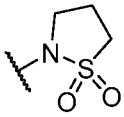

R^{2b}-22 ,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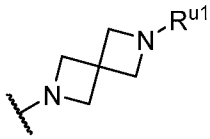
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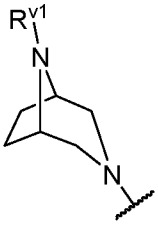
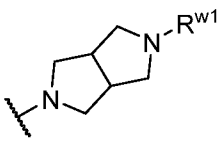
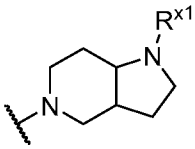
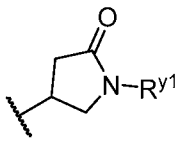
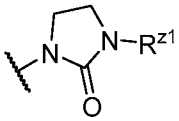
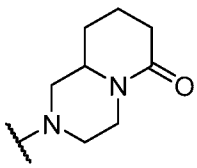

R^{2b}-25 ,


R^{2b}-26 ,


R^{2b}-27 ,


R^{2b}-28 ,


R^{2b}-29 and


R^{2b}-30 ;

[0125] R^{a1} is selected from the group consisting of $-N(R^{3a})C(=O)R^{4a}$; $-NR^{5a}R^{5b}$; unsubstituted 4- to 10-membered heterocyclo; substituted 4- to 10-membered heterocyclo having one, two, or three substituents independently selected from the group consisting of hydroxy, $-NR^{5c}R^{5d}$, C_1-C_4 alkyl, C_1-C_6 alkoxy, $-C(R^{6a})(R^{6b})C(=O)NR^{5e}R^{5f}$, $-C(=O)R^{4b}$, (hydroxy)C_1-C_4 alkyl, and halo;

[0126] R^{a2} and R^{a3} are each hydrogen; or

[0127] R^{a2} and R^{a3} taken together with the carbon atom to which they are attached form a C(=O) group;

[0128] R^{a4} is selected from the group consisting of hydrogen, halo, and hydroxy;

[0129] R^{a5} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_3-C_6 cycloalkyl;

[0130] R^{b1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_3-C_6 cycloalkyl;

[0131] R^{c1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and $-C(=O)R^{4c}$;

[0132] R^{c2} and R^{c3} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl; or

[0133] R^{c2} and R^{c3} taken together with the carbon atom to which they are attached form a C(=O) group;

[0134] R^{c4} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

[0135] m is 1 or 2;

[0136] R^{d1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and $-C(=O)R^{4c}$,

[0137] R^{d2} and R^{d3} are each independently selected from the group consisting of hydrogen and fluoro;

[0138] R^{e1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and $-C(=O)R^{4c}$;

[0139] R^{f1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and $-C(=O)R^{4c}$,

[0140] R^{g1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, $-C(=O)R^{4c}$, C_1-C_4 haloalkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl

[0141] R^{h1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and $-C(=O)R^{4c}$;

[0142] R^{h2} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

[0143] R^{h3} and R^{h4} are each independently selected from the group consisting of hydrogen and C_1-C_4 alkyl; or

[0144] R^{h3} and R^{h4} taken together with the carbon atom to which they are attached form a C(=O) group;

[0145] R^{i1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, (hydroxy)C_1-C_4 alkyl, -N(R^{3a})C(=O)R^{4a}, and (amino)C_1-C_4 alkyl;

[0146] Z^1 is selected from the group consisting of -CH_2- and -O-;

[0147] R^{j1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and -C(=O)R^{4c};

[0148] R^{k1} is selected from the group consisting of C_1-C_4 alkyl, unsubstituted 4- to 14-membered heterocyclo and -N$R^{5a}R^{5b}$;

[0149] R^{k2} is selected from the group consisting of hydrogen, hydroxy, and C_1-C_4 alkyl;

[0150] r is 0, 1, or 2;

[0151] Z^2 is selected from the group consisting of -O- and -N(R^{m3})-;

[0152] R^{m3} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl;

[0153] R^{n3} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

[0154] R^{o1} is selected from the group consisting of hydroxy, (hydroxy)C_1-C_4 alkyl, (amino)C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, C_1-C_4 alkoxy, -N$R^{5a}R^{5b}$, unsubstituted 4- to 14-membered heterocyclo, substituted 4- to 14-membered heterocyclo having one, two, or three substituents independently selected from the group consisting of halo, C_1-C_4 alkyl and C_1-C_4 alkoxy;

[0155] R^{o2} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and (C_1-C_4 alkoxy)C_1-C_4 alkyl

[0156] R^{o3} is selected from the group consisting of hydrogen, fluoro, and C_1-C_4 alkyl;

[0157] R^{p1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

[0158] Z^3 is selected from the group consisting of -O- and -N(R^{q1})-;

[0159] R^{q1} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

[0160] R^{r1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

[0161] R^{s1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

[0162] R^{t1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

[0163] R^{u1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

[0164] R^{v1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

[0165] R^{w1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

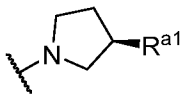
[0166] R^{x1} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and -C(=O)R^{4c};

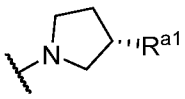
[0167] R^{y1} is selected from the group consisting of hydrogen and C_1-C_4 alkyl; and

[0168] R^{z1} is selected from the group consisting of hydrogen and C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0169] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein:

[0170] R^{2b} is selected from the group consisting of:


R^{2b}-1A ,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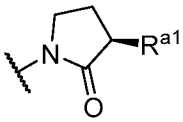
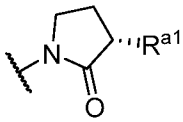
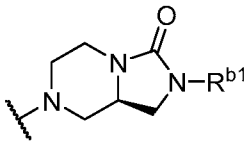
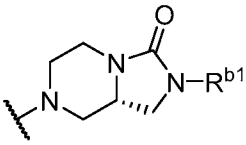
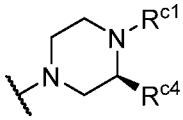
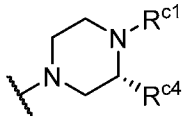

R^{2b}-1C ,

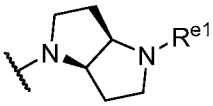

R^{2b}-1D ,

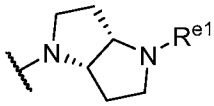

R^{2b}-2A ,


R^{2b}-2B ,


R^{2b}-3A ,


R^{2b}-3B ,


R^{2b}-5A ,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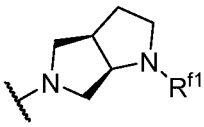
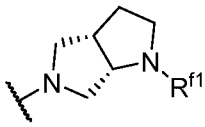
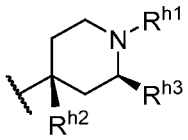
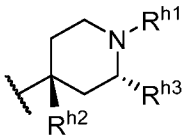

R^{2b}-6A ,


R^{2b}-6B ,


R^{2b}-8A ,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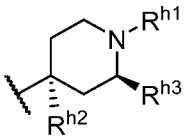
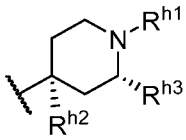
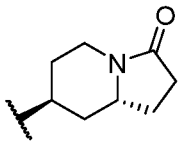

R^{2b}-8C ,


R^{2b}-8D ,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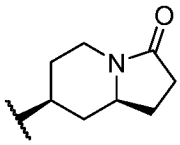
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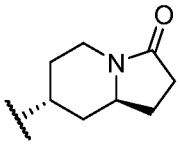
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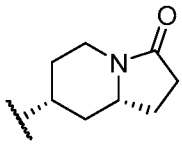
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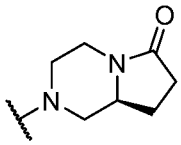
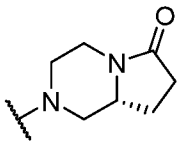

R^{2b}-11A ,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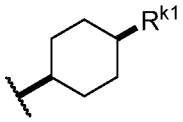
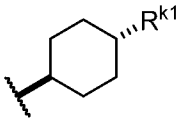

R^{2b}-13A ,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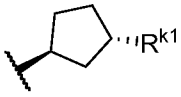
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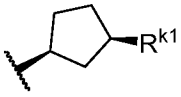
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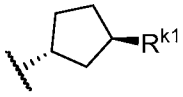
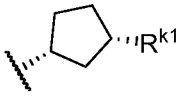
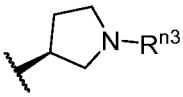
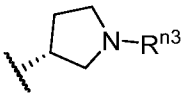
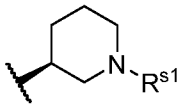
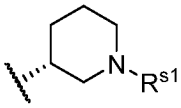

R^{2b}-13E ,

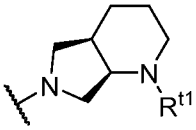

R^{2b}-13F ,


R^{2b}-16A ,


R^{2b}-16B ,


R^{2b}-21A ,


R^{2b}-21B ,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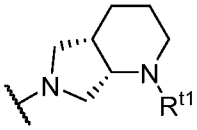
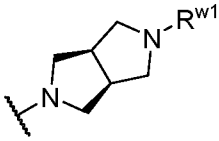

R^{2b}-22B ,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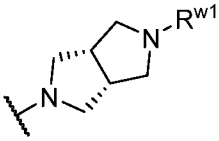
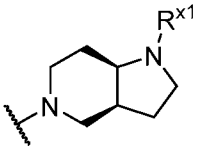

R^{2b}-26B ,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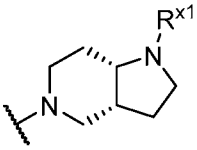
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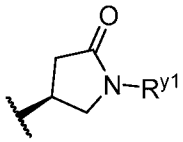
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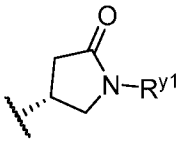
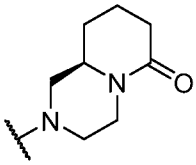
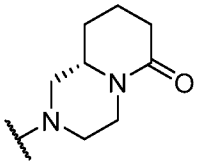

R^{2b}-28B ,


R^{2b}-30A and


R^{2b}-30B ,

or a pharmaceutically acceptable salt or solvate thereof.

[0171] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-1, R^{2b}-1A, R^{2b}-1B, R^{2b}-1C, or R^{2b}-1D, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{a1} is $-N(R^{3a})C(=O)R^{4a}$. In another embodiment, R^{a1} is $-NR^{5a}R^{5b}$. In another embodiment, R^{a1} is $-NR^{5a}R^{5b}$ and R^{5a} and R^{5b} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl. In another embodiment, R^{a1} is optionally substituted 4- to 10-membered heterocyclo.

[0172] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-2, R^{2b}-2A, or R^{2b}-2B, or a

pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{b1} is C_1-C_4 alkyl.

[0173] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-3, R^{2b}-3A, or R^{2b}-3B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{c1} is selected from the group consisting of C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and -C(=O)R^{4c}. In another embodiment, R^{c2} and R^{c3} are each hydrogen. In another embodiment, R^{c2} and R^{c3} taken together with the carbon atom to which they are attached form a C(=O) group. In another embodiment, R^{c4} is hydrogen. In another embodiment, m is 1.

[0174] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-4, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{d1} is C(=O)R^{4c}. In another embodiment, R^{d2} and R^{d3} are each hydrogen or fluoro.

[0175] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-5, R^{2b}-5A, or R^{2b}-5B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{e1} is -C(=O)R^{4c}.

[0176] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-6, R^{2b}-6A, or R^{2b}-6B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{f1} is C(=O)R^{4c}.

[0177] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-7, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{g1} is C(=O)R^{4c}.

[0178] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-8, R^{2b}-8A, R^{2b}-8B, R^{2b}-8C, or R^{2b}-8D, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{h1} is -C(=O)R^{4c}. In another embodiment, R^{h2} is selected from the group consisting of hydrogen and C_1-C_3 alkyl. In another embodiment, R^{h3} is hydrogen.

[0179] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-9, or a pharmaceutically acceptable salt or solvate thereof.

[0180] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-10, R^{2b}-10A, R^{2b}-10B, R^{2b}-10C, and R^{2b}-10d, or a pharmaceutically acceptable salt or solvate thereof.

[0181] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-11, R^{2b}-11A and R^{2b}-11B, or a pharmaceutically acceptable salt or solvate thereof.

[0182] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-12, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{j1} is -C(=O)R^{4c}.

[0183] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-13, R^{2b}-13A, R^{2b}-13B, R^{2b}-13C, R^{2b}-13D, R^{2b}-13E, and R^{2b}-13F, or a pharmaceutically acceptable salt or solvate thereof.

[0184] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-14, or a pharmaceutically acceptable salt or solvate thereof.

[0185] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-15, or a pharmaceutically acceptable salt or solvate thereof.

[0186] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-16, R^{2b}-16A and R^{2b}-16B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{n3} is -C(=O)R^{4c}.

[0187] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-17, or a pharmaceutically acceptable salt or solvate thereof.

[0188] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-18, or a pharmaceutically acceptable salt or solvate thereof.

[0189] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-19, or a pharmaceutically acceptable salt or solvate thereof.

[0190] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-20, or a pharmaceutically acceptable salt or solvate thereof.

[0191] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-21, R^{2b}-21A and R^{2b}-21B, or a pharmaceutically acceptable salt or solvate thereof.

[0192] In another embodiment, Compounds of the Disclosure are compounds having Formula **III**, wherein R^{2b} is selected from the group consisting of R^{2b}-22, R^{2b}-22A and R^{2b}-22B, or a pharmaceutically acceptable salt or solvate thereof.

[0193] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-23, or a pharmaceutically acceptable salt or solvate thereof.

[0194] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-24, or a pharmaceutically acceptable salt or solvate thereof.

[0195] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-25, or a pharmaceutically acceptable salt or solvate thereof.

[0196] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-26, R^{2b}-26A and R^{2b}-26B, or a pharmaceutically acceptable salt or solvate thereof.

[0197] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-27, R^{2b}-27A and R^{2b}-27B, or a pharmaceutically acceptable salt or solvate thereof.

[0198] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is selected from the group consisting of R^{2b}-28, R^{2b}-28A and R^{2b}-28B, or a pharmaceutically acceptable salt or solvate thereof.

[0199] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-29, or a pharmaceutically acceptable salt or solvate thereof.

[0200] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is R^{2b}-30, R^{2b}-30A, or R^{2b}-30B, or a pharmaceutically acceptable salt or solvate thereof.

[0201] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2b} is any one or more of the R^{11a} groups provided in connection with Formula **IV**, *see* below, or a pharmaceutically acceptable salt or solvate thereof.

[0202] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{4c} is C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

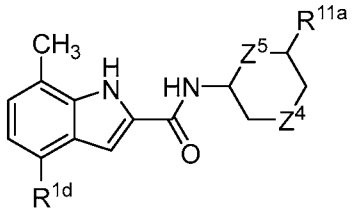
[0203] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2d} is selected from the group consisting of hydrogen, fluoro, and chloro, or a pharmaceutically acceptable salt or solvate thereof.

[0204] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2d} is hydrogen, or a pharmaceutically acceptable salt or solvate thereof.

[0205] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** in any of the above described embodiments, wherein A^1 and A^2 are -C(H)=; R^{2e} is hydrogen; and R^{2d} is selected from the group consisting of hydrogen and halogen, or a pharmaceutically acceptable salt or solvate thereof.

[0206] In another embodiment, Compounds of the Disclosure are compounds having Formula **III** or Formula **III-A**, wherein R^{2d} is fluoro, or a pharmaceutically acceptable salt or solvate thereof.

[0207] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV**:



IV,

wherein:

[0208] Z^4 is selected from the group consisting of -O-, -C(R^{28a})(R^{28b})-, and -N(R^{23})-; or Z^4 is absent;

[0209] Z^5 is selected from the group consisting of -CH_2- and -CH_2CH_2-;

[0210] R^{11a} is selected from the group consisting of optionally substituted alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, and $-N(R^{12b})C(=O)R^{13c}$;

[0211] R^{12b} is selected from the group consisting of hydrogen, alkyl, cycloalkyl, and heterocyclo;

[0212] R^{13c} is selected from the group consisting of alkyl, haloalkyl, alkoxy, (alkoxy)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocycle, amino, (amino)alkyl, (C_3-C_6 cycloalkyl)oxy, and (4- to 8-membered heterocyclo)oxy;

[0213] R^{23} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

[0214] R^{28a} and R^{28b} are independently selected from the group consisting of hydrogen, alkyl, and halo; and

R^{1d} is as defined in connection with Formula **I**, or a pharmaceutically acceptable salt or solvate thereof.

[0215] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV**, wherein Z^4 is selected from the group consisting of -O- and $-CH_2-$; or Z^4 is absent, or a pharmaceutically acceptable salt or solvate thereof.

[0216] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV**, wherein:

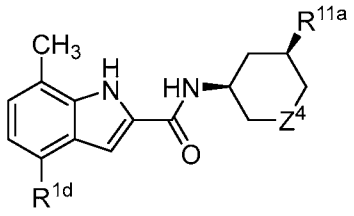
[0217] Z^4 is selected from the group consisting of -O- and $-CH_2-$; or Z^4 is absent;

[0218] Z^5 is selected from the group consisting of $-CH_2-$ and $-CH_2CH_2-$;

[0219] R^{13c} is selected from the group consisting of alkyl, haloalkyl, alkoxy, (alkoxy)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocycle, and

[0220] R^{1d} is as defined in connection with Formula **I**, or a pharmaceutically acceptable salt or solvate thereof.

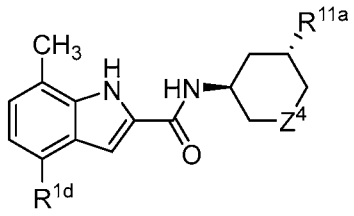
[0221] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV-A**:



IV-A,

or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1d}, R^{11a}, and Z^4 are as defined in connection with Formula **IV**.

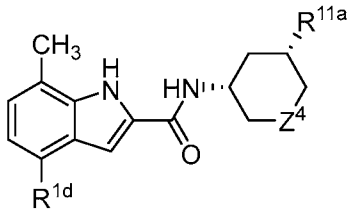
[0222] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV-B**:



IV-B,

or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1d}, R^{11a}, and Z^4 are as defined in connection with Formula **IV**.

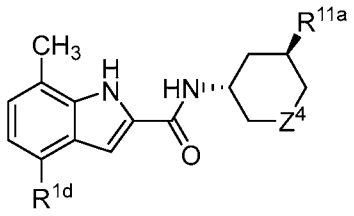
[0223] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV-C**:



IV-C,

or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1d}, R^{11a}, and Z^4 are as defined in connection with Formula **IV**.

[0224] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV-D**:



IV-D,

or a pharmaceutically acceptable salt or solvate thereof, wherein R^{1d}, R^{11a}, and Z^4 are as defined in connection with Formula **IV**.

[0225] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein:

[0226] R^{11a} is selected from the group consisting of: (A) unsubstituted 4- to 14-membered heterocyclo; (B) substituted 4- to 14-membered heterocyclo having one, two or three substituents independently selected from the group consisting of -$N(R^{12a})C(=O)R^{13a}$; -$C(=O)R^{13b}$; C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (hydroxy)C_1-C_4 alkyl; C_1-C_4 haloalkyl; amino; hydroxy; -$N(R^{12a})S(=O)_2R^{24}$; -$S(=O)_2R^{24}$; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C) unsubstituted 5- to 10-membered heteroaryl; (D) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, and (amino)alkyl; (E) C_1-C_6 alkyl; and (F) -$N(R^{12b})C(=O)R^{13c}$;

[0227] R^{12a} and R^{12b} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, and (hydroxy)C_1-C_4 alkyl;

[0228] R^{13a}, R^{13b}, and R^{13c} are each independently selected from the group consisting of C_1-C_6 alkyl; C_1-C_6 haloalkyl; unsubstituted C_3-C_6 cycloalkyl; C_1-C_6 alkoxy; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (hydroxy)C_1-C_4 alkyl; (cyano)alkyl; unsubstituted C_6-C_{10} aryl; substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; amino; (amino)alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy; and

[0229] R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl.

[0230] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein Z^4 is -$C(R^{28a})(R^{28b})$-; and R^{28a} and R^{28b}

are independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, and fluoro, or a pharmaceutically acceptable salt or solvate thereof.

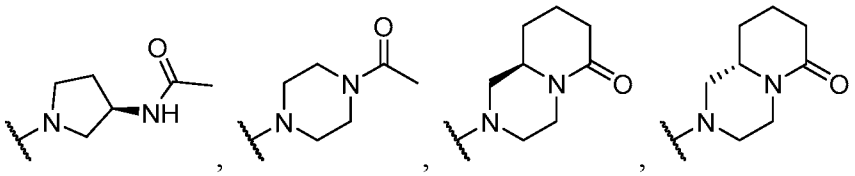
[0231] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein Z^4 is $-C(R^{28a})(R^{28b})-$; R^{28a} is hydrogen; and R^{28b} is selected from the group consisting of C_1-C_4 alkyl and fluoro, or a pharmaceutically acceptable salt or solvate thereof.

[0232] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein Z^4 is $-C(R^{28a})(R^{28b})-$; and R^{28a} and R^{28b} are independently C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0233] In another embodiment, Compounds of the Disclosure are compounds having Formula **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein Z^4 is selected from the group consisting of -O-, $-CH_2-$, and $-N(R^{23})$, or Z^4 is absent, or a pharmaceutically acceptable salt or solvate thereof.

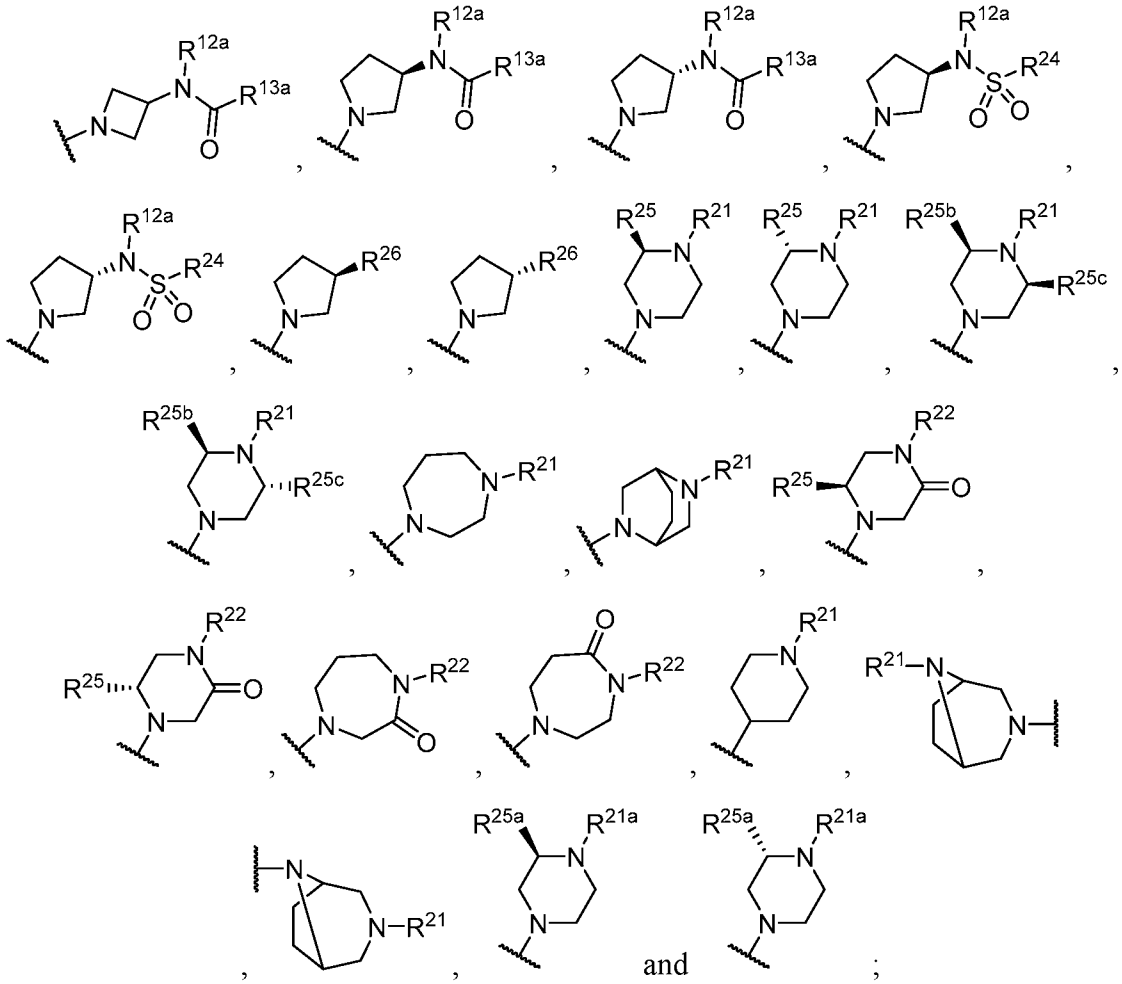
[0234] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein Z^4 is $-CH_2-$, or a pharmaceutically acceptable salt or solvate thereof.

[0235] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is an optionally substituted 3- to 10-membered heterocycle linked to the rest of the molecule through a nitrogen atom, e.g., R^{11a} is



, and the like.

[0236] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:



[0237] R^{12a} is selected from the group consisting of hydrogen, C_1-C_3 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl; and (hydroxy)C_1-C_4 alkyl;

[0238] R^{13a} is selected from the group consisting of C_1-C_4 alkyl; amino; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (hydroxy)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl;

[0239] R^{13b} is selected from the group consisting of C_1-C_4 alkyl; amino; C_1-C_4 haloalkyl; C_1-C_4 alkoxy; (hydroxy)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (amino)alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently

selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy;

[0240] R^{21} is selected from the group consisting of hydrogen, -C(=O)R^{13b}, C_1-C_4 alkyl, C_1-C_4 haloalkyl, unsubstituted 4- to 14-membered heterocyclo, and -S(=O)$_2$$R^{24}$;

[0241] R^{22} is C_1-C_4 alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl;

[0242] R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl;

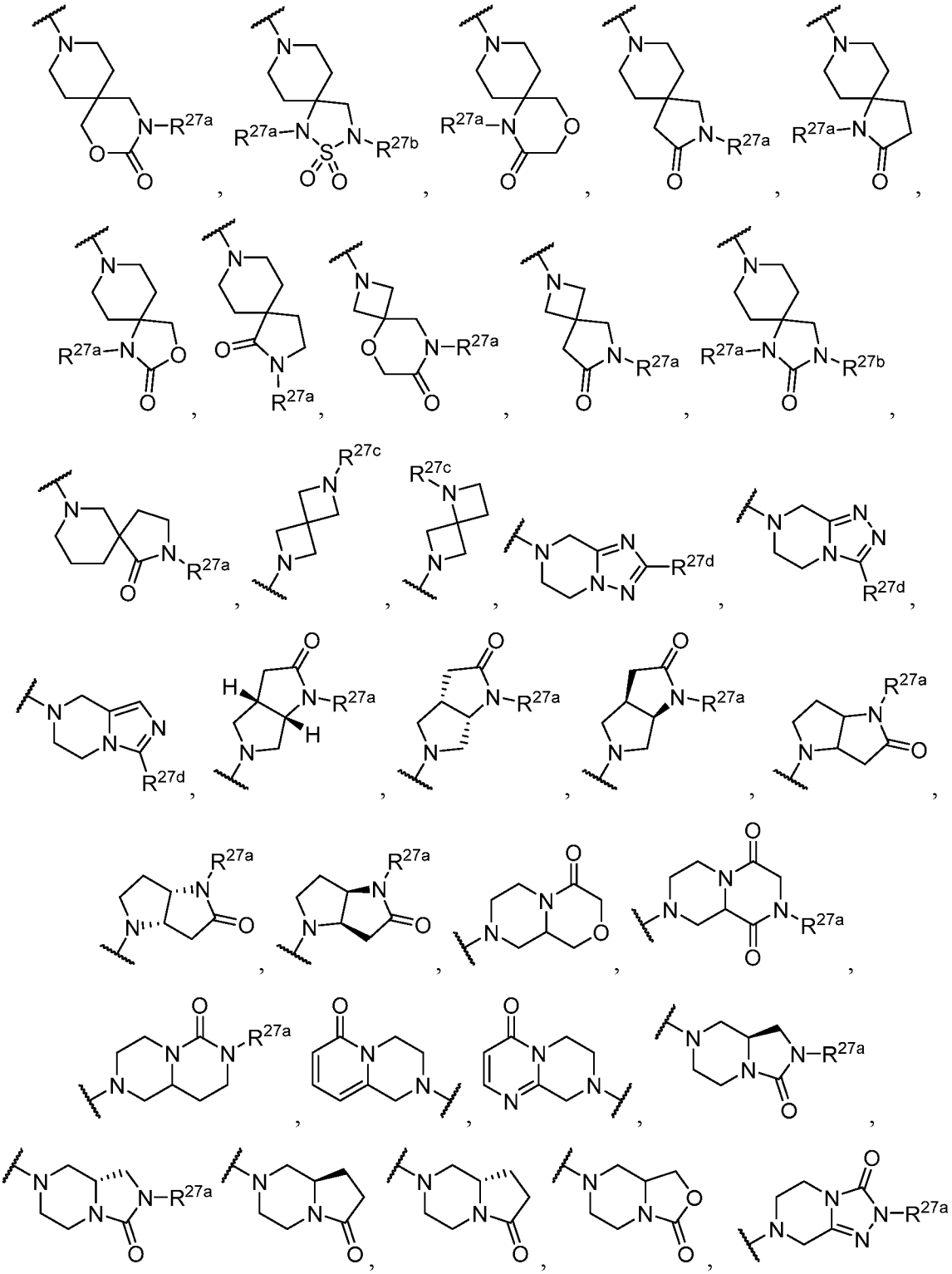
[0243] R^{25} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl;

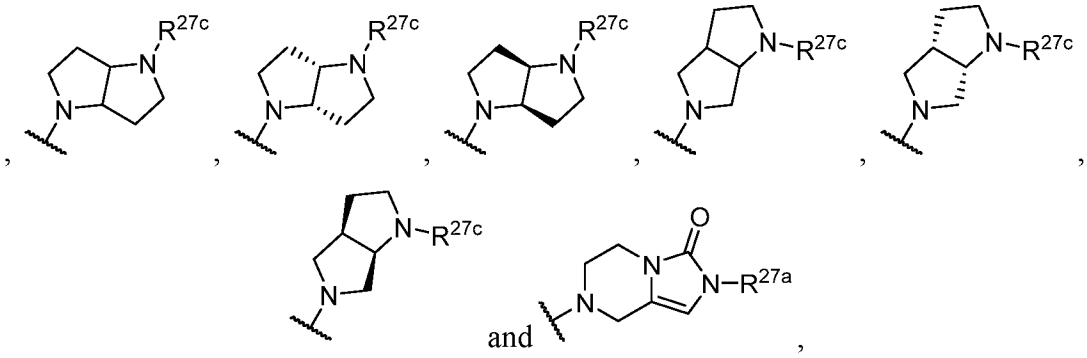
[0244] R^{25b} and R^{25c} are independently selected from the group consisting of C_1-C_4 alkyl and C_1-C_4 haloalkyl;

[0245] R^{26} is selected from the group consisting of unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; and

[0246] R^{21a} and R^{25a} taken together with the atoms to which they are attached form an optionally substituted 4- to 8-membered heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

[0247] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of:





wherein:

[0248] R^{27a} and R^{27b} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl; and (hydroxy)C_1-C_4 alkyl;

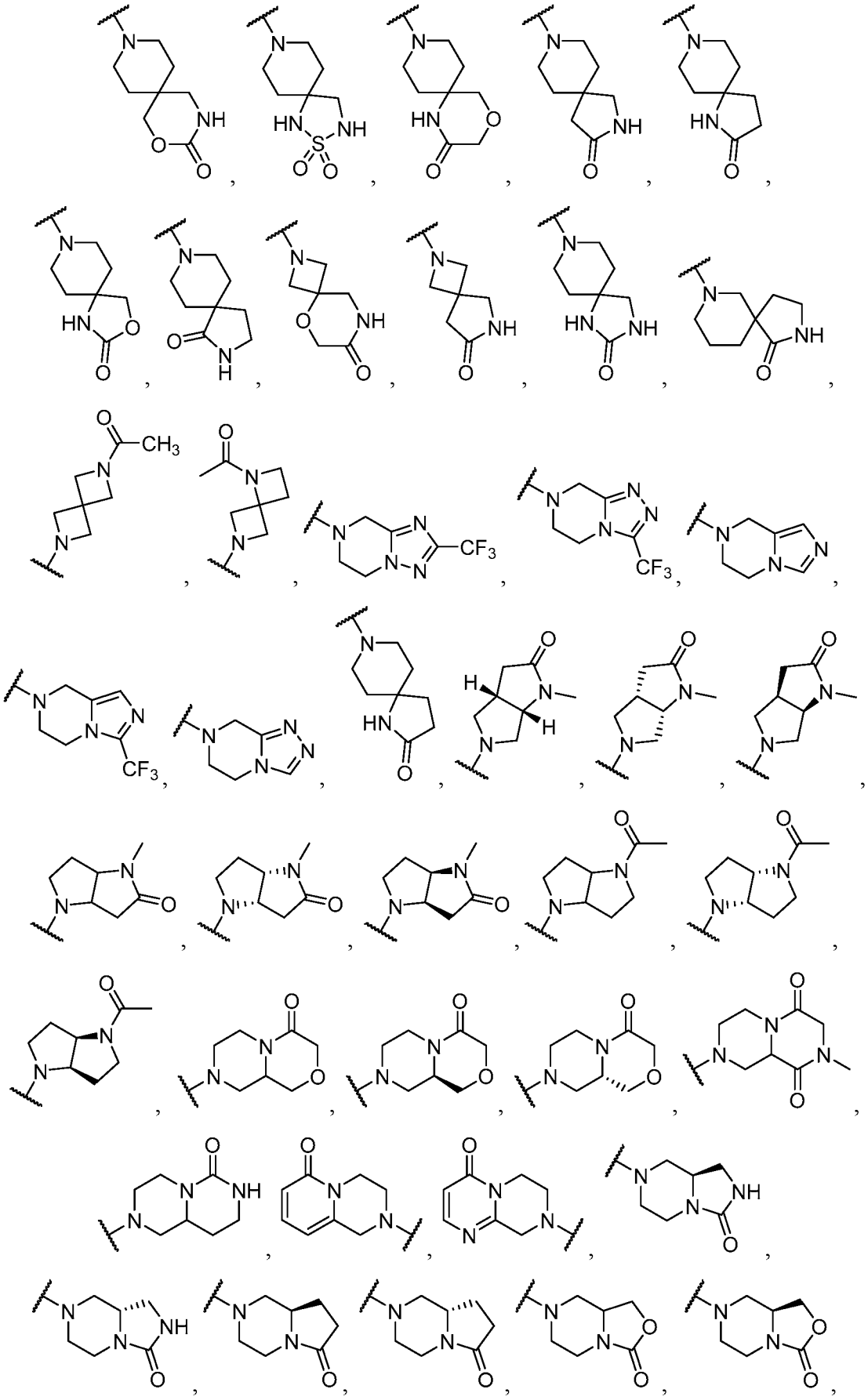
[0249] R^{27c} is selected from the group consisting of hydrogen; -C(=O)R^{13b}; C_1-C_4 alkyl; C_1-C_4 haloalkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; and -S(=O)$_2$$R^{24}$;

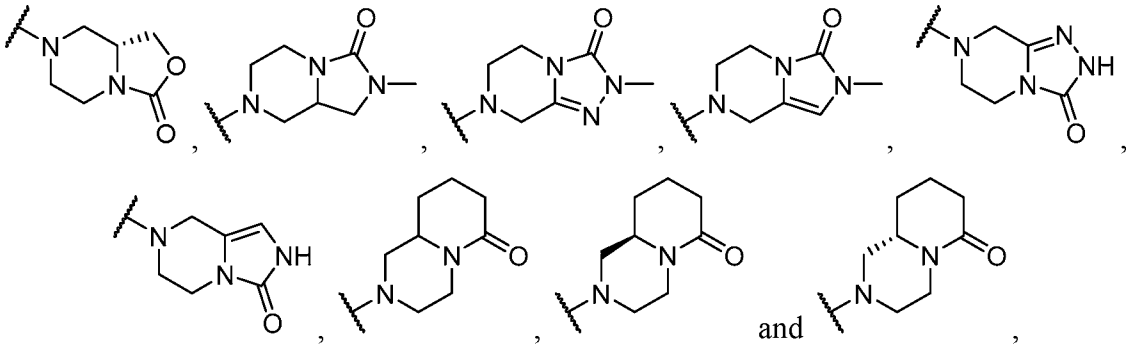
[0250] R^{27d} is selected from the group consisting of hydrogen; C_1-C_4 alkyl; and C_1-C_4 haloalkyl;

[0251] R^{13b} is selected from the group consisting of C_1-C_4 alkyl; aminoC_1-C_4 haloalkyl; C_1-C_4 alkoxy; (hydroxy)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (amino)alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy; and

[0252] R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0253] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of

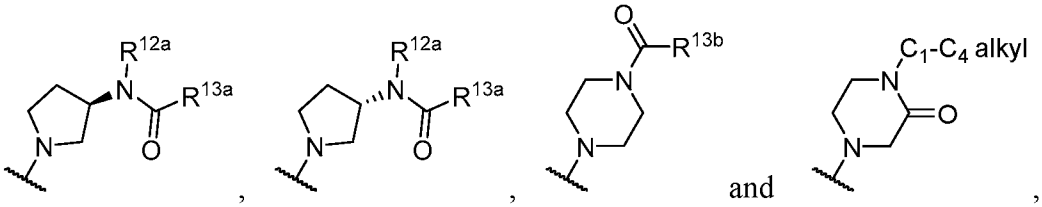




or a pharmaceutically acceptable salt or solvate thereof

[0254] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of $-N(R^{12a})C(=O)R^{13a}$, $-C(=O)R^{13b}$, and C_1-C_4 alkyl; unsubstituted 5- to 10-membered heteroaryl; and substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of halo and C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0255] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo is selected from the group consisting of:

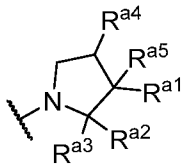


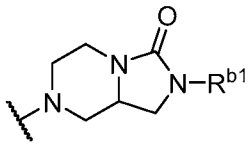
or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{12a} is selected from the group consisting of hydrogen and C_1-C_3 alkyl; R^{13a} is C_1-C_4 alkyl; and R^{13b} is C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{12a} is selected from the group consisting of hydrogen and methyl; R^{13a} is methyl; and R^{13b} is methyl, or a pharmaceutically acceptable salt or solvate thereof.

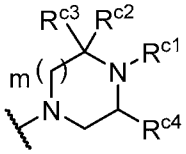
[0256] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is any one or more of the R^{2b} groups provided in connection with Formula **III**, *see* above, or a pharmaceutically acceptable salt or solvate thereof.

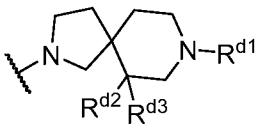
[0257] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein:

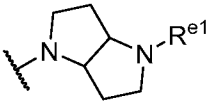
[0258] R^{11a} is selected from the group consisting of:

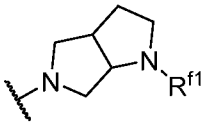

R^{11a}-1 ,

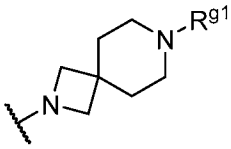

R^{11a}-2 ,

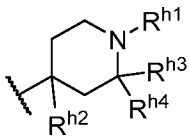

R^{11a}-3 ,

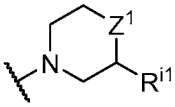

R^{11a}-4 ,

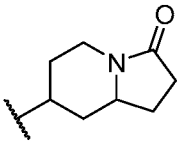

R^{11a}-5 ,

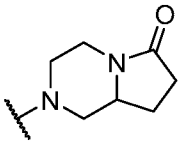

R^{11a}-6 ,

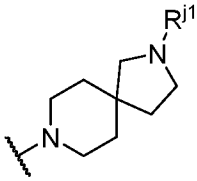

R^{11a}-7 ,

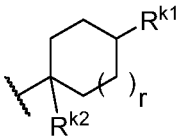

R^{11a}-8 ,

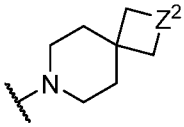

R^{11a}-9 ,

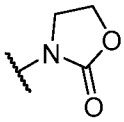

R^{11a}-10 ,

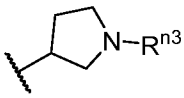

R^{11a}-11 ,

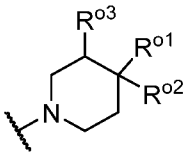

R^{11a}-12 ,

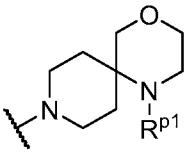

R^{11a}-13

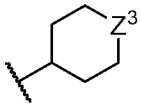

R^{11a}-14

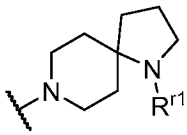

R^{11a}-15

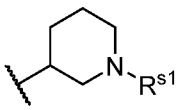

R^{11a}-16 ,

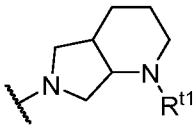

R^{11a}-17

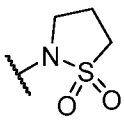

R^{11a}-18

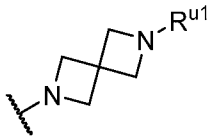

R^{11a}-19 ,

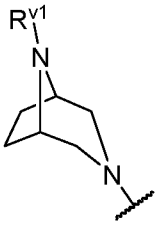

R^{11a}-20 ,

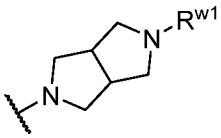

R^{11a}-21 ,

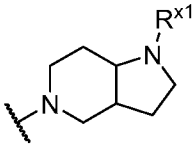

R^{11a}-22 ,

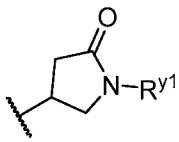

R^{11a}-23 ,

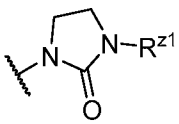

R^{11a}-24 ,

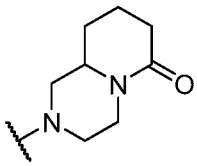

R^{11a}-25 ,


R^{11a}-26 ,


R^{11a}-27 ,


R^{11a}-28 ,

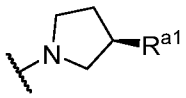

R^{11a}-29 and

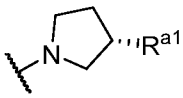

R^{11a}-30 ;

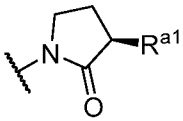
[0259] and R^{a1}, R^{a2}, R^{a3}, R^{a4}, R^{a5}, R^{b1}, R^{c1}, R^{c2}, R^{c3}, R^{c4}, m, R^{d1}, R^{d2}, R^{d3}, R^{e1}, R^{f1}, R^{g1}, R^{h1}, R^{h2}, R^{h3}, R^{h4}, R^{i1}, Z^1, R^{j1}, R^{k1}, R^{k2}, r, Z^2, R^{n3}, R^{o1}, R^{o2}, R^{o3}, R^{p1}, Z^3, R^{r1}, R^{s1}, R^{t1}, R^{u1}, R^{v1}, R^{w1}, R^{x1}, R^{y1}, and R^{z1} are as defined in connection with Formula **III**; or a pharmaceutically acceptable salt or solvate thereof.

[0260] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein:

[0261] R^{11a} is selected from the group consisting of:


R^{11a}-1A ,


R^{11a}-1B ,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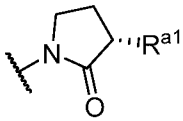
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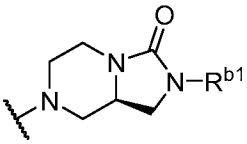
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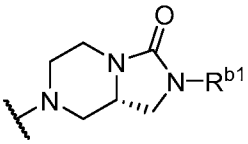
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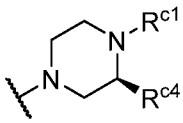
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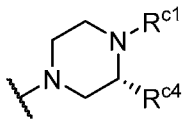
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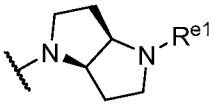
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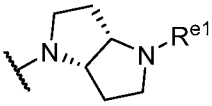
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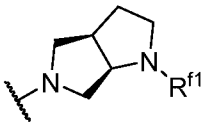
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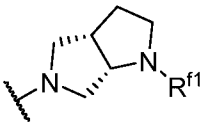
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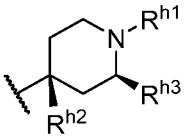
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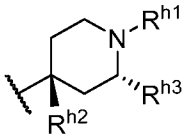
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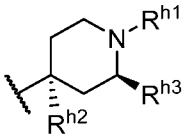
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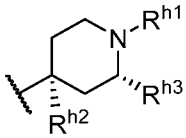
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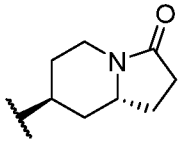
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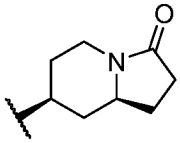
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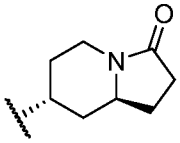
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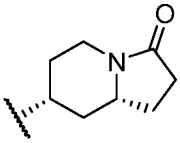
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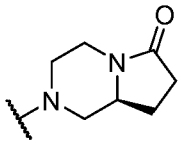
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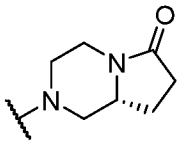
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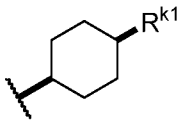
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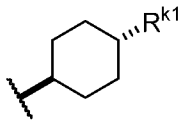
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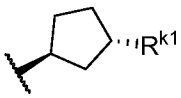
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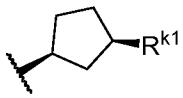
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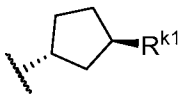
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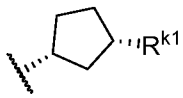
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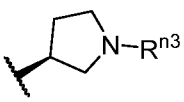
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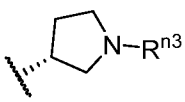
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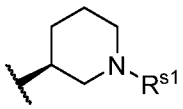
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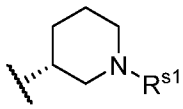
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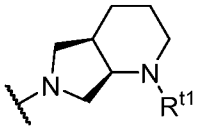
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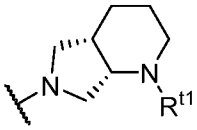
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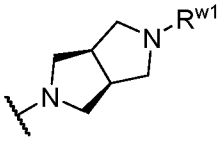
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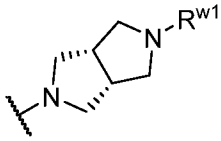
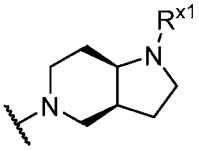
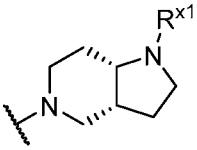
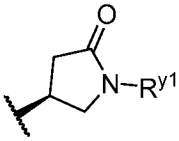
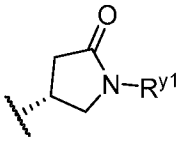
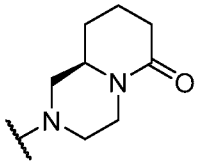

R^{11a}-26B


R^{11a}-27A

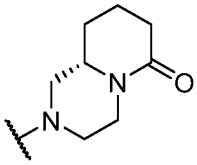

R^{11a}-27B


R^{11a}-28A


R^{11a}-28B


R^{11a}-30A

and


R^{11a}-30B

[0262] and R^{a1}, R^{a5}, R^{b1}, R^{e1}, R^{f1}, R^{h1}, R^{h2}, R^{h3}, R^{k1}, R^{n3}, R^{s1}, R^{t1}, R^{w1}, R^{x1}, and R^{y1} are as defined in connection with Formula **III**; or a pharmaceutically acceptable salt or solvate thereof.

[0263] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-1, R^{11a}-1A, R^{11a}-1B, R^{11a}-1C, or R^{11a}-1D, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{a1} is $-N(R^{3a})C(=O)R^{4a}$. In another embodiment, R^{a1} is $-NR^{5a}R^{5b}$. In another embodiment, R^{a1} is $-NR^{5a}R^{5b}$ and R^{5a} and R^{5b} are independently selected from the group consisting of hydrogen and C_1-C_4 alkyl. In another embodiment, R^{a1} is optionally substituted 4- to 10-membered heterocyclo.

[0264] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-2, R^{11a}-2A, or R^{11a}-2B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{b1} is C_1-C_4 alkyl.

[0265] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-3, R^{11a}-3A, or R^{11a}-3B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{c1} is selected from the group consisting of C_1-C_4 alkyl, C_3-C_6 cycloalkyl, and $-C(=O)R^{4c}$. In another embodiment, R^{c2} and R^{c3} are each hydrogen. In another embodiment, R^{c2} and R^{c3} taken together with the carbon atom to which they are attached form a C(=O) group. In another embodiment, R^{c4} is hydrogen. In another embodiment, m is 1.

[0266] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-4, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{d1} is $C(=O)R^{4c}$. In another embodiment, R^{d2} and R^{d3} are each hydrogen or fluoro.

[0267] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-5, R^{11a}-5A, or R^{11a}-5B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{e1} is $-C(=O)R^{4c}$.

[0268] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-6, R^{11a}-6A, or R^{11a}-6B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{f1} is $C(=O)R^{4c}$.

[0269] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-7, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{g1} is $C(=O)R^{4c}$.

[0270] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-8, R^{11a}-8A, R^{11a}-8B, R^{11a}-8C, or R^{11a}-8D, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{h1} is $-C(=O)R^{4c}$. In another embodiment, R^{h2} is selected from the group consisting of hydrogen and C_1-C_3 alkyl. In another embodiment, R^{h3} is hydrogen.

[0271] In another embodiment, Compounds of the Disclosure are compounds any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-9, or a pharmaceutically acceptable salt or solvate thereof.

[0272] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-10, R^{11a}-10A, R^{11a}-10B, R^{11a}-10C, and R^{11a}-10D, or a pharmaceutically acceptable salt or solvate thereof.

[0273] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-11, R^{11a}-11A and R^{11a}-11B, or a pharmaceutically acceptable salt or solvate thereof.

[0274] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-12, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{j1} is -C(=O)R^{4c}.

[0275] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-13, R^{11a}-13A, R^{11a}-13B, R^{11a}-13C, R^{11a}-13D, R^{11a}-13E, and R^{11a}-13F, or a pharmaceutically acceptable salt or solvate thereof.

[0276] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-14, or a pharmaceutically acceptable salt or solvate thereof.

[0277] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-15, or a pharmaceutically acceptable salt or solvate thereof.

[0278] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-16, R^{11a}-16A and R^{11a}-16B, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{n3} is -C(=O)R^{4c}.

[0279] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-17, or a pharmaceutically acceptable salt or solvate thereof.

[0280] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-18, or a pharmaceutically acceptable salt or solvate thereof.

[0281] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-19, or a pharmaceutically acceptable salt or solvate thereof.

[0282] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-20, or a pharmaceutically acceptable salt or solvate thereof.

[0283] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group

consisting of R^{11a}-21, R^{11a}-21A and R^{11a}-21B, or a pharmaceutically acceptable salt or solvate thereof.

[0284] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-22, R^{11a}-22A and R^{11a}-22B, or a pharmaceutically acceptable salt or solvate thereof.

[0285] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-23, or a pharmaceutically acceptable salt or solvate thereof.

[0286] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-24, or a pharmaceutically acceptable salt or solvate thereof.

[0287] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-25, or a pharmaceutically acceptable salt or solvate thereof.

[0288] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-26, R^{11a}-26A and R^{11a}-26B, or a pharmaceutically acceptable salt or solvate thereof.

[0289] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-27, R^{11a}-27A and R^{11a}-27B, or a pharmaceutically acceptable salt or solvate thereof.

[0290] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is selected from the group consisting of R^{11a}-28, R^{11a}-28A and R^{11a}-28B, or a pharmaceutically acceptable salt or solvate thereof.

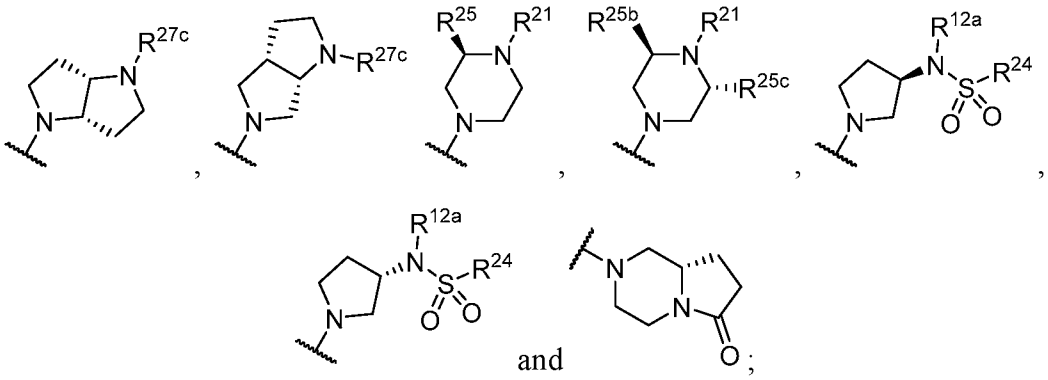
[0291] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-29, or a pharmaceutically acceptable salt or solvate thereof.

[0292] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV**, **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein R^{11a} is R^{11a}-30, R^{11a}-30A, or R^{11a}-30B, or a pharmaceutically acceptable salt or solvate thereof.

[0293] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein:

[0294] Z^4 is $-CH_2-$;

[0295] R^{11a} is selected from the group consisting of:



[0296] R^{12a} is selected from the group consisting of hydrogen and C_1-C_3 alkyl;

[0297] R^{21} is $-C(=O)R^{13b}$;

[0298] R^{27c} is $-C(=O)R^{13b}$;

[0299] R^{13b} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl;

[0300] R^{24} is C_1-C_4 alkyl;

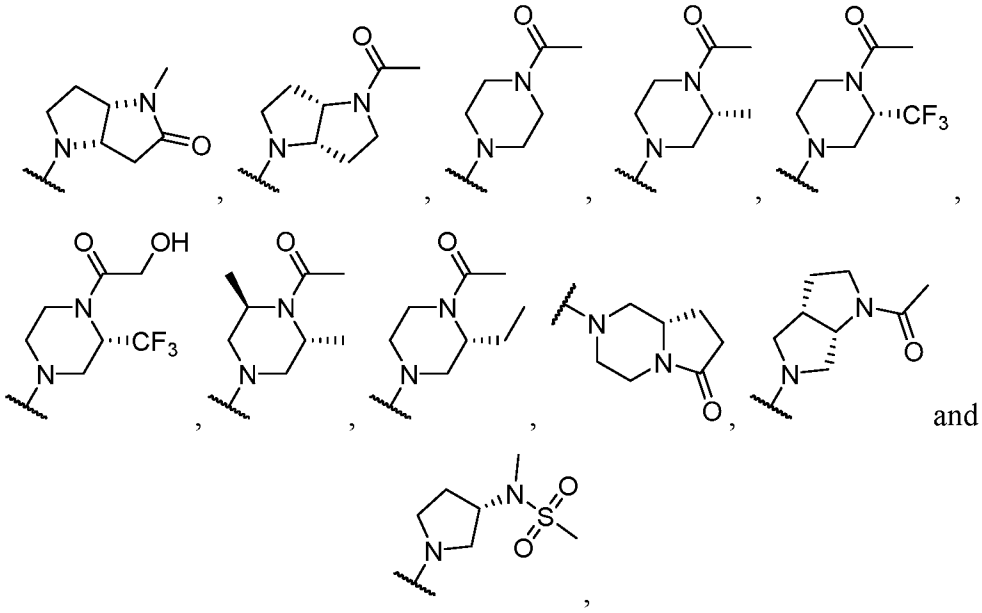
[0301] R^{25} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl; and

[0302] R^{25b} and R^{25c} are independently selected from the group consisting of C_1-C_4 alkyl and C_1-C_4 haloalkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0303] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein:

[0304] Z^4 is $-CH_2-$; and

[0305] R^{11a} is selected from the group consisting of:

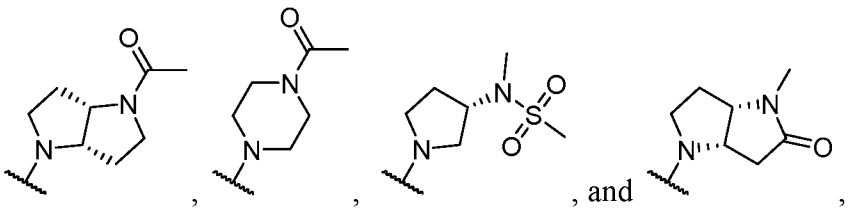


or a pharmaceutically acceptable salt or solvate thereof.

[0306] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein:

[0307] Z^4 is $-CH_2-$; and

[0308] R^{11a} is selected from the group consisting of:

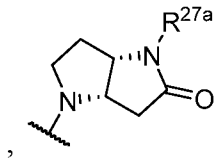


or a pharmaceutically acceptable salt or solvate thereof.

[0309] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **IV-A**, **IV-B**, **IV-C**, or **IV-D**, wherein:

[0310] Z^4 is $-CH_2-$;

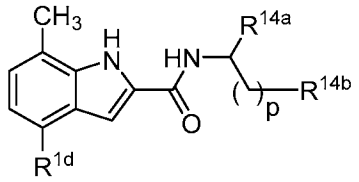
[0311] R^{11a} is:



; and

R^{27a} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, and (hydroxy)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof. In another embodiment, R^{27a} is methyl.

[0312] In another embodiment, Compounds of the Disclosure are compounds Formula **V**:



V,

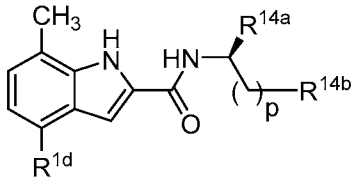
wherein:

[0313] R^{14a} is selected from the group consisting of optionally substituted alkyl and optionally substituted heteroaryl;

[0314] R^{14b} is selected from the group consisting of optionally substituted alkyl, optionally substituted heteroaryl, optionally substituted aryl, optionally substituted heterocyclo, optionally substituted cycloalkyl, and carboxamido; and

[0315] p is 0, 1, 2, or 3; or a pharmaceutically acceptable salt or solvate thereof.

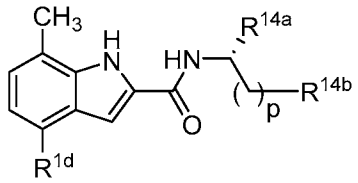
[0316] In another embodiment, Compounds of the Disclosure are compounds having Formula **V-A**:



V-A,

wherein R^{1d}, R^{14a}, R^{14d}, and p are as defined in connection with Formula **V**, or a pharmaceutically acceptable salt or solvate thereof.

[0317] In another embodiment, Compounds of the Disclosure are compounds having Formula **V-B**:



V-B,

wherein R^{1d}, R^{14a}, R^{14d}, and p are as defined in connection with Formula **V**, or a pharmaceutically acceptable salt or solvate thereof.

[0318] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **V**, **V-A**, or **V-B**, wherein:

[0319] R^{14a} is selected from the group consisting of (A) unsubstituted 5- to 10-membered heteroaryl; (B) substituted 5- or 10-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of (i) halo; (ii) C_1-C_4 alkyl; (iii) C_1-C_4 alkoxy; (iv) (3- to 8-membered heterocyclo)C_1-C_4 alkyl; (v) (5- to 9-membered heteroaryl)C_1-C_4 alkyl; (vi) -C(=O)$NR^{15a}R^{15b}$; (vii) unsubstituted 5- to 10-

membered heteroaryl; (viii) substituted 5- or 10-membered heteroaryl having one, two, or three substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, (3- to 8-membered heterocyclo)C_1-C_4 alkyl, 5- to 9-membered heteroaryl, and -$NR^{15e}R^{15f}$; (ix) -OR^{16} (x) unsubstituted C_3-C_6 cycloalkyl; (xi) substituted C_3-C_6 cycloalkyl having one, two, three, or four substituents independently selected from the group consisting of C_1-C_4 alkyl and -$N(R^{17a})C(=O)R^{18a}$; (xii) cyano; (xiii) unsubstituted 4- to 14-membered heterocyclo; (xiv) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of C_1-C_4 alkyl, (5- to 9-membered heteroaryl)C_1-C_4 alkyl; (xv) (carboxy)C_1-C_4 alkyl; (xvi) (carboxamido)C_1-C_4 alkyl; and (xvii) carboxy; and (C) C_1-C_6 alkyl;

[0320] R^{14b} is selected from the group consisting of: (A) unsubstituted 5- to 10-membered heteroaryl; (B) substituted 5- or 10-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, and (C_3-C_6 cycloalkyl)C_1-C_4 alkyl; (C) unsubstituted C_6-C_{10} aryl; (D) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, and (3- to 8-membered heterocyclo)C_1-C_4 alkyl; (E) unsubstituted 4- to 14-membered heterocyclo; (F) substituted 4- to 14-membered heterocyclo having one, two, three, or four substituents independently selected from the group consisting of hydroxy, amino, and C_1-C_4 alkyl; (G) -$C(=O)NR^{15c}R^{15d}$; (H) unsubstituted C_3-C_6 cycloalkyl; and (I) C_1-C_6 alkyl;

[0321] p is 0, 1, 2, or 3;

[0322] R^{15a} and R^{15b} are independently selected from the group consisting of: (A) hydrogen; (B) C_1-C_6 alkyl; (C) C_1-C_6 haloalkyl; (D) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (E) (hydroxy)C_1-C_4 alkyl; (F) (cyano)alkyl; (G) unsubstituted C_6-C_{10} aryl; (H) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (I) unsubstituted 5- or 6-membered heteroaryl; (J) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (K) unsubstituted 4- to 14-membered heterocyclo; (L) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (M) unsubstituted C_3-C_8 cycloalkyl; and (N) substituted C_3-C_8 cycloalkyl having one, two, three, or four

substituents independently selected from the group consisting of C_1-C_6 alkyl and -$NR^{15g}R^{15h}$; or

[0323] R^{15a} and R^{15b} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0324] R^{15c} and R^{15d} are independently selected from the group consisting of: (A) hydrogen; (B) C_1-C_6 alkyl; (C) C_1-C_6 haloalkyl; (D) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (E) (hydroxy)C_1-C_4 alkyl; (F) (cyano)alkyl; (G) unsubstituted C_6-C_{10} aryl; (H) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (I) unsubstituted 5- or 6-membered heteroaryl; (J) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (K) unsubstituted 4- to 14-membered heterocyclo; (L) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (M) unsubstituted C_3-C_8 cycloalkyl; and (N) substituted C_3-C_8 cycloalkyl having one, two, three, or four substituents independently selected from the group consisting of C_1-C_6 alkyl and -$NR^{15g}R^{15h}$; or

[0325] R^{15c} and R^{15d} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0326] R^{15e} and R^{15f} are independently selected from the group consisting of: (A) hydrogen; (B) C_1-C_6 alkyl; (C) C_1-C_6 haloalkyl; (D) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (E) (hydroxy)C_1-C_4 alkyl; (F) (cyano)alkyl; (G) unsubstituted C_6-C_{10} aryl; (H) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (I) unsubstituted 5- or 6-membered heteroaryl; (J) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (K) unsubstituted 4- to 14-membered heterocyclo; (L) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (M) unsubstituted C_3-C_8 cycloalkyl; and (N) substituted C_3-C_8 cycloalkyl having one, two, three, or four substituents independently selected from the group consisting of C_1-C_6 alkyl and -$NR^{15g}R^{15h}$; or

[0327] R^{15e} and R^{15f} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0328] R^{15g} and R^{15h} are independently selected from the group consisting of: (A) hydrogen; (B) C_1-C_6 alkyl; (C) C_1-C_6 haloalkyl; (D) C_1-C_6 alkoxy; (E) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (F) (hydroxy)C_1-C_4 alkyl; (G) (cyano)alkyl; (H) unsubstituted C_6-C_{10} aryl; (I) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (J) unsubstituted 5- or 6-membered heteroaryl; (K) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (L) unsubstituted 4- to 14-membered heterocyclo; (M) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (N) unsubstituted C_3-C_8 cycloalkyl; and (O) substituted C_3-C_8 cycloalkyl having one, two, three, or four substituents independently selected from the group consisting of C_1-C_6 alkyl and $-NR^{15g}R^{15h}$; or

[0329] R^{15g} and R^{15g} taken together with the nitrogen atom to which they are attached form an optionally substituted 4- to 14- membered heterocyclo;

[0330] R^{16} is (amino)(hydroxy)C_1-C_4 alkyl;

[0331] R^{17a} is selected from the group consisting of hydrogen and C_1-C_4 alkyl;

[0332] R^{18a} is selected from the group consisting of: (A) C_1-C_6 alkyl; (B) C_1-C_6 haloalkyl; (C) C_1-C_6 alkoxy; (D) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (E) (hydroxy)C_1-C_4 alkyl; (F) (cyano)alkyl; (G) unsubstituted C_6-C_{10} aryl; (H) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (I) unsubstituted 5- or 6-membered heteroaryl; (J) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (K) unsubstituted 4- to 14-membered heterocyclo; (L) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (M) unsubstituted C_3-C_8 cycloalkyl; and (N) substituted C_3-C_8 cycloalkyl having one, two, three, or four substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl,

[0333] or a pharmaceutically acceptable salt or solvate thereof.

[0334] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **V**, **V-A**, or **V-B**, wherein R^{14a} is selected from the group consisting of unsubstituted 5- to 10-membered heteroaryl; and substituted 5- or 10-membered heteroaryl having one, two, or three substituents independently selected from the group consisting of C_1-C_4 alkyl; C_1-C_4 alkoxy; (3- to 8-membered heterocyclo)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; -C(=O)$NR^{15a}R^{15b}$; unsubstituted 5- to 10-membered heteroaryl; substituted 5- or 10-membered heteroaryl having one, two, or three substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, (3- to 8-membered heterocyclo)C_1-C_4 alkyl, 5- to 9-membered heteroaryl, and -$NR^{15e}R^{15f}$; unsubstituted C_3-C_6 cycloalkyl; and substituted C_3-C_6 cycloalkyl having one, two, or three substituents independently selected from the group consisting of C_1-C_4 alkyl and -N(R^{17a})C(=O)R^{18a}, or a pharmaceutically acceptable salt or solvate thereof.

[0335] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **V**, **V-A**, or **V-B**, wherein R^{14a} is a substituted pyridyl having one, two, or three substituents independently selected from the group consisting of C_1-C_4 alkyl; C_1-C_4 alkoxy; (3- to 8-membered heterocyclo)C_1-C_4 alkyl; (5- to 9-membered heteroaryl)C_1-C_4 alkyl; -C(=O)$NR^{15a}R^{15b}$; unsubstituted 5- to 10-membered heteroaryl; substituted 5- to 10-membered heteroaryl having one, two, or three substituents independently selected from the group consisting of halo, C_1-C_4 alkyl, (3- to 8-membered heterocyclo)C_1-C_4 alkyl, 5- to 9-membered heteroaryl, and -$NR^{15e}R^{15f}$; unsubstituted C_3-C_6 cycloalkyl; and substituted C_3-C_6 cycloalkyl having one, two, or three substituents independently selected from the group consisting of C_1-C_4 alkyl and -N(R^{17a})C(=O)R^{18a}, or a pharmaceutically acceptable salt or solvate thereof.

[0336] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **V**, **V-A**, or **V-B**, wherein R^{14b} is selected from the group consisting of unsubstituted 5- to 10-membered heteroaryl; substituted 5- to 10-membered heteroaryl having one or two substituents independently selected from the group consisting of C_1-C_4 alkyl and (C_3-C_6 cycloalkyl)C_1-C_4 alkyl; unsubstituted C_6-C_{10} aryl; substituted C_6-C_{10} aryl, having one or two substituents independently selected from the group consisting of C_1-C_4 alkyl and (3- to 8-membered heterocyclo)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of hydroxy, amino, and C_1-

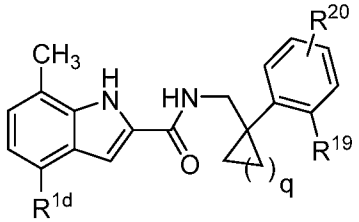
C_4 alkyl; and unsubstituted C_3-C_6 cycloalkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0337] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **V**, **V-A**, or **V-B**, wherein R^{14b} is selected from the group consisting of unsubstituted 5- or 6-membered heteroaryl; substituted 5- or 6-membered heteroaryl having one or two substituents independently selected from the group consisting of C_1-C_4 alkyl and (C_3-C_6 cycloalkyl)C_1-C_4 alkyl; unsubstituted phenyl; substituted phenyl, having one or two substituents independently selected from the group consisting of C_1-C_4 alkyl and (3- to 8-membered heterocyclo)C_1-C_4 alkyl; and unsubstituted C_3-C_6 cycloalkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0338] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **V**, **V-A**, or **V-B**, wherein p is 0, or a pharmaceutically acceptable salt or solvate thereof.

[0339] In another embodiment, Compounds of the Disclosure are compounds having any one of Formulae **V**, **V-A**, or **V-B**, wherein p is 1, or a pharmaceutically acceptable salt or solvate thereof.

[0340] In another embodiment, Compounds of the Disclosure are compounds having Formula **VI**:



VI,

wherein:

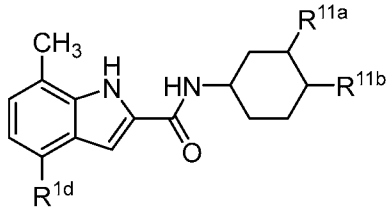
[0341] R^{19} is selected from the group consisting of unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl;

[0342] R^{20} is selected from the group consisting of hydrogen, halo, and C_1-C_4 alkyl; and

[0343] q is 1, 2, or 3, or a pharmaceutically acceptable salt or solvate thereof.

[0344] In another embodiment, Compounds of the Disclosure are compounds having Formula **VI**, wherein q is 1.

[0345] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII**:



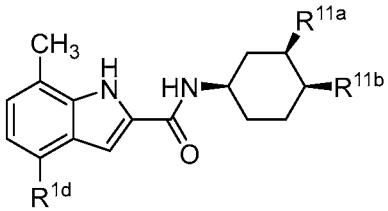
VII,

[0346] wherein:

[0347] R^{11b} is selected from the group consisting of C_1-C_4 alkyl, halo, and C_1-C_4 haloalkyl; and

[0348] R^{1d} and R^{11a} are as defined in connection with Formula **IV**, or a pharmaceutically acceptable salt or solvate thereof.

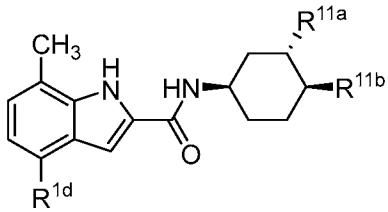
[0349] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-A**:



VII-A,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

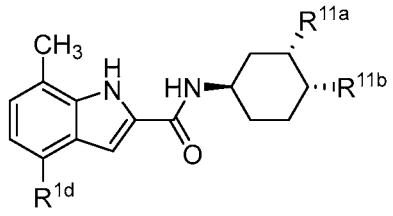
[0350] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-B**:



VII-B,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

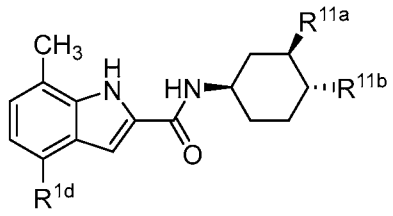
[0351] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-C**:



VII-C,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

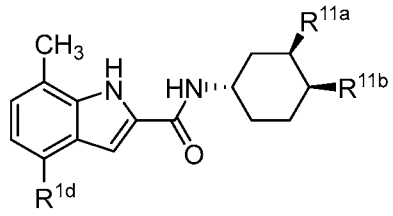
[0352] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-D**:



VII-D,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

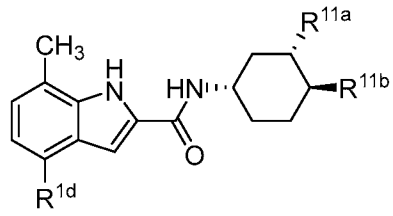
[0353] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-E**:



VII-E,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

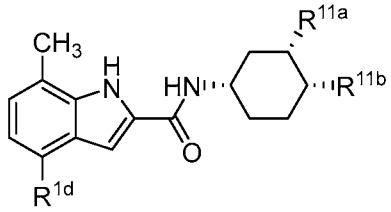
[0354] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-F**:



VII-F,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

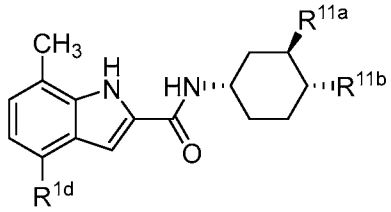
[0355] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-G**:



VII-G,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

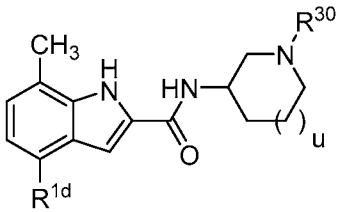
[0356] In another embodiment, Compounds of the Disclosure are compounds having Formula **VII-H**:



VII-H,

wherein R^{1d}, R^{11a}, and R^{11b} are as defined in connection with Formula **VII**, or a pharmaceutically acceptable salt or solvate thereof.

[0357] In another embodiment, Compounds of the Disclosure are compounds having Formula **VIII**:



VIII,

wherein:

[0358] R^{30} is selected from the group consisting of hydrogen; C_1-C_6 alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; -C(=O)R^{13b}, and -S(=O)$_2R^{24}$;

[0359] R^{13b} is selected from the group consisting of C_1-C_4 alkyl; amino; C_1-C_4 haloalkyl; C_1-C_4 alkoxy; (hydroxy)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (amino)alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two

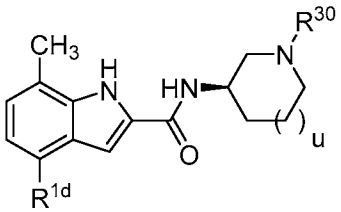
substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy;

[0360] R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl;

[0361] u is 0, 1, 2, or 3; and

[0362] R^{1d} is as defined in connection with Formula **I**, or a pharmaceutically acceptable salt or solvate thereof.

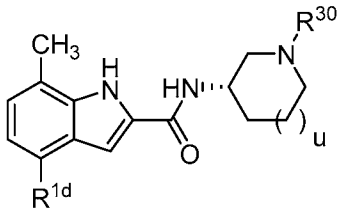
[0363] In another embodiment, Compounds of the Disclosure are compounds having Formula **VIII-A**:



VIII-A,

wherein R^{1d}, R^{30}, and u are as defined in connection with Formula **VIII**, or a pharmaceutically acceptable salt or solvate thereof.

[0364] In another embodiment, Compounds of the Disclosure are compounds having Formula **VIII-B**:



VIII-B,

wherein R^{1d}, R^{30}, and u are as defined in connection with Formula **VIII**, or a pharmaceutically acceptable salt or solvate thereof.

[0365] In another embodiment, Compounds of the Disclosure are compounds of Table 1, and the pharmaceutically acceptable salts or solvates thereof. The chemical names of the compounds of Table 1 were generated by Chemdraw® Professional version 17.0.0.206. Mass spectroscopy and biological data of representative Compounds of the Disclosure are provided in Table 1B and/or WO 2020/037079 and/or WO 2021/168313. In another embodiment, Compounds of the Disclosure are compounds of Table 1B, and the

pharmaceutically acceptable salts or solvates thereof. The biological data in Table 1B were generated following the protocols described in EXAMPLES 11 and 12 of WO 2020/037079.

[0366] In another embodiment, Compounds of the Disclosure are selected from the group consisting of Cpd. Nos. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 824, 828, 839, 870, 922, 930, 942, 995, 1007, 1025, 1043, 1044, 1045, 1048, 1051, 1055, 1070, 1078, 1083, 1097, 1117, 1138, 1180, 1184, and 1192, and the pharmaceutically acceptable salts or solvates thereof. In another embodiment, Compounds of the Disclosure are selected from the group consisting of Cpd. Nos. 15, 922, 930, 942, 1055, 1070, 1117, 1180, 1184, and 1192, and the pharmaceutically acceptable salts or solvates thereof. In another embodiment, Compounds of the Disclosure are selected from the group consisting of Cpd. Nos. 1228, 1229, 1230, 1231, 1232, 1233, 1234 and 1235, and the pharmaceutically acceptable salts or solvates thereof.

[0367] In another embodiment, Compounds of the Disclosure are selected from the group consisting of Cpd. Nos. 15, 942, 1184, and 1232, and the pharmaceutically acceptable salts or solvates thereof.

[0368] In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 15. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1228. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1229. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1230. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1231. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1232. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1233. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1234. In a non-limiting embodiment, the Compound of the Disclosure is Cpd. No. 1235. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 15. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1228. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1229. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1230. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1231. In a non-limiting

embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1232. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1233. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1234. In a non-limiting embodiment, the Compound of the Disclosure is a pharmaceutically acceptable salt or solvate of Cpd. No. 1235.

Table 1

Cpd. No.	Chemical Name
1	4-fluoro-N-(3-fluoro-5-(3-(N-methylacetamido)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
2	4-fluoro-N-(3-fluoro-5-(3-(2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
3	N-(3-(3-(dimethylamino)-2-oxopyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
4	N-(3-(3-(4-(2-(dimethylamino)-2-oxoethyl)piperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
5	N-(3-(8-acetyl-2,8-diazaspiro[4.5]decan-2-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
6	N-(3-(3-(4-(2-amino-2-oxoethyl)piperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
7	N-(3-(4-acetylpiperazin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
8	N-(3-(3-(1,1-dioxidothiomorpholino)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
9	N-(3-(3-(4-acetylpiperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
10	N-(3-(4-cyclopropyl-3-oxopiperazin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
11	4-fluoro-N-(3-fluoro-5-(3-morpholinopyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
12	4-fluoro-N-(3-fluoro-5-(4-(2-methoxyacetyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
13	N-(3-(4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
14	N-(3-(1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
15	N-((1R,3S)-3-(4-acetylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
16	4-fluoro-N-(3-fluoro-5-(3-(2-(hydroxymethyl)morpholino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
17	4-fluoro-N-(3-fluoro-5-(3-(4-methyl-3-oxopiperazin-1-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide

18	4-fluoro-N-(3-fluoro-5-(2-oxo-[1,3'-bipyrrolidin]-1'-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
19	N-(3-(7-acetyl-2,7-diazaspiro[3.5]nonan-2-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
20	4-fluoro-N-(3-fluoro-5-(4-methyl-3-oxopiperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
21	4-fluoro-N-(3-fluoro-5-(4-methyl-5-oxo-1,4-diazepan-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
22	N-(3-chloro-5-(3-morpholinopyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
23	N-(3-(1-acetyl-4-methylpiperidin-4-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
24	4-fluoro-N-(3-fluoro-5-(2-(2-hydroxyethyl)morpholino)phenyl)-7-methyl-1H-indole-2-carboxamide
25	N-(3-(4-(dimethylcarbamoyl)piperazin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
26	4-fluoro-N-(3-fluoro-5-((7S,8aS)-3-oxooctahydroindolizin-7-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
27	4-fluoro-7-methyl-N-(3-(6-oxohexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)phenyl)-1H-indole-2-carboxamide
28	N-(3-(6,6-difluoro-2,8-diazaspiro[4.5]decan-2-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
29	N-(3-(3-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
30	N-(3-(2-acetyl-2,8-diazaspiro[4.5]decan-8-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
31	N-(3-(4-acetylpiperazin-1-yl)-5-chlorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
32	N-(3-(4-acetyl-3-methylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
34	N-(3-(4-acetylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
35	4-fluoro-N-(3-fluoro-5-((1s,4s)-4-morpholinocyclohexyl)phenyl)-7-methyl-1H-indole-2-carboxamide
36	4-fluoro-7-methyl-N-(3-(4-propionylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
37	4-fluoro-7-methyl-N-(3-(3-oxooctahydroindolizin-7-yl)phenyl)-1H-indole-2-carboxamide
38	4-fluoro-7-methyl-N-(3-(3-(N-methylacetamido)pyrrolidin-1-yl)phenyl)-1H-indole-2-carboxamide
39	N-(3-(3-(4-(dimethylglycyl)piperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
40	N-(3-(7-(2,2-difluoroethyl)-2,7-diazaspiro[3.5]nonan-2-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
41	N-(3-(7-(2,2-difluoroethyl)-2,7-diazaspiro[3.5]nonan-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
42	4-fluoro-7-methyl-N-(3-(3-(N-methylacetamido)piperidin-1-yl)phenyl)-1H-indole-2-carboxamide

43	N-(3-(4-(dimethylalanyl)piperazin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
44	4-fluoro-N-(3-(4-(2-methoxyacetyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
45	N-(3-(1-acetylpiperidin-4-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
46	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
47	4-fluoro-N-(3-fluoro-5-(3-((2-fluoroethyl)(methyl)amino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
48	4-fluoro-N-(3-fluoro-5-(2-(hydroxymethyl)morpholino)phenyl)-7-methyl-1H-indole-2-carboxamide
49	4-fluoro-7-methyl-N-(3-(4-nicotinoylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
50	4-fluoro-N-(3-(2-(2-hydroxyethyl)morpholino)phenyl)-7-methyl-1H-indole-2-carboxamide
51	4-fluoro-7-methyl-N-(3-((7R,8aR)-3-oxooctahydroindolizin-7-yl)phenyl)-1H-indole-2-carboxamide
52	N-(3-(4-acetylpiperazin-1-yl)-2-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
53	N-(3-(3-(dimethylamino)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
54	4-fluoro-7-methyl-N-(3-(2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)phenyl)-1H-indole-2-carboxamide
55	N-(3-(4-(dimethylcarbamoyl)piperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
56	N-(3-(1-acetylpyrrolidin-3-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
57	N-(3-(2-oxa-7-azaspiro[3.5]nonan-7-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
58	4-fluoro-7-methyl-N-(3-(4-methyl-3-oxopiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
59	N-(3-(3-(dimethylamino)pyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
60	N-(3-(1,3,4-oxadiazol-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
61	N-(3-((3S,4S)-3-(dimethylamino)-4-hydroxypyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
62	N-(3-(4-(dimethylglycyl)piperazin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
63	N-(3-(3-(dimethylamino)-4-fluoropyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
64	4-fluoro-7-methyl-N-(3-(pyrimidin-5-yl)phenyl)-1H-indole-2-carboxamide
65	4-fluoro-7-methyl-N-(3-(5-methyl-1,3,4-thiadiazol-2-yl)phenyl)-1H-indole-2-carboxamide
66	4-fluoro-7-methyl-N-(3-(2-oxooxazolidin-3-yl)phenyl)-1H-indole-2-carboxamide
68	N-(3-((1r,4r)-4-(dimethylamino)cyclohexyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
69	N-(3-((1s,4s)-4-(dimethylamino)cyclohexyl)-5-fluorophenyl)-4-fluoro-7-methyl-

	1H-indole-2-carboxamide
70	N-(3-(4-(dimethylglycyl)-3-methylpiperazin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
71	N-(3-(4-acetyl-3-ethylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
72	4-fluoro-N-(3-(4-(2-hydroxyacetyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
73	N-(3-(1-acetylpyrrolidin-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
74	4-fluoro-7-methyl-N-(3-(3-morpholinopyrrolidin-1-yl)phenyl)-1H-indole-2-carboxamide
75	4-fluoro-N-(3-(4-(3-methoxypropanoyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
76	4-fluoro-7-methyl-N-(3-(4-morpholinopiperidin-1-yl)phenyl)-1H-indole-2-carboxamide
77	N-(3-(4-acetyl-3-(trifluoromethyl)piperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
78	4-fluoro-7-methyl-N-(3-(4-(N-methylacetamido)piperidin-1-yl)phenyl)-1H-indole-2-carboxamide
79	N-(3-(4-acetylpiperazin-1-yl)-4-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
80	N-(3-(4-(dimethylamino)piperidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
81	4-fluoro-N-(3-(5-(methoxymethyl)-1,3,4-thiadiazol-2-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
82	4-fluoro-N-(7-fluoroisoquinolin-5-yl)-7-methyl-1H-indole-2-carboxamide
83	methyl 2-(3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)phenyl)-2,8-diazaspiro[4.5]decane-8-carboxylate
84	N-(3-(4-acetylpiperazin-1-yl)phenyl)-7-bromo-4-fluoro-1H-indole-2-carboxamide
85	4-fluoro-7-methyl-N-(2-(1-methyl-1H-pyrazol-4-yl)-1-(3-methylpyridin-2-yl)ethyl)-1H-indole-2-carboxamide
86	N-(3-(1,8-diazaspiro[4.5]decan-8-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
87	4-fluoro-N-(3-(4-hydroxy-4-methylpiperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
88	N-(3-(4-ethyl-3-oxopiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
89	4-fluoro-N-(3-fluoro-5-(1'-methyl-5'-oxo-[1,3'-bipyrrolidin]-3-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
90	4-fluoro-7-methyl-N-(3-((7S,8aS)-3-oxooctahydroindolizin-7-yl)phenyl)-1H-indole-2-carboxamide
91	N-(3-chloro-5-(4-methylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
92	4-fluoro-N-(3-(4-(2-fluoroacetyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
93	N-(3-(4-(cyclopropanecarbonyl)piperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
94	(R)-N-(3-(3-(dimethylamino)pyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-

	indole-2-carboxamide
95	N-(3-(4-oxa-1,9-diazaspiro[5.5]undecan-9-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
96	4-fluoro-N-(3-fluoro-5-((7R,8aS)-3-oxooctahydroindolizin-7-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
97	N-(3-((3R,5S)-4-acetyl-3,5-dimethylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
98	4-fluoro-7-methyl-N-(3-(2-methyl-2,7-diazaspiro[3.5]nonan-7-yl)phenyl)-1H-indole-2-carboxamide
99	N-(3-(4-(dimethylamino)-3-methylpiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
100	N-(3-(4-cyclopropyl-3-oxopiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
101	4-fluoro-7-methyl-N-(3-(tetrahydro-2H-pyran-4-yl)phenyl)-1H-indole-2-carboxamide
102	(S)-N-(3-(3-(dimethylamino)pyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
103	N-(3-(4,4-bis(hydroxymethyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
104	N-(3-(1-acetyl-1,8-diazaspiro[4.5]decan-8-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
105	4-fluoro-N-(3-fluoro-5-((3aS,6aS)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
106	N-(3-chloro-5-((1s,4s)-4-(dimethylamino)cyclohexyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
107	4-fluoro-N-(3-(5-(hydroxymethyl)-1,3,4-thiadiazol-2-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
108	4-fluoro-7-methyl-N-(3-(oxazol-5-yl)phenyl)-1H-indole-2-carboxamide
109	4-fluoro-N-(3-(7-(2-methoxyethyl)-2,7-diazaspiro[3.5]nonan-2-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
110	4-fluoro-7-methyl-N-(3-(2-(2,2,2-trifluoroethyl)-2,7-diazaspiro[3.5]nonan-7-yl)phenyl)-1H-indole-2-carboxamide
111	N-(3-((3R,4S)-4-(dimethylamino)-3-methylpiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
112	methyl 2-(3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)phenyl)-2,7-diazaspiro[3.5]nonane-7-carboxylate
113	N-(3-(4-(dimethylamino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
114	4-fluoro-N-(3-fluoro-5-((8aR)-3-oxooctahydroindolizin-7-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
115	4-fluoro-N-(3-(2-(hydroxymethyl)morpholino)phenyl)-7-methyl-1H-indole-2-carboxamide
116	4-fluoro-7-methyl-N-(3-(pyridin-4-yl)phenyl)-1H-indole-2-carboxamide
117	N-(3-(4-((dimethylamino)methyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
118	4-fluoro-7-methyl-N-(3-(2-oxopyrrolidin-1-yl)phenyl)-1H-indole-2-carboxamide
119	N-(3-(5-cyclopropyl-1,3,4-oxadiazol-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide

120	N-(3-chloro-5-(3-(dimethylamino)pyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
121	methyl 4-(3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)phenyl)piperazine-1-carboxylate
122	4-fluoro-N-(3-fluoro-5-((3aR,6aR)-1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
123	N-(3-(1-acetylpiperidin-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
124	4-fluoro-7-methyl-N-(3-(octahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)phenyl)-1H-indole-2-carboxamide
125	N-(3-(1,1-dioxidoisothiazolidin-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
126	4-fluoro-N-(3-(4-hydroxypiperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
127	methyl 8-(3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)phenyl)-2,8-diazaspiro[4.5]decane-2-carboxylate
128	4-fluoro-7-methyl-N-(3-(3-(methylamino)pyrrolidin-1-yl)phenyl)-1H-indole-2-carboxamide
129	4-fluoro-7-methyl-N-(3-(2-methylmorpholino)phenyl)-1H-indole-2-carboxamide
130	4-fluoro-N-(3-(3-((2-fluoroethyl)(methyl)amino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
131	4-fluoro-7-methyl-N-((1S,3R)-3-(pyrimidin-5-yl)cyclohexyl)-1H-indole-2-carboxamide
132	N-(3-(5-((dimethylamino)methyl)-1,3,4-thiadiazol-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
133	4-fluoro-N-(3-(2-(methoxymethyl)morpholino)phenyl)-7-methyl-1H-indole-2-carboxamide
134	4-fluoro-N-(isoquinolin-5-yl)-7-methyl-1H-indole-2-carboxamide
135	4-fluoro-7-methyl-N-(3-(6-methyl-2,6-diazaspiro[3.3]heptan-2-yl)phenyl)-1H-indole-2-carboxamide
136	4-fluoro-7-methyl-N-(4'-(methylsulfonamidomethyl)-[1,1'-biphenyl]-3-yl)-1H-indole-2-carboxamide
137	4-fluoro-7-methyl-N-(3-(pyridin-3-yl)phenyl)-1H-indole-2-carboxamide
138	4-fluoro-7-methyl-N-(3-(4-(1-methylpiperidine-3-carbonyl)piperazin-1-yl)phenyl)-1H-indole-2-carboxamide
139	4-fluoro-7-methyl-N-(3-(4-(methylcarbamoyl)piperazin-1-yl)phenyl)-1H-indole-2-carboxamide
140	N-(3-(1-(dimethylglycyl)pyrrolidin-3-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
141	N-(2-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-1-(3-methylpyridin-2-yl)ethyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
142	N-(3-(1-(2,2-difluoroethyl)-1,8-diazaspiro[4.5]decan-8-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
143	N-(3-(2-cyclopropylmorpholino)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
144	4-fluoro-7-methyl-N-(3-(4-(methylamino)piperidin-1-yl)phenyl)-1H-indole-2-carboxamide
145	N-(3-chloro-5-(pyrimidin-5-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-

	carboxamide
146	4-fluoro-7-methyl-N-(3-(4-(tetrahydrofuran-3-yl)piperazin-1-yl)phenyl)-1H-indole-2-carboxamide
147	4-fluoro-7-methyl-N-(3-(3-oxopiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
148	4-fluoro-N-(3-(3-((2-hydroxyethyl)(methyl)amino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
149	4-fluoro-N-(3-(4-(3-hydroxypropanoyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
150	N-(3-(4-(3-aminopropyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
151	4-fluoro-7-methyl-N-(3-(1-methyl-1H-pyrazol-4-yl)phenyl)-1H-indole-2-carboxamide
152	4-fluoro-7-methyl-N-(3-(4-(4-methylpiperazin-1-yl)piperidin-1-yl)phenyl)-1H-indole-2-carboxamide
153	N-(3-(3-(4,4-difluoropiperidin-1-yl)pyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
154	N-(3-((3R,4R)-3-(dimethylamino)-4-hydroxypyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
155	4-fluoro-N-(3-(4-(3-methoxyazetidin-1-yl)piperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
156	4-fluoro-N-(3-(3-((2-methoxyethyl)(methyl)amino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
157	4-fluoro-7-methyl-N-(3-(4-(pyridin-3-ylamino)piperidin-1-yl)phenyl)-1H-indole-2-carboxamide
159	4-fluoro-N-(3-fluoro-5-(3-methyl-3-morpholinopyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
160	4-fluoro-7-methyl-N-(3-(1-methyl-2-oxopiperidin-4-yl)phenyl)-1H-indole-2-carboxamide
161	N-((5-((1H-imidazol-1-yl)methyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
162	N-(3-(1H-1,2,4-triazol-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
163	N-(3-(8-acetyl-3,8-diazabicyclo[3.2.1]octan-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
164	4-fluoro-7-methyl-N-(3-(1-(2-morpholinoethyl)-1H-pyrazol-4-yl)phenyl)-1H-indole-2-carboxamide
165	4-fluoro-7-methyl-N-(3-(5-methylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)phenyl)-1H-indole-2-carboxamide
166	4-fluoro-7-methyl-N-(3-((7S,8aR)-3-oxooctahydroindolizin-7-yl)phenyl)-1H-indole-2-carboxamide
167	N-(3-(2-((dimethylamino)methyl)morpholino)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
168	4-fluoro-7-methyl-N-(3-(1-methylpiperidin-4-yl)phenyl)-1H-indole-2-carboxamide
169	4-fluoro-7-methyl-N-((1R,3S)-3-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
170	N-(3-(4-(2-cyanoacetyl)piperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
171	4-fluoro-7-methyl-N-(3-(1-methyl-1H-imidazol-2-yl)phenyl)-1H-indole-2-

	carboxamide
172	4-fluoro-7-methyl-N-(3-(1-methyloctahydro-5H-pyrrolo[3,2-c]pyridin-5-yl)phenyl)-1H-indole-2-carboxamide
173	N-(3-(4,4-bis(methoxymethyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
174	4-fluoro-N-(3-(3-(3-hydroxyazetidin-1-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
175	N-(2-(1-(cyclopropylmethyl)-1H-pyrazol-4-yl)-1-(3-methylpyridin-2-yl)ethyl)-7-methyl-1H-indole-2-carboxamide
176	4-fluoro-7-methyl-N-(3-(4-(methylsulfonyl)piperazin-1-yl)phenyl)-1H-indole-2-carboxamide
177	4-fluoro-7-methyl-N-(3-(5-oxopyrrolidin-3-yl)phenyl)-1H-indole-2-carboxamide
178	N-(3-(3-(azetidin-1-yl)pyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
179	N-(3-(2,7-diazaspiro[3.5]nonan-7-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
180	4-fluoro-7-methyl-N-(3-(4-(pyrrolidin-1-yl)piperidin-1-yl)phenyl)-1H-indole-2-carboxamide
181	4-fluoro-7-methyl-N-(3-(3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)phenyl)-1H-indole-2-carboxamide
182	4-fluoro-7-methyl-N-(3-(1-methyloctahydro-6H-pyrrolo[3,4-b]pyridin-6-yl)phenyl)-1H-indole-2-carboxamide
183	4-fluoro-N-(3-fluoro-5-(4-methyl-3-oxo-1,4-diazepan-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
184	N-(3-(2,7-diazaspiro[3.5]nonan-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
185	N-(5-(4-acetylpiperazin-1-yl)-2-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
186	N-(3-((3R,4S)-4-(dimethylamino)-3-fluoropiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
187	N-(3-(4-(dimethylamino)piperidin-1-yl)-5-methylphenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
188	N-(3-chloro-5-(4-(3-morpholinopropyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
189	N-(3-(2,8-diazaspiro[4.5]decan-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
190	N-(3-chloro-5-(4-(dimethylamino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
191	4-fluoro-7-methyl-N-(3-(3-methyl-2-oxoimidazolidin-1-yl)phenyl)-1H-indole-2-carboxamide
192	N-(3-(4-aminopiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
193	N-(3-(4-acetyl-3-isobutylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
194	4-fluoro-7-methyl-N-(3-morpholinophenyl)-1H-indole-2-carboxamide
195	N-(3-(4-(dimethylamino)-1-hydroxycyclohexyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
196	4-fluoro-N-(3-(isoxazol-5-yl)phenyl)-7-methyl-1H-indole-2-carboxamide

197	4-fluoro-7-methyl-N-(3-(1-methyl-1H-imidazol-5-yl)phenyl)-1H-indole-2-carboxamide
198	4-fluoro-N-(3-(4-methoxypiperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
199	N-(3-(4-(cyclopropylmethyl)piperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
200	4-fluoro-7-methyl-N-(3-(5-oxo-1,4-diazepan-1-yl)phenyl)-1H-indole-2-carboxamide
201	4-fluoro-N-(3-(4-isopropyl-3-oxopiperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
202	N-(3-((3S,4R)-4-(dimethylamino)-3-methylpiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
203	N-(3-(2-((ethylamino)methyl)morpholino)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
204	4-fluoro-N-(3-(4-(2-hydroxyethyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
205	4-fluoro-N-(3-(4-isopropyl-3-methylpiperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
206	N-(3-(2-(2,2-difluoroethyl)-2,8-diazaspiro[4.5]decan-8-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
207	4-fluoro-7-methyl-N-(3-(4-(tetrahydro-2H-pyran-4-yl)piperazin-1-yl)phenyl)-1H-indole-2-carboxamide
208	N-(3-(4-(dimethylglycyl)piperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
209	4-fluoro-7-methyl-N-(3-(3-oxomorpholino)phenyl)-1H-indole-2-carboxamide
210	4-fluoro-N-(3-(4-((2-hydroxyethyl)amino)piperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
211	4-fluoro-7-methyl-N-((1R,3S)-3-morpholinocyclohexyl)-1H-indole-2-carboxamide
212	4-fluoro-7-methyl-N-(3-(1-methyl-1,8-diazaspiro[4.5]decan-8-yl)phenyl)-1H-indole-2-carboxamide
213	N-(1-((1r,4r)-4-(dimethylamino)cyclohexyl)-1H-indazol-4-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
214	N-(3-((3R,5R)-4-acetyl-3,5-dimethylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
215	4-fluoro-7-methyl-N-(3-(pyrrolo[1,2-a]pyrazin-7-yl)phenyl)-1H-indole-2-carboxamide
216	4-fluoro-7-methyl-N-(3-(3-methylmorpholino)phenyl)-1H-indole-2-carboxamide
217	N-(3-((1R,3R)-3-(dimethylamino)cyclopentyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
218	N-(3-(6-oxa-3-azabicyclo[3.1.1]heptan-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
219	4-fluoro-N-(3-(1-(2-hydroxyethyl)-1H-pyrazol-4-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
220	4-fluoro-N-(3-(hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
221	N-(3-(1H-imidazol-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
222	N-(3-(4-(dimethylamino)-4-methylpiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-

	indole-2-carboxamide
223	4-fluoro-N-(3-(4-(2-methoxyethyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
224	4-fluoro-7-methyl-N-(3-(oxetan-3-yl)phenyl)-1H-indole-2-carboxamide
225	4-fluoro-7-methyl-N-(3-(4-(propylamino)piperidin-1-yl)phenyl)-1H-indole-2-carboxamide
226	N-(3-(1-(dimethylglycyl)pyrrolidin-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
227	N-(3-(4-(bis(2-hydroxyethyl)amino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
228	N-(4'-((1H-imidazol-1-yl)methyl)-[1,1'-biphenyl]-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
229	4-fluoro-7-methyl-N-(3-(4-methyl-3-(trifluoromethyl)piperazin-1-yl)phenyl)-1H-indole-2-carboxamide
230	4-fluoro-N-(3-fluoro-5-(1'-methyl-2'-oxo-[1,3'-bipyrrolidin]-3-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
231	4-fluoro-N-(4'-(2-hydroxyethoxy)-[1,1'-biphenyl]-3-yl)-7-methyl-1H-indole-2-carboxamide
232	4-fluoro-7-methyl-N-(5-(4-methylpiperazin-1-yl)imidazo[1,5-a]pyridin-7-yl)-1H-indole-2-carboxamide
233	N-(3-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
234	4-fluoro-7-methyl-N-(3-(4-methylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
235	4-fluoro-7-methyl-N-(3-(pyrazolo[1,5-a]pyridin-4-yl)phenyl)-1H-indole-2-carboxamide
236	N-(3-(4-cyclopropylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
237	4-fluoro-7-methyl-N-(3-(4-methyl-4H-1,2,4-triazol-3-yl)phenyl)-1H-indole-2-carboxamide
238	4-fluoro-7-methyl-N-(quinolin-5-yl)-1H-indole-2-carboxamide
239	4-fluoro-7-methyl-N-(3-(1-methyl-1H-pyrazol-5-yl)phenyl)-1H-indole-2-carboxamide
240	N-(3-(4-(2-aminoethoxy)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
241	N-(3-(2,8-diazaspiro[4.5]decan-8-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
242	N-(3-(4-acetylpiperazin-1-yl)-5-(trifluoromethyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
243	4-fluoro-N-(3-(4-isopropylpiperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
244	4-fluoro-7-methyl-N-(3-(2-(4-methylpiperazin-1-yl)ethyl)phenyl)-1H-indole-2-carboxamide
245	4-fluoro-7-methyl-N-(3-(1-methylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)phenyl)-1H-indole-2-carboxamide
246	N-(3-(4-(3-aminopropyl)piperidin-1-yl)-5-chlorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
247	4-fluoro-7-methyl-N-(1-(1-methylpiperidin-4-yl)-1H-indazol-4-yl)-1H-indole-2-

	carboxamide
248	N-(3-(4-acetyl-1,4-diazepan-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
249	N-(3-(1,2,4-oxadiazol-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
250	N-(3-(8-oxa-3-azabicyclo[3.2.1]octan-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
251	N-(3-(4-(dimethylamino)bicyclo[4.1.0]heptan-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
252	N-(3-(1H-pyrazol-4-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
253	N-(3-(4-(dimethylamino)-4-(methoxymethyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
254	N-(3-(4-((dimethylamino)methyl)-4-hydroxypiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
255	N-(3-(1-cyano-4-(dimethylamino)cyclohexyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
256	N-(3-(2-(dimethylamino)-2-oxoethyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
257	N-(3-(6-acetyl-3,6-diazabicyclo[3.1.1]heptan-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
258	4-fluoro-7-methyl-N-(1-(3-methyl-5-(2-(4-methylpiperazin-1-yl)ethyl)pyridin-2-yl)-2-phenylethyl)-1H-indole-2-carboxamide
259	N-(3-(8-(2,2-difluoroethyl)-2,8-diazaspiro[4.5]decan-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
260	tert-butyl 4-(3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)phenyl)piperazine-1-carboxylate
261	4-fluoro-7-methyl-N-(3-(oxazol-2-yl)phenyl)-1H-indole-2-carboxamide
262	4-fluoro-N-(3-(4-methoxy-4-methylpiperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
263	N-(3'-acetamido-[1,1'-biphenyl]-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
264	N-(3-((1S,3S)-3-(dimethylamino)cyclopentyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
265	4-fluoro-N-(3-(3-(hydroxymethyl)morpholino)phenyl)-7-methyl-1H-indole-2-carboxamide
266	N-(3'-((dimethylamino)methyl)-[1,1'-biphenyl]-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
267	N-(3-(1-acetyl-4-carbamoylpiperidin-4-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
268	4-fluoro-N-(3-(4-hydroxy-1'-methyl-[4,4'-bipiperidin]-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
269	N-(cyclopropyl(4-methoxy-3-methylpyridin-2-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
270	4-fluoro-7-methyl-N-(4-methyl-3-(4-methylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
271	N-(3-(4-acetylpiperazin-1-yl)-5-fluorophenyl)-4-fluoro-1H-indole-2-carboxamide
272	4-fluoro-N-(3-(imidazo[1,2-a]pyridin-5-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
273	N-(cyclopropyl(3-methyl-5-((2-oxo-2,3-dihydro-1H-imidazol-1-

	yl)methyl)pyridin-2-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
274	N-(3-(4-(dimethylamino)piperidin-1-yl)-5-(fluoromethyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
275	N-(3-chloro-5-(4-(3-morpholinopropyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
276	N-(3-(3-((dimethylamino)methyl)-1H-1,2,4-triazol-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
277	4-fluoro-N-(3-(2-(hydroxymethyl)-4-methylpiperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
278	4-fluoro-N-(3-(imidazo[1,5-a]pyridin-6-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
279	4-fluoro-7-methyl-N-(3-(4-methyl-1,4-diazepan-1-yl)phenyl)-1H-indole-2-carboxamide
280	4-fluoro-N-(3-(4-isopropyl-2-methylpiperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
281	N-(3-(4H-1,2,4-triazol-4-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
282	N-(3-(3-(dimethylamino)cyclopentyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
283	4-fluoro-7-methyl-N-(3-(pyrrolidin-3-yl)phenyl)-1H-indole-2-carboxamide
284	N-(3-(2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
285	4-fluoro-7-methyl-N-(3-(pyridin-2-yl)phenyl)-1H-indole-2-carboxamide
286	4-fluoro-N-(3-(imidazo[1,2-a]pyridin-2-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
287	N-(3-(4-oxa-7-azaspiro[2.5]octan-7-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
288	4-fluoro-7-methyl-N-(3-(4-(methylamino)-4-oxobutyl)phenyl)-1H-indole-2-carboxamide
289	N-(3-(2,5-dimethylmorpholino)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
290	4-fluoro-7-methyl-N-(3-(pyrazolo[1,5-a]pyridin-3-yl)phenyl)-1H-indole-2-carboxamide
291	N-(3-(3-oxa-8-azabicyclo[3.2.1]octan-8-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
292	N-(3-(5-acetyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
293	4-fluoro-7-methyl-N-(3-(3-(methylamino)-3-oxopropyl)phenyl)-1H-indole-2-carboxamide
294	4-fluoro-7-methyl-N-(3-(1-methyloctahydro-1H-indol-5-yl)phenyl)-1H-indole-2-carboxamide
295	N-(2-(4-acetylpiperazin-1-yl)pyrimidin-4-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
296	N-(3-(1,2,4-oxadiazol-5-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
297	4-fluoro-7-methyl-N-(3-(piperidin-1-yl)phenyl)-1H-indole-2-carboxamide
298	N-(3-((3S,5S)-4-acetyl-3,5-dimethylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
299	4-fluoro-N-(3-(imidazo[1,5-a]pyridin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide

300	N-(3-(2-amino-2-oxoethyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
301	N-(3-((3S,4R)-4-(dimethylamino)-3-fluoropiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
302	N-(3-((1R,3S)-3-(dimethylamino)cyclopentyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
303	N-(3-((2S,4R)-4-(dimethylamino)-2-methylpiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
304	N-(3-(4H-1,2,4-triazol-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
305	4-fluoro-7-methyl-N-(5-(3-(N-methylacetamido)piperidin-1-yl)tetrahydro-2H-pyran-3-yl)-1H-indole-2-carboxamide
306	N-(3-(3-cyclopropylmorpholino)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
307	4-fluoro-7-methyl-N-(3-(morpholin-3-yl)phenyl)-1H-indole-2-carboxamide
308	N-(3-((2R,4R)-4-(dimethylamino)-2-methylpiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
309	N-((5-((1H-imidazol-1-yl)methyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
310	N-(3-(3-aminopiperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
311	N-(3-(difluoromethyl)-5-(4-(dimethylamino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
312	4-fluoro-7-methyl-N-(3-(4-phenylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
313	N-(3-((1r,4r)-4-(dimethylamino)cyclohexyl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
314	4-fluoro-7-methyl-N-(3-(pyrrolidine-2-carboxamido)phenyl)-1H-indole-2-carboxamide
315	``` ```4-fluoro-N-(3-(2-hydroxypropan-2-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
316	4-fluoro-7-methyl-N-(3-(pyrimidin-2-yl)phenyl)-1H-indole-2-carboxamide
317	N-(cyclopropyl(5-((2,4-dimethyl-1H-imidazol-1-yl)methyl)-3-methylpyridin-2-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
318	N-(3-(2,4-dimethylpiperazin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
319	N-(3-(5-amino-1,3,4-oxadiazol-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
320	4-fluoro-7-methyl-N-(2-methyl-3-(4-methylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
321	4-fluoro-7-methyl-N-(3-(2-oxopiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
322	N-(3-(1H-pyrazol-5-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
323	N-(3-(2-(dimethylamino)ethoxy)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
324	N-(3-((1S,3R)-3-(dimethylamino)cyclopentyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
325	4-fluoro-7-methyl-N-(3-(methyl(piperidin-4-yl)amino)phenyl)-1H-indole-2-carboxamide
326	4-fluoro-7-methyl-N-(3-(6-(methylamino)pyridin-2-yl)phenyl)-1H-indole-2-carboxamide

327	4-fluoro-7-methyl-N-(2-oxo-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-yl)-1H-indole-2-carboxamide
328	N-(3-(5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
329	N-(3-(dimethylcarbamoyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
330	4-fluoro-7-methyl-N-(3-((1-methylpyrrolidin-3-yl)amino)phenyl)-1H-indole-2-carboxamide
331	4-fluoro-N-(3-(3-(2-hydroxyethyl)morpholino)phenyl)-7-methyl-1H-indole-2-carboxamide
332	4-fluoro-7-methyl-N-(3-(pyrrolidin-1-yl)phenyl)-1H-indole-2-carboxamide
333	N-(3-chloro-5-(morpholinomethyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
334	4-fluoro-7-methyl-N-(1-(3-methylpyridin-2-yl)-4-morpholino-4-oxobutyl)-1H-indole-2-carboxamide
335	N-(3-(3-(dimethylamino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
336	4-fluoro-N-(3-(4-isopropylpiperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
337	N-(3-(1H-imidazol-4-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
338	4-fluoro-7-methyl-N-(8-(4-methylpiperazin-1-yl)imidazo[1,2-a]pyridin-6-yl)-1H-indole-2-carboxamide
339	N-(3-chloro-5-((1r,4r)-4-(dimethylamino)cyclohexyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
340	4-fluoro-7-methyl-N-(2-(4-methylpiperazin-1-yl)pyridin-4-yl)-1H-indole-2-carboxamide
341	4-fluoro-N-(3-(2-hydroxyethyl)phenyl)-7-methyl-1H-indole-2-carboxamide
342	4-fluoro-7-methyl-N-(3-(methyl(1-methylpyrrolidin-3-yl)amino)phenyl)-1H-indole-2-carboxamide
343	N-(3-((1s,4s)-4-(dimethylamino)cyclohexyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
344	4-fluoro-7-methyl-N-(6-(4-methylpiperazin-1-yl)pyridin-2-yl)-1H-indole-2-carboxamide
345	N-(3-cyano-5-(4-(dimethylamino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
346	4-fluoro-N-(4'-(hydroxymethyl)-[1,1'-biphenyl]-3-yl)-7-methyl-1H-indole-2-carboxamide
347	N-(3-(3-(4-aminopiperidin-1-yl)pyrrolidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
348	4-fluoro-7-methyl-N-(3-(5-methyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)phenyl)-1H-indole-2-carboxamide
349	4-fluoro-7-methyl-N-(3-(3-methyl-3,8-diazabicyclo[3.2.1]octan-8-yl)phenyl)-1H-indole-2-carboxamide
350	4-fluoro-7-methyl-N-(8-(4-methylpiperazin-1-yl)quinolin-6-yl)-1H-indole-2-carboxamide
351	4-fluoro-7-methyl-N-(3-(methyl(1-methylpiperidin-4-yl)amino)phenyl)-1H-indole-2-carboxamide
352	4-fluoro-7-methyl-N-(3-((1-methylpiperidin-3-yl)methyl)phenyl)-1H-indole-2-carboxamide

353	4-fluoro-N-(3-fluoro-5-((1r,4r)-4-morpholinocyclohexyl)phenyl)-7-methyl-1H-indole-2-carboxamide
354	4-fluoro-7-methyl-N-(3-(pyrazolo[1,5-a]pyridin-2-yl)phenyl)-1H-indole-2-carboxamide
355	4-fluoro-7-methyl-N-(5-(4-methylpiperazin-1-yl)imidazo[1,2-a]pyridin-7-yl)-1H-indole-2-carboxamide
356	N-(2-(1-(cyclopropylmethyl)-1H-imidazol-4-yl)-1-(3-methylpyridin-2-yl)ethyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
357	N-(3-((1H-imidazol-2-yl)methyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
358	4-fluoro-7-methyl-N-(1-(3-methylpyridin-2-yl)-2-(4-(morpholinomethyl)phenyl)ethyl)-1H-indole-2-carboxamide
359	N-((1S,3S)-3-(4-acetylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
360	N-(5-(4-acetylpiperazin-1-yl)-1-methylpiperidin-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
361	4-fluoro-7-methyl-N-(8-oxo-6,7,8,9-tetrahydro-5H-pyrido[2,3-d]azepin-9-yl)-1H-indole-2-carboxamide
362	N-((1S,3S)-3-(1,4-oxazepan-4-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
363	N-(5-(4-acetylpiperazin-1-yl)tetrahydro-2H-pyran-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
364	4-fluoro-7-methyl-N-(2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-yl)-1H-indole-2-carboxamide
365	N-(3-(3-acetyl-3,6-diazabicyclo[3.1.1]heptan-6-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
366	N-(1'-acetyl-[1,4'-bipiperidin]-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
367	4-fluoro-7-methyl-N-(1'-methyl-2'-oxo-[1,4'-bipiperidin]-3-yl)-1H-indole-2-carboxamide
368	4-fluoro-7-methyl-N-(5-(pyrimidin-5-yl)tetrahydro-2H-pyran-3-yl)-1H-indole-2-carboxamide
369	4-fluoro-7-methyl-N-((1S,3S)-3-(pyrimidin-5-yl)cyclohexyl)-1H-indole-2-carboxamide
370	4-fluoro-7-methyl-N-((1S,3S)-3-(4-methyl-3-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
371	4-fluoro-7-methyl-N-(5-(1-methylpiperidin-4-yl)-1H-imidazol-2-yl)-1H-indole-2-carboxamide
372	N-((1R,3R)-3-(4-acetylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
373	N-((1S,3R)-3-(4-acetylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
374	4-fluoro-7-methyl-N-(3-morpholinocyclohexyl)-1H-indole-2-carboxamide
375	N-(3-(4-(dimethylamino)-4-(trifluoromethyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
376	N-(3-(4-acetylpiperazin-1-yl)cyclopentyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
377	N-(1-(2-(dimethylamino)-2-oxoethyl)piperidin-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide

378	N-(1-(3-(dimethylamino)-3-oxopropyl)piperidin-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
379	4-fluoro-7-methyl-N-((1R,3R)-3-(pyrimidin-5-yl)cyclohexyl)-1H-indole-2-carboxamide
380	4-fluoro-7-methyl-N-((1R,3S)-3-(pyrimidin-5-yl)cyclohexyl)-1H-indole-2-carboxamide
381	4-fluoro-7-methyl-N-((1R,3R)-3-morpholinocyclohexyl)-1H-indole-2-carboxamide
382	4-fluoro-7-methyl-N-((1R,3R)-3-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
383	N-(4-(4-acetylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
384	4-fluoro-7-methyl-N-(1-(2-(methylamino)-2-oxoethyl)piperidin-3-yl)-1H-indole-2-carboxamide
385	4-fluoro-7-methyl-N-((1R,3R)-3-(3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
386	4-fluoro-7-methyl-N-(1-(3-(methylamino)-3-oxopropyl)piperidin-3-yl)-1H-indole-2-carboxamide
387	4-fluoro-7-methyl-N-((1R,3R)-3-(4-methyl-3-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
388	N-((1R,3R)-3-(1,4-oxazepan-4-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
389	4-fluoro-7-methyl-N-(1-(3-(N-methylacetamido)propyl)piperidin-3-yl)-1H-indole-2-carboxamide
390	4-fluoro-7-methyl-N-(3-methyl-2-oxo-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-yl)-1H-indole-2-carboxamide
391	4-fluoro-7-methyl-N-(3-(4-methylpiperazin-1-yl)-2H-indazol-7-yl)-1H-indole-2-carboxamide
392	4-fluoro-7-methyl-N-((1-(2-(4-methylpiperazin-1-yl)phenyl)cyclopropyl)methyl)-1H-indole-2-carboxamide
393	7-methyl-N-(3-morpholinophenyl)-1H-indole-2-carboxamide
394	4-fluoro-7-methyl-N-(3-(1-methyl-1H-pyrazol-3-yl)phenyl)-1H-indole-2-carboxamide
395	N-(3-(1-aminocyclopropyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
396	N-(3-(4-glycylpiperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
397	N-(3-(5-amino-1H-pyrazol-4-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
398	N-(3-(4-(dimethylamino)piperidin-1-yl)-5-ethylphenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
399	4-fluoro-7-methyl-N-(3-(methylsulfonyl)phenyl)-1H-indole-2-carboxamide
400	N-(cyclopropyl(3-methylimidazo[1,2-a]pyridin-2-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
401	4-fluoro-7-methyl-N-(8-(4-methylpiperazin-1-yl)isoquinolin-6-yl)-1H-indole-2-carboxamide
402	N-(cyclopropyl(5-methyl-6'-(morpholinomethyl)-[3,3'-bipyridin]-6-yl)methyl)-7-methyl-1H-indole-2-carboxamide
403	4-fluoro-7-methyl-N-(5,6,7,8-tetrahydroisoquinolin-5-yl)-1H-indole-2-carboxamide

404	N-(cyclopropyl(3-methyl-5-(pyrimidin-2-yl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
405	N-(3-(4-((2-(diethylamino)ethyl)sulfonyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
406	N-(cyclopropyl(5-methyl-[3,3'-bipyridin]-6-yl)methyl)-7-methyl-1H-indole-2-carboxamide
407	4-fluoro-7-methyl-N-(2-methyl-5-(4-methylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
408	7-methyl-N-(1-(3-methylpyridin-2-yl)-2-phenylethyl)-1H-indole-2-carboxamide
409	4-fluoro-7-methyl-N-(3-((4-methylpiperazin-1-yl)methyl)isoquinolin-6-yl)-1H-indole-2-carboxamide
410	4-fluoro-7-methyl-N-(5-(4-methylpiperazin-1-yl)pyridin-3-yl)-1H-indole-2-carboxamide
411	4-fluoro-7-methyl-N-(3-(3-methyl-2-oxo-3,8-diazabicyclo[3.2.1]octan-8-yl)phenyl)-1H-indole-2-carboxamide
412	N-(cyclopropyl(3-methyl-5-((1-methylpiperidin-4-yl)carbamoyl)pyridin-2-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
413	N-(3-(4-((2-aminoethyl)amino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
414	4-fluoro-7-methyl-N-(1-(3-methyl-5-(2-(4-methylpiperazin-1-yl)ethyl)pyridin-2-yl)-3-phenylpropyl)-1H-indole-2-carboxamide
415	N-(3-(4-(dimethylamino)piperidin-1-yl)-2H-indazol-7-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
416	4-fluoro-7-methyl-N-(2-(piperidin-4-ylamino)quinazolin-6-yl)-1H-indole-2-carboxamide
417	4-fluoro-7-methyl-N-(3-(4-(1-phenylethyl)piperazin-1-yl)phenyl)-1H-indole-2-carboxamide
418	N-(3-(2-aminoethyl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
419	N-((3-chloropyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
420	7-methyl-N-(1-(3-methylpyridin-2-yl)-4-morpholino-4-oxobutyl)-1H-indole-2-carboxamide
421	4-fluoro-7-methyl-N-(3-((4-methylpiperazin-1-yl)methyl)phenyl)-1H-indole-2-carboxamide
422	N-(3-(3-oxa-6-azabicyclo[3.1.1]heptan-6-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
423	N-(cyclopropyl(3-methyl-5-(4-(2-(pyridin-3-yl)acetamido)cyclohexyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
424	N-(cyclopropyl(3-methylpyrazolo[1,5-a]pyridin-2-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
425	4-fluoro-7-methyl-N-(3-(pyrrolidin-2-yl)phenyl)-1H-indole-2-carboxamide
426	N-((6'-amino-5-methyl-[3,3'-bipyridin]-6-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
427	N-(3-((dimethylamino)methyl)imidazo[1,2-a]pyridin-6-yl)-7-methyl-1H-indole-2-carboxamide
428	N-(3-(1H-imidazol-2-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
429	N-(3-(4-((4-aminocyclohexyl)sulfonyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide

430	N-(cyclopropyl(5-(2-hydroxy-3-((pyridin-3-ylmethyl)amino)propoxy)-3-methylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
431	7-methyl-N-(1-(3-methylpyridin-2-yl)-4-morpholino-4-oxobutyl)-4-vinyl-1H-indole-2-carboxamide
432	N-((4-cyano-3-methylpyridin-2-yl)(cyclopropyl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
433	N-(3-(4-(((1H-imidazol-5-yl)methyl)amino)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
434	N-(4-(4-hydroxypiperidin-1-yl)-1-(3-methylpyridin-2-yl)-4-oxobutyl)-7-methyl-1H-indole-2-carboxamide
435	N-(cyclopropyl(3-methyl-5-(2-(4-methylpiperazin-1-yl)ethyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
436	N-(3-(8-(dimethylamino)-3-azabicyclo[3.2.1]octan-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
437	N-(isoquinolin-6-yl)-7-methyl-1H-indole-2-carboxamide
438	4-fluoro-7-methyl-N-(3-(piperidin-2-yl)phenyl)-1H-indole-2-carboxamide
439	N-(3-(4-(2-aminoacetamido)piperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
440	N-(cyclopropyl(3-methyl-5-(4-(3-(pyridin-3-yl)propyl)piperazin-1-yl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
441	N-(cyclopropyl(3-methyl-5-(2-(4-methylpiperazin-1-yl)-2-oxoethyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
442	7-methyl-N-(2-methyl-5-(morpholinomethyl)phenyl)-1H-indole-2-carboxamide
443	N-(6-(4-((2-aminoethyl)sulfonyl)piperazin-1-yl)pyridin-2-yl)-7-methyl-1H-indole-2-carboxamide
444	N-(3-(5-amino-1H-pyrazol-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
445	N-((5-(1H-imidazol-2-yl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
446	N-(4-(dimethylamino)-1-(3-methylpyridin-2-yl)-4-oxobutyl)-7-methyl-1H-indole-2-carboxamide
447	N-(cyclopropyl(3-methyl-5-(2-(2-(pyridin-3-yl)acetamido)ethyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
448	7-methyl-N-(7-(4-methylpiperazine-1-carbonyl)naphthalen-2-yl)-1H-indole-2-carboxamide
449	N-(3-(4-((2-aminoethyl)sulfonyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
450	N-(cyclopropyl(4-methylpyridazin-3-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
451	N-((5-(((1S,2R)-2-aminocyclobutyl)carbamoyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
452	N-(3-(4-((2-aminoethyl)amino)piperidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
453	7-methyl-N-(7-((4-methylpiperazin-1-yl)methyl)naphthalen-2-yl)-1H-indole-2-carboxamide
454	4-fluoro-7-methyl-N-(3-sulfamoylphenyl)-1H-indole-2-carboxamide
455	N-((5-(((1R,2R)-2-aminocyclobutyl)carbamoyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide

456	7-methyl-N-(4-methyl-3-(morpholinomethyl)phenyl)-1H-indole-2-carboxamide
457	7-methyl-N-((1-(2-morpholinophenyl)cyclopropyl)methyl)-1H-indole-2-carboxamide
458	4-fluoro-7-methyl-N-(3-oxo-1,2,3,4-tetrahydroisoquinolin-4-yl)-1H-indole-2-carboxamide
459	N-(imidazo[1,2-a]pyridin-6-yl)-7-methyl-1H-indole-2-carboxamide
460	N-(4-(5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)-1-(3-methylpyridin-2-yl)-4-oxobutyl)-7-methyl-1H-indole-2-carboxamide
461	N-(cyclopropyl(5-(2-hydroxy-3-((3-methoxybenzyl)amino)propoxy)-3-methylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
462	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
463	(R)-N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
464	7-ethyl-N-(1-(3-methylpyridin-2-yl)-4-morpholino-4-oxobutyl)-1H-indole-2-carboxamide
465	7-methyl-N-(3-((4-methylpiperazin-1-yl)methyl)isoquinolin-6-yl)-1H-indole-2-carboxamide
466	7-methyl-N-(quinazolin-7-yl)-1H-indole-2-carboxamide
467	N-(3-(4-(2-aminoethyl)piperazin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
468	N-(3-(3-((dimethylamino)methyl)morpholino)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
469	7-methyl-N-(2-methyl-5-(4-methylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
470	N-(cyclopropyl(3-methyl-5-((1-methylpiperidin-4-yl)carbamoyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
471	7-methyl-N-(1-(3-methylpyridin-2-yl)propyl)-1H-indole-2-carboxamide
472	N-(cyclopropyl(3-methylquinolin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
473	7-methyl-N-(2-(piperidin-4-ylamino)quinazolin-6-yl)-1H-indole-2-carboxamide
474	7-methyl-N-(2-methyl-1-(3-methylpyridin-2-yl)propyl)-1H-indole-2-carboxamide
475	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
476	N-(5-(4-((2-aminoethyl)sulfonyl)piperazin-1-yl)-2-methylphenyl)-7-methyl-1H-indole-2-carboxamide
477	N-(cyclopropyl(3-methyl-5-((4-methylpiperazin-1-yl)methyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
478	7-methyl-N-(3-(morpholinomethyl)phenyl)-1H-indole-2-carboxamide
479	7-methyl-N-phenyl-1H-indole-2-carboxamide
480	7-methyl-N-(1-(3-methylpyridin-2-yl)ethyl)-1H-indole-2-carboxamide
481	N-(cyclopropyl(7-methylimidazo[1,2-b]pyridazin-6-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
482	7-methyl-N-(2-oxo-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-yl)-1H-indole-2-carboxamide
483	7-methyl-N-(2-(2-morpholinophenyl)propyl)-1H-indole-2-carboxamide
484	N-(imidazo[1,2-a]pyrimidin-6-yl)-7-methyl-1H-indole-2-carboxamide
485	4-ethyl-7-methyl-N-(1-(3-methylpyridin-2-yl)-4-morpholino-4-oxobutyl)-1H-

	indole-2-carboxamide
486	N-(3-((diethylamino)methyl)phenyl)-7-methyl-1H-indole-2-carboxamide
487	7-methyl-N-(7-(morpholinomethyl)naphthalen-2-yl)-1H-indole-2-carboxamide
488	7-methyl-N-(3-((4-methylpiperazin-1-yl)methyl)phenyl)-1H-indole-2-carboxamide
489	7-methyl-N-(1-(3-methylpyridin-2-yl)-2-morpholinoethyl)-1H-indole-2-carboxamide
490	7-methyl-N-(2-methyl-5-morpholinophenyl)-1H-indole-2-carboxamide
491	N-(2-(dimethylamino)-2-oxo-1-(pyridin-2-yl)ethyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
492	N-(cyclopropyl(2-hydroxy-6-methylphenyl)methyl)-7-methyl-1H-indole-2-carboxamide
493	N-(cyclopropyl(5-methylpyrimidin-4-yl)methyl)-7-methyl-1H-indole-2-carboxamide
494	7-methyl-N-(1-(3-methylpyridin-2-yl)-5-morpholino-5-oxopentyl)-1H-indole-2-carboxamide
495	N-(3-((dimethylamino)methyl)-5-methylimidazo[1,2-a]pyridin-6-yl)-7-methyl-1H-indole-2-carboxamide
496	N-((5-(((1r,4r)-4-aminocyclohexyl)carbamoyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
497	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-5-fluoro-7-methyl-1H-indole-2-carboxamide
498	4-fluoro-7-methyl-N-(5,6,7,8-tetrahydroquinolin-8-yl)-1H-indole-2-carboxamide
499	N-(2-(4-acetylpiperazin-1-yl)benzyl)-7-methyl-1H-indole-2-carboxamide
500	N-(2-cyclopropyl-1-(3-methylpyridin-2-yl)ethyl)-7-methyl-1H-indole-2-carboxamide
501	N-(3-(2-amino-1H-imidazol-4-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
502	N-(3-(5-aminoisoxazol-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
503	N-(2-amino-2-oxo-1-(pyridin-2-yl)ethyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
504	7-methyl-N-((1r,4r)-4-methylcyclohexyl)-1H-indole-2-carboxamide
505	7-methyl-N-(tetrahydro-2H-pyran-4-yl)-1H-indole-2-carboxamide
506	N-(cyclopropyl(3-methyl-6-oxo-1,6-dihydropyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
507	N-(cyclopropyl(isoquinolin-1-yl)methyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
508	7-methyl-N-((2-morpholinocyclohexyl)methyl)-1H-indole-2-carboxamide
509	N-(3-(4-acetylpiperazin-1-yl)phenyl)-7-cyclopropyl-1H-indole-2-carboxamide
510	N-(cyclopropyl(3-methyl-5-(pyrrolidin-3-ylcarbamoyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
511	7-methyl-N-(2-morpholinophenethyl)-1H-indole-2-carboxamide
512	N-((1r,4r)-4-acetamidocyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
513	N-(cyclobutyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
514	4-methoxy-7-methyl-N-(1-(3-methylpyridin-2-yl)-4-morpholino-4-oxobutyl)-1H-indole-2-carboxamide
515	7-methoxy-N-(1-(3-methylpyridin-2-yl)-4-morpholino-4-oxobutyl)-1H-indole-2-carboxamide

516	N-((5-(((1R,3R)-3-aminocyclopentyl)carbamoyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
517	4-fluoro-7-methyl-N-(2-oxo-2-(phenylamino)-1-(pyridin-2-yl)ethyl)-1H-indole-2-carboxamide
518	N-(cyclopropyl(3-methylpyrazin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
519	4-fluoro-7-methyl-N-(5-(1-methylpiperidin-4-yl)-1,3,4-thiadiazol-2-yl)-1H-indole-2-carboxamide
520	7-methyl-N-(2-oxo-2,3,4,5-tetrahydro-1H-benzo[b]azepin-4-yl)-1H-indole-2-carboxamide
521	N-(cyclopropyl(3-ethylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
522	N-cyclohexyl-7-methyl-1H-indole-2-carboxamide
523	7-methyl-N-(1-(3-methylpyridin-2-yl)-4-oxo-4-(pyridin-3-ylamino)butyl)-1H-indole-2-carboxamide
524	N-(3-(5-amino-1H-1,2,4-triazol-3-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
525	methyl (R)-3-(4-bromophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
526	7-methyl-N-(naphthalen-2-yl)-1H-indole-2-carboxamide
527	methyl (R)-3-(4-cyanophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
528	7-methyl-N-(2-(pyrrolidin-1-yl)benzyl)-1H-indole-2-carboxamide
529	N-(cyclopropyl(3,6-dimethyl-5-((1-methylpiperidin-4-yl)carbamoyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
530	N-(3-(4-amino-[1,4'-bipiperidin]-1'-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
531	N-(6-(4-((2-aminoethyl)amino)piperidin-1-yl)pyridin-2-yl)-7-methyl-1H-indole-2-carboxamide
532	4-fluoro-7-methyl-N-(3-(5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)phenyl)-1H-indole-2-carboxamide
533	7-methyl-N-(quinazolin-6-yl)-1H-indole-2-carboxamide
534	4-fluoro-7-methyl-N-(quinazolin-8-yl)-1H-indole-2-carboxamide
535	N-((5-(azetidin-3-ylcarbamoyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
536	N-(3-((dimethylamino)methyl)imidazo[1,2-a]pyridin-6-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
537	N-(6-(diethylamino)-5,6,7,8-tetrahydronaphthalen-2-yl)-7-methyl-1H-indole-2-carboxamide
538	7-methyl-N-(4-oxo-3,4-dihydroquinazolin-6-yl)-1H-indole-2-carboxamide
539	4-fluoro-7-methyl-N-(3-(4-methyl-2-phenylpiperazin-1-yl)phenyl)-1H-indole-2-carboxamide
540	4-fluoro-7-methyl-N-(2-(4-methylpiperazin-1-yl)phenethyl)-1H-indole-2-carboxamide
541	7-methyl-N-(2-(piperazin-1-ylmethyl)quinazolin-6-yl)-1H-indole-2-carboxamide
542	2-(6-(cyclopropyl(4-fluoro-7-methyl-1H-indole-2-carboxamido)methyl)-5-methylpyridin-3-yl)acetic acid
543	N-((3R,4S)-1-(4-aminobutanoyl)-3-methylpiperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
544	6-(cyclopropyl(4-fluoro-7-methyl-1H-indole-2-carboxamido)methyl)-5-

	methylnicotinic acid
545	4-fluoro-7-methyl-N-(3-(5-oxo-4,5-dihydro-1,2,4-oxadiazol-3-yl)phenyl)-1H-indole-2-carboxamide
546	N-(2-((dimethylamino)methyl)imidazo[1,2-a]pyridin-6-yl)-7-methyl-1H-indole-2-carboxamide
547	N-(3-(2,3-dihydro-4H-benzo[b][1,4]oxazin-4-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
548	4-fluoro-7-methyl-N-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-3-yl)-1H-indole-2-carboxamide
549	N-(2-(4-(2-(dimethylamino)ethyl)piperidin-1-yl)phenethyl)-7-methyl-1H-indole-2-carboxamide
550	N-(2-(benzylamino)-2-oxo-1-(pyridin-2-yl)ethyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
551	N-(3-((dimethylamino)methyl)-7-methylimidazo[1,2-a]pyridin-6-yl)-7-methyl-1H-indole-2-carboxamide
552	N-((1R,3s,5S)-8-(4-aminobutanoyl)-8-azabicyclo[3.2.1]octan-3-yl)-7-methyl-1H-indole-2-carboxamide
553	N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-7-bromo-1H-indole-2-carboxamide
554	7-methyl-N-(2-(4-methylpiperazin-1-yl)benzyl)-1H-indole-2-carboxamide
555	N-(3-(4-cyclopropyl-3,4-dihydroquinoxalin-1(2H)-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
556	methyl 3-(2-fluorophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
557	4-fluoro-7-methyl-N-(5-(1-methylpiperidin-4-yl)-1,3,4-oxadiazol-2-yl)-1H-indole-2-carboxamide
558	4-fluoro-7-methyl-N-(5-(1-methylpiperidin-4-yl)-1H-pyrazol-3-yl)-1H-indole-2-carboxamide
559	4-fluoro-7-methyl-N-(5-(1-methylpiperidin-4-yl)-4H-1,2,4-triazol-3-yl)-1H-indole-2-carboxamide
560	4-fluoro-7-methyl-N-(2-morpholino-2-oxo-1-(pyridin-2-yl)ethyl)-1H-indole-2-carboxamide
561	4-fluoro-7-methyl-N-(1-(1-methylpiperidin-4-yl)-1H-imidazol-4-yl)-1H-indole-2-carboxamide
562	4-fluoro-7-methyl-N-(2-(1-methylpiperidin-4-yl)-1H-imidazol-5-yl)-1H-indole-2-carboxamide
563	N-(cyclopentyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
564	N-(cyclopropyl(2-oxoindolin-7-yl)methyl)-7-methyl-1H-indole-2-carboxamide
565	N-(1-(4-(dimethylamino)cyclohexyl)-1H-pyrazol-4-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
566	N-(2-(2-((dimethylamino)methyl)morpholino)phenethyl)-7-methyl-1H-indole-2-carboxamide
567	7-methyl-N-(1-(3-methylpyridin-2-yl)-4-(piperazin-1-yl)butyl)-1H-indole-2-carboxamide
568	N-(2,2-dimethyl-1-(3-methylpyridin-2-yl)propyl)-7-methyl-1H-indole-2-carboxamide
569	4-fluoro-7-methyl-N-(1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)-1H-indole-2-carboxamide
570	7-methyl-N-(pyrazolo[1,5-a]pyridin-7-ylmethyl)-1H-indole-2-carboxamide

571	7-methyl-N-(1-(3-methylpyridin-2-yl)-4-oxo-4-((tetrahydrofuran-3-yl)amino)butyl)-1H-indole-2-carboxamide
572	7-methyl-N-(1-(3-methylpyridin-2-yl)-4-oxo-4-(piperazin-1-yl)butyl)-1H-indole-2-carboxamide
573	N-((5-(((1S,2S)-2-aminocyclobutyl)carbamoyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
574	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-(hydroxymethyl)-1H-indole-2-carboxamide
575	7-methyl-N-(2-morpholinobenzyl)-1H-indole-2-carboxamide
576	2-(cyclopropyl(7-methyl-1H-indole-2-carboxamido)methyl)-3-methylpyridine 1-oxide
577	N-(cyclopropyl(2-methyl-4-(piperazine-1-carbonyl)phenyl)methyl)-7-methyl-1H-indole-2-carboxamide
578	N-(imidazo[1,2-a]pyridin-7-yl)-7-methyl-1H-indole-2-carboxamide
579	N-(4-((4-aminocyclohexyl)amino)-1-(3-methylpyridin-2-yl)-4-oxobutyl)-7-methyl-1H-indole-2-carboxamide
580	N-(2-(1H-imidazol-1-yl)phenethyl)-7-methyl-1H-indole-2-carboxamide
581	N-((1r,4r)-4-((3-aminopropyl)sulfonamido)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
582	N-(4-(diethylamino)-1-(3-methylpyridin-2-yl)butyl)-7-methyl-1H-indole-2-carboxamide
583	N-(cyclopropyl(2-methyl-5-(piperazine-1-carbonyl)phenyl)methyl)-7-methyl-1H-indole-2-carboxamide
584	N-((5-(((1R,2S)-2-aminocyclobutyl)carbamoyl)-3-methylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
585	4-fluoro-7-methyl-N-(2-(methylamino)-2-oxo-1-(pyridin-2-yl)ethyl)-1H-indole-2-carboxamide
586	ethyl 3-(7-methyl-1H-indole-2-carboxamido)-3-phenylpropanoate
587	7-methyl-N-((1r,4r)-4-(3-(piperidin-1-yl)propanamido)cyclohexyl)-1H-indole-2-carboxamide
588	N-((3S,4R)-1-(4-aminobutanoyl)-3-methylpiperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
589	N-((1r,4r)-4-(3-(diethylamino)propanamido)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
590	N-((3R,4R)-1-(4-aminobutanoyl)-3-methylpiperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
591	7-methyl-N-(3-(3-methylpyridin-2-yl)azetidin-3-yl)-1H-indole-2-carboxamide
592	N-((1s,4s)-4-(3-aminopropanamido)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
593	N-(1-(4-aminobutanoyl)pyrrolidin-3-yl)-7-methyl-1H-indole-2-carboxamide
594	N-(1-(4-aminobutanoyl)azetidin-3-yl)-7-methyl-1H-indole-2-carboxamide
595	7-methyl-N-(2-(3-methylpyridin-2-yl)propan-2-yl)-1H-indole-2-carboxamide
596	N-((1s,3s)-3-(3-aminopropanamido)cyclobutyl)-7-methyl-1H-indole-2-carboxamide
597	N-((1r,3r)-3-(3-aminopropanamido)cyclobutyl)-7-methyl-1H-indole-2-carboxamide
598	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-pyrrolo[2,3-c]pyridine-2-carboxamide

599	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-pyrrolo[3,2-b]pyridine-2-carboxamide
600	N-(3-(3-aminopropanamido)cyclopentyl)-7-methyl-1H-indole-2-carboxamide
601	N,7-dimethyl-N-(1-(3-methylpyridin-2-yl)-2-morpholinoethyl)-1H-indole-2-carboxamide
602	N-((5-(aminomethyl)-3-methylisoxazol-4-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
603	N-(2-(dimethylamino)-1-(pyridin-3-yl)ethyl)-7-methyl-1H-indole-2-carboxamide
604	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)pyrazolo[1,5-a]pyrimidine-2-carboxamide
605	7-methyl-N-((1r,4r)-4-(2-(pyridin-3-yl)acetamido)cyclohexyl)-1H-indole-2-carboxamide
606	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-4-(hydroxymethyl)-7-methyl-1H-indole-2-carboxamide
607	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-methylindoline-2-carboxamide
608	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-pyrrolo[3,2-c]pyridine-2-carboxamide
609	4-fluoro-7-methyl-N-(quinolin-8-yl)-1H-indole-2-carboxamide
612	4-fluoro-7-methyl-N-(4-(4-methylpiperazin-1-yl)pyridin-2-yl)-1H-indole-2-carboxamide
613	(S)-N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
614	N-((3S,4S)-1-(4-aminobutanoyl)-3-methylpiperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
615	N-(cyclopropyl(6-((dimethylamino)methyl)pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
616	(R)-N-(2-hydroxy-1-phenylethyl)-7-methyl-1H-indole-2-carboxamide
617	7-methyl-N-(2-oxo-6-phenylazepan-4-yl)-1H-indole-2-carboxamide
618	7-((1H-pyrazol-5-yl)methyl)-N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-1H-indole-2-carboxamide
619	(2,3-dihydrospiro[indene-1,2'-pyrrolidin]-1'-yl)(7-methyl-1H-indol-2-yl)methanone
620	7-methyl-N-(1-oxo-2,3,4,5-tetrahydro-1H-benzo[c]azepin-5-yl)-1H-indole-2-carboxamide
622	N-(5-chloro-2-morpholinophenethyl)-7-methyl-1H-indole-2-carboxamide
623	N-(imidazo[1,2-a]pyrazin-6-yl)-7-methyl-1H-indole-2-carboxamide
624	7-methyl-N-(2-methyl-3-(morpholinomethyl)phenyl)-1H-indole-2-carboxamide
625	N-((1S,4S,5S)-2-(4-aminobutanoyl)-2-azabicyclo[2.2.2]octan-5-yl)-7-methyl-1H-indole-2-carboxamide
626	7-methyl-N-(1-(pyrimidin-2-yl)piperidin-3-yl)-1H-indole-2-carboxamide
627	N-(2-(dimethylamino)-1-(3-methylpyridin-2-yl)ethyl)-7-methyl-1H-indole-2-carboxamide
628	ethyl 4-(7-methyl-1H-indole-2-carboxamido)piperidine-1-carboxylate
629	N-((1r,4r)-4-(3-aminopropanamido)-4-methylcyclohexyl)-7-methyl-1H-indole-2-carboxamide
630	ethyl 3-cyclobutyl-2-(7-methyl-1H-indole-2-carboxamido)propanoate
631	N-((1R,4R,5S)-2-(3-aminopropanoyl)-2-azabicyclo[2.2.2]octan-5-yl)-7-methyl-1H-indole-2-carboxamide

632	7-methyl-N-(pyridin-4-yl)-1H-indole-2-carboxamide
633	7-methyl-N-(6-(morpholinomethyl)pyridin-2-yl)-1H-indole-2-carboxamide
634	methyl (R)-3-(3-chlorophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
635	N-(2-(2'-(aminomethyl)-[1,1'-biphenyl]-2-yl)ethyl)-7-methyl-1H-indole-2-carboxamide
636	7-methyl-N-(2-(piperazin-1-yl)benzyl)-1H-indole-2-carboxamide
637	N-(di(pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
638	N-(2-(dimethylamino)benzyl)-7-methyl-1H-indole-2-carboxamide
639	N-(1-(4-aminobutanoyl)piperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
640	N-(8-(3-aminopropanamido)bicyclo[3.2.1]octan-3-yl)-7-methyl-1H-indole-2-carboxamide
641	N-((1s,4s)-4-(3-aminopropanamido)-4-methylcyclohexyl)-7-methyl-1H-indole-2-carboxamide
642	7-methyl-N-(2,2,2-trifluoro-1-(3-fluorophenyl)ethyl)-1H-indole-2-carboxamide
643	7-methyl-N-(1-(pyridin-3-yl)cyclopropyl)-1H-indole-2-carboxamide
644	N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-4,7-dimethyl-1H-indole-2-carboxamide
645	N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-N,7-dimethyl-1H-indole-2-carboxamide
646	N-(1-((3-aminopropyl)sulfonyl)piperidin-3-yl)-7-methyl-1H-indole-2-carboxamide
648	methyl 3-(furan-2-yl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
649	methyl 3-(7-methyl-1H-indole-2-carboxamido)-3-(thiophen-3-yl)propanoate
650	methyl 3-(7-methyl-1H-indole-2-carboxamido)-3-(thiophen-2-yl)propanoate
652	N-(1-(4-(1H-pyrazol-1-yl)phenyl)ethyl)-7-methyl-1H-indole-2-carboxamide
653	N-(4-chloro-2-morpholinophenethyl)-7-methyl-1H-indole-2-carboxamide
654	N-((1S,4R)-bicyclo[2.2.1]heptan-2-yl)-7-methyl-1H-indole-2-carboxamide
655	N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-3,7-dimethyl-1H-indole-2-carboxamide
656	N-((1R,3r,5S)-8-(4-aminobutanoyl)-8-azabicyclo[3.2.1]octan-3-yl)-7-methyl-3a,7a-dihydro-1H-indole-2-carboxamide
657	N-((1S,4S,5R)-2-(4-aminobutanoyl)-2-azabicyclo[2.2.2]octan-5-yl)-7-methyl-1H-indole-2-carboxamide
658	methyl (R)-3-(7-methyl-1H-indole-2-carboxamido)-3-(pyridin-3-yl)propanoate
659	methyl 3-(3-methoxyphenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
660	N-(cyclopropyl(pyridin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
661	N-((1r,4r)-4-((2-aminoethyl)sulfonamido)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
662	N-((1s,4s)-4-(hydroxymethyl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
663	N-(1-((3-aminopropyl)sulfonyl)piperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
664	N-(1-(4-aminobutanoyl)piperidin-3-yl)-7-methyl-1H-indole-2-carboxamide
665	7-methyl-N-(pyrimidin-5-yl)-1H-indole-2-carboxamide
666	methyl (R)-3-(7-methyl-1H-indole-2-carboxamido)-3-phenylpropanoate
667	N-((6-(2-amino-2-oxoethyl)pyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
668	7-methyl-N-(1-(3-methyl-1,2,4-oxadiazol-5-yl)propyl)-1H-indole-2-carboxamide
669	methyl 3-(3-bromophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate

670	N-(1-acetylpiperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
671	methyl 3-(7-methyl-1H-indole-2-carboxamido)-3-(pyridin-3-yl)propanoate
672	N-((1R,4R,5R)-2-(3-aminopropanoyl)-2-azabicyclo[2.2.2]octan-5-yl)-7-methyl-1H-indole-2-carboxamide
673	7-methyl-N-(pyridin-2-yl)-1H-indole-2-carboxamide
674	7-methyl-N-(3-(pyrrolidin-1-ylmethyl)benzyl)-1H-indole-2-carboxamide
675	ethyl 3,3,3-trifluoro-2-(7-methyl-1H-indole-2-carboxamido)propanoate
676	methyl (S)-3-(7-methyl-1H-indole-2-carboxamido)-3-(pyridin-3-yl)propanoate
677	methyl (S)-3-(7-methyl-1H-indole-2-carboxamido)-3-(o-tolyl)propanoate
678	7-methyl-N-(3,3,3-trifluoro-2-hydroxypropyl)-1H-indole-2-carboxamide
679	7-methyl-N-(2-(5-oxopyrrolidin-2-yl)phenyl)-1H-indole-2-carboxamide
680	N-(cyclopropyl(pyrimidin-2-yl)methyl)-7-methyl-1H-indole-2-carboxamide
681	N-(2-(3,5-dimethoxyphenyl)-2-hydroxyethyl)-7-methyl-1H-indole-2-carboxamide
682	7-methyl-N-(3-(methylamino)-1-(3-methylpyridin-2-yl)-3-oxopropyl)-1H-indole-2-carboxamide
683	methyl (S)-3-(4-chlorophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
684	(3,4-dihydroisoquinolin-2(1H)-yl)(7-methyl-1H-indol-2-yl)methanone
685	N-(3-(3-aminopropanamido)bicyclo[3.2.1]octan-8-yl)-7-methyl-1H-indole-2-carboxamide
686	N-(2-hydroxy-2-(o-tolyl)ethyl)-7-methyl-1H-indole-2-carboxamide
687	(S)-7-methyl-N-(2,2,2-trifluoro-1-phenylethyl)-1H-indole-2-carboxamide
688	7-methyl-N-(1-(4-methylthiazol-2-yl)ethyl)-1H-indole-2-carboxamide
689	N-(cyclopropyl(pyridin-3-yl)methyl)-7-methyl-1H-indole-2-carboxamide
690	methyl (S)-3-(7-methyl-1H-indole-2-carboxamido)-3-phenylpropanoate
691	7-methyl-N-(4-(morpholinomethyl)phenyl)-1H-indole-2-carboxamide
692	(R)-N-(1-hydroxy-3-phenylpropan-2-yl)-7-methyl-1H-indole-2-carboxamide
693	7-methyl-N-((1-methyl-1H-pyrazol-5-yl)methyl)-1H-indole-2-carboxamide
694	dimethyl (7-methyl-1H-indole-2-carbonyl)-D-aspartate
695	N-(2-hydroxy-2-(3-methoxyphenyl)ethyl)-7-methyl-1H-indole-2-carboxamide
697	N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-7-chloro-1H-indole-2-carboxamide
698	N-((1r,4r)-4-acetamidocyclohexyl)-7-methyl-1H-indole-2-carboxamide
699	7-methyl-N-(2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1H-indole-2-carboxamide
700	ethyl 3-(7-methyl-1H-indole-2-carboxamido)-3-(pyridin-4-yl)propanoate
701	methyl 2-(7-methyl-1H-indole-2-carboxamido)-2-phenylacetate
702	7-methyl-N-((5-methylisoxazol-4-yl)methyl)-1H-indole-2-carboxamide
703	(S)-N-(2-hydroxy-1-phenylethyl)-7-methyl-1H-indole-2-carboxamide
704	7-methyl-N-(2-oxo-2,3,4,5-tetrahydro-1H-benzo[b]azepin-5-yl)-1H-indole-2-carboxamide
705	N-(2-hydroxy-1-phenylethyl)-7-methyl-1H-indole-2-carboxamide
706	N-((1r,4r)-4-aminocyclohexyl)-7-bromo-1H-indole-2-carboxamide
707	methyl 3-(3-fluorophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
708	dimethyl (7-methyl-1H-indole-2-carbonyl)-L-aspartate
709	7-methyl-N-(3-(morpholinomethyl)benzyl)-1H-indole-2-carboxamide
710	N-(imidazo[1,2-a]pyrazin-6-ylmethyl)-7-methyl-1H-indole-2-carboxamide
711	N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-3-ethyl-7-methyl-1H-indole-2-carboxamide
712	7-methyl-N-(1-(1-methyl-1H-pyrazol-3-yl)ethyl)-1H-indole-2-carboxamide

713	(R)-7-methyl-N-(1-(m-tolyl)ethyl)-1H-indole-2-carboxamide
714	7-methyl-N-(1-(naphthalen-1-yl)ethyl)-1H-indole-2-carboxamide
715	7-methyl-N-(piperidin-4-yl)-1H-indole-2-carboxamide
716	7-methyl-N-(2-(piperidin-1-yl)benzyl)-1H-indole-2-carboxamide
717	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-(trifluoromethyl)-1H-indole-2-carboxamide
718	(7-methyl-1H-indol-2-yl)(1,3,4,5-tetrahydro-2H-benzo[c]azepin-2-yl)methanone
719	7-methyl-N-((5-methylisoxazol-3-yl)methyl)-1H-indole-2-carboxamide
720	N-(2-(2,6-difluorophenyl)-2-hydroxyethyl)-7-methyl-1H-indole-2-carboxamide
721	N-((2,5-dimethyloxazol-4-yl)methyl)-7-methyl-1H-indole-2-carboxamide
722	7-methyl-N-((3-methylpyridin-2-yl)(pyrrolidin-3-yl)methyl)-1H-indole-2-carboxamide
723	7-methyl-N-((5-methylpyrazin-2-yl)methyl)-1H-indole-2-carboxamide
724	7-methyl-N-(4-(morpholinomethyl)pyridin-2-yl)-1H-indole-2-carboxamide
725	N-(3-(dimethylamino)-1-(pyridin-3-yl)propyl)-7-methyl-1H-indole-2-carboxamide
726	(R)-7-methyl-N-(2,2,2-trifluoro-1-phenylethyl)-1H-indole-2-carboxamide
727	N-(cyclopropyl(5-((dimethylamino)methyl)pyridin-3-yl)methyl)-7-methyl-1H-indole-2-carboxamide
728	N-(3-(dimethylamino)-1-(3-methylpyridin-2-yl)propyl)-7-methyl-1H-indole-2-carboxamide
729	N-((1H-imidazol-5-yl)methyl)-7-methyl-1H-indole-2-carboxamide
730	N-((1r,4r)-4-aminocyclohexyl)-4,7-dimethyl-1H-indole-2-carboxamide
731	N-(2-cyclopropyl-2-hydroxyethyl)-7-methyl-1H-indole-2-carboxamide
732	7-methyl-N-((4-methyl-1,2,5-oxadiazol-3-yl)methyl)-1H-indole-2-carboxamide
733	7-methyl-N-(oxazol-4-ylmethyl)-1H-indole-2-carboxamide
735	7-methyl-N-(1-(3-methyl-1,2,4-oxadiazol-5-yl)ethyl)-1H-indole-2-carboxamide
736	N-((1r,4r)-4-aminocyclohexyl)-3,7-dimethyl-1H-indole-2-carboxamide
738	N-((1r,4r)-4-(3-aminopropanamido)cyclohexyl)-5,7-dimethyl-1H-indole-2-carboxamide
746	7-methyl-N-(2-morpholinoethyl)-1H-indole-2-carboxamide
747	7-methyl-N-((tetrahydrofuran-2-yl)methyl)-1H-indole-2-carboxamide
748	N-(2,3-dihydro-1H-inden-1-yl)-7-methyl-1H-indole-2-carboxamide
749	7-methyl-N-(1-phenylethyl)-1H-indole-2-carboxamide
750	7-methyl-N-(3-(piperidin-1-yl)benzyl)-1H-indole-2-carboxamide
751	7-methyl-N-(3-(piperidin-1-ylsulfonyl)benzyl)-1H-indole-2-carboxamide
752	N-(1-benzylpiperidin-4-yl)-7-methyl-1H-indole-2-carboxamide
753	7-methyl-N-(1,2,3,4-tetrahydronaphthalen-1-yl)-1H-indole-2-carboxamide
754	N-(2-hydroxy-2-(4-methoxyphenyl)ethyl)-7-methyl-1H-indole-2-carboxamide
755	7-methyl-N-(4-(morpholinomethyl)benzyl)-1H-indole-2-carboxamide
756	N-((1r,4r)-4-aminocyclohexyl)-5,7-dimethyl-1H-indole-2-carboxamide
757	2-(4-(7-methyl-1H-indole-2-carbonyl)piperazin-1-yl)nicotinamide
758	7-methyl-N-(4-(piperidin-1-ylsulfonyl)benzyl)-1H-indole-2-carboxamide
759	N-((1s,3s)-3-(hydroxymethyl)cyclobutyl)-7-methyl-1H-indole-2-carboxamide
761	N-((1r,4r)-4-aminocyclohexyl)-N,7-dimethyl-1H-indole-2-carboxamide
763	(S)-N-(1-hydroxy-3-methylbutan-2-yl)-7-methyl-1H-indole-2-carboxamide
764	methyl 3-(4-chlorophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
765	(S)-N-(1-hydroxy-3-phenylpropan-2-yl)-7-methyl-1H-indole-2-carboxamide

766	tert-butyl (2-(7-methyl-1H-indole-2-carboxamido)propyl)carbamate
767	N-(2-(cyclopropylmethoxy)benzyl)-7-methyl-1H-indole-2-carboxamide
768	7-methyl-N-((1-methyl-1H-1,2,4-triazol-5-yl)methyl)-1H-indole-2-carboxamide
769	N-(1-cyclopropyl-2,2,2-trifluoroethyl)-7-methyl-1H-indole-2-carboxamide
771	1-(7-methyl-1H-indole-2-carbonyl)piperidine-4-carboxamide
773	methyl 3-(4-isopropylphenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
774	methyl 3-(2-bromophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
775	methyl 3-(7-methyl-1H-indole-2-carboxamido)-3-phenylpropanoate
776	methyl 3-(4-fluorophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
777	methyl 3-(4-methoxyphenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
778	methyl 3-(4-bromophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
779	N-(benzo[d]oxazol-2-ylmethyl)-7-methyl-1H-indole-2-carboxamide
780	7-methyl-N-((1r,4r)-4-(trifluoromethyl)cyclohexyl)-1H-indole-2-carboxamide
781	2-(4-(7-methyl-1H-indole-2-carbonyl)piperazin-1-yl)acetamide
782	7-methyl-N-(2-(5-methyl-1,2,4-oxadiazol-3-yl)ethyl)-1H-indole-2-carboxamide
783	methyl 3-(7-methyl-1H-indole-2-carboxamido)-3-(p-tolyl)propanoate
784	N-(3,3-difluoro-2-hydroxypropyl)-7-methyl-1H-indole-2-carboxamide
785	7-methyl-N-(1-(5-methyl-1,2,4-oxadiazol-3-yl)ethyl)-1H-indole-2-carboxamide
786	1-(7-methyl-1H-indole-2-carbonyl)pyrrolidine-2-carboxamide
787	4-(7-methyl-1H-indole-2-carbonyl)piperazine-1-carboxamide
788	7-methyl-N-(1-(2-(trifluoromethyl)phenyl)ethyl)-1H-indole-2-carboxamide
790	7-methyl-N-(1-(3-(trifluoromethyl)phenyl)ethyl)-1H-indole-2-carboxamide
791	7-methyl-N-((1r,4r)-4-(2,2,2-trifluoroacetamido)cyclohexyl)-1H-indole-2-carboxamide
793	7-methyl-N-(2-morpholinophenyl)-1H-indole-2-carboxamide
794	(3-aminopiperidin-1-yl)(7-methyl-1H-indol-2-yl)methanone
795	7-methyl-N-(pyridin-3-yl)-1H-indole-2-carboxamide
796	N-(imidazo[1,2-a]pyridin-2-yl)-7-methyl-1H-indole-2-carboxamide
797	ethyl (1R,2R)-2-(7-methyl-1H-indole-2-carboxamido)cyclohexane-1-carboxylate
798	3-amino-N-(1-(7-methyl-1H-indole-2-carbonyl)piperidin-3-yl)propanamide
799	(3-(dimethylamino)piperidin-1-yl)(7-methyl-1H-indol-2-yl)methanone
800	(7-methyl-1H-indol-2-yl)(3-(methylamino)piperidin-1-yl)methanone
801	N-(cyclopropyl(o-tolyl)methyl)-7-methyl-1H-indole-2-carboxamide
802	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-isopropyl-1H-indole-2-carboxamide
803	N-(cyclopropyl(pyridin-2-yl)methyl)-7-ethyl-1H-indole-2-carboxamide
804	7-methyl-N-(quinazolin-2-yl)-1H-indole-2-carboxamide
805	7-cyclopropyl-N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-1H-indole-2-carboxamide
808	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-6-fluoro-7-methyl-1H-indole-2-carboxamide
809	7-methyl-N-(3-(methylamino)-3-oxo-1-(pyridin-3-yl)propyl)-1H-indole-2-carboxamide
810	(5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)(7-methyl-1H-indol-2-yl)methanone
811	(5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)(7-methyl-1H-indol-2-yl)methanone
812	(5,6-dihydro-[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)(7-methyl-1H-indol-2-yl)methanone

814	2-(7-methyl-1H-indole-2-carbonyl)-1,2,3,4-tetrahydro-5H-benzo[c]azepin-5-one
815	N-(3-(dimethylamino)-2-phenylpropyl)-7-methyl-1H-indole-2-carboxamide
816	7-methyl-N-(2-oxo-7-phenylazepan-4-yl)-1H-indole-2-carboxamide
817	N-((3-benzylpyridin-2-yl)(cyclopropyl)methyl)-7-methyl-1H-indole-2-carboxamide
818	N-(2-([1,1'-biphenyl]-2-yl)ethyl)-7-methyl-1H-indole-2-carboxamide
819	N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-7-propyl-1H-indole-2-carboxamide
820	(2,3-dihydrospiro[indene-1,3'-pyrrolidin]-1'-yl)(7-methyl-1H-indol-2-yl)methanone
821	7-(cyclobutylmethyl)-N-(cyclopropyl(3-methylpyridin-2-yl)methyl)-1H-indole-2-carboxamide
822	4-fluoro-7-methyl-N-((1R,3R)-3-(3-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
823	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
824	ethyl 4-((1S,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
825	ethyl 4-((1R,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
826	4-fluoro-7-methyl-N-((1R,3S)-3-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
827	4-fluoro-7-methyl-N-((1R,3R)-3-(4-(2,2,2-trifluoroethyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
828	4-fluoro-7-methyl-N-((1R,3S)-3-(4-(morpholine-4-carbonyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
829	4-fluoro-7-methyl-N-((1R,3R)-3-(4-(morpholine-4-carbonyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
830	N-((1R,3S)-3-(4-(cyclopropanecarbonyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
831	N-((1R,3R)-3-(4-(cyclopropanecarbonyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
832	4-fluoro-7-methyl-N-((1R)-3-(4-methyl-5-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
833	N-((1R,3S)-3-(3-acetamidopyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
834	N-((1R,3R)-3-(3-acetamidopyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
835	N-((1R,3S)-3-(4-ethyl-3-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
836	N-((1R,3R)-3-(4-ethyl-3-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
837	4-fluoro-N-((1R,3S)-3-(4-isobutyrylpiperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
838	4-fluoro-N-((1R,3R)-3-(4-isobutyrylpiperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
839	4-fluoro-7-methyl-N-((1R,3S)-3-(4-propionylpiperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
840	4-fluoro-7-methyl-N-((1R,3R)-3-(4-propionylpiperazin-1-yl)cyclohexyl)-1H-

	indole-2-carboxamide
841	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
842	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
843	4-fluoro-N-((1R,3S)-3-(3-(N-(2-methoxyethyl)acetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
844	4-fluoro-N-((1R,3R)-3-(3-(N-(2-methoxyethyl)acetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
845	4-fluoro-N-((1R,3R)-3-(3-(N-(2-methoxyethyl)acetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
846	4-fluoro-N-((1R,3S)-3-(4-(2-methoxyacetyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
847	4-fluoro-N-((1R,3R)-3-(4-(2-methoxyacetyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
848	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
849	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
850	4-fluoro-7-methyl-N-((1R,3S)-3-(4-(methylsulfonyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
851	4-fluoro-7-methyl-N-((1R,3R)-3-(4-(methylsulfonyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
852	N-((1R,3S)-3-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
853	N-((1R,3R)-3-(5,6-dihydroimidazo[1,2-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
854	N-((1R,3S)-3-(4-(dimethylglycyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
855	N-((1R,3R)-3-(4-(dimethylglycyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
856	N-((1R,3S)-3-(4-acetylpiperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
857	N-((1R,3R)-3-(4-acetylpiperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
858	4-fluoro-7-methyl-N-((1R)-3-(4-(2-(methylamino)-2-oxoethyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
859	N-((1R)-3-(4-(2-(dimethylamino)-2-oxoethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
860	N-((1R,3S)-3-(5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
861	N-((1R,3R)-3-(5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
862	4-fluoro-N-((1R)-3-(3-(N-isopropylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
863	4-fluoro-7-methyl-N-((1R,3S)-3-(6-oxohexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
864	4-fluoro-7-methyl-N-((1R,3R)-3-(6-oxohexahydropyrrolo[1,2-a]pyrazin-2(1H)-

	yl)cyclohexyl)-1H-indole-2-carboxamide
865	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxotetrahydro-3H-oxazolo[3,4-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
866	4-fluoro-7-methyl-N-((1R,3R)-3-(3-oxotetrahydro-3H-oxazolo[3,4-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
867	N-(1-(1-acetylpiperidin-4-yl)azepan-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
868	N-((1R,3S)-3-(5,6-dihydro-[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
869	N-((1R,3R)-3-(5,6-dihydro-[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
870	4-fluoro-N-((1R,3S)-3-(4-(2-hydroxyacetyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
871	4-fluoro-N-((1R,3R)-3-(4-(2-hydroxyacetyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
872	4-fluoro-N-((1R,3S)-3-(3-(N-(2-hydroxyethyl)acetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
873	4-fluoro-N-((1R,3R)-3-(3-(N-(2-hydroxyethyl)acetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
874	4-fluoro-7-methyl-N-((1R)-3-(1-oxo-2,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
875	ethyl (R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)-[1,4'-bipiperidine]-1'-carboxylate
876	ethyl (S)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)-[1,4'-bipiperidine]-1'-carboxylate
877	1-(4-((1-(4-fluoro-7-methyl-1H-indole-2-carbonyl)piperidin-3-yl)methyl)piperazin-1-yl)ethan-1-one
878	N-((1R,3S)-3-(4-(2,2-difluoroacetyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
879	N-((1R,3R)-3-(4-(2,2-difluoroacetyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
880	4-fluoro-N-((1R,3S)-3-(3-(2-methoxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
881	4-fluoro-N-((1R,3R)-3-(3-(2-methoxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
882	4-fluoro-7-methyl-N-((1R,3S)-3-(1-oxo-2,7-diazaspiro[4.5]decan-7-yl)cyclohexyl)-1H-indole-2-carboxamide
883	4-fluoro-7-methyl-N-((1R,3R)-3-(1-oxo-2,7-diazaspiro[4.5]decan-7-yl)cyclohexyl)-1H-indole-2-carboxamide
884	N-((1R,3S)-3-(2,4-dimethyl-3-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
885	N-((1R,3R)-3-(2,4-dimethyl-3-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
886	1-(4-(1-(4-fluoro-7-methyl-1H-indole-2-carbonyl)piperidine-3-carbonyl)piperazin-1-yl)ethan-1-one
887	4-fluoro-7-methyl-N-((1R,3S)-3-(4-methyl-3-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
888	N-((1R,3S)-3-(6-acetyl-2,6-diazaspiro[3.3]heptan-2-yl)cyclohexyl)-4-fluoro-7-

	methyl-1H-indole-2-carboxamide
889	N-((1R,3R)-3-(6-acetyl-2,6-diazaspiro[3.3]heptan-2-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
890	4-fluoro-7-methyl-N-((1R)-3-(2-oxo-1,3,8-triazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
891	(R)-N-(1'-(dimethylglycyl)-[1,4'-bipiperidin]-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
892	(S)-N-(1'-(dimethylglycyl)-[1,4'-bipiperidin]-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
893	4-fluoro-7-methyl-N-((1R)-3-(5-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
894	4-fluoro-7-methyl-N-((1R)-3-(2-oxo-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
895	4-fluoro-7-methyl-N-(3-(2-oxo-3-oxa-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
896	4-fluoro-7-methyl-N-((1R)-3-(3-oxo-2,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
897	4-fluoro-7-methyl-N-((1R,3S)-3-(7-oxo-2,6-diazaspiro[3.4]octan-2-yl)cyclohexyl)-1H-indole-2-carboxamide
898	4-fluoro-7-methyl-N-((1R,3R)-3-(7-oxo-2,6-diazaspiro[3.4]octan-2-yl)cyclohexyl)-1H-indole-2-carboxamide
899	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(N-methylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
900	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-3-(N-methylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
901	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-3-(N-methylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
902	4-fluoro-7-methyl-N-((1R,3R)-3-(pyridin-3-yl)cyclohexyl)-1H-indole-2-carboxamide
903	4-fluoro-7-methyl-N-((1R,3S)-3-(pyridin-3-yl)cyclohexyl)-1H-indole-2-carboxamide
904	4-fluoro-7-methyl-N-((1S,3S)-3-(pyridin-3-yl)cyclohexyl)-1H-indole-2-carboxamide
905	4-fluoro-7-methyl-N-((1S,3R)-3-(pyridin-3-yl)cyclohexyl)-1H-indole-2-carboxamide
906	N-((1R,3S)-3-(4-acetyl-3-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
907	N-((1R,3R)-3-(4-acetyl-3-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
908	N-((1R,3S)-3-(3-(2-(dimethylamino)-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
909	N-((1R,3R)-3-(3-(2-(dimethylamino)-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
910	4-fluoro-7-methyl-N-((1R,3S)-3-(2-oxo-[1,3'-bipyrrolidin]-1'-yl)cyclohexyl)-1H-indole-2-carboxamide
911	4-fluoro-7-methyl-N-((1R,3R)-3-(2-oxo-[1,3'-bipyrrolidin]-1'-yl)cyclohexyl)-1H-indole-2-carboxamide
912	4-fluoro-7-methyl-N-((1R,3R)-3-(pyridin-4-yl)cyclohexyl)-1H-indole-2-

	carboxamide
913	4-fluoro-7-methyl-N-((1R,3S)-3-(pyridin-4-yl)cyclohexyl)-1H-indole-2-carboxamide
914	4-fluoro-7-methyl-N-((1S,3R)-3-(pyridin-4-yl)cyclohexyl)-1H-indole-2-carboxamide
915	4-fluoro-7-methyl-N-((1S,3S)-3-(pyridin-4-yl)cyclohexyl)-1H-indole-2-carboxamide
916	4-fluoro-7-methyl-N-((1R,3S)-3-(4-methyl-2-oxopiperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
917	4-fluoro-7-methyl-N-((1R,3R)-3-(4-methyl-2-oxopiperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
918	4-fluoro-7-methyl-N-((1R,3S)-3-(4-(oxetane-3-carbonyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
919	4-fluoro-7-methyl-N-((1R,3R)-3-(4-(oxetane-3-carbonyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
920	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-6-oxohexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
921	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-6-oxohexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
922	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-6-oxohexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
923	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-6-oxohexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
924	4-fluoro-7-methyl-N-((1R,3S)-3-(4-(tetrahydrofuran-3-yl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
925	4-fluoro-7-methyl-N-((1R,3R)-3-(4-(tetrahydrofuran-3-yl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
926	N-((1R,3S)-3-(8-acetyl-3,8-diazabicyclo[3.2.1]octan-3-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
927	N-((1R,3R)-3-(8-acetyl-3,8-diazabicyclo[3.2.1]octan-3-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
928	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-2,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
929	4-fluoro-7-methyl-N-((1R,3R)-3-(3-oxo-2,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
930	N-((1R,3S)-3-((R)-4-acetyl-3-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
931	N-((1R,3R)-3-((R)-4-acetyl-3-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
932	4-fluoro-7-methyl-N-((1R,3S)-3-(5-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
933	4-fluoro-7-methyl-N-((1R,3R)-3-(5-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
934	4-fluoro-N-((1R,3S)-3-(3-(2-hydroxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
935	4-fluoro-N-((1R,3R)-3-(3-(2-hydroxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
936	N-((1R,3S)-3-(5-acetyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)cyclohexyl)-4-fluoro-

	7-methyl-1H-indole-2-carboxamide
937	N-((1R,3R)-3-(5-acetyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
938	4-fluoro-7-methyl-N-((1R,3S)-3-(2-oxo-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
939	4-fluoro-7-methyl-N-((1R,3R)-3-(2-oxo-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
940	4-fluoro-7-methyl-N-((1R,3S)-3-(2-oxo-1,3,8-triazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
941	4-fluoro-7-methyl-N-((1R,3R)-3-(2-oxo-1,3,8-triazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
942	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-3-(N-methylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
943	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-3-(N-methylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
944	4-fluoro-7-methyl-N-((1R,3S)-3-(4-methyl-5-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
945	4-fluoro-7-methyl-N-((1R,3R)-3-(4-methyl-5-oxo-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
946	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(N-methyloxetane-3-carboxamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
947	4-fluoro-7-methyl-N-((1R,3R)-3-(3-(N-methyloxetane-3-carboxamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
948	N-((1R,3S)-3-(4-(ethylcarbamoyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
949	N-((1R,3R)-3-(4-(ethylcarbamoyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
950	N-((1R,3S)-3-(1-acetyl-1,6-diazaspiro[3.3]heptan-6-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
951	N-((1R,3R)-3-(1-acetyl-1,6-diazaspiro[3.3]heptan-6-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
952	N-((1R,3S)-3-(3-acetyl-3,8-diazabicyclo[3.2.1]octan-8-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
953	N-((1R,3R)-3-(3-acetyl-3,8-diazabicyclo[3.2.1]octan-8-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
954	N-((1R,3S)-3-(5-((dimethylamino)methyl)-1,3,4-oxadiazol-2-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
955	N-((1S,3R)-3-(5-((dimethylamino)methyl)-1,3,4-oxadiazol-2-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
956	4-fluoro-7-methyl-N-((1R,3R)-3-(piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
957	4-fluoro-7-methyl-N-((1R,3R)-3-(piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
958	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
959	4-fluoro-7-methyl-N-((1R,3R)-3-(3-(2-oxooxazolidin-3-yl)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
960	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(N-methylacetamido)azetidin-1-

	yl)cyclohexyl)-1H-indole-2-carboxamide
961	N-((1R,3S)-3-(5-acetyl-2,5-diazabicyclo[2.2.2]octan-2-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
962	N-((1R,3R)-3-(5-acetyl-2,5-diazabicyclo[2.2.2]octan-2-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
963	4-fluoro-7-methyl-N-((1R,3S)-3-(2-oxo-3-oxa-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
964	4-fluoro-7-methyl-N-((1R,3R)-3-(2-oxo-3-oxa-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
965	4-fluoro-7-methyl-N-((1R,3S)-3-(2-oxo-1-(2,2,2-trifluoroethyl)-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
966	4-fluoro-7-methyl-N-((1R,3R)-3-(2-oxo-1-(2,2,2-trifluoroethyl)-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
967	N-((1R,3S)-3-((S)-4-acetyl-3-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
968	N-((1R,3R)-3-((S)-4-acetyl-3-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
969	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(N-methylisobutyramido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
970	4-fluoro-7-methyl-N-((1R,3R)-3-(3-(N-methylisobutyramido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
971	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(N-methylcyclopropanecarboxamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
972	4-fluoro-7-methyl-N-((1R,3R)-3-(3-(N-methylcyclopropanecarboxamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
973	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-4-(tetrahydrofuran-3-yl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
974	4-fluoro-7-methyl-N-((1R,3R)-3-(3-oxo-4-(tetrahydrofuran-3-yl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
975	4-fluoro-7-methyl-N-((1R,3S)-3-(5-methyl-1,3,4-oxadiazol-2-yl)cyclohexyl)-1H-indole-2-carboxamide
976	4-fluoro-7-methyl-N-((1S,3R)-3-(5-methyl-1,3,4-oxadiazol-2-yl)cyclohexyl)-1H-indole-2-carboxamide
977	N-((1R,3S)-3-(4-cyclopropyl-3-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
978	N-((1R,3R)-3-(4-cyclopropyl-3-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
979	N-((1R,3S)-3-(4-acetyl-1,4-diazepan-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
980	N-((1R,3R)-3-(4-acetyl-1,4-diazepan-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
981	4-fluoro-7-methyl-N-((1R,3S)-3-(4-(methylsulfonyl)-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
982	4-fluoro-7-methyl-N-((1R,3R)-3-(4-(methylsulfonyl)-1,4-diazepan-1-yl)cyclohexyl)-1H-indole-2-carboxamide
983	4-fluoro-N-((1R,3S)-3-((R)-3-(2-hydroxy-N-methylacetamido)pyrrolidin-1-

	yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
984	4-fluoro-N-((1R,3R)-3-((R)-3-(2-hydroxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
985	N-((3S,5S)-5-(4-acetylpiperazin-1-yl)tetrahydro-2H-pyran-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
986	N-((3S,5R)-5-(4-acetylpiperazin-1-yl)tetrahydro-2H-pyran-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
987	N-((3R,5R)-5-(4-acetylpiperazin-1-yl)tetrahydro-2H-pyran-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
988	N-((3R,5S)-5-(4-acetylpiperazin-1-yl)tetrahydro-2H-pyran-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
989	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide
990	4-fluoro-7-methyl-N-((1R,3R)-3-(3-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide
991	N-((1R,3S)-3-(5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
992	N-((1R,3R)-3-(5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
993	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(trifluoromethyl)-5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide
994	4-fluoro-7-methyl-N-((1R,3R)-3-(3-(trifluoromethyl)-5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide
995	4-fluoro-N-((1R,3S)-3-((S)-3-(2-hydroxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
996	4-fluoro-N-((1R,3R)-3-((S)-3-(2-hydroxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
997	isopropyl 4-((1S,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
998	isopropyl 4-((1R,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
999	tetrahydro-2H-pyran-4-yl 4-((1S,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
1000	tetrahydro-2H-pyran-4-yl 4-((1R,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
1001	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(trifluoromethyl)-5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1002	N-((1R,3S)-3-(3-(dimethylamino)-2-oxopyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1003	4-fluoro-7-methyl-N-((1R,3S)-3-(pyrimidin-4-yl)cyclohexyl)-1H-indole-2-carboxamide
1004	4-fluoro-7-methyl-N-((1R,3S)-3-(2-oxo-4-(tetrahydrofuran-3-yl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1005	N-((1R,3S)-3-(4-ethyl-2-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1006	N-((3S,5R)-5-(4-acetylpiperazin-1-yl)-1-methylpiperidin-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1007	N-((1R,3S)-3-(1-acetylpiperidin-4-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-

	carboxamide
1008	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-2-oxa-4,9-diazaspiro[5.5]undecan-9-yl)cyclohexyl)-1H-indole-2-carboxamide
1009	N-((1R,3S)-3-(2,2-dioxido-2-thia-1,3,8-triazaspiro[4.5]decan-8-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1010	4-fluoro-7-methyl-N-((1R,3S)-3-(2-oxo-4-oxa-1,9-diazaspiro[5.5]undecan-9-yl)cyclohexyl)-1H-indole-2-carboxamide
1011	4-fluoro-7-methyl-N-((1R,3S)-3-(5-methyl-1,2,4-oxadiazol-3-yl)cyclohexyl)-1H-indole-2-carboxamide
1012	4-fluoro-7-methyl-N-((1R,3S)-3-(6-oxo-1,6-dihydro-1,2,4-triazin-3-yl)cyclohexyl)-1H-indole-2-carboxamide
1013	4-fluoro-7-methyl-N-((1R,3S)-3-(6-oxo-1,6-dihydropyrimidin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1014	N-((1R,3S)-3-(5-((dimethylamino)methyl)-1,2,4-oxadiazol-3-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1015	N-((1R,3R)-3-(4-acetylpiperazin-1-yl)-4-fluorocyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1016	N-((1R,3R)-3-(4-acetylpiperazin-1-yl)-4-(trifluoromethyl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1017	N-((1R,3S)-3-(4-acetyl-2-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1018	N-((1R,3S)-3-(4-acetyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1019	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-2,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
1020	4-fluoro-7-methyl-N-((1R,3S)-3-(7-oxo-5-oxa-2,8-diazaspiro[3.5]nonan-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1021	N-((1R,3S)-3-(4-acetyl-2-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1022	N-((1R,3S)-3-(4-acetyl-3-(hydroxymethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1023	N-((1R,3S)-3-(4-acetyl-2-(hydroxymethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1024	N-((1R,3S)-3-(7-acetyl-4,7-diazaspiro[2.5]octan-4-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1025	N-((1R,3S)-3-(4-acetyl-4,7-diazaspiro[2.5]octan-7-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1026	N-((1R,3S)-3-(3,4-dimethyl-2-oxopiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1027	4-fluoro-7-methyl-N-(1-(pyridin-4-yl)piperidin-3-yl)-1H-indole-2-carboxamide
1028	4-fluoro-7-methyl-N-(1'-methyl-2'-oxo-[1,4'-bipiperidin]-3-yl)-1H-indole-2-carboxamide
1029	isopropyl 4-((1S,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
1030	tetrahydro-2H-pyran-4-yl 4-((1S,3R)-3-(4-fluoro-7-methyl-1H-indole-2-carboxamido)cyclohexyl)piperazine-1-carboxylate
1031	4-fluoro-7-methyl-N-((1R,3S)-3-(2-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide

1032	N-((1R,3S)-3-((4-acetylpiperazin-1-yl)methyl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1033	N-((1R,3S)-3-(5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1034	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(trifluoromethyl)-5,6-dihydroimidazo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1035	4-fluoro-N-((1R,3R,4R)-4-fluoro-3-(2-oxo-1,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1036	4-fluoro-N-((1R,3R,4R)-4-fluoro-3-((S)-3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1037	4-fluoro-7-methyl-N-((1R,3S)-3-(4-((tetrahydro-2H-pyran-4-yl)carbamoyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1038	4-fluoro-7-methyl-N-((1R,3S)-3-((3aS,6aS)-1-methyl-2-oxohexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1039	4-fluoro-7-methyl-N-((1R,3S)-3-((3aR,6aR)-1-methyl-2-oxohexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1040	4-fluoro-7-methyl-N-((1R,3S)-3-(4-methyl-5-oxohexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1041	4-fluoro-N-((1R,3S)-3-((S)-3-(2-hydroxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1042	4-fluoro-N-((1R,3S)-3-((R)-3-(2-methoxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1043	4-fluoro-N-((1R,3S)-3-((S)-3-(2-methoxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1044	4-fluoro-7-methyl-N-((1R,3S)-3-(6-oxooctahydro-2H-pyrido[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1045	4-fluoro-7-methyl-N-((1R,3S)-3-(4-oxohexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1046	4-fluoro-7-methyl-N-((1R,3S)-3-(8-methyl-6,9-dioxooctahydro-2H-pyrazino[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1047	4-fluoro-7-methyl-N-((1R,3S)-3-(6-oxooctahydro-2H-pyrazino[1,2-c]pyrimidin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1048	4-fluoro-7-methyl-N-((1R,3S)-3-(6-oxo-1,3,4,6-tetrahydro-2H-pyrido[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1049	4-fluoro-7-methyl-N-((1R,3S)-3-(4-oxo-4,6,7,9-tetrahydro-8H-pyrazino[1,2-a]pyrimidin-8-yl)cyclohexyl)-1H-indole-2-carboxamide
1050	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1051	4-fluoro-7-methyl-N-((1R,3S)-3-(2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1052	4-fluoro-N-((1R,3S)-3-(3-(2-hydroxy-N,2-dimethylpropanamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1053	N-((1R,3S)-3-(3-(N-ethyl-2-hydroxyacetamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1054	N-((1R,3S)-3-(3-(N-ethylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide

1055	N-((1R,3S)-3-(4-acetyl-3-ethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1056	4-fluoro-7-methyl-N-((1R,3S)-3-(2-methyl-3-oxo-2,5,6,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1057	4-fluoro-7-methyl-N-((1R,3S)-3-(2-methyl-3-oxo-2,5,6,8-tetrahydroimidazo[1,5-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1058	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-2,5,6,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1059	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-2,5,6,8-tetrahydroimidazo[1,5-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1060	4-fluoro-N-((1R,3S)-3-((S)-3-((1-hydroxy-N-methylmethyl)sulfonamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1061	4-fluoro-N-((1R,3S)-3-((S)-3-(N-(2-hydroxyethyl)methylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1062	N-((1R,3S)-3-((3R,5R)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1063	4-fluoro-N-((1R,3R)-3-((S)-3-(2-methoxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1064	4-fluoro-7-methyl-N-((1R,3R)-3-(pyrimidin-4-yl)cyclohexyl)-1H-indole-2-carboxamide
1065	4-fluoro-7-methyl-N-((1S,3R)-3-(5-methyl-1,2,4-oxadiazol-3-yl)cyclohexyl)-1H-indole-2-carboxamide
1066	4-fluoro-7-methyl-N-((1R,3R)-3-(2-(trifluoromethyl)-5,6-dihydro-[1,2,4]triazolo[1,5-a]pyrazin-7(8H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1067	4-fluoro-7-methyl-N-((1R,3R)-3-(4-oxohexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1068	4-fluoro-7-methyl-N-((1R,3S)-3-(6-oxo-1,6-dihydropyrimidin-4-yl)cyclohexyl)-1H-indole-2-carboxamide
1069	N-((1R,3S)-3-((R)-4-acetyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1070	N-((1R,3S)-3-((S)-4-acetyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1071	N-((1R,3R)-3-((R)-4-acetyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1072	N-((1R,3R)-3-((S)-4-acetyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1073	N-((1R,3S)-3-((S)-4-acetyl-2-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1074	N-((1R,3R)-3-((S)-4-acetyl-2-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1075	N-((1R,3R)-3-((R)-4-acetyl-3-(hydroxymethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1076	N-((1R,3R)-3-((S)-4-acetyl-3-(hydroxymethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1077	N-((1S,3R)-3-((4-acetylpiperazin-1-yl)methyl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1078	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-6-oxooctahydro-2H-pyrido[1,2-a]pyrazin-2-

	yl)cyclohexyl)-1H-indole-2-carboxamide
1079	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-6-oxooctahydro-2H-pyrido[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1080	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-6-oxooctahydro-2H-pyrido[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1081	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1082	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1083	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1084	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1085	N-((1R,3S)-3-((S)-4-acetyl-3-ethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1086	N-((1R,3R)-3-((S)-4-acetyl-3-ethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1087	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-3-(methylamino)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1088	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-3-(methylamino)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1089	N-((1R,3S)-3-((R)-3-(dimethylamino)-2-oxopyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1090	N-((1R,3S)-3-((S)-3-(dimethylamino)-2-oxopyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1091	N-((1R,3R)-3-((R)-4-acetyl-2-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1092	N-((1R,3S)-3-((R)-4-acetyl-2-methylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1093	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-6-oxooctahydro-2H-pyrido[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1094	N-((1R,3S)-3-((R)-4-acetyl-3-ethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1095	N-((1R,3R)-3-((R)-4-acetyl-3-ethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1096	N-((1R,3R)-3-((3R,5S)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1097	N-((1R,3S)-3-((3R,5S)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1098	N-((1R,3S)-3-((S)-4-acetyl-3-(hydroxymethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1099	N-((1R,3S)-3-((R)-4-acetyl-3-(hydroxymethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1100	N-((1R,3R)-3-(4-acetyl-4,7-diazaspiro[2.5]octan-7-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1101	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-8-methyl-6,9-dioxooctahydro-2H-pyrazino[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1102	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-8-methyl-6,9-dioxooctahydro-2H-

	pyrazino[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1103	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-8-methyl-6,9-dioxooctahydro-2H-pyrazino[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1104	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-8-methyl-6,9-dioxooctahydro-2H-pyrazino[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1105	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-2,5,6,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1106	4-fluoro-7-methyl-N-((1R,3R)-3-(3-oxo-2,5,6,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1107	N-((3S,5S)-5-(4-acetylpiperazin-1-yl)-1-methylpiperidin-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1108	N-((3R,5R)-5-(4-acetylpiperazin-1-yl)-1-methylpiperidin-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1109	N-((3R,5S)-5-(4-acetylpiperazin-1-yl)-1-methylpiperidin-3-yl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1110	N-((1S,3R)-3-(5-((dimethylamino)methyl)-1,2,4-oxadiazol-3-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1111	4-fluoro-7-methyl-N-(3-(3-oxotetrahydro-3H-oxazolo[3,4-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1112	4-fluoro-N-((1R,3S)-3-(4-isobutyryl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1113	4-fluoro-7-methyl-N-((1R,3S)-3-(4-propionyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1114	N-((1R,3S)-3-(4-((E)-N'-cyano-N-methylcarbamimidoyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1115	4-fluoro-7-methyl-N-((1R,3S)-3-(4-((E)-1-(methylamino)-2-nitrovinyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1116	N-((1R,3S)-3-(4-((E)-1-(cyanoimino)ethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1117	4-fluoro-N-((1R,3S)-3-(4-(2-hydroxyacetyl)-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1118	N-((1R,3S)-3-(1-(4-acetylpiperazin-1-yl)ethyl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1119	N-((1R,3S)-3-((R)-3-(N-ethyl-2-hydroxyacetamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1120	N-((1R,3R)-3-((R)-3-(N-ethyl-2-hydroxyacetamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1121	N-((1R,3S)-3-((R)-3-(N-ethylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1122	N-((1R,3R)-3-((R)-3-(N-ethylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1123	N-((1R,3R)-3-((3R,5R)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1124	N-((1R,3R)-3-(1-acetylpiperidin-4-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1125	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1126	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-2-methyl-3-oxohexahydroimidazo[1,5-

	a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1127	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1128	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1129	N-((1R,3S)-3-((S)-3-(N-ethyl-2-hydroxyacetamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1130	N-((1R,3R)-3-((S)-3-(N-ethyl-2-hydroxyacetamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1131	N-((1R,3S)-3-((S)-3-(N-ethylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1132	N-((1R,3R)-3-((S)-3-(N-ethylmethylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1133	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-3-oxotetrahydro-3H-oxazolo[3,4-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1134	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-3-oxotetrahydro-3H-oxazolo[3,4-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1135	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-3-oxotetrahydro-3H-oxazolo[3,4-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1136	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-3-oxotetrahydro-3H-oxazolo[3,4-a]pyrazin-7(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1137	N-((1R,3R)-3-(7-acetyl-4,7-diazaspiro[2.5]octan-4-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1138	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-4-oxohexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1139	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-4-oxohexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1140	4-fluoro-7-methyl-N-((1R,3S)-3-((R)-4-oxohexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1141	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-4-oxohexahydropyrazino[2,1-c][1,4]oxazin-8(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1142	4-fluoro-7-methyl-N-((1R,3R)-3-(2-methyl-3-oxo-2,5,6,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1143	4-fluoro-7-methyl-N-((1R,3R)-3-(6-oxo-1,3,4,6-tetrahydro-2H-pyrido[1,2-a]pyrazin-2-yl)cyclohexyl)-1H-indole-2-carboxamide
1144	4-fluoro-N-((1R,3S)-3-((S)-3-(2-hydroxy-N,2-dimethylpropanamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1145	4-fluoro-N-((1R,3R)-3-((S)-3-(2-hydroxy-N,2-dimethylpropanamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1146	4-fluoro-N-((1R,3S)-3-((R)-3-(2-hydroxy-N,2-dimethylpropanamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1147	4-fluoro-N-((1R,3R)-3-((R)-3-(2-hydroxy-N,2-dimethylpropanamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1148	N-((1R,3R)-3-(4-((E)-1-(cyanoimino)ethyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1149	4-fluoro-N-((1R,3S)-3-((R)-3-(N-(2-hydroxyethyl)methylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1150	4-fluoro-N-((1R,3R)-3-((R)-3-(N-(2-hydroxyethyl)methylsulfonamido)pyrrolidin-

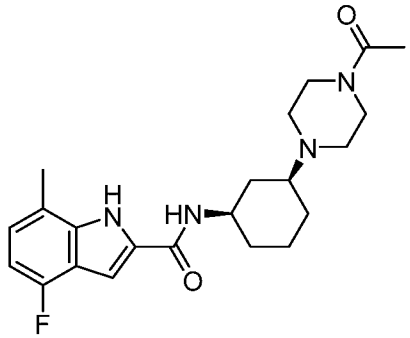
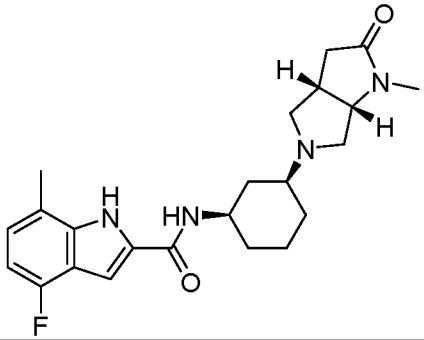
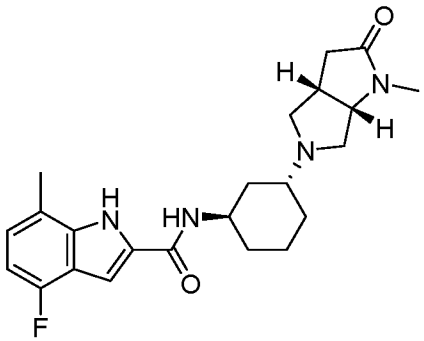
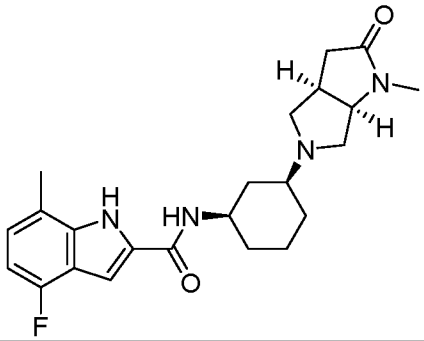
	1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1151	4-fluoro-N-((1R,3R)-3-((S)-3-(N-(2-hydroxyethyl)methylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1152	N-((1R,3R)-3-(4-((E)-N'-cyano-N-methylcarbamimidoyl)piperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1153	N-(2-chlorobenzyl)-7-methyl-1H-indole-2-carboxamide
1154	(S)-N-(1-(2-chlorophenyl)ethyl)-7-methyl-1H-indole-2-carboxamide
1155	N-(1-(4-(1H-1,2,4-triazol-1-yl)phenyl)ethyl)-7-methyl-1H-indole-2-carboxamide
1156	N-(1-(2-chlorophenyl)ethyl)-7-methyl-1H-indole-2-carboxamide
1157	methyl 3-(2-chlorophenyl)-3-(7-methyl-1H-indole-2-carboxamido)propanoate
1158	N-(3-chloro-5-(4-(3-(pyrrolidin-1-yl)propyl)piperidin-1-yl)phenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1159	4-fluoro-7-methyl-N-(1-methyl-5-(1-methylpiperidin-4-yl)-1H-imidazol-2-yl)-1H-indole-2-carboxamide
1160	4-fluoro-N-((1R,3R)-3-((R)-3-(2-methoxy-N-methylacetamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1161	4-fluoro-N-((1R,3S)-3-((R)-3-(N-(2-hydroxyethyl)methylsulfonamido)pyrrolidin-1-yl)cyclohexyl)-7-methyl-1H-indene-2-carboxamide
1162	N-((1R,3S)-3-((3S,5S)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1163	N-((1R,3R)-3-((3S,5S)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1164	4-fluoro-7-methyl-N-((1R,3R)-3-((R)-4-propionyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1165	4-fluoro-7-methyl-N-((1R,3R)-3-(4-oxo-4,6,7,9-tetrahydro-8H-pyrazino[1,2-a]pyrimidin-8-yl)cyclohexyl)-1H-indole-2-carboxamide
1166	4-fluoro-7-methyl-N-((1R,3R)-3-(3-oxo-2,5,6,8-tetrahydroimidazo[1,5-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1167	4-fluoro-7-methyl-N-((1R,3S)-3-((S)-4-propionyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1168	4-fluoro-7-methyl-N-((1R,3R)-3-((S)-4-propionyl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1169	4-fluoro-7-methyl-N-((1R,3R)-3-(4-((E)-1-(methylamino)-2-nitrovinyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1170	4-fluoro-7-methyl-N-((1R,3R)-3-(4-((tetrahydro-2H-pyran-4-yl)carbamoyl)piperazin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1171	4-fluoro-N-((1R,3S)-3-((S)-4-isobutyryl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1172	4-fluoro-N-((1R,3R)-3-((S)-4-isobutyryl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1173	4-fluoro-N-((1R,3S)-3-((S)-4-(2-hydroxyacetyl)-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1174	4-fluoro-N-((1R,3R)-3-((S)-4-(2-hydroxyacetyl)-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1175	4-fluoro-N-((1R,3R)-3-((R)-4-isobutyryl-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide
1176	4-fluoro-N-((1R,3R)-3-((R)-4-(2-hydroxyacetyl)-3-(trifluoromethyl)piperazin-1-yl)cyclohexyl)-7-methyl-1H-indole-2-carboxamide

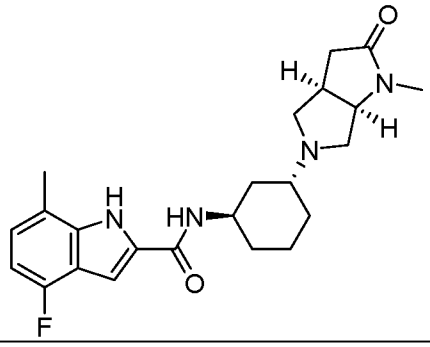
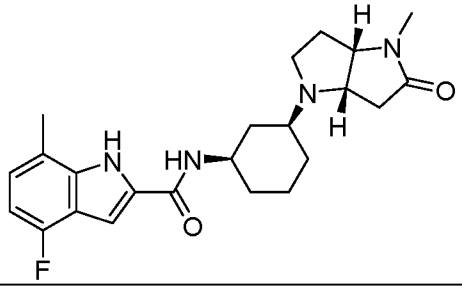
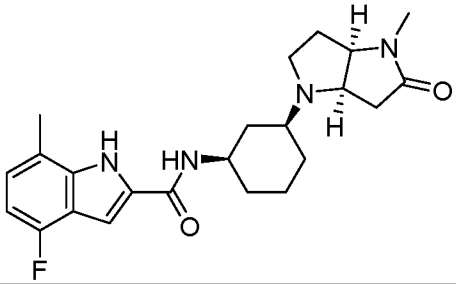
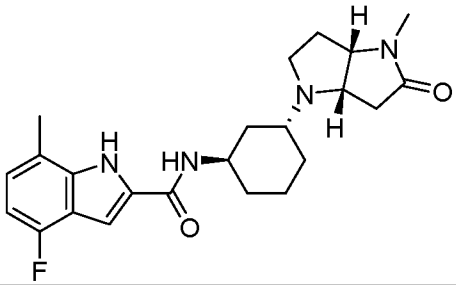
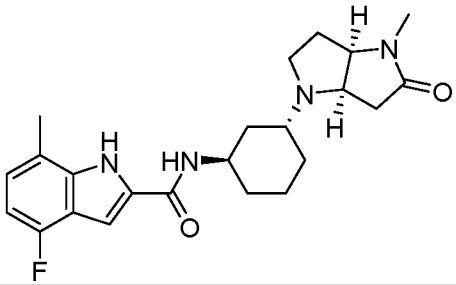
1177	N-((1R,3S)-3-((3aR,6aS)-5-acetylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1178	N-((1R,3R)-3-((3aR,6aS)-5-acetylhexahydropyrrolo[3,4-c]pyrrol-2(1H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1179	4-fluoro-7-methyl-N-((1R,3R)-3-(2-methyl-3-oxo-2,5,6,8-tetrahydroimidazo[1,5-a]pyrazin-7(3H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1180	N-((1R,3S)-3-((3aS,6aS)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1181	N-((1R,3R)-3-((3aS,6aS)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1182	N-((1R,3S)-3-((3aR,6aR)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1183	N-((1R,3R)-3-((3aR,6aR)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1184	N-((1R,3S)-3-((3aS,6aS)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1185	N-((1R,3S)-3-((3aR,6aR)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1186	N-((1R,3R)-3-((3aS,6aS)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1187	N-((1R,3R)-3-((3aR,6aR)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1188	4-fluoro-7-methyl-N-((1S,3R)-3-(6-oxo-1,4,5,6-tetrahydro-1,2,4-triazin-3-yl)cyclohexyl)-1H-indole-2-carboxamide
1189	4-fluoro-7-methyl-N-((1R,3S)-3-(3-(N-(oxetan-3-yl)acetamido)pyrrolidin-1-yl)cyclohexyl)-1H-indole-2-carboxamide
1190	4-fluoro-7-methyl-N-((1R,3S)-3-(3-oxo-2,8-diazaspiro[4.5]decan-8-yl)cyclohexyl)-1H-indole-2-carboxamide
1191	4-fluoro-7-methyl-N-(1'-methyl-2'-oxo-[1,4'-bipiperidin]-3-yl)-1H-indole-2-carboxamide
1192	N-((1R,3S)-3-((3R,5R)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1193	N-((1R,3R)-3-((3R,5R)-4-acetyl-3,5-dimethylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1194	(R)-4-fluoro-N-(3-fluoro-5-(3-(N-methylacetamido)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1195	(S)-4-fluoro-N-(3-fluoro-5-(3-(N-methylacetamido)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1196	4-fluoro-N-(3-fluoro-5-((S)-3-((R)-2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1197	4-fluoro-N-(3-fluoro-5-((S)-3-((S)-2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1198	4-fluoro-N-(3-fluoro-5-((R)-3-((S)-2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1199	4-fluoro-N-(3-fluoro-5-((R)-3-((R)-2-methyl-3-oxohexahydroimidazo[1,5-a]pyrazin-7(1H)-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1200	(R)-N-(3-(3-(dimethylamino)-2-oxopyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide

1201	(S)-N-(3-(3-(dimethylamino)-2-oxopyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1202	(R)-N-(3-(3-(4-(2-(dimethylamino)-2-oxoethyl)piperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1203	(R)-N-(3-(3-(4-(2-(dimethylamino)-2-oxoethyl)piperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1204	(S)-N-(3-(3-(4-(2-amino-2-oxoethyl)piperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1205	(R)-N-(3-(3-(4-(2-amino-2-oxoethyl)piperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1206	(S)-N-(3-(3-(1,1-dioxidothiomorpholino)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1207	(R)-N-(3-(3-(1,1-dioxidothiomorpholino)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1208	(R)-N-(3-(3-(4-acetylpiperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1209	(S)-N-(3-(3-(4-acetylpiperazin-1-yl)pyrrolidin-1-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1210	(S)-4-fluoro-N-(3-fluoro-5-(3-morpholinopyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1211	(R)-4-fluoro-N-(3-fluoro-5-(3-morpholinopyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1212	N-(3-((3aR,6aR)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1213	N-(3-((3aR,6aS)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1214	N-(3-((3aS,6aS)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1215	N-(3-((3aS,6aR)-4-acetylhexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1216	N-(3-((3aR,6aR)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1217	N-(3-((3aS,6aR)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1218	N-(3-((3aS,6aS)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1219	N-(3-((3aR,6aS)-1-acetylhexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)-5-fluorophenyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide
1220	4-fluoro-N-(3-fluoro-5-((S)-3-((S)-2-(hydroxymethyl)morpholino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1221	4-fluoro-N-(3-fluoro-5-((S)-3-((R)-2-(hydroxymethyl)morpholino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1222	4-fluoro-N-(3-fluoro-5-((R)-3-((R)-2-(hydroxymethyl)morpholino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1223	4-fluoro-N-(3-fluoro-5-((R)-3-((S)-2-(hydroxymethyl)morpholino)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1224	(R)-4-fluoro-N-(3-fluoro-5-(3-(4-methyl-3-oxopiperazin-1-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide

1225	(S)-4-fluoro-N-(3-fluoro-5-(3-(4-methyl-3-oxopiperazin-1-yl)pyrrolidin-1-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1226	(S)-4-fluoro-N-(3-fluoro-5-(2-oxo-[1,3'-bipyrrolidin]-1'-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1227	(R)-4-fluoro-N-(3-fluoro-5-(2-oxo-[1,3'-bipyrrolidin]-1'-yl)phenyl)-7-methyl-1H-indole-2-carboxamide
1228	4-fluoro-7-methyl-N-((1R,3S)-3-((3aS,6aS)-1-methyl-2-oxohexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1229	4-fluoro-7-methyl-N-((1R,3R)-3-((3aS,6aS)-1-methyl-2-oxohexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1230	4-fluoro-7-methyl-N-((1R,3S)-3-((3aR,6aR)-1-methyl-2-oxohexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1231	4-fluoro-7-methyl-N-((1R,3R)-3-((3aR,6aR)-1-methyl-2-oxohexahydropyrrolo[3,4-b]pyrrol-5(1H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1232	4-fluoro-7-methyl-N-((1R,3S)-3-((3aS,6aS)-4-methyl-5-oxohexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1233	4-fluoro-7-methyl-N-((1R,3S)-3-((3aR,6aR)-4-methyl-5-oxohexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1234	4-fluoro-7-methyl-N-((1R,3R)-3-((3aS,6aS)-4-methyl-5-oxohexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-1H-indole-2-carboxamide
1235	4-fluoro-7-methyl-N-((1R,3R)-3-((3aR,6aR)-4-methyl-5-oxohexahydropyrrolo[3,2-b]pyrrol-1(2H)-yl)cyclohexyl)-1H-indole-2-carboxamide

Table 1B

Cpd. No.	STRUCTURE	SETD2 (1434-1711)	SETD2 A549
15		0.02	0.05
1228		0.04	0.09
1229		8.8	2
1230		0.04	0.09

1231		9.8	2
1232		0.008	0.01
1233		0.04	0.04
1234		4.2	2
1235		10	2

[0369] The present disclosure encompasses the preparation and use of salts of the Compounds of the Disclosure, including non-toxic pharmaceutically acceptable salts. Examples of pharmaceutically acceptable addition salts include inorganic and organic acid addition salts and basic salts. The pharmaceutically acceptable salts include, but are not limited to, metal salts such as sodium salt, potassium salt, cesium salt and the like;

alkaline earth metals such as calcium salt, magnesium salt and the like; organic amine salts such as triethylamine salt, pyridine salt, picoline salt, ethanolamine salt, triethanolamine salt, dicyclohexylamine salt, N,N'-dibenzylethylenediamine salt and the like; inorganic acid salts such as hydrochloride, hydrobromide, phosphate, sulphate and the like; organic acid salts such as citrate, lactate, tartrate, maleate, fumarate, mandelate, acetate, dichloroacetate, trifluoroacetate, oxalate, formate and the like; sulfonates such as methanesulfonate, benzenesulfonate, p-toluenesulfonate and the like; and amino acid salts such as arginate, asparginate, glutamate and the like. The term "pharmaceutically acceptable salt" as used herein, refers to any salt, *e.g.*, obtained by reaction with an acid or a base, of a Compound of the Disclosure that is physiologically tolerated in the target subject (*e.g.*, a mammal, *e.g.,* a human).

[0370] Acid addition salts can be formed by mixing a solution of the particular Compound of the Disclosure with a solution of a pharmaceutically acceptable non-toxic acid such as hydrochloric acid, fumaric acid, maleic acid, succinic acid, acetic acid, citric acid, tartaric acid, carbonic acid, phosphoric acid, oxalic acid, dichloroacetic acid, or the like. Basic salts can be formed by mixing a solution of the compound of the present disclosure with a solution of a pharmaceutically acceptable non-toxic base such as sodium hydroxide, potassium hydroxide, choline hydroxide, sodium carbonate and the like.

[0371] The present disclosure encompasses the preparation and use of solvates of Compounds of the Disclosure. Solvates typically do not significantly alter the physiological activity or toxicity of the compounds, and as such may function as pharmacological equivalents. The term "solvate" as used herein is a combination, physical association and/or solvation of a compound of the present disclosure with a solvent molecule such as, *e.g.* a disolvate, monosolvate or hemisolvate, where the ratio of solvent molecule to compound of the present disclosure is about 2:1, about 1:1 or about 1:2, respectively. This physical association involves varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances, the solvate can be isolated, such as when one or more solvent molecules are incorporated into the crystal lattice of a crystalline solid. Thus, "solvate" encompasses both solution-phase and isolatable solvates. Compounds of the Disclosure can be present as solvated forms with a pharmaceutically acceptable solvent, such as water, methanol, ethanol, and the like, and it is intended that the disclosure includes both solvated and unsolvated forms of

Compounds of the Disclosure. One type of solvate is a hydrate. A "hydrate" relates to a particular subgroup of solvates where the solvent molecule is water. Solvates typically can function as pharmacological equivalents. Preparation of solvates is known in the art. See, for example, M. Caira *et al*, *J. Pharmaceut. Sci., 93(3)*:601-611 (2004), which describes the preparation of solvates of fluconazole with ethyl acetate and with water. Similar preparation of solvates, hemisolvates, hydrates, and the like are described by E.C. van Tonder *et al.*, *AAPS Pharm. Sci. Tech., 5(1)*:Article 12 (2004), and A.L. Bingham *et al.*, *Chem. Commun.* 603-604 (2001). A typical, non-limiting, process of preparing a solvate would involve dissolving a Compound of the Disclosure in a desired solvent (organic, water, or a mixture thereof) at temperatures above 20°C to about 25°C, then cooling the solution at a rate sufficient to form crystals, and isolating the crystals by known methods, *e.g.*, filtration. Analytical techniques such as infrared spectroscopy can be used to confirm the presence of the solvent in a crystal of the solvate.

II. Second Therapeutic Agents

[0372] In one embodiment, the therapeutic methods, uses, compositions, and kits of the present disclosure comprise administering a therapeutically effective amount of a Compound of the Disclosure in combination with a therapeutically effective amount of a Second Therapeutic Agent to a subject in need thereof.

[0373] The term "Second Therapeutic Agent" as used herein comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

[0374] In one embodiment, the Second Therapeutic Agent comprises one compound from one drug class, i.e., one BTK inhibitor, one anti-CD20 monoclonal antibody, one alkylating agent, one topoisomerase II inhibitor, one vinca alkaloid, one platinum-based drug, one nucleoside anticancer agent, one PI3K inhibitor, one CDK4/6 inhibitor, one CARM1 inhibitor, inhibitor of an enzyme of DNA damage repair, one SYK inhibitor, or one MEK inhibitor.

[0375] In another embodiment, the Second Therapeutic Agent comprises ibrutinib, acalabrutinib, zanubrutinib, rituximab, mafosfamide, doxorubicin, vincristine, cytarabine, carboplatin, etoposide, gemcitabine, oxaliplatin, copanlisib, palbociclib, or EZM2302.

[0376] In another embodiment, the Second Therapeutic Agent comprises two different compounds from one drug class, e.g., two different BTK inhibitors, two different anti-CD20 monoclonal antibodies, two different alkylating agents, two different topoisomerase II inhibitors, two different vinca alkaloids, two different platinum-based drugs, two different nucleoside anticancer agents, two different PI3K inhibitors, two different CDK4/6 inhibitors, or two different CARM1 inhibitors.

[0377] In another embodiment, the Second Therapeutic Agent comprises three different compounds from one drug class, e.g., three different BTK inhibitors, three different anti-CD20 monoclonal antibodies, three different alkylating agents, three different topoisomerase II inhibitors, three different vinca alkaloids, three different platinum-based drugs, three different nucleoside anticancer agents, three different PI3K inhibitors, three different CDK4/6 inhibitors, or three different CARM1 inhibitors.

[0378] In another embodiment, the Second Therapeutic Agent comprises three different compounds from two drug classes, e.g., two different BTK inhibitors and one PI3Ki inhibitor; two different CDK4/6 inhibitors and one CARM1 inhibitor ; and so on.

[0379] In another embodiment, the Second Therapeutic Agent comprises compounds from two different drug classes. For example, in one embodiment, the Second Therapeutic Agent comprises a first compound from a first drug class and second compound from a second drug class, wherein the first drug class and the second drug class are different. In a specific non-limiting example, the Second Therapeutic Agent comprises a BTK inhibitor, e.g., ibrutinib, and a PI3Ki inhibitor, e.g., copanlisib. Non-limiting examples of combinations of first and second drug classes of the Second Therapeutic Agent are provided in Table 4.

Table 4

No.	Drug Class # 1	Drug Class # 2
1	BTK inhibitor	anti-CD20 mAb
2	BTK inhibitor	alkylating agent
3	BTK inhibitor	topoisomerase II inhibitor
4	BTK inhibitor	vinca alkaloid
5	BTK inhibitor	platinum-based drug
6	BTK inhibitor	nucleoside anticancer agent
7	BTK inhibitor	PI3K inhibitor

8	BTK inhibitor	CDK4/6 inhibitor
9	BTK inhibitor	CARM1 inhibitor
10	anti-CD20 mAb	alkylating agent
11	anti-CD20 mAb	topoisomerase II inhibitor
12	anti-CD20 mAb	vinca alkaloid
13	anti-CD20 mAb	platinum-based drug
14	anti-CD20 mAb	nucleoside anticancer agent
15	anti-CD20 mAb	PI3K inhibitor
16	anti-CD20 mAb	CDK4/6 inhibitor
17	anti-CD20 mAb	CARM1 inhibitor
18	alkylating agent	topoisomerase II inhibitor
19	alkylating agent	vinca alkaloid
20	alkylating agent	platinum-based drug
21	alkylating agent	nucleoside anticancer agent
22	alkylating agent	PI3K inhibitor
23	alkylating agent	CDK4/6 inhibitor
24	alkylating agent	CARM1 inhibitor
25	topoisomerase II inhibitor	vinca alkaloid
26	topoisomerase II inhibitor	platinum-based drug
27	topoisomerase II inhibitor	nucleoside anticancer agent
28	topoisomerase II inhibitor	PI3K inhibitor
29	topoisomerase II inhibitor	CDK4/6 inhibitor
30	topoisomerase II inhibitor	CARM1 inhibitor
31	vinca alkaloid	platinum-based drug
32	vinca alkaloid	nucleoside anticancer agent
33	vinca alkaloid	PI3K inhibitor
34	vinca alkaloid	CDK4/6 inhibitor
35	vinca alkaloid	CARM1 inhibitor
36	platinum-based drug	nucleoside anticancer agent
37	platinum-based drug	PI3K inhibitor
38	platinum-based drug	CDK4/6 inhibitor
39	platinum-based drug	CARM1 inhibitor
40	nucleoside anticancer agent	PI3K inhibitor
41	nucleoside anticancer agent	CDK4/6 inhibitor
42	nucleoside anticancer agent	CARM1 inhibitor
43	PI3K inhibitor	CDK4/6 inhibitor
44	PI3K inhibitor	CARM1 inhibitor
45	CDK4/6 inhibitor	CARM1 inhibitor

[0380] In another embodiment, the Second Therapeutic Agent comprises compounds from three different drug classes. For example, in one embodiment, the Second Therapeutic Agent comprises a first compound from a first drug class, and a second compound from a second drug class, and a third compound from a third drug class, wherein the first drug class, the second drug class, and the third drug class are different.

Non-limiting examples of combinations of first, second, and third drug classes of the Second Therapeutic Agent are provided in Table 5.

Table 5

No.	Drug Class # 1	Drug Class # 2	Drug Class # 3
1	BTK inhibitor	anti-CD20 mAb	alkylating agent
2	BTK inhibitor	anti-CD20 mAb	topoisomerase II inhibitor
3	BTK inhibitor	anti-CD20 mAb	vinca alkaloid
4	BTK inhibitor	anti-CD20 mAb	platinum-based drug
5	BTK inhibitor	anti-CD20 mAb	nucleoside anticancer agent
6	BTK inhibitor	anti-CD20 mAb	PI3K inhibitor
7	BTK inhibitor	anti-CD20 mAb	CDK4/6 inhibitor
8	BTK inhibitor	anti-CD20 mAb	CARM1 inhibitor
9	BTK inhibitor	alkylating agent	topoisomerase II inhibitor
10	BTK inhibitor	alkylating agent	vinca alkaloid
11	BTK inhibitor	alkylating agent	platinum-based drug
12	BTK inhibitor	alkylating agent	nucleoside anticancer agent
13	BTK inhibitor	alkylating agent	PI3K inhibitor
14	BTK inhibitor	alkylating agent	CDK4/6 inhibitor
15	BTK inhibitor	alkylating agent	CARM1 inhibitor
16	BTK inhibitor	topoisomerase II inhibitor	vinca alkaloid
17	BTK inhibitor	topoisomerase II inhibitor	platinum-based drug
18	BTK inhibitor	topoisomerase II inhibitor	nucleoside anticancer agent
19	BTK inhibitor	topoisomerase II inhibitor	PI3K inhibitor
20	BTK inhibitor	topoisomerase II inhibitor	CDK4/6 inhibitor
21	BTK inhibitor	topoisomerase II inhibitor	CARM1 inhibitor
22	BTK inhibitor	vinca alkaloid	platinum-based drug
23	BTK inhibitor	vinca alkaloid	nucleoside anticancer agent
24	BTK inhibitor	vinca alkaloid	PI3K inhibitor
25	BTK inhibitor	vinca alkaloid	CDK4/6 inhibitor
26	BTK inhibitor	vinca alkaloid	CARM1 inhibitor
27	BTK inhibitor	platinum-based drug	nucleoside anticancer agent
28	BTK inhibitor	platinum-based drug	PI3K inhibitor
29	BTK inhibitor	platinum-based drug	CDK4/6 inhibitor
30	BTK inhibitor	platinum-based drug	CARM1 inhibitor
31	BTK inhibitor	nucleoside anticancer agent	PI3K inhibitor
32	BTK inhibitor	nucleoside anticancer agent	CDK4/6 inhibitor
33	BTK inhibitor	nucleoside anticancer agent	CARM1 inhibitor
34	BTK inhibitor	PI3K inhibitor	CDK4/6 inhibitor
35	BTK inhibitor	PI3K inhibitor	CARM1 inhibitor
36	BTK inhibitor	CDK4/6 inhibitor	CARM1 inhibitor
37	anti-CD20 mAb	alkylating agent	topoisomerase II inhibitor
38	anti-CD20 mAb	alkylating agent	vinca alkaloid
39	anti-CD20 mAb	alkylating agent	platinum-based drug

40	anti-CD20 mAb	alkylating agent	nucleoside anticancer agent
41	anti-CD20 mAb	alkylating agent	PI3K inhibitor
42	anti-CD20 mAb	alkylating agent	CDK4/6 inhibitor
43	anti-CD20 mAb	alkylating agent	CARM1 inhibitor
44	anti-CD20 mAb	topoisomerase II inhibitor	vinca alkaloid
45	anti-CD20 mAb	topoisomerase II inhibitor	platinum-based drug
46	anti-CD20 mAb	topoisomerase II inhibitor	nucleoside anticancer agent
47	anti-CD20 mAb	topoisomerase II inhibitor	PI3K inhibitor
48	anti-CD20 mAb	topoisomerase II inhibitor	CDK4/6 inhibitor
49	anti-CD20 mAb	topoisomerase II inhibitor	CARM1 inhibitor
50	anti-CD20 mAb	vinca alkaloid	platinum-based drug
51	anti-CD20 mAb	vinca alkaloid	nucleoside anticancer agent
52	anti-CD20 mAb	vinca alkaloid	PI3K inhibitor
53	anti-CD20 mAb	vinca alkaloid	CDK4/6 inhibitor
54	anti-CD20 mAb	vinca alkaloid	CARM1 inhibitor
55	anti-CD20 mAb	platinum-based drug	nucleoside anticancer agent
56	anti-CD20 mAb	platinum-based drug	PI3K inhibitor
57	anti-CD20 mAb	platinum-based drug	CDK4/6 inhibitor
58	anti-CD20 mAb	platinum-based drug	CARM1 inhibitor
59	anti-CD20 mAb	nucleoside anticancer agent	PI3K inhibitor
60	anti-CD20 mAb	nucleoside anticancer agent	CDK4/6 inhibitor
61	anti-CD20 mAb	nucleoside anticancer agent	CARM1 inhibitor
62	anti-CD20 mAb	PI3K inhibitor	CDK4/6 inhibitor
63	anti-CD20 mAb	PI3K inhibitor	CARM1 inhibitor
64	anti-CD20 mAb	CDK4/6 inhibitor	CARM1 inhibitor
65	alkylating agent	topoisomerase II inhibitor	vinca alkaloid
66	alkylating agent	topoisomerase II inhibitor	platinum-based drug
67	alkylating agent	topoisomerase II inhibitor	nucleoside anticancer agent
68	alkylating agent	topoisomerase II inhibitor	PI3K inhibitor
69	alkylating agent	topoisomerase II inhibitor	CDK4/6 inhibitor
70	alkylating agent	topoisomerase II inhibitor	CARM1 inhibitor
71	alkylating agent	vinca alkaloid	platinum-based drug
72	alkylating agent	vinca alkaloid	nucleoside anticancer agent
73	alkylating agent	vinca alkaloid	PI3K inhibitor
74	alkylating agent	vinca alkaloid	CDK4/6 inhibitor
75	alkylating agent	vinca alkaloid	CARM1 inhibitor
76	alkylating agent	platinum-based drug	nucleoside anticancer agent
77	alkylating agent	platinum-based drug	PI3K inhibitor
78	alkylating agent	platinum-based drug	CDK4/6 inhibitor
79	alkylating agent	platinum-based drug	CARM1 inhibitor
80	alkylating agent	nucleoside anticancer agent	PI3K inhibitor
81	alkylating agent	nucleoside anticancer agent	CDK4/6 inhibitor

82	alkylating agent	nucleoside anticancer agent	CARM1 inhibitor
83	alkylating agent	PI3K inhibitor	CDK4/6 inhibitor
84	alkylating agent	PI3K inhibitor	CARM1 inhibitor
85	alkylating agent	CDK4/6 inhibitor	CARM1 inhibitor
86	topoisomerase II inhibitor	vinca alkaloid	platinum-based drug
87	topoisomerase II inhibitor	vinca alkaloid	nucleoside anticancer agent
88	topoisomerase II inhibitor	vinca alkaloid	PI3K inhibitor
89	topoisomerase II inhibitor	vinca alkaloid	CDK4/6 inhibitor
90	topoisomerase II inhibitor	vinca alkaloid	CARM1 inhibitor
91	topoisomerase II inhibitor	platinum-based drug	nucleoside anticancer agent
92	topoisomerase II inhibitor	platinum-based drug	PI3K inhibitor
93	topoisomerase II inhibitor	platinum-based drug	CDK4/6 inhibitor
94	topoisomerase II inhibitor	platinum-based drug	CARM1 inhibitor
95	topoisomerase II inhibitor	nucleoside anticancer agent	PI3K inhibitor
96	topoisomerase II inhibitor	nucleoside anticancer agent	CDK4/6 inhibitor
97	topoisomerase II inhibitor	nucleoside anticancer agent	CARM1 inhibitor
98	topoisomerase II inhibitor	PI3K inhibitor	CDK4/6 inhibitor
99	topoisomerase II inhibitor	PI3K inhibitor	CARM1 inhibitor
100	topoisomerase II inhibitor	CDK4/6 inhibitor	CARM1 inhibitor
101	vinca alkaloid	platinum-based drug	nucleoside anticancer agent
102	vinca alkaloid	platinum-based drug	PI3K inhibitor
103	vinca alkaloid	platinum-based drug	CDK4/6 inhibitor
104	vinca alkaloid	platinum-based drug	CARM1 inhibitor
105	vinca alkaloid	nucleoside anticancer agent	PI3K inhibitor
106	vinca alkaloid	nucleoside anticancer agent	CDK4/6 inhibitor
107	vinca alkaloid	nucleoside anticancer agent	CARM1 inhibitor
108	vinca alkaloid	PI3K inhibitor	CDK4/6 inhibitor
109	vinca alkaloid	PI3K inhibitor	CARM1 inhibitor
110	vinca alkaloid	CDK4/6 inhibitor	CARM1 inhibitor

111	platinum-based drug	nucleoside anticancer agent	PI3K inhibitor
112	platinum-based drug	nucleoside anticancer agent	CDK4/6 inhibitor
113	platinum-based drug	nucleoside anticancer agent	CARM1 inhibitor
114	platinum-based drug	PI3K inhibitor	CDK4/6 inhibitor
115	platinum-based drug	PI3K inhibitor	CARM1 inhibitor
116	platinum-based drug	CDK4/6 inhibitor	CARM1 inhibitor
117	nucleoside anticancer agent	PI3K inhibitor	CDK4/6 inhibitor
118	nucleoside anticancer agent	PI3K inhibitor	CARM1 inhibitor
119	nucleoside anticancer agent	CDK4/6 inhibitor	CARM1 inhibitor
120	PI3K inhibitor	CDK4/6 inhibitor	CARM1 inhibitor

III. Third Therapeutic Agents

[0381] In one embodiment, the therapeutic methods, uses, compositions, and kits of the present disclosure comprise administering a therapeutically effective amount of a Compound of the Disclosure in combination with a therapeutically effective amount of a Second Therapeutic Agent and a therapeutically effective amount of a Third Therapeutic Agent to a subject in need thereof.

[0382] The term "Third Therapeutic Agent" as used herein comprises one or more glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

[0383] In one embodiment, the Third Therapeutic Agent comprises one compound from one drug class, i.e., one glucocorticoid receptor agonist, one immunomodulatory drug, one proteasome inhibitor, one Bcl-2 inhibitor, one pleiotropic pathway modulator, one XPO1 inhibitor, one histone deacetylase inhibitor, or one EZH2 inhibitor.

[0384] In another embodiment, the Third Therapeutic Agent comprises two different compounds from one drug class, e.g., two different glucocorticoid receptor agonists, e.g., dexamethasone and prednisone, two different immunomodulatory drugs, two different proteasome inhibitors, two different Bcl-2 inhibitors, two different pleiotropic pathway modulators, two different XPO1 inhibitors, two different histone deacetylase inhibitors, or two different EZH2 inhibitors.

[0385] In another embodiment, the Third Therapeutic Agent comprises three different compounds from one drug class, e.g., three different glucocorticoid receptor agonists, e.g., dexamethasone, prednisone, and methylprednisolone, three different immunomodulatory drugs, three different proteasome inhibitors, three different Bcl-2 inhibitors, three different pleiotropic pathway modulators, three different XPO1 inhibitors, three different histone deacetylase inhibitors, or three different EZH2 inhibitors.

[0386] In another embodiment, the Third Therapeutic Agent comprises three different compounds from two drug classes, e.g., two different glucocorticoid receptor agonists, e.g., dexamethasone and prednisone, and one immunomodulatory drug; two different glucocorticoid receptor agonists and one proteasome inhibitor; and so on.

[0387] In another embodiment, the Third Therapeutic Agent comprises compounds from two different drug classes. For example, in one embodiment, the Second Therapeutic Agent comprises a first compound from a first drug class and second compound from a second drug class, wherein the first drug class and the second drug class are different. In a specific non-limiting example, the Third Therapeutic Agent comprises an EZH2 inhibitor, e.g., tazemetostat, and an immunomodulatory drug, e.g., lenoliminide. Non-limiting examples of combinations of first and second drug classes of the Third Therapeutic Agent are provided in Table 6.

Table 6

No.	Drug Class # 1	Drug Class # 2
1	GR agonist	IMiD
2	GR agonist	Proteasome inhibitor
3	GR agonist	Bcl-2 inhibitor
4	GR agonist	Pleiotropic pathway modulator
5	GR agonist	XPO1 inhibitor
6	GR agonist	HDAC inhibitor
7	GR agonist	EZH2 inhibitor
8	IMiD	Proteasome inhibitor
9	IMiD	Bcl-2 inhibitor
10	IMiD	Pleiotropic pathway modulator
11	IMiD	XPO1 inhibitor
12	IMiD	HDAC inhibitor
13	IMiD	EZH2 inhibitor
14	Proteasome inhibitor	Bcl-2 inhibitor
15	Proteasome inhibitor	Pleiotropic pathway modulator
16	Proteasome inhibitor	XPO1 inhibitor
17	Proteasome inhibitor	HDAC inhibitor

18	Proteasome inhibitor	EZH2 inhibitor
19	Bcl-2 inhibitor	Pleiotropic pathway modulator
20	Bcl-2 inhibitor	XPO1 inhibitor
21	Bcl-2 inhibitor	HDAC inhibitor
22	Bcl-2 inhibitor	EZH2 inhibitor
23	Pleiotropic pathway modulator	XPO1 inhibitor
24	Pleiotropic pathway modulator	HDAC inhibitor
25	Pleiotropic pathway modulator	EZH2 inhibitor
26	XPO1 inhibitor	HDAC inhibitor
27	XPO1 inhibitor	EZH2 inhibitor
28	HDAC inhibitor	EZH2 inhibitor

[0388] In another embodiment, the Third Therapeutic Agent comprises compounds from three different drug classes. For example, in one embodiment, the Second Therapeutic Agent comprises a first compound from a first drug class, and a second compound from a second drug class, and a third compound from a third drug class, wherein the first drug class, the second drug class, and the third drug class are different. Non-limiting examples of combinations of first, second, and third drug classes of the Third Therapeutic Agent are provided in Table 7.

Table 7

No.	Drug Class # 1	Drug Class # 2	Drug Class # 3
1	GR agonist	IMiD	Proteasome inhibitor
2	GR agonist	IMiD	Bcl-2 inhibitor
3	GR agonist	IMiD	Pleiotropic pathway modulator
4	GR agonist	IMiD	XPO1 inhibitor
5	GR agonist	IMiD	HDAC inhibitor
6	GR agonist	IMiD	EZH2 inhibitor
7	GR agonist	Proteasome inhibitor	Bcl-2 inhibitor
8	GR agonist	Proteasome inhibitor	Pleiotropic pathway modulator
9	GR agonist	Proteasome inhibitor	XPO1 inhibitor
10	GR agonist	Proteasome inhibitor	HDAC inhibitor
11	GR agonist	Proteasome inhibitor	EZH2 inhibitor
12	GR agonist	Bcl-2 inhibitor	Pleiotropic pathway modulator
13	GR agonist	Bcl-2 inhibitor	XPO1 inhibitor
14	GR agonist	Bcl-2 inhibitor	HDAC inhibitor
15	GR agonist	Bcl-2 inhibitor	EZH2 inhibitor
16	GR agonist	Pleiotropic pathway modulator	XPO1 inhibitor
17	GR agonist	Pleiotropic pathway modulator	HDAC inhibitor
18	GR agonist	Pleiotropic pathway modulator	EZH2 inhibitor
19	GR agonist	XPO1 inhibitor	HDAC inhibitor
20	GR agonist	XPO1 inhibitor	EZH2 inhibitor

21	GR agonist	HDAC inhibitor	EZH2 inhibitor
22	IMiD	Proteasome inhibitor	Bcl-2 inhibitor
23	IMiD	Proteasome inhibitor	Pleiotropic pathway modulator
24	IMiD	Proteasome inhibitor	XPO1 inhibitor
25	IMiD	Proteasome inhibitor	HDAC inhibitor
26	IMiD	Proteasome inhibitor	EZH2 inhibitor
27	IMiD	Bcl-2 inhibitor	Pleiotropic pathway modulator
28	IMiD	Bcl-2 inhibitor	XPO1 inhibitor
29	IMiD	Bcl-2 inhibitor	HDAC inhibitor
30	IMiD	Bcl-2 inhibitor	EZH2 inhibitor
31	IMiD	Pleiotropic pathway modulator	XPO1 inhibitor
32	IMiD	Pleiotropic pathway modulator	HDAC inhibitor
33	IMiD	Pleiotropic pathway modulator	EZH2 inhibitor
34	IMiD	XPO1 inhibitor	HDAC inhibitor
35	IMiD	XPO1 inhibitor	EZH2 inhibitor
36	IMiD	HDAC inhibitor	EZH2 inhibitor
37	Proteasome inhibitor	Bcl-2 inhibitor	Pleiotropic pathway modulator
38	Proteasome inhibitor	Bcl-2 inhibitor	XPO1 inhibitor
39	Proteasome inhibitor	Bcl-2 inhibitor	HDAC inhibitor
40	Proteasome inhibitor	Bcl-2 inhibitor	EZH2 inhibitor
41	Proteasome inhibitor	Pleiotropic pathway modulator	XPO1 inhibitor
42	Proteasome inhibitor	Pleiotropic pathway modulator	HDAC inhibitor
43	Proteasome inhibitor	Pleiotropic pathway modulator	EZH2 inhibitor
44	Proteasome inhibitor	XPO1 inhibitor	HDAC inhibitor
45	Proteasome inhibitor	XPO1 inhibitor	EZH2 inhibitor
46	Proteasome inhibitor	HDAC inhibitor	EZH2 inhibitor
47	Bcl-2 inhibitor	Pleiotropic pathway modulator	XPO1 inhibitor
48	Bcl-2 inhibitor	Pleiotropic pathway modulator	HDAC inhibitor
49	Bcl-2 inhibitor	Pleiotropic pathway modulator	EZH2 inhibitor
50	Bcl-2 inhibitor	XPO1 inhibitor	HDAC inhibitor
51	Bcl-2 inhibitor	XPO1 inhibitor	EZH2 inhibitor
52	Bcl-2 inhibitor	HDAC inhibitor	EZH2 inhibitor
53	Pleiotropic pathway modulator	XPO1 inhibitor	HDAC inhibitor
54	Pleiotropic pathway modulator	XPO1 inhibitor	EZH2 inhibitor
55	Pleiotropic pathway modulator	HDAC inhibitor	EZH2 inhibitor
56	XPO1 inhibitor	HDAC inhibitor	EZH2 inhibitor

[0389] Non-limiting examples of combinations of a Second Therapeutic Agent and a Third Therapeutic Agent are provided in Table 8.

Table 8

No.	Drug Class # 1	Drug Class # 2
1	BTK inhibitor	IMiD
2	BTK inhibitor	GR agonist
3	BTK inhibitor	Proteasome inhibitor
4	BTK inhibitor	Bcl-2 inhibitor
5	BTK inhibitor	Pleiotropic pathway modulator
6	BTK inhibitor	XPO1 inhibitor
7	BTK inhibitor	HDAC inhibitor
8	BTK inhibitor	EZH2 inhibitor
9	anti-CD20 mAb	IMiD
10	anti-CD20 mAb	GR agonist
11	anti-CD20 mAb	Proteasome inhibitor
12	anti-CD20 mAb	Bcl-2 inhibitor
13	anti-CD20 mAb	Pleiotropic pathway modulator
14	anti-CD20 mAb	XPO1 inhibitor
15	anti-CD20 mAb	HDAC inhibitor
16	anti-CD20 mAb	EZH2 inhibitor
17	alkylating agent	IMiD
18	alkylating agent	GR agonist
19	alkylating agent	Proteasome inhibitor
20	alkylating agent	Bcl-2 inhibitor
21	alkylating agent	Pleiotropic pathway modulator
22	alkylating agent	XPO1 inhibitor
23	alkylating agent	HDAC inhibitor
24	alkylating agent	EZH2 inhibitor
25	topoisomerase II inhibitor	IMiD
26	topoisomerase II inhibitor	GR agonist
27	topoisomerase II inhibitor	Proteasome inhibitor
28	topoisomerase II inhibitor	Bcl-2 inhibitor
29	topoisomerase II inhibitor	Pleiotropic pathway modulator
30	topoisomerase II inhibitor	XPO1 inhibitor
31	topoisomerase II inhibitor	HDAC inhibitor
32	topoisomerase II inhibitor	EZH2 inhibitor
33	vinca alkaloid	IMiD
34	vinca alkaloid	GR agonist
35	vinca alkaloid	Proteasome inhibitor
36	vinca alkaloid	Bcl-2 inhibitor
37	vinca alkaloid	Pleiotropic pathway modulator
38	vinca alkaloid	XPO1 inhibitor
39	vinca alkaloid	HDAC inhibitor
40	vinca alkaloid	EZH2 inhibitor
41	platinum-based drug	IMiD
42	platinum-based drug	GR agonist
43	platinum-based drug	Proteasome inhibitor
44	platinum-based drug	Bcl-2 inhibitor
45	platinum-based drug	Pleiotropic pathway modulator
46	platinum-based drug	XPO1 inhibitor

47	platinum-based drug	HDAC inhibitor
48	platinum-based drug	EZH2 inhibitor
49	nucleoside anticancer agents	IMiD
50	nucleoside anticancer agents	GR agonist
51	nucleoside anticancer agents	Proteasome inhibitor
52	nucleoside anticancer agents	Bcl-2 inhibitor
53	nucleoside anticancer agents	Pleiotropic pathway modulator
54	nucleoside anticancer agents	XPO1 inhibitor
55	nucleoside anticancer agents	HDAC inhibitor
56	nucleoside anticancer agents	EZH2 inhibitor
57	PI3K inhibitor	IMiD
58	PI3K inhibitor	GR agonist
59	PI3K inhibitor	Proteasome inhibitor
60	PI3K inhibitor	Bcl-2 inhibitor
61	PI3K inhibitor	Pleiotropic pathway modulator
62	PI3K inhibitor	XPO1 inhibitor
63	PI3K inhibitor	HDAC inhibitor
64	PI3K inhibitor	EZH2 inhibitor
65	CDK4/6 inhibitor	IMiD
66	CDK4/6 inhibitor	GR agonist
67	CDK4/6 inhibitor	Proteasome inhibitor
68	CDK4/6 inhibitor	Bcl-2 inhibitor
69	CDK4/6 inhibitor	Pleiotropic pathway modulator
70	CDK4/6 inhibitor	XPO1 inhibitor
71	CDK4/6 inhibitor	HDAC inhibitor
72	CDK4/6 inhibitor	EZH2 inhibitor
73	CARM1 inhibitor	IMiD
74	CARM1 inhibitor	GR agonist
75	CARM1 inhibitor	Proteasome inhibitor
76	CARM1 inhibitor	Bcl-2 inhibitor
77	CARM1 inhibitor	Pleiotropic pathway modulator
78	CARM1 inhibitor	XPO1 inhibitor
79	CARM1 inhibitor	HDAC inhibitor
80	CARM1 inhibitor	EZH2 inhibitor

[0390] The term "drug class" as used herein refers to the grouping of biologically active molecules, i.e., drugs, based on their chemical nature, mechanism of action, e.g., binding to the same biological target, and/or mode of action to treat a disease, disorder, or condition in a subject. A Second Therapeutic Agent of the disclosure comprises one or more biologically active molecules from one or more drug classes. These drug classes include BTK inhibitors, anti-CD20 monoclonal antibodies, alkylating agents, topoisomerase II inhibitors, vinca alkaloids, platinum-based drugs, nucleoside anticancer agents, PI3K inhibitors, CDK4/6 inhibitors, CARM1 inhibitors, inhibitors of an enzyme

of DNA damage repair, SYK inhibitors and MEK inhibitors. Likewise, a Third Therapeutic Agent of the disclosure comprises one or more biologically active molecules from one or more drug classes. These drug classes include glucocorticoid receptor agonists, immunomodulatory drugs, proteasome inhibitors, Bcl-2 inhibitors, pleiotropic pathway modulators, XPO1 inhibitors, histone deacetylase inhibitors, and EZH2 inhibitors.

[0391] The terms "BTK inhibitor" or "BTKi" as used herein refers to a compound that inhibits Bruton's tyrosine kinase, including wild-type BTK and mutant BTK. BTK inhibitors and methods of administering BTK inhibitors to a subject are known in the art. Exemplary BTK inhibitors include, but are not limited to, ibrutinib, evobrutinib, tirabrutinib, spebrutinib, poseltinib, pirtobrutinib (LOXO-305), acalabrutinib, and zanubrutinib.

[0392] The terms "anti-CD20 monoclonal antibody" or "anti CD20 mAb" as used herein refers to a compound that binds to CD20. Anti-CD20 monoclonal antibodies may include bispecific antibodies (BsAb). A non-limiting exemplary anti-CD20 bispecific antibody is BsAb CD20/CD3. CD20 is a surface antigen on B cells, whereas CD3 is an antigen on the surface of T-cells. Anti-CD20 monoclonal antibodies and methods of administering anti-CD20 monoclonal antibodies to a subject are known in the art. A non-limiting exemplary anti-CD20 monoclonal antibody is rituximab, obinutuzumab, ocaratuzumab, ibritumomab, tiuxetan, tositumomab, ofatumumab, ocrelizumab, and veltuzumab. Exemplary examples of a BsAb is mosunetuzumab, golimumab, and RGN1979.

[0393] The term "alkylating agent" as used herein refers to an alkylating agent for use in treating cancer that attaches an alkyl group to DNA. A non-limiting exemplary alkylating agent is mafosfamide.

[0394] The term "topoisomerase II inhibitor" as used herein refers to a compound for use in treating cancer that inhibits Type II topoisomerase. Exemplary topoisomerase II inhibitors include, but are not limited to, doxorubicin, etoposide, novobiocin, ciprofloxacin, teniposide, HU-331, ICRF-187, ICRF-193, and mitindomide.

[0395] The term "vinca alkaloid" as used herein refers to anti-mitotic and anti-microtubule alkaloid agents originally derived from vinca plants. Exemplary vinca alkaloids include, but are not limited to, vincristine, vinblastine, vindesine, vinorelbine, vincaminol, vineridine, vinburnine, vinpocetine, minovincine, methoxyminovincine, minovincinine, vincadifformine, desoxyvincaminol, and vincamajine.

[0396] The term "platinum-based drug" as used herein refers to platinum containing agents that coordinate to DNA to interfere with DNA repair. Exemplary platinum-based drugs include, but are not limited to, carboplatin, cisplatin, oxaliplatin, dicycloplatin, eptaplatin, lobaplatin, miriplatin, nedaplatin, picoplatin, satraplatin, and triplatin tetranitrate.

[0397] The term "nucleoside anticancer agent" as used herein refers to nucleoside analogs for treating cancer. Exemplary nucleoside anticancer agents include, but are not limited to, gemcitabine and cytarabine.

[0398] The terms "PI3K inhibitor" or "PIK3i" as used herein refers to a compound that inhibits phosphoinositide 3-kinase. PI3K inhibitors and methods of administering PI3K inhibitors to a subject are known in the art. Exemplary PI3K inhibitors include, but are not limited to, copanlisib, idelalisib, duvelisib, taselisib, buparlisib, alpelisib, umbralisib, dactolisib, and voxtalisib.

[0399] The term "CDK4/6 inhibitor" or "CDK4/6i" as used herein refers to a compound that inhibits two types of cyclin-dependent kinase - CDK4 and CDK6. CDK4/6 inhibitors and methods of administering CDK4/6 inhibitors to a subject are known in the art. Exemplary CDK4/6 inhibitors include but are not limited to, abemaciclib, ribociclib, and palbociclib .

[0400] The term "CARM1 inhibitor" or "CARM1i" as used herein refers to a compound that inhibits coactivator-associated arginine methyltransferase 1. CARM1 inhibitors and methods of administering CARM1 inhibitors to a subject are known in the art. A non-limiting exemplary CARM1 inhibitor is EZM2302.

[0401] The term "glucocorticoid receptor agonist" or "GR agonist" as used herein refers to a compound that activates the glucocorticoid receptor. Glucocorticoid receptor agonists and methods of administering glucocorticoid receptor agonists to a subject are known in the art. *See, e.g.*, Pufall, M. A., *Adv Exp Med Biol. 872*:315–333 (2015). Exemplary glucocorticoid receptor agonists include, but are not limited to, dexamethasone, hydrocortisone, corticosterone, prednisolone, methylprednisolone, prednisone, triamcinolone, mapracorat, ciclesonide, and (20S)-protopanaxatriol. In one embodiment, the glucocorticoid receptor agonist is prednisone. In another embodiment, the glucocorticoid receptor agonist is dexamethasone.

[0402] The term "immunomodulatory drug" or "IMiD" as used herein refers to a compound that inhibits the production of tumour necrosis factor, interleukin 6,

immunoglobulin G, and/or VEGF, andand/or co-stimulates T cells and NK cells, and/or increases interferon gamma and interleukin 2 production. Immunomodulatory drugs and methods of administering immunomodulatory drugs to a subject are known in the art. Exemplary immunomodulatory drugs include, but art not limited to, thalidomide, lenalidomide, and pomalidomide. In one embodiment, the immunomodulatory drug is pomalidomide.

[0403] The term "proteasome inhibitor" as used herein refers to a compound that blocks the action of proteasomes and thus prevents the degredation of pro-apoptotic factors such as p53 protein. Proteasome inhibitors and methods of administering proteasome inhibitors to a subject are known in the art. Exemplary proteasome inhibitors include, but art not limited to, bortezomib, carfilzomib, and ixazomib. In one embodiment, the proteasome inhibitor is bortezomib.

[0404] The term "Bcl-2 inhibitor" as used herein refers to a compound that inhibits the anti-apoptotic Bcl-2 protein. Bcl-2 inhibitors and methods of administering Bcl-2 inhibitors to a subject are known in the art. Examplary Bcl-2 inhibitors include but are not limited to, navitoclax (ABT-263), ABT-737, Sabutoclax, AT-1019 (Gossypol), TW-37, venetoclax (ABT-199), obatoclax, HA14-1, A-1155463, A-1331852, and WEHI-539. In one embodiment, the Bcl-2 inhibitor is venetoclax.

[0405] The term "pleiotropic pathway modulator" as used herein refers to compound that binds to cereblon to promote protein degredation. Pleiotropic pathway modulators and methods of administering pleiotropic pathway modulators to a subject are known in the art are known in the art. *See, e.g.*, Hagner *et al.*, *Blood 126*:779-789 (2017). A non-limiting exemplary pleiotropic pathway modulator is CC-122.

[0406] The term "XPO1 inhibitor" as used herein refers to an inhibitor of exportin-1 (also known as chromosome region maintenance 1 protein homolog; CRM1). XPO1 inhibitors and methods of administering XPO1 inhibitors to a subject are known in the art. *See, e.g.*, Wang and Liu, *Stem Cell Invest 6*:6 (2019). A non-limiting exemplary XPO1 inhibitor is selinexor.

[0407] The term "histone deacetylase inhibitor" or "HDAC inhibitor" as used herein refers to a compound that inhibits histone deactylase enzymes. Histone deacetylase inhibitors and methods of administering histone deacetylase inhibitors to a subject are known in the art. *See, e.g.*, Eckschlager *et al.*, *Int. J. Mol. Sci. 18*:1414 (2017) doi:10.3390/ijms18071414. Exemplary histone deacetylase inhibitors include, but are

not limited to, romidepsin, belinostat, panobinostat, and vorinostate. In one embodiment, the histone deacetylase inhibitor is panobinostat.

[0408] The term "EZH2 inhibitor" as used herein refers to a compound that inhibits the enhancer of zeste homolog 2 enzyme. EZH2 inhibitors and methods of administering EZH2 inhibitors to a subject are known in the art. *See, e.g.,* Lue and Amengual, *Curr Hematol Malig Rep 13*:369–382 (2018). Exemplary EZH2 inhibitors include, but are not limited to, tazemetostat (Tazverik®), EPZ011989, EPZ005687, GSK126, PF-06821497, and valemetostat. In one embodiment, the EZH2 inhibitor is tazemetostat.

[0409] The term "inhibitor of an enzyme of DNA damage repair" or "DNA repair enzyme inhibitor" refers to a compound that inhibits an enzyme that recognizes and corrects physical damage in DNA. Enzymes involved in DNA damage response pathways and frequently mutated in cancer include, but are not limited to, enzymes encoded by the genes *ATM*, *ATR*, *PAXIP*, *BRCA1*, *BRCA2*, *RAD51*, *FRC*, *XRCC1*, *PCNA*, *PARP1*, *ERCC1*, and *MSH3*.

[0410] The term "ATM inhibitor" as used herein refers to a compound that inhibits ataxia telangiectasia mutated kinase. ATM inhibitors and methods of administering ATM inhibitors to a subject are known in the art. Exemplary ATM inhibitors include, but are not limited to, AZD0156, dactolisib, KU-55933, CP-466722, and AZD1390.

[0411] The term "ATR inhibitor" as used herein refers to a compound that inhibits the ataxia telangiectasia and Rad3-related protein. ATR inhibitors and methods of administering ATR inhibitors to a subject are known in the art. Exemplary ATR inhibitors include, but are not limited to, AZD6738, VX-803, and elimusertib.

[0412] The term "Chk1 inhibitor" as used herein refers to a compound that inhibits the serine/threonine-specific protein kinase that, in humans, is encoded by the gene *CHEK1*. Chk1 inhibitors and methods of administering Chk1 inhibitors to a subject are known in the art. Exemplary Chk1 inhibitors include, but are not limited to, AZD7762, rabusertib, MK-8776, CHIR-124, and PF-477736.

[0413] The term "Wee1 inhibitor" as used herein refers to a compound that inhibits the tyrosine kinase belonging to the serine/threonine family of protein kinases, that in humans, is encoded by the gene *Wee1*. Wee1 inhibitors and methods of administering Wee1 inhibitors to a subject are known in the art. Exemplary Wee1 inhibitors include, but are not limited to, AZD1755.

[0414] The term "RAD51 inhibitor" as used herein refers to a compound that inhibits DNA repair protein RAD51 homolog 1 that, in humans, is encoded by the gene *RAD51*. RAD51 inhibitors and methods of administering RAD51 inhibitors to a subject are known in the art. Exemplary RAD51 inhibitors include, but are not limited to, B02 and RI-1.

[0415] The term "PARP inhibitor" as used herein refers to a compound that inhibits poly (ADP-ribose) polymerase protein(s). PARP inhibitors and methods of administering PARP inhibitors to a subject are known in the art. Exemplary PARP inhibitors include, but are not limited to, olaparib, niraparib, rucaparib, and talazoparib.

[0416] The term "AKT inhibitor" as used herein refers to a compound that inhibits serine/threonine-specific protein kinases that, in humans, are encoded by the genes *AKT1*, *AKT2*, and *AKT3*. AKT inhibitors and methods of administering AKT inhibitors to a subject are known in the art. Exemplary AKT inhibitors include, but are not limited to, MK2206.

[0417] The term "SYK inhibitor" as used herein refers to a compound that inhibits spleen tyrosine kinase that, in humans, is encoded by the gene *SYK*. SYK inhibitors and methods of administering SYK inhibitors to a subject are known in the art. Exemplary SYK inhibitors include, but are not limited to, tamatinib, fostamatinib, R406, MNS, lanraplenib, TAK-659, entospletinib, and BAY-61-3606.

[0418] The term "MEK inhibitor" as used herein refers to a compound that inhibits mitogen-activated protein kinase kinase enzymes. MEK inhibitors and methods of administering MEK inhibitors to a subject are known in the art. Exemplary MEK inhibitors include, but are not limited to, trametinib, selumetinib, and merdametinib.

IV. Therapeutic Methods

[0419] In one embodiment, the present disclosure is directed to a method for treating a disease, condition, or disorder in a subject suffering from, or at risk of suffering from, the disease, condition, or disorder, the method comprising administering to the subject an effective amount of a Compound of the Disclosure and a Second Therapeutic Agent.

[0420] In another embodiment, present disclosure is directed to a method for treating a disease, condition, or disorder in a subject suffering from, or at risk of suffering from, the disease, condition, or disorder, the method comprising administering to the subject an

effective amount of a Compound of the Disclosure, a Second Therapeutic Agent, and a Third Therapeutic Agent.

[0421] In one embodiment, the disease, condition, or disorder is responsive to or mediated by the inhibition of SETD2 protein by a Compound of the Disclosure.

[0422] In the therapeutic methods and uses provided herein, the Compound of the Disclosure, the Second Therapeutic Agent, and the optional Third Therapeutic Agent can be administered in combination under one or more of the following conditions: as separate pharmaceutical compositions, at different periodicities, e.g., simultaneously or sequentially, at different durations, at different concentrations, by different administration routes, etc. Other therapeutic, e.g., anticancer, agents may also be administered to the cancer patient.

[0423] In another embodiment, the present disclosure provides a method of treating a disease, disorder, or condition in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure in combination with a Second Therapeutic Agent.

[0424] In another embodiment, the present disclosure provides a method of treating a disease, disorder, or condition in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure in combination with a Second Therapeutic Agent to provide an additive effect.

[0425] In another embodiment, the present disclosure provides a method of treating a disease, disorder, or condition in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure in combination with a Second Therapeutic Agent to provide a synergistic effect, e.g., the combined therapeutic effects of the Compound of the Disclosure and the Second Therapeutic Agent have an effect that is more significant than each agent alone.

[0426] In another embodiment, the present disclosure provides a method of treating a disease, disorder, or condition in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure in combination with a Second Therapeutic Agent and a Third Therapeutic Agent.

[0427] In another embodiment, the present disclosure provides a method of treating a disease, disorder, or condition in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure in combination with a Second Therapeutic Agent and a Third Therapeutic Agent to provide an additive effect.

[0428] In another embodiment, the present disclosure provides a method of treating a disease, disorder, or condition in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure in combination with a Second Therapeutic Agent and a Third Therapeutic Agent to provide a synergistic effect.

[0429] In another aspect, the present disclosure provides a method of treating cancer in a subject comprising administering a therapeutically effective amount of a Compound of the Disclosure in combination with a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent. While not being limited to a specific mechanism, in some embodiments, Compounds of the Disclosure treat cancer by inhibiting SETD2 protein. Examples of treatable cancers include, but are not limited to, the cancers listed in Table 2.

Table 2

adrenal cancer	lymphoepithelioma
acinic cell carcinoma	lymphoma
acoustic neuroma	acute lymphocytic leukemia
acral lentigious melanoma	acute myelogeous leukemia
acrospiroma	chronic lymphocytic leukemia
acute eosinophilic leukemia	liver cancer
acute erythroid leukemia	small cell lung cancer
acute lymphoblastic leukemia	non-small cell lung cancer
acute megakaryoblastic leukemia	MALT lymphoma
acute monocytic leukemia	malignant fibrous histiocytoma
acute promyelocytic leukemia	malignant peripheral nerve sheath tumor
adenocarcinoma	malignant triton tumor
adenoid cystic carcinoma	mantle cell lymphoma
adenoma	marginal zone B-cell lymphoma
adenomatoid odontogenic tumor	mast cell leukemia
adenosquamous carcinoma	mediastinal germ cell tumor
adipose tissue neoplasm	medullary carcinoma of the breast
adrenocortical carcinoma	medullary thyroid cancer
adult T-cell leukemia/lymphoma	medulloblastoma
aggressive NK-cell leukemia	melanoma
AIDS-related lymphoma	meningioma
alveolar rhabdomyosarcoma	merkel cell cancer
alveolar soft part sarcoma	mesothelioma
ameloblastic fibroma	metastatic urothelial carcinoma
anaplastic large cell lymphoma	mixed Mullerian tumor
anaplastic thyroid cancer	mucinous tumor
angioimmunoblastic T-cell lymphoma	multiple myeloma
angiomyolipoma	muscle tissue neoplasm
angiosarcoma	mycosis fungoides

astrocytoma	myxoid liposarcoma
atypical teratoid rhabdoid tumor	myxoma
B-cell chronic lymphocytic leukemia	myxosarcoma
B-cell prolymphocytic leukemia	nasopharyngeal carcinoma
B-cell lymphoma	neurinoma
basal cell carcinoma	neuroblastoma
biliary tract cancer	neurofibroma
bladder cancer	neuroma
blastoma	nodular melanoma
bone cancer	ocular cancer
Brenner tumor	oligoastrocytoma
Brown tumor	oligodendroglioma
Burkitt's lymphoma	oncocytoma
breast cancer	optic nerve sheath meningioma
brain cancer	optic nerve tumor
carcinoma	oral cancer
carcinoma in situ	osteosarcoma
carcinosarcoma	ovarian cancer
cartilage tumor	Pancoast tumor
cementoma	papillary thyroid cancer
myeloid sarcoma	paraganglioma
chondroma	pinealoblastoma
chordoma	pineocytoma
choriocarcinoma	pituicytoma
choroid plexus papilloma	pituitary adenoma
clear-cell sarcoma of the kidney	pituitary tumor
craniopharyngioma	plasmacytoma
cutaneous T-cell lymphoma	polyembryoma
cervical cancer	precursor T-lymphoblastic lymphoma
colorectal cancer	primary central nervous system lymphoma
Degos disease	primary effusion lymphoma
desmoplastic small round cell tumor	preimary peritoneal cancer
diffuse large B-cell lymphoma	prostate cancer
dysembryoplastic neuroepithelial tumor	pancreatic cancer
dysgerminoma	pharyngeal cancer
embryonal carcinoma	pseudomyxoma periotonei
endocrine gland neoplasm	renal cell carcinoma
endodermal sinus tumor	renal medullary carcinoma
enteropathy-associated T-cell lymphoma	retinoblastoma
esophageal cancer	rhabdomyoma
fetus in fetu	rhabdomyosarcoma
fibroma	Richter's transformation
fibrosarcoma	rectal cancer
follicular lymphoma	sarcoma
follicular thyroid cancer	Schwannomatosis

ganglioneuroma	seminoma
gastrointestinal cancer	Sertoli cell tumor
germ cell tumor	sex cord-gonadal stromal tumor
gestational choriocarcinoma	signet ring cell carcinoma
giant cell fibroblastoma	skin cancer
giant cell tumor of the bone	small blue round cell tumors
glial tumor	small cell carcinoma
glioblastoma multiforme	soft tissue sarcoma
glioma	somatostatinoma
gliomatosis cerebri	soot wart
glucagonoma	spinal tumor
gonadoblastoma	splenic marginal zone lymphoma
granulosa cell tumor	squamous cell carcinoma
gynandroblastoma	synovial sarcoma
gallbladder cancer	Sezary's disease
gastric cancer	small intestine cancer
hairy cell leukemia	squamous carcinoma
hemangioblastoma	stomach cancer
head and neck cancer	T-cell lymphoma
hemangiopericytoma	testicular cancer
hematological malignancy	thecoma
hepatoblastoma	thyroid cancer
hepatosplenic T-cell lymphoma	transitional cell carcinoma
Hodgkin's lymphoma	throat cancer
non-Hodgkin's lymphoma	urachal cancer
invasive lobular carcinoma	urogenital cancer
intestinal cancer	urothelial carcinoma
kidney cancer	uveal melanoma
laryngeal cancer	uterine cancer
lentigo maligna	verrucous carcinoma
lethal midline carcinoma	visual pathway glioma
leukemia	vulvar cancer
leydig cell tumor	vaginal cancer
liposarcoma	Waldenstrom's macroglobulinemia
lung cancer	Warthin's tumor
lymphangioma	Wilms' tumor.
lymphangiosarcoma	

[0430] In another embodiment, the cancer is pancreatic cancer or esophageal cancer.

[0431] In another embodiment, the cancer is selected from the group consisting of esophageal cancer, kidney cancer, stomach cancer, hepatocellular carcinoma, glioblastoma, central nervous system (CNS) cancer, soft tissue cancer, lung cancer, breast cancer, bladder/urinary tract cancer, head and neck cancer, prostate cancer, hematological

cancer, pancreatic cancer, skin cancer, endometrial cancer, ovarian cancer, and colorectal cancer.

[0432] In another embodiment, the cancer or cancer cell is a hematological cancer. Exemplary hematological cancers include, but are not limited to, the cancers listed in Table 3.

Table 3

acute lymphocytic leukemia (ALL)	acute eosinophilic leukemia
acute myeloid leukemia (AML)	acute erythroid leukemia
chronic lymphocytic leukemia (CLL)	acute lymphoblastic leukemia
small lymphocytic lymphoma (SLL)	acute megakaryoblastic leukemia
multiple myeloma (MM)	acute monocytic leukemia
Hodgkins lymphoma (HL)	acute promyelocytic leukemia
non-Hodgkin's lymphoma (NHL)	acute myelogeous leukemia
mantle cell lymphoma (MCL)	B-cell prolymphocytic leukemia
marginal zone B-cell lymphoma	B-cell lymphoma
splenic marginal zone lymphoma	MALT lymphoma
follicular lymphoma (FL)	precursor T-lymphoblastic lymphoma
Waldenstrom's macroglobulinemia (WM)	T-cell lymphoma
diffuse large B-cell lymphoma (DLBCL)	mast cell leukemia
marginal zone lymphoma (MZL)	adult T cell leukemia/lymphoma
hairy cell leukemia (HCL)	aggressive NK-cell leukemia
Burkitt's lymphoma (BL)	angioimmunoblastic T-cell lymphoma
Richter's transformation	

[0433] In another embodiment, the cancer is multiple myeloma.

[0434] In another embodiment, the multiple myeloma is characterized as having chromosomal translocations involving the immunoglobulin heavy chain locus at 14q32. In another embodiment, the chromosomal translocation is a t(4;14) translocation, i.e., the multiple myeloma is t(4;14) multiple myeloma.

[0435] In another embodiment, the cancer is mantle cell lymphoma.

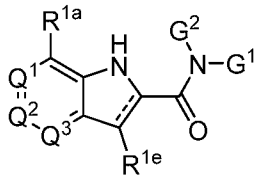
[0436] In another embodiment, the cancer is diffuse large B-cell lymphoma.

[0437] In another embodiment, the present disclosure provides a therapeutic method of modulating protein methylation, gene expression, cell proliferation, cell differentiation and/or apoptosis *in vivo* in the cancers mentioned above by administering a therapeutically effective amount of a Compound of the Disclosure to a subject in need of such therapy and a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent.

[0438] The present disclosure also provides the following particular embodiments.

[0439] Embodiment 1. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of:

[0440] (a) compound of Formula **I**:



I,

or a pharmaceutically acceptable salt or solvate thereof ,wherein:

[0441] R^{1a} is selected from the group consisting of halogen, alkyl, alkoxy, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

[0442] Q^1 is selected from the group consisting of -C(R^{1b})= and –N=;

[0443] Q^2 is selected from the group consisting of -C(R^{1c})= and –N=;

[0444] Q^3 is selected from the group consisting of -C(R^{1d})= and –N=;

[0445] provided that at least one of Q^1, Q^2, or Q^3 is -C(R^{1b})=, -C(R^{1c})=, or -C(R^{1d})=, respectively;

[0446] R^{1b}, R^{1c}, and R^{1d} are each independently selected from the group consisting of hydrogen, halogen, alkyl, alkenyl, (hydroxy)alkyl, and alkoxy;

[0447] R^{1e} is selected from the group consisting of hydrogen, halogen, alkyl, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

[0448] ═ is a single or double bond;

[0449] G^1 is selected from the group consisting of: optionally substituted aryl;

[0450] optionally substituted heteroaryl; optionally substituted heterocyclo; optionally substituted cycloalkyl; (aryl)alkyl; (heteroaryl)alkyl; (heterocyclo)alkyl; (amino)(aryl)alkyl; (heteroaryl)(aryl)alkyl; (heteroaryl)(heterocyclo)alkyl; (heteroaryl)(carboxamido)alkyl; (heteroaryl)(cycloalkyl)alkyl; (aryl)(alkoxycarbonyl)alkyl; (cycloalkyl)alkyl; (heteroaryl)(amino)alkyl; (cycloalkyl)(alkoxycarbonyl)alkyl; (heteroaryl)(alkoxycarbonyl)alkyl; (heterocyclo)(cycloalkyl)alkyl; (aryl)(cycloalkyl)alkyl; (aryl)(hydroxy)alkyl; (cycloalkyl)(hydroxy)alkyl; (hydroxy)alkyl; optionally substituted alkyl; (aryl)(haloalkyl)alkyl; (cycloalkyl)(haloalkyl)alkyl; (hydroxy)(haloalkyl)alkyl; and (alkoxycarbonyl)(haloalkyl)alkyl; and

[0451] G^2 is selected from the group consisting of hydrogen and alkyl; or

[0452] G^1 and G^2 taken together with the nitrogen atom to which they are attached form an optionally substituted heterocyclo; or

[0453] (b) a pharmaceutical composition comprising the compound of Formula **I**, a pharmaceutically acceptable salt or solvate thereof, or a pharmaceutical composition comprising a Compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier; and

[0454] (c) a Second Therapeutic Agent,

[0455] wherein the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more DNA repair enzyme inhibitors, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

[0456] Embodiment 2. The method of Embodiment 1, wherein the Second Therapeutic Agent comprises a BTK inhibitor.

[0457] Embodiment 3. The method of Embodiment 2, wherein the BTK inhibitor is ibrutinib, acalabrutinib, or zanubrutinib.

[0458] Embodiment 4. The method of any one of Embodiments 1-3, wherein the Second Therapeutic Agent comprises an anti-CD20 monoclonal antibody.

[0459] Embodiment 5. The method of Embodiment 4, wherein the anti CD20 monoclonal antibody is rituximab.

[0460] Embodiment 6. The method of any one of Embodiments 1-5, wherein the Second Therapeutic Agent comprises a PI3K inhibitor.

[0461] Embodiment 7. The method of Embodiment 6, wherein the PI3K inhibitor is copanlisib.

[0462] Embodiment 8. The method of any one of Embodiments 1-7, wherein the Second Therapeutic Agent comprises a CDK4/6 inhibitor.

[0463] Embodiment 9. The method of Embodiment 8, wherein the CDK4/6 inhibitor is palbociclib.

[0464] Embodiment 10. The method of any one of Embodiments 1-9, wherein the Second Therapeutic Agent comprises a CARM1 inhibitor.

[0465] Embodiment 11. The method of Embodiment 10, wherein the CARM1 inhibitor is EZM2302.

[0466] Embodiment 12. The method of any one of Embodiments 1-11, wherein the Second Therapeutic Agent comprises an alkylating agent.

[0467] Embodiment 13. The method of Embodiment 12, wherein the alkylating agent is mafosfamide.

[0468] Embodiment 14. The method of any one of Embodiments 1-13, wherein the Second Therapeutic Agent comprises a topoisomerase II inhibitor.

[0469] Embodiment 15. The method of Embodiment 14, wherein the topoisomerase II inhibitor is doxorubicin and etoposide.

[0470] Embodiment 16. The method of any one of Embodiments 1-15, wherein the Second Therapeutic Agent comprises a vinca alkaloid.

[0471] Embodiment 17. The method of Embodiment 16, wherein the vinca alkaloid is vincristine.

[0472] Embodiment 18. The method of any one of Embodiments 1-17, wherein the Second Therapeutic Agent comprises a platinum-based drug.

[0473] Embodiment 19. The method of Embodiment 18, wherein the platinum-based drug is carboplatin or oxaliplatin.

[0474] Embodiment 20. The method of any one of Embodiments 1-19, wherein the Second Therapeutic Agent comprises a nucleoside anticancer agent.

[0475] Embodiment 21. The method of Embodiment 20, wherein the nucleoside anticancer agent is gemcitabine.

[0476] Embodiment 22. The method of any one of Embodiments 1-21 further comprising administering a therapeutically effective amount of a Third Therapeutic Agent to the subject, wherein the Third Therapeutic Agent comprises one or more glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

[0477] Embodiment 23. The method of Embodiment 22, wherein the Third Therapeutic Agent comprises a glucocorticoid receptor agonist.

[0478] Embodiment 24. The method of Embodiment 23, wherein the glucocorticoid receptor agonist is dexamethasone or prednisolone.

[0479] Embodiment 25. The method of any one of Embodiments 22-24, wherein the Third Therapeutic Agent comprises an immunomodulatory drug.

[0480] Embodiment 26. The method of Embodiment 25, wherein the immunomodulatory drug is pomalidomide or lenalidomide.

[0481] Embodiment 27. The method of any one of Embodiments 22-26, wherein the Third Therapeutic Agent comprises a proteasome inhibitor.

[0482] Embodiment 28. The method of Embodiment 27, wherein the proteasome inhibitor is bortezomib.

[0483] Embodiment 29. The method of any one of Embodiments 22-29, wherein the Third Therapeutic Agent comprises a Bcl-2 inhibitor.

[0484] Embodiment 30. The method of Embodiment 29, wherein the Bcl-2 inhibitor is venetoclax.

[0485] Embodiment 31. The method of any one of Embodiments 22-30, wherein the Third Therapeutic Agent comprises a pleiotropic pathway modulator.

[0486] Embodiment 32. The method of Embodiment 31, wherein the pleiotropic pathway modulator is CC-122.

[0487] Embodiment 33. The method of any one of Embodiments 22-32, wherein the Third Therapeutic Agent comprises a XPO1 inhibitor.

[0488] Embodiment 34. The method of Embodiment 33, wherein the XPO1 inhibitor is selinexor.

[0489] Embodiment 35. The method of any one of Embodiments 22-34, wherein the Third Therapeutic Agent comprises a histone deacetylase inhibitor.

[0490] Embodiment 36. The method of Embodiment 35, wherein the histone deacetylase inhibitor is panobinostat.

[0491] Embodiment 37. The method of any one of Embodiments 22-36, wherein the Third Therapeutic Agent comprises an EZH2 inhibitor.

[0492] Embodiment 38. The method of Embodiment 37, wherein the EZH2 inhibitor is tazemetostat.

[0493] Embodiment 39. The method of Embodiment 1, wherein the Second Therapeutic Agent comprises a combination set forth in Table 4.

[0494] Embodiment 40. The method of Embodiment 1, wherein the Second Therapeutic Agent comprises a combination set forth in Table 5.

[0495] Embodiment 41. The method of Embodiment 22, wherein the Second Therapeutic Agent and Third Therapeutic Agent comprise a combination set forth in Table 8.

[0496] Embodiment 42. The method of any one of Embodiments 1-21, wherein the Compound of the Disclosure and the Second Therapeutic Agent are administered sequentially.

[0497] Embodiment 43. The method of any one of Embodiments 1-21, wherein the Compound of the Disclosure and the Second Therapeutic Agent are administered simultaneously.

[0498] Embodiment 44. The method of Embodiments 22-43, wherein the Compound of the Disclosure, the Second Therapeutic Agent, and the Third Therapeutic Agent are administered sequentially.

[0499] Embodiment 45. The method of any one of Embodiments 1-44, wherein the subject has cancer.

[0500] Embodiment 46. The method of Embodiment 45, wherein the cancer is any one or more of the cancers of Table 2.

[0501] Embodiment 47. The method of Embodiment 45, wherein the cancer is a hematological cancer.

[0502] Embodiment 48. The method of Embodiment 47, wherein the hematological cancer is any one or more of the cancers of Table 3.

[0503] Embodiment 49. The method of Embodiment 48, wherein the hematological cancer is multiple myeloma, mantle cell lymphoma, or diffuse large B-cell lymphoma.

[0504] Embodiment 50. The method of Embodiment 49, wherein the hematological cancer is t(4;14) multiple myeloma.

[0505] Embodiment 51. A compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, *see* Embodiment 1, or a pharmaceutical composition comprising a compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier for use in treating cancer in a subject, wherein the compound or composition is to be administered in combination with a Second Therapeutic Agent, and the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K

inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

[0506] Embodiment 52. The compound or composition for use of Embodiment 51, wherein the Second Therapeutic Agent comprises a BTK inhibitor.

[0507] Embodiment 53. The compound or composition for use of Embodiment 52, wherein the BTK inhibitor is ibrutinib, acalabrutinib, or zanubrutinib.

[0508] Embodiment 54. The compound or composition for use of any one of Embodiments 51-53, wherein the Second Therapeutic Agent comprises an anti-CD20 monoclonal antibody.

[0509] Embodiment 55. The compound or composition for use of Embodiment 54, wherein the anti CD20 monoclonal antibody is rituximab.

[0510] Embodiment 56. The compound or composition for use of any one of Embodiments 51-55, wherein the Second Therapeutic Agent comprises a PI3K inhibitor.

[0511] Embodiment 57. The compound or composition for use of Embodiment 56, wherein the PI3K inhibitor is copanlisib.

[0512] Embodiment 58. The compound or composition for use of any one of Embodiments 51-57, wherein the Second Therapeutic Agent comprises a CDK4/6 inhibitor.

[0513] Embodiment 59. The compound or composition for use of Embodiment 58, wherein the CDK4/6 inhibitor is palbociclib.

[0514] Embodiment 60. The compound or composition for use of any one of Embodiments 51-59, wherein the Second Therapeutic Agent comprises a CARM1 inhibitor.

[0515] Embodiment 61. The compound or composition for use of Embodiment 60, wherein the CARM1 inhibitor is EZM2302.

[0516] Embodiment 62. The compound or composition for use of any one of Embodiments 51-61, wherein the Second Therapeutic Agent comprises an alkylating agent.

[0517] Embodiment 63. The compound or composition for use of Embodiment 62, wherein the alkylating agent is mafosfamide.

[0518] Embodiment 64. The compound or composition for use of any one of Embodiments 51-63, wherein the Second Therapeutic Agent comprises a topoisomerase II inhibitor.

[0519] Embodiment 65. The compound or composition for use of Embodiment 64, wherein the topoisomerase II inhibitor is doxorubicin and etoposide.

[0520] Embodiment 66. The compound or composition for use of any one of Embodiments 51-65, wherein the Second Therapeutic Agent comprises a vinca alkaloid.

[0521] Embodiment 67. The compound or composition for use of Embodiment 66, wherein the vinca alkaloid is vincristine.

[0522] Embodiment 68. The compound or composition for use of any one of Embodiments 51-67, wherein the Second Therapeutic Agent comprises a platinum-based drug.

[0523] Embodiment 69. The compound or composition for use of Embodiment 68, wherein the platinum-based drug is carboplatin or oxaliplatin.

[0524] Embodiment 70. The compound or composition for use of any one of Embodiments 51-69, wherein the Second Therapeutic Agent comprises a nucleoside anticancer agent.

[0525] Embodiment 71. The compound or composition for use of Embodiment 70, wherein the nucleoside anticancer agent is gemcitabine.

[0526] Embodiment 72. The compound or composition for use of any one of Embodiments 51-71 further comprising a therapeutically effective amount of a Third Therapeutic Agent to be administered to the subject, wherein the Third Therapeutic Agent comprises one or more glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

[0527] Embodiment 73. The compound or composition for use of Embodiment 72, wherein the Third Therapeutic Agent comprises a glucocorticoid receptor agonist.

[0528] Embodiment 74. The compound or composition for use of Embodiment 73, wherein the glucocorticoid receptor agonist is dexamethasone or prednisolone.

[0529] Embodiment 75. The compound or composition for use of any one of Embodiments 72-74, wherein the Third Therapeutic Agent comprises an immunomodulatory drug.

[0530] Embodiment 76. The compound or composition for use of Embodiment 75, wherein the immunomodulatory drug is pomalidomide or lenalidomide.

[0531] Embodiment 77. The compound or composition for use of any one of Embodiments 72-76, wherein the Third Therapeutic Agent comprises a proteasome inhibitor.

[0532] Embodiment 78. The compound or composition for use of Embodiment 77, wherein the proteasome inhibitor is bortezomib.

[0533] Embodiment 79. The compound or composition for use of any one of Embodiments 72-79, wherein the Third Therapeutic Agent comprises a Bcl-2 inhibitor.

[0534] Embodiment 80. The compound or composition for use of Embodiment 79, wherein the Bcl-2 inhibitor is venetoclax.

[0535] Embodiment 81. The compound or composition for use of any one of Embodiments 72-80, wherein the Third Therapeutic Agent comprises a pleiotropic pathway modulator.

[0536] Embodiment 82. The compound or composition for use of Embodiment 81, wherein the pleiotropic pathway modulator is CC-122.

[0537] Embodiment 83. The compound or composition for use of any one of Embodiments 72-82, wherein the Third Therapeutic Agent comprises a XPO1 inhibitor.

[0538] Embodiment 84. The compound or composition for use of Embodiment 73, wherein the XPO1 inhibitor is selinexor.

[0539] Embodiment 85. The compound or composition for use of any one of Embodiments 72-84, wherein the Third Therapeutic Agent comprises a histone deacetylase inhibitor.

[0540] Embodiment 86. The compound or composition for use of Embodiment 75, wherein the histone deacetylase inhibitor is panobinostat.

[0541] Embodiment 87. The compound or composition for use of any one of Embodiments 72-86, wherein the Third Therapeutic Agent comprises an EZH2 inhibitor.

[0542] Embodiment 88. The compound or composition for use of Embodiment 87, wherein the EZH2 inhibitor is tazemetostat.

[0543] Embodiment 89. The compound or composition for use of Embodiment 51, wherein the Second Therapeutic Agent comprises a combination set forth in Table 4.

[0544] Embodiment 90. The compound or composition for use of Embodiment 51, wherein the Second Therapeutic Agent comprises a combination set forth in Table 5.

[0545] Embodiment 91. The compound or composition for use of Embodiment 72, wherein the Second Therapeutic Agent and Third Therapeutic Agent comprise a combination set forth in Table 8.

[0546] Embodiment 92. The compound or composition for use of any one of Embodiments 51-71, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered sequentially.

[0547] Embodiment 93. The compound or composition for use of any one of Embodiments 51-71, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered simultaneously.

[0548] Embodiment 94. The compound or composition for use of Embodiments 72-93, wherein the Compound of the Disclosure, the Second Therapeutic Agent, and the Third Therapeutic Agent are to be administered sequentially.

[0549] Embodiment 95. The compound or composition for use of any one of Embodiments 51-94, wherein the subject has cancer.

[0550] Embodiment 96. The compound or composition for use of Embodiment 95, wherein the cancer is any one or more of the cancers of Table 2.

[0551] Embodiment 97. The compound or composition for use of Embodiment 95, wherein the cancer is a hematological cancer.

[0552] Embodiment 98. The compound or composition for use of Embodiment 97, wherein the hematological cancer is any one or more of the cancers of Table 3.

[0553] Embodiment 99. The compound or composition for use of Embodiment 98, wherein the hematological cancer is multiple myeloma, mantle cell lymphoma, or diffuse large B-cell lymphoma.

[0554] Embodiment 100. The compound or composition for use of Embodiment 99, wherein the hematological cancer is t(4;14) multiple myeloma.

[0555] Embodiment 101. Use of a compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, *see* Embodiment 1, or a pharmaceutical composition comprising a compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier for the manufacture of a medicament

for treating cancer in a subject, wherein the compound or composition is to be administered in combination with a Second Therapeutic Agent and the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, or one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

[0556] Embodiment 102. The use of Embodiment 101, wherein the Second Therapeutic Agent comprises a BTK inhibitor.

[0557] Embodiment 103. The use of Embodiment 102, wherein the BTK inhibitor is ibrutinib, acalabrutinib, or zanubrutinib.

[0558] Embodiment 104. The use of any one of Embodiments 101-103, wherein the Second Therapeutic Agent comprises an anti-CD20 monoclonal antibody.

[0559] Embodiment 105. The use of Embodiment 104, wherein the anti CD20 monoclonal antibody is rituximab.

[0560] Embodiment 106. The use of any one of Embodiments 101-105, wherein the Second Therapeutic Agent comprises a PI3K inhibitor.

[0561] Embodiment 107. The use of Embodiment 106, wherein the PI3K inhibitor is copanlisib.

[0562] Embodiment 108. The use of any one of Embodiments 101-107, wherein the Second Therapeutic Agent comprises a CDK4/6 inhibitor.

[0563] Embodiment 109. The use of Embodiment 108, wherein the CDK4/6 inhibitor is palbociclib.

[0564] Embodiment 110. The use of any one of Embodiments 101-109, wherein the Second Therapeutic Agent comprises a CARM1 inhibitor.

[0565] Embodiment 111. The use of Embodiment 110, wherein the CARM1 inhibitor is EZM2302.

[0566] Embodiment 112. The use of any one of Embodiments 101-111, wherein the Second Therapeutic Agent comprises an alkylating agent.

[0567] Embodiment 113. The use of Embodiment 112, wherein the alkylating agent is mafosfamide.

[0568] Embodiment 114. The use of any one of Embodiments 101-113, wherein the Second Therapeutic Agent comprises a topoisomerase II inhibitor.

[0569] Embodiment 115. The use of Embodiment 114, wherein the topoisomerase II inhibitor is doxorubicin and etoposide.

[0570] Embodiment 116. The use of any one of Embodiments 51-115, wherein the Second Therapeutic Agent comprises a vinca alkaloid.

[0571] Embodiment 117. The use of Embodiment 116, wherein the vinca alkaloid is vincristine.

[0572] Embodiment 118. The use of any one of Embodiments 101-117, wherein the Second Therapeutic Agent comprises a platinum-based drug.

[0573] Embodiment 119. The use of Embodiment 118, wherein the platinum-based drug is carboplatin or oxaliplatin.

[0574] Embodiment 120. The use of any one of Embodiments 101-119, wherein the Second Therapeutic Agent comprises a nucleoside anticancer agent.

[0575] Embodiment 121. The use of Embodiment 120, wherein the nucleoside anticancer agent is gemcitabine.

[0576] Embodiment 122. The use of any one of Embodiments 101-121 further comprising a therapeutically effective amount of a Third Therapeutic Agent to be administered to the subject, wherein the Third Therapeutic Agent comprises one or more glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

[0577] Embodiment 123. The use of Embodiment 122, wherein the Third Therapeutic Agent comprises a glucocorticoid receptor agonist.

[0578] Embodiment 124. The use of Embodiment 123, wherein the glucocorticoid receptor agonist is dexamethasone or prednisolone.

[0579] Embodiment 125. The use of any one of Embodiments 122-124, wherein the Third Therapeutic Agent comprises an immunomodulatory drug.

[0580] Embodiment 126. The use of Embodiment 125, wherein the immunomodulatory drug is pomalidomide or lenalidomide.

[0581] Embodiment 127. The use of any one of Embodiments 122-126, wherein the Third Therapeutic Agent comprises a proteasome inhibitor.

[0582] Embodiment 128. The use of Embodiment 127, wherein the proteasome inhibitor is bortezomib.

[0583] Embodiment 129. The use of any one of Embodiments 122-129, wherein the Third Therapeutic Agent comprises a Bcl-2 inhibitor.

[0584] Embodiment 130. The use of Embodiment 129, wherein the Bcl-2 inhibitor is venetoclax.

[0585] Embodiment 131. The use of any one of Embodiments 122-130, wherein the Third Therapeutic Agent comprises a pleiotropic pathway modulator.

[0586] Embodiment 132. The use of Embodiment 131, wherein the pleiotropic pathway modulator is CC-122.

[0587] Embodiment 133. The use of any one of Embodiments 122-132, wherein the Third Therapeutic Agent comprises a XPO1 inhibitor.

[0588] Embodiment 134. The use of Embodiment 123, wherein the XPO1 inhibitor is selinexor.

[0589] Embodiment 135. The use of any one of Embodiments 122-134, wherein the Third Therapeutic Agent comprises a histone deacetylase inhibitor.

[0590] Embodiment 136. The use of Embodiment 125, wherein the histone deacetylase inhibitor is panobinostat.

[0591] Embodiment 137. The use of any one of Embodiments 122-136, wherein the Third Therapeutic Agent comprises an EZH2 inhibitor.

[0592] Embodiment 138. The use of Embodiment 137, wherein the EZH2 inhibitor is tazemetostat.

[0593] Embodiment 139. The use of Embodiment 101, wherein the Second Therapeutic Agent comprises a combination set forth in Table 4.

[0594] Embodiment 140. The use of Embodiment 101, wherein the Second Therapeutic Agent comprises a combination set forth in Table 5.

[0595] Embodiment 141. The use of Embodiment 122, wherein the Second Therapeutic Agent and Third Therapeutic Agent comprise a combination set forth in Table 8.

[0596] Embodiment 142. The use of any one of Embodiments 101-121, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered sequentially.

[0597] Embodiment 143. The use of any one of Embodiments 101-121, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered simultaneously.

[0598] Embodiment 144. The use of Embodiments 122-143, wherein the Compound of the Disclosure, the Second Therapeutic Agent, and the Third Therapeutic Agent are to be administered sequentially.

[0599] Embodiment 145. The use of any one of Embodiments 101-144, wherein the subject has cancer.

[0600] Embodiment 146. The use of Embodiment 145, wherein the cancer is any one or more of the cancers of Table 2.

[0601] Embodiment 147. The use of Embodiment 145, wherein the cancer is a hematological cancer.

[0602] Embodiment 148. The use of Embodiment 147, wherein the hematological cancer is any one or more of the cancers of Table 3.

[0603] Embodiment 149. The use of Embodiment 148, wherein the hematological cancer is multiple myeloma, mantle cell lymphoma, or diffuse large B-cell lymphoma.

[0604] Embodiment 150. The use of Embodiment 149, wherein the hematological cancer is t(4;14) multiple myeloma.

[0605] Embodiment 151. A kit for carrying out the method of any one of claims 1-50 or the use of any one of claims 51-150, the kit comprising: (a) a therapeutically effective amount compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, or (b) a pharmaceutical composition comprising a compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier; and (c) a therapeutically effective amount of a Second Therapeutic Agent, wherein the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof and, optionally, (d) instructions for administering the Compound or Composition of the Disclosure and the Second Therapeutic Agent to the subject.

[0606] Embodiment 152. The kit of Embodiment 151, wherein the Second Therapeutic Agent comprises a BTK inhibitor.

[0607] Embodiment 153. The kit of Embodiment 152, wherein the BTK inhibitor is ibrutinib, acalabrutinib, or zanubrutinib.

[0608] Embodiment 154. The kit of any one of Embodiments 151-153, wherein the Second Therapeutic Agent comprises an anti-CD20 monoclonal antibody.

[0609] Embodiment 155. The kit of Embodiment 154, wherein the anti CD20 monoclonal antibody is rituximab.

[0610] Embodiment 156. The kit of any one of Embodiments 151-155, wherein the Second Therapeutic Agent comprises a PI3K inhibitor.

[0611] Embodiment 157. The kit of Embodiment 156, wherein the PI3K inhibitor is copanlisib.

[0612] Embodiment 158. The kit of any one of Embodiments 151-157, wherein the Second Therapeutic Agent comprises a CDK4/6 inhibitor.

[0613] Embodiment 159. The kit of Embodiment 158, wherein the CDK4/6 inhibitor is palbociclib.

[0614] Embodiment 160. The kit of any one of Embodiments 151-159, wherein the Second Therapeutic Agent comprises a CARM1 inhibitor.

[0615] Embodiment 161. The kit of Embodiment 160, wherein the CARM1 inhibitor is EZM2302.

[0616] Embodiment 162. The kit of any one of Embodiments 151-161, wherein the Second Therapeutic Agent comprises an alkylating agent.

[0617] Embodiment 163. The kit of Embodiment 162, wherein the alkylating agent is mafosfamide.

[0618] Embodiment 164. The kit of any one of Embodiments 151-163, wherein the Second Therapeutic Agent comprises a topoisomerase II inhibitor.

[0619] Embodiment 165. The kit of Embodiment 164, wherein the topoisomerase II inhibitor is doxorubicin and etoposide.

[0620] Embodiment 166. The kit of any one of Embodiments 51-165, wherein the Second Therapeutic Agent comprises a vinca alkaloid.

[0621] Embodiment 167. The kit of Embodiment 166, wherein the vinca alkaloid is vincristine.

[0622] Embodiment 168. The kit of any one of Embodiments 151-167, wherein the Second Therapeutic Agent comprises a platinum-based drug.

[0623] Embodiment 169. The kit of Embodiment 168, wherein the platinum-based drug is carboplatin or oxaliplatin.

[0624] Embodiment 170. The kit of any one of Embodiments 151-169, wherein the Second Therapeutic Agent comprises a nucleoside anticancer agent.

[0625] Embodiment 171. The kit of Embodiment 170, wherein the nucleoside anticancer agent is gemcitabine.

[0626] Embodiment 172. The kit of any one of Embodiments 151-171 further comprising a therapeutically effective amount of a Third Therapeutic Agent to be administered to the subject, wherein the Third Therapeutic Agent comprises one or more glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

[0627] Embodiment 173. The kit of Embodiment 172, wherein the Third Therapeutic Agent comprises a glucocorticoid receptor agonist.

[0628] Embodiment 174. The kit of Embodiment 173, wherein the glucocorticoid receptor agonist is dexamethasone or prednisolone.

[0629] Embodiment 175. The kit of any one of Embodiments 172-174, wherein the Third Therapeutic Agent comprises an immunomodulatory drug.

[0630] Embodiment 176. The kit of Embodiment 175, wherein the immunomodulatory drug is pomalidomide or lenalidomide.

[0631] Embodiment 177. The kit of any one of Embodiments 172-176, wherein the Third Therapeutic Agent comprises a proteasome inhibitor.

[0632] Embodiment 178. The kit of Embodiment 177, wherein the proteasome inhibitor is bortezomib.

[0633] Embodiment 179. The kit of any one of Embodiments 172-179, wherein the S Third econd Therapeutic Agent comprises a Bcl-2 inhibitor.

[0634] Embodiment 180. The kit of Embodiment 179, wherein the Bcl-2 inhibitor is venetoclax.

[0635] Embodiment 181. The kit of any one of Embodiments 172-180, wherein the Third Therapeutic Agent comprises a pleiotropic pathway modulator.

[0636] Embodiment 182. The kit of Embodiment 181, wherein the pleiotropic pathway modulator is CC-122.

[0637] Embodiment 183. The kit of any one of Embodiments 172-182, wherein the Third Therapeutic Agent comprises a XPO1 inhibitor.

[0638] Embodiment 184. The kit of Embodiment 173, wherein the XPO1 inhibitor is selinexor

[0639] Embodiment 185. The kit of any one of Embodiments 172-184, wherein the Third Therapeutic Agent comprises a histone deacetylase inhibitor.

[0640] Embodiment 186. The kit of Embodiment 185, wherein the histone deacetylase inhibitor is panobinostat.

[0641] Embodiment 187. The kit of any one of Embodiments 172-186, wherein the Third Therapeutic Agent comprises an EZH2 inhibitor.

[0642] Embodiment 188. The kit of Embodiment 187, wherein the EZH2 inhibitor is tazemetostat.

[0643] Embodiment 189. The kit of Embodiment 151, wherein the Second Therapeutic Agent comprises a combination set forth in Table 4.

[0644] Embodiment 190. The kit of Embodiment 151, wherein the Second Therapeutic Agent comprises a combination set forth in Table 5.

[0645] Embodiment 191. The kit of Embodiment 172, wherein the Second Therapeutic Agent and Third Therapeutic Agent comprise a combination set forth in Table 8.

[0646] Embodiment 192. The kit of any one of Embodiments 151-171, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered sequentially.

[0647] Embodiment 193. The kit of any one of Embodiments 151-171, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered simultaneously.

[0648] Embodiment 194. The kit of Embodiments 172-193, wherein the Compound of the Disclosure, the Second Therapeutic Agent, and the Third Therapeutic Agent are to be administered sequentially.

[0649] Embodiment 195. The kit of any one of Embodiments 151-194, wherein the subject has cancer.

[0650] Embodiment 196. The kit of Embodiment 195, wherein the cancer is any one or more of the cancers of Table 2.

[0651] Embodiment 197. The kit of Embodiment 195, wherein the cancer is a hematological cancer.

[0652] Embodiment 198. The kit of Embodiment 197, wherein the hematological cancer is any one or more of the cancers of Table 3.

[0653] Embodiment 199. The kit of Embodiment 198, wherein the hematological cancer is multiple myeloma, mantle cell lymphoma, or diffuse large B-cell lymphoma.

[0654] Embodiment 200. The kit of Embodiment 199, wherein the hematological cancer is t(4;14) multiple myeloma.

[0655] Embodiment 201. A kit comprising (a) a therapeutically effective amount of compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, *see* Embodiment 1, or (b) a pharmaceutical composition comprising a compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier; and (c) a therapeutically effective amount of a Second Therapeutic Agent, wherein the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof and, optionally, (d) instructions for administering the Compound or Composition of the Disclosure and the Second Therapeutic Agent to a subject.

[0656] Embodiment 202. The kit of Embodiment 201, wherein the Second Therapeutic Agent comprises a BTK inhibitor.

[0657] Embodiment 203. The kit of Embodiment 202, wherein the BTK inhibitor is ibrutinib, acalabrutinib, or zanubrutinib.

[0658] Embodiment 204. The kit of any one of Embodiments 201-203, wherein the Second Therapeutic Agent comprises an anti-CD20 monoclonal antibody.

[0659] Embodiment 205. The kit of Embodiment 204, wherein the anti CD20 monoclonal antibody is rituximab.

[0660] Embodiment 206. The kit of any one of Embodiments 201-205, wherein the Second Therapeutic Agent comprises a PI3K inhibitor.

[0661] Embodiment 207. The kit of Embodiment 206, wherein the PI3K inhibitor is copanlisib.

[0662] Embodiment 208. The kit of any one of Embodiments 201-207, wherein the Second Therapeutic Agent comprises a CDK4/6 inhibitor.

[0663] Embodiment 209. The kit of Embodiment 208, wherein the CDK4/6 inhibitor is palbociclib.

[0664] Embodiment 210. The kit of any one of Embodiments 201-209, wherein the Second Therapeutic Agent comprises a CARM1 inhibitor.

[0665] Embodiment 211. The kit of Embodiment 210, wherein the CARM1 inhibitor is EZM2302.

[0666] Embodiment 212. The kit of any one of Embodiments 201-211, wherein the Second Therapeutic Agent comprises an alkylating agent.

[0667] Embodiment 213. The kit of Embodiment 212, wherein the alkylating agent is mafosfamide.

[0668] Embodiment 214. The kit of any one of Embodiments 201-213, wherein the Second Therapeutic Agent comprises a topoisomerase II inhibitor.

[0669] Embodiment 215. The kit of Embodiment 214, wherein the topoisomerase II inhibitor is doxorubicin and etoposide.

[0670] Embodiment 216. The kit of any one of Embodiments 51-215, wherein the Second Therapeutic Agent comprises a vinca alkaloid.

[0671] Embodiment 217. The kit of Embodiment 216, wherein the vinca alkaloid is vincristine.

[0672] Embodiment 218. The kit of any one of Embodiments 201-217, wherein the Second Therapeutic Agent comprises a platinum-based drug.

[0673] Embodiment 219. The kit of Embodiment 218, wherein the platinum-based drug is carboplatin or oxaliplatin.

[0674] Embodiment 220. The kit of any one of Embodiments 201-219, wherein the Second Therapeutic Agent comprises a nucleoside anticancer agent.

[0675] Embodiment 221. The kit of Embodiment 220, wherein the nucleoside anticancer agent is gemcitabine.

[0676] Embodiment 222. The kit of any one of Embodiments 201-221 further comprising a therapeutically effective amount of a Third Therapeutic Agent to be administered to the subject, wherein the Third Therapeutic Agent comprises one or more

glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

[0677] Embodiment 223. The kit of Embodiment 222, wherein the Third Therapeutic Agent comprises a glucocorticoid receptor agonist.

[0678] Embodiment 224. The kit of Embodiment 223, wherein the glucocorticoid receptor agonist is dexamethasone or prednisolone.

[0679] Embodiment 225. The kit of any one of Embodiments 222-224, wherein the Third Therapeutic Agent comprises an immunomodulatory drug.

[0680] Embodiment 226. The kit of Embodiment 225, wherein the immunomodulatory drug is pomalidomide or lenalidomide.

[0681] Embodiment 227. The kit of any one of Embodiments 222-226, wherein the Third Therapeutic Agent comprises a proteasome inhibitor.

[0682] Embodiment 228. The kit of Embodiment 227, wherein the proteasome inhibitor is bortezomib.

[0683] Embodiment 229. The kit of any one of Embodiments 222-229, wherein the Third Therapeutic Agent comprises a Bcl-2 inhibitor.

[0684] Embodiment 230. The kit of Embodiment 229, wherein the Bcl-2 inhibitor is venetoclax.

[0685] Embodiment 231. The kit of any one of Embodiments 222-230, wherein the Third Therapeutic Agent comprises a pleiotropic pathway modulator.

[0686] Embodiment 232. The kit of Embodiment 231, wherein the pleiotropic pathway modulator is CC-122.

[0687] Embodiment 233. The kit of any one of Embodiments 222-232, wherein the Third Therapeutic Agent comprises a XPO1 inhibitor.

[0688] Embodiment 234. The kit of Embodiment 223, wherein the XPO1 inhibitor is selinexor

[0689] Embodiment 235. The kit of any one of Embodiments 222-234, wherein the Third Therapeutic Agent comprises a histone deacetylase inhibitor.

[0690] Embodiment 236. The kit of Embodiment 235, wherein the histone deacetylase inhibitor is panobinostat.

[0691] Embodiment 237. The kit of any one of Embodiments 222-236, wherein the Third Therapeutic Agent comprises an EZH2 inhibitor.

[0692] Embodiment 238. The kit of Embodiment 237, wherein the EZH2 inhibitor is tazemetostat.

[0693] Embodiment 239. The kit of Embodiment 201, wherein the Second Therapeutic Agent comprises a combination set forth in Table 4.

[0694] Embodiment 240. The kit of Embodiment 201, wherein the Second Therapeutic Agent comprises a combination set forth in Table 5.

[0695] Embodiment 241. The kit of Embodiment 222, wherein the Second Therapeutic Agent and Third Therapeutic Agent comprise a combination set forth in Table 8.

[0696] Embodiment 242. The kit of any one of Embodiments 201-221, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered sequentially.

[0697] Embodiment 243. The kit of any one of Embodiments 201-221, wherein the Compound of the Disclosure and the Second Therapeutic Agent are to be administered simultaneously.

[0698] Embodiment 244. The kit of Embodiments 222-243, wherein the Compound of the Disclosure, the Second Therapeutic Agent, and the Third Therapeutic Agent are to be administered sequentially.

[0699] Embodiment 245. The kit of any one of Embodiments 201-244, wherein the subject has cancer.

[0700] Embodiment 246. The kit of Embodiment 245, wherein the cancer is any one or more of the cancers of Table 2.

[0701] Embodiment 247. The kit of Embodiment 245, wherein the cancer is a hematological cancer.

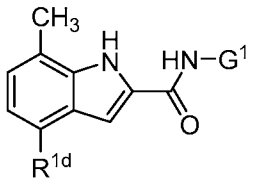
[0702] Embodiment 248. The kit of Embodiment 247, wherein the hematological cancer is any one or more of the cancers of Table 3.

[0703] Embodiment 249. The kit of Embodiment 248, wherein the hematological cancer is multiple myeloma, mantle cell lymphoma, or diffuse large B-cell lymphoma.

[0704] Embodiment 250. The kit of Embodiment 249, wherein the hematological cancer is t(4;14) multiple myeloma.

[0705] Embodiment 251. The method of any one of Embodiments 1-50, the compound for use of any one of claims 51-100, the use of any one of claims 101-150, or the kit of any one of Embodiments 151-250, wherein ═ is double bond.

[0706] Embodiment 252. The method, compound for use, use, or kit of Embodiment 251, wherein the compound is a compound of Formula **II**:

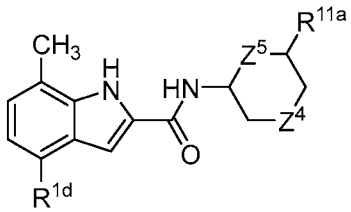


II,

[0707] or a pharmaceutically acceptable salt or solvate thereof.

[0708] Embodiment 253. The method, compound for use, use, or kit of Embodiments 251 or 252, wherein G^1 is selected from the group consisting of: optionally substituted C_6-C_{10} aryl; optionally substituted 5- to 9-membered heteroaryl; optionally substituted 3- to 10-membered heterocyclo; optionally substituted C_6-C_8 cycloalkyl; (5- to 9-membered heteroaryl)C_1-C_6 alkyl; (5- to 9-membered heteroaryl)(C_{6-10} aryl)C_1-C_4 alkyl; (5- to 9-membered heteroaryl heteroaryl)(C_3-C_6 cycloalkyl)C_1-C_4 alkyl; and (C_3-C_6 cycloalkyl)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

[0709] Embodiment 254. The method, compound for use, use, or kit of Embodiment 253, wherein the compound is a compound of of Formula **IV**:



IV,

wherein:

[0710] Z^4 is selected from the group consisting of -O-, -C(R^{28a})(R^{28b})-, and -N(R^{23})-; or Z^4 is absent;

[0711] Z^5 is selected from the group consisting of -CH_2- and -CH_2CH_2-;

[0712] R^{11a} is selected from the group consisting of optionally substituted alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, and -N(R^{12b})C(=O)R^{13c};

[0713] R^{12b} is selected from the group consisting of hydrogen, alkyl, cycloalkyl, and heterocyclo, (C_1-C_4 alkoxy)C_1-C_4 alkyl, and (hydroxy)C_1-C_4 alkyl; and

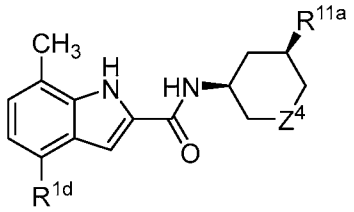
[0714] R^{13c} is selected from the group consisting of alkyl, haloalkyl, alkoxy, (alkoxy)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocycle, amino, (amino)alkyl, (C_3-C_6 cycloalkyl)oxy, and (4- to 8-membered heterocyclo)oxy;

[0715] R^{23} is selected from the group consisting of hydrogen and C_1-C_4 alkyl; and

[0716] R^{28a} and R^{28b} are independently selected from the group consisting of hydrogen, alkyl, and halo;,

[0717] or a pharmaceutically acceptable salt or solvate thereof.

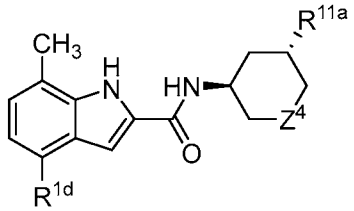
[0718] Embodiment 255. The method, compound for use, use, or kit of Embodiment 254, wherein the compound is a compound of Formula **IV-A**:



IV-A,

or a pharmaceutically acceptable salt or solvate thereof.

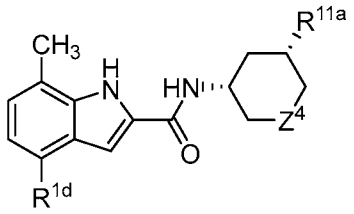
[0719] Embodiment 256. The method, compound for use, use, or kit of Embodiment 254, wherein the compound is a compound of Formula **IV-B**:



IV-B,

or a pharmaceutically acceptable salt or solvate thereof.

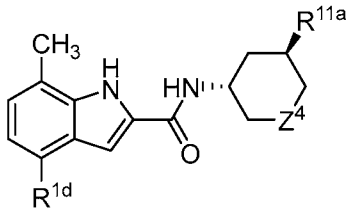
[0720] Embodiment 257. The method, compound for use, use, or kit of Embodiment 254, wherein the compound is a compound of Formula **IV-C**:



IV-C,

or a pharmaceutically acceptable salt or solvate thereof.

[0721] Embodiment 258. The method, compound for use, use, or kit of Embodiment 254, wherein the compound is a compound of Formula **IV-D**:



IV-D,

or a pharmaceutically acceptable salt or solvate thereof.

[0722] Embodiment 259. The method, compound for use, use, or kit of any one of Embodiments 254-258, wherein:

[0723] R^{11a} is selected from the group consisting of:

[0724] (A) unsubstituted 4- to 14-membered heterocyclo;

[0725] (B) substituted 4- to 14-membered heterocyclo having one, two or three substituents independently selected from the group consisting of:

[0726] (i) $-N(R^{12a})C(=O)R^{13a}$; (ii) $-C(=O)R^{13b}$; (iii) C_1-C_4 alkyl; (iv) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (v) (hydroxy)C_1-C_4 alkyl; (vi) C_1-C_4 haloalkyl; (vii) amino; (vii) hydroxy; (viii) $-N(R^{12a})S(=O)_2R^{24}$; (ix) $-S(=O)_2R^{24}$; (x) unsubstituted C_3-C_6 cycloalkyl; (xi) substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; (xii) unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (xiii) $-C(=N-R^{60})R^{61}$; and(xiv) $-C(=C-NO_2)R^{64}$;

[0727] (C) unsubstituted 5- to 10-membered heteroaryl;

[0728] (D) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo and C_1-C_4 alkyl;

[0729] (E) C_1-C_6 alkyl; and

[0730] (F) $-N(R^{12b})C(=O)R^{13c}$;

[0731] R^{12a} and R^{12b} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, and (hydroxy)C_1-C_4 alkyl;

[0732] R^{13a}, R^{13b}, and R^{13c} are each independently selected from the group consisting of (A) C_1-C_6 alkyl; (B) C_1-C_6 haloalkyl; (C) unsubstituted C_3-C_6 cycloalkyl; (D) C_1-C_6 alkoxy; (E) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (F) (hydroxy)C_1-C_4 alkyl; (G) (cyano)alkyl; (H) unsubstituted C_6-C_{10} aryl; (I) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (J) unsubstituted 5- or 6-membered heteroaryl; (K) substituted 5- or 6-

membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (L) unsubstituted 4- to 14-membered heterocyclo; (M) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (N) amino; (O) (amino)alkyl; (P) (C_3-C_6 cycloalkyl)oxy; and (Q) (4- to 8-membered heterocyclo)oxy; and

[0733] R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl;

[0734] R^{60} is selected from the group consisting of cyano, nitro, hydroxy, C_1-C_6 alkoxy, -C(=O)R^{62}, and -S(=O)$_2R^{62}$;

[0735] R^{61} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and -$NR^{63a}R^{63b}$;

[0736] R^{62} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and -$NR^{63a}R^{63b}$;

[0737] R^{63a} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

[0738] R^{63b} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl; or

[0739] R^{63a} and R^{63b} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo;

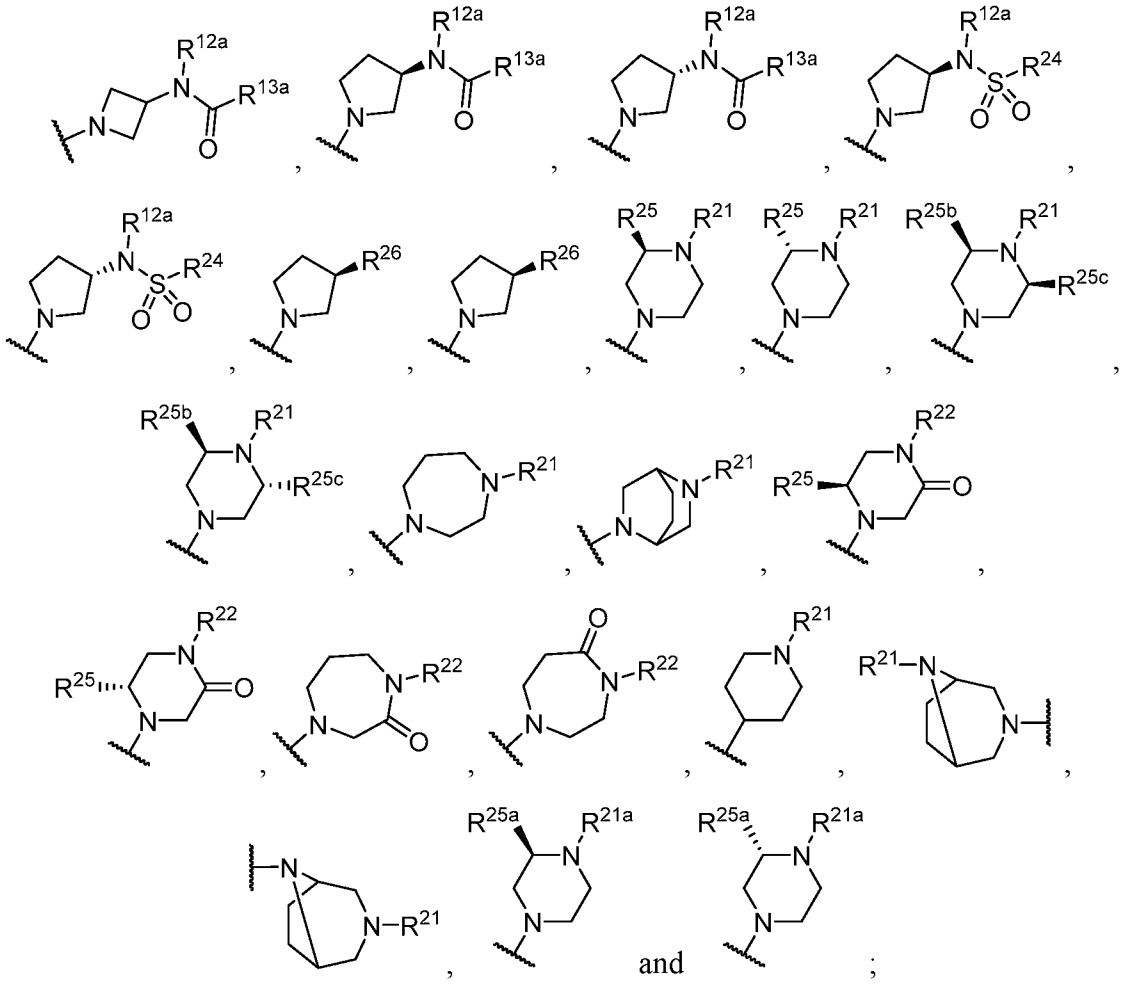
[0740] R^{64} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and -$NR^{63c}R^{63d}$;

[0741] R^{63c} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

[0742] R^{63d} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl; or

[0743] R^{63c} and R^{63d} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

[0744] Embodiment 260. The method, compound for use, use, or kit of Embodiment 259, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:



[0745] R^{12a} is selected from the group consisting of hydrogen, C_1-C_3 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl; and (hydroxy)C_1-C_4 alkyl;

[0746] R^{13a} is selected from the group consisting of C_1-C_4 alkyl; amino; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (hydroxy)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl;

[0747] R^{13b} is selected from the group consisting of C_1-C_4 alkyl; amino; C_1-C_4 haloalkyl; C_1-C_4 alkoxy; (hydroxy)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (amino)alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently

selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy;

[0748] R^{21} is selected from the group consisting of hydrogen, -C(=O)R^{13b}, C_1-C_4 alkyl, C_1-C_4 haloalkyl, unsubstituted 4- to 14-membered heterocyclo, and -S(=O)$_2$$R^{24}$;

[0749] R^{22} is C_1-C_4 alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl;

[0750] R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl;

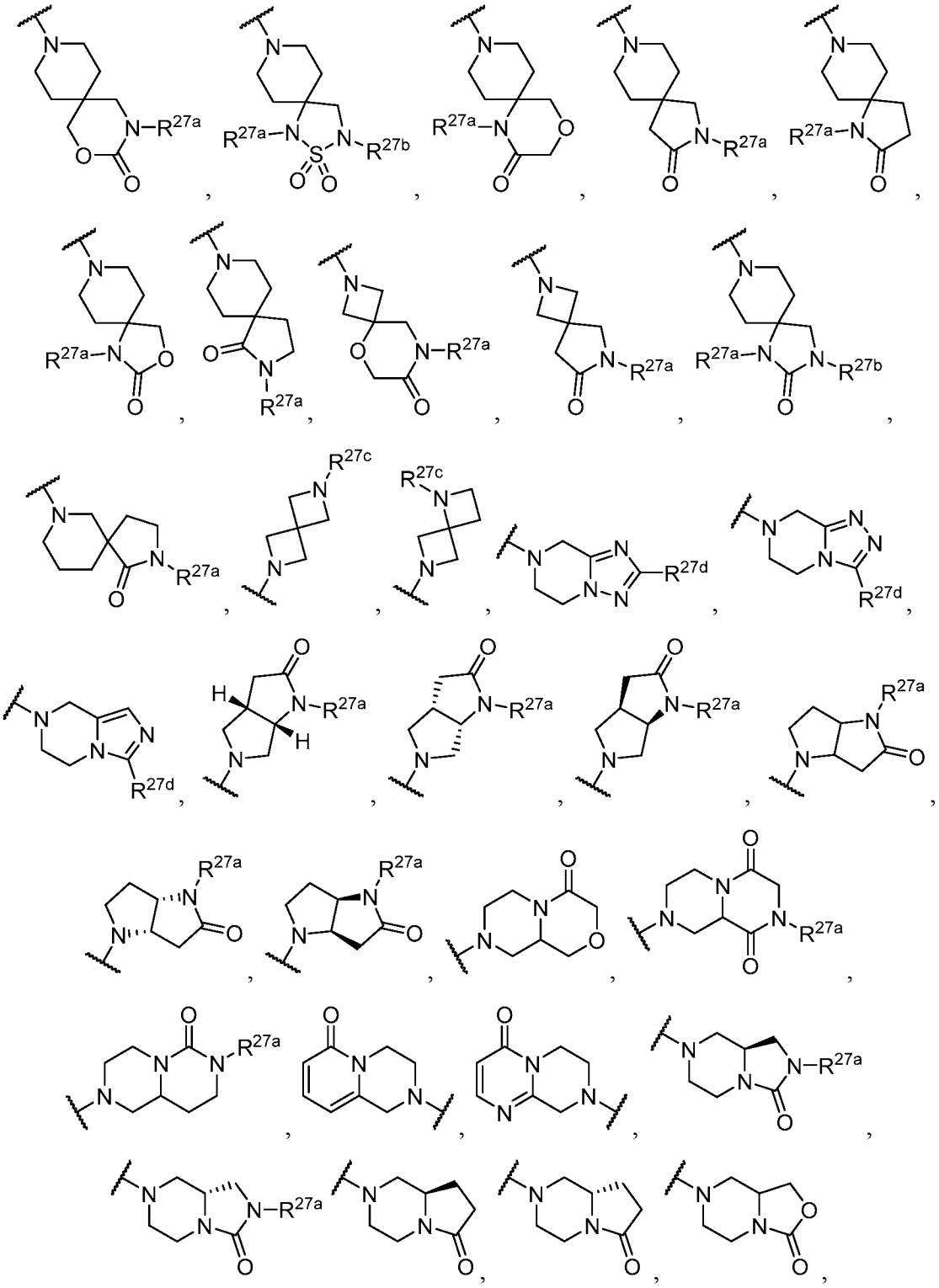
[0751] R^{25} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl;

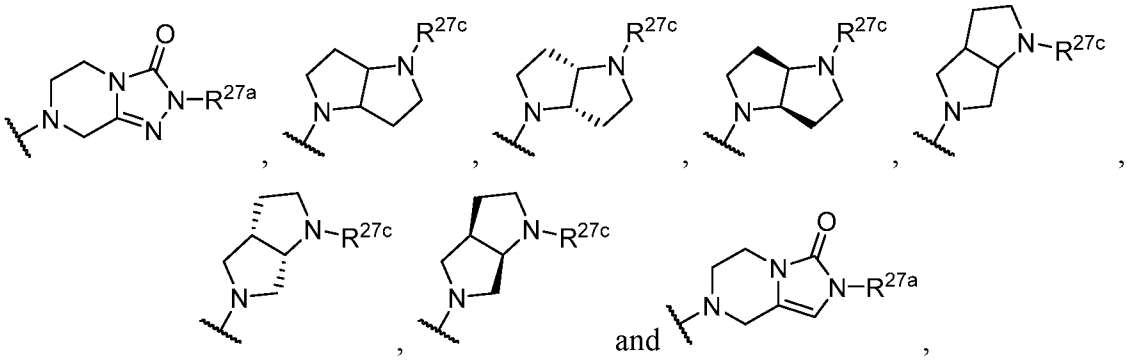
[0752] R^{25b} and R^{25c} are independently selected from the group consisting of C_1-C_4 alkyl and C_1-C_4 haloalkyl;

[0753] R^{26} is selected from the group consisting of unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; and

[0754] R^{21a} and R^{25a} taken together with the atoms to which they are attached form an optionally substituted 4- to 8-membered heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

[0755] Embodiment 261. The method, compound for use, use, or kit of Embodiment 259, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:





[0756] R^{27a} and R^{27b} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl; and (hydroxy)C_1-C_4 alkyl;

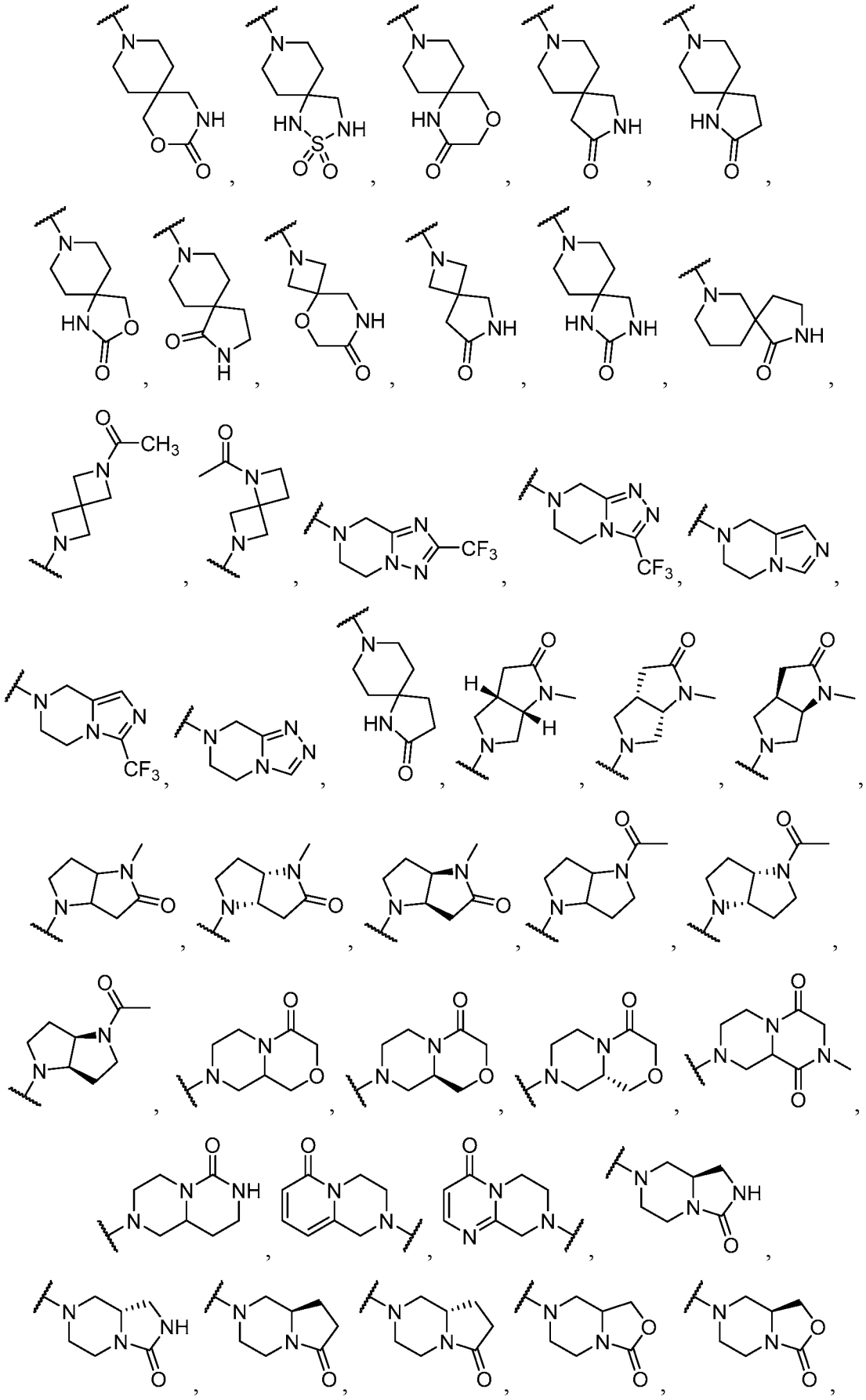
[0757] R^{27c} is selected from the group consisting of hydrogen; -C(=O)R^{13b}; C_1-C_4 alkyl; C_1-C_4 haloalkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; and -S(=O)$_2$$R^{24}$;

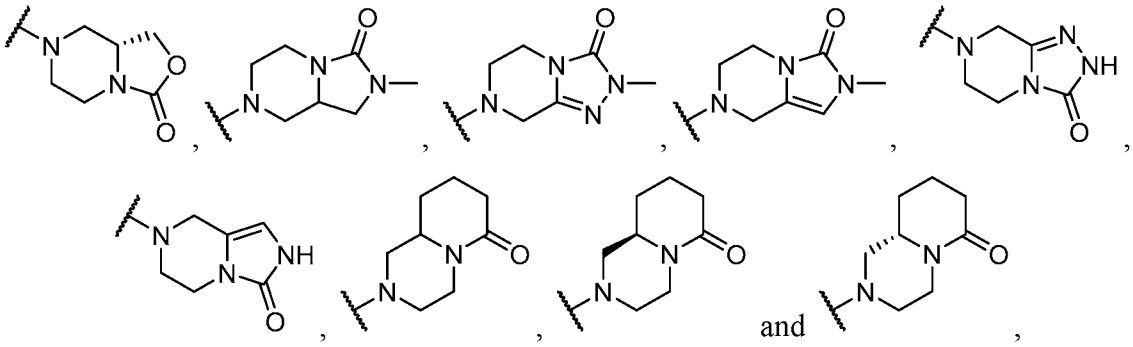
[0758] R^{27d} is selected from the group consisting of hydrogen; C_1-C_4 alkyl; and C_1-C_4 haloalkyl;

[0759] R^{13b} is selected from the group consisting of C_1-C_4 alkyl; aminoC_1-C_4 haloalkyl; C_1-C_4 alkoxy; (hydroxy)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (amino)alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy; and

[0760] R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

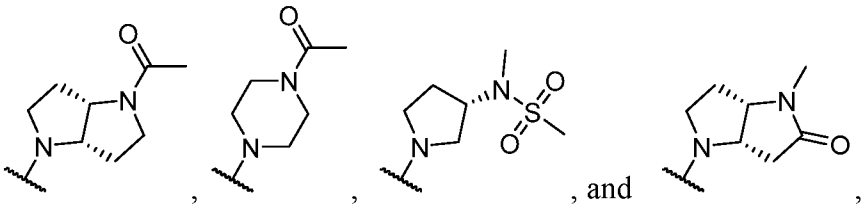
[0761] Embodiment 262. The method, compound for use, use, or kit of Embodiment 261, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:





or a pharmaceutically acceptable salt or solvate thereof.

[0762] Embodiment 263. The method, compound for use, use, or kit of Embodiment 259, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:



or a pharmaceutically acceptable salt or solvate thereof.

[0763] Embodiment 264. The method, compound for use, use, or kit of any one of Embodiments 254-263, wherein Z^4 is $-CH_2-$, or a pharmaceutically acceptable salt or solvate thereof.

[0764] Embodiment 265. The method, compound for use, use, or kit of any one of Embodiments 251-264, wherein R^{1d} is fluoro, or a pharmaceutically acceptable salt or solvate thereof.

[0765] Embodiment 266. The method, compound for use, use, or kit of Embodiment 251, wherein the compound is a compound of Table 1, or a pharmaceutically acceptable salt or solvate thereof.

[0766] Embodiment 267. The method, compound for use, use, or kit of Embodiment 251, wherein the compound is a compound of Table 1B, or a pharmaceutically acceptable salt or solvate thereof.

[0767] Embodiment 268. The method of any one of Embodiments 1-50 or 251-267, the compound for use of any one of claims 51-100 or 251-267, the use of any one of Embodiments 101-150 or 251-267, or the kit of any one of Embodiments 151-250 or 251-267, wherein the Second Therapeutic Agent comprises a DNA repair enzyme inhibitor.

[0768] Embodiment 269. The method, compound for use, use, or kit of Embodiment 268, wherein the DNA repair enzyme inhibitor is an ATM inhibitor, ATR inhibitor, Chk1 inhibitor, Wee1 inhibitor, RAD51 inhibitor, PARP inhibitor, or AKT inhibitor.

[0769] Embodiment 270. The method of any one of Embodiments 1-50 or 251-269, the compound for use of any one of claims 51-100 or 251-269, the use of any one of Embodiments 101-150 or 251-269, or the kit of any one of Embodiments 151-250 or 251-269, wherein the Second Therapeutic Agent comprises a SYK inhibitor.

[0770] Embodiment 271. The method of any one of Embodiments 1-50 or 251-270, the compound for use of any one of claims 51-100 or 2251-270, the use of any one of Embodiments 101-150 or 251-270, or the kit of any one of Embodiments 151-250 or 251-270, wherein the Second Therapeutic Agent comprises a MEK inhibitor.

[0771] Compounds of the Disclosure can be administered to a subject in the form of a raw chemical without any other components present. Compounds of the Disclosure can also be administered to a subject as part of a pharmaceutical composition containing the compound combined with a suitable pharmaceutically acceptable carrier. Such a carrier can be selected from pharmaceutically acceptable excipients and auxiliaries. The term "pharmaceutically acceptable carrier" or "pharmaceutically acceptable vehicle" encompasses any of the standard pharmaceutical carriers, solvents, surfactants, or vehicles. Suitable pharmaceutically acceptable vehicles include aqueous vehicles and nonaqueous vehicles. Standard pharmaceutical carriers and their formulations are described in Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, PA, 19th ed. 1995. Pharmaceutical compositions comprising a Compound of the Disclosure and a pharmaceutically acceptable carrier are collectively referred to as "Compositions of the Disclosure."

[0772] Pharmaceutical compositions within the scope of the present disclosure include all compositions where a Compound of the Disclosure is combined with one or more pharmaceutically acceptable carriers. In one embodiment, the Compound of the Disclosure is present in the composition in an amount that is effective to achieve its intended therapeutic purpose. While individual needs may vary, a determination of optimal ranges of effective amounts of each compound is within the skill of the art. Typically, a Compound of the Disclosure can be administered to a mammal, e.g., a human, orally at a dose of from about 0.0025 to about 1500 mg per kg body weight of the mammal, or an equivalent amount of a pharmaceutically acceptable salt or solvate

thereof, per day to treat the particular disorder. A useful oral dose of a Compound of the Disclosure administered to a mammal is from about 0.0025 to about 50 mg per kg body weight of the mammal, or an equivalent amount of the pharmaceutically acceptable salt or solvate thereof. For intramuscular injection, the dose is typically about one-half of the oral dose.

[0773] A unit oral dose may comprise from about 0.01 mg to about 1 g of the Compound of the Disclosure, e.g., about 0.01 mg to about 500 mg, about 0.01 mg to about 250 mg, about 0.01 mg to about 100 mg, 0.01 mg to about 50 mg, e.g., about 0.1 mg to about 10 mg, of the compound. The unit dose can be administered one or more times daily, e.g., as one or more tablets or capsules, each containing from about 0.01 mg to about 1 g of the compound, or an equivalent amount of a pharmaceutically acceptable salt or solvate thereof.

[0774] A Compound of Disclosure or pharmaceutical composition comprising a Compound of the Disclosure and, optionally a Second Therapeutic Agent can be administered to any subject, e.g., a cancer patient in need thereof, that may experience the beneficial effects of a Compound of the Disclosure. Foremost among such subject are mammals, e.g., humans and companion animals, although the disclosure is not intended to be so limited. In one embodiment, the subject is a human.

[0775] A pharmaceutical composition of the present disclosure can be administered by any means that achieves its intended purpose. For example, administration can be by the oral, parenteral, subcutaneous, intravenous, intramuscular, intraperitoneal, transdermal, intranasal, transmucosal, rectal, intravaginal or buccal route, or by inhalation. The dosage administered and route of administration will vary, depending upon the circumstances of the particular subject, and taking into account such factors as age, gender, health, and weight of the recipient, condition or disorder to be treated, kind of concurrent treatment, if any, frequency of treatment, and the nature of the effect desired.

[0776] In one embodiment, a pharmaceutical composition of the present disclosure can be administered orally. In another embodiment, a pharmaceutical composition of the present disclosure can be administered orally and is formulated into tablets, dragees, capsules, or an oral liquid preparation. In one embodiment, the oral formulation comprises extruded multiparticulates comprising the Compound of the Disclosure.

[0777] Alternatively, a pharmaceutical composition of the present disclosure can be administered rectally, and is formulated in suppositories.

[0778] Alternatively, a pharmaceutical composition of the present disclosure can be administered by injection.

[0779] Alternatively, a pharmaceutical composition of the present disclosure can be administered transdermally.

[0780] Alternatively, a pharmaceutical composition of the present disclosure can be administered by inhalation or by intranasal or transmucosal administration.

[0781] Alternatively, a pharmaceutical composition of the present disclosure can be administered by the intravaginal route.

[0782] A pharmaceutical composition of the present disclosure can contain from about 0.01 to 99 percent by weight, e.g., from about 0.25 to 75 percent by weight, of a Compound of the Disclosure, e.g., about 1%, about 5%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, or about 75% by weight of a Compound of the Disclosure.

[0783] A pharmaceutical composition of the present disclosure is manufactured in a manner which itself will be known in view of the instant disclosure, for example, by means of conventional mixing, granulating, dragee-making, dissolving, extrusion, or lyophilizing processes. Thus, pharmaceutical compositions for oral use can be obtained by combining the active compound with solid excipients, optionally grinding the resulting mixture and processing the mixture of granules, after adding suitable auxiliaries, if desired or necessary, to obtain tablets or dragee cores.

[0784] Suitable excipients include fillers such as saccharides (for example, lactose, sucrose, mannitol or sorbitol), cellulose preparations, calcium phosphates (for example, tricalcium phosphate or calcium hydrogen phosphate), as well as binders such as starch paste (using, for example, maize starch, wheat starch, rice starch, or potato starch), gelatin, tragacanth, methyl cellulose, hydroxypropylmethylcellulose, sodium carboxymethylcellulose, and/or polyvinyl pyrrolidone. If desired, one or more disintegrating agents can be added, such as the above-mentioned starches and also carboxymethyl-starch, cross-linked polyvinyl pyrrolidone, agar, or alginic acid or a salt thereof, such as sodium alginate.

[0785] Auxiliaries are typically flow-regulating agents and lubricants such as, for example, silica, talc, stearic acid or salts thereof (e.g., magnesium stearate or calcium stearate), and polyethylene glycol. Dragee cores are provided with suitable coatings that

are resistant to gastric juices. For this purpose, concentrated saccharide solutions can be used, which may optionally contain gum arabic, talc, polyvinyl pyrrolidone, polyethylene glycol and/or titanium dioxide, lacquer solutions and suitable organic solvents or solvent mixtures. In order to produce coatings resistant to gastric juices, solutions of suitable cellulose preparations such as acetylcellulose phthalate or hydroxypropylmethyl-cellulose phthalate can be used. Dye stuffs or pigments can be added to the tablets or dragee coatings, for example, for identification or in order to characterize combinations of active compound doses.

[0786] Examples of other pharmaceutical preparations that can be used orally include push-fit capsules made of gelatin, or soft, sealed capsules made of gelatin and a plasticizer such as glycerol or sorbitol. The push-fit capsules can contain a compound in the form of granules, which can be mixed with fillers such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers, or in the form of extruded multiparticulates. In soft capsules, the active compounds are preferably dissolved or suspended in suitable liquids, such as fatty oils or liquid paraffin. In addition, stabilizers can be added.

[0787] Possible pharmaceutical preparations for rectal administration include, for example, suppositories, which consist of a combination of one or more active compounds with a suppository base. Suitable suppository bases include natural and synthetic triglycerides, and paraffin hydrocarbons, among others. It is also possible to use gelatin rectal capsules consisting of a combination of active compound with a base material such as, for example, a liquid triglyceride, polyethylene glycol, or paraffin hydrocarbon.

[0788] Suitable formulations for parenteral administration include aqueous solutions of the active compound in a water-soluble form such as, for example, a water-soluble salt, alkaline solution, or acidic solution. Alternatively, a suspension of the active compound can be prepared as an oily suspension. Suitable lipophilic solvents or vehicles for such as suspension may include fatty oils (for example, sesame oil), synthetic fatty acid esters (for example, ethyl oleate), triglycerides, or a polyethylene glycol such as polyethylene glycol-400 (PEG-400). An aqueous suspension may contain one or more substances to increase the viscosity of the suspension, including, for example, sodium carboxymethyl cellulose, sorbitol, and/or dextran. The suspension may optionally contain stabilizers.

[0789] In some embodiments, the Compound of the Disclosure, the Second Therapeutic Agent and, optionally, the Third Therapeutic Agent are administered in combination to a subject as part of a single pharmaceutical composition.

[0790] In some embodiments, the Compound of the Disclosure, the Second Therapeutic Agent and, optionally, the Third Therapeutic Agent are administered in combination to a subject separately, e.g., as two or more separate pharmaceutical compositions. For example, the Second Therapeutic Agent may comprise one of a BTK inhibitor, an anti-CD20 monoclonal antibody, an alkylating agent, a topoisomerase II inhibitor, a vinca alkaloid, a platinum-based drug, a nucleoside anticancer agent, a PI3K inhibitor, a CDK4/6 inhibitor, a CARM1 inhibitor, an inhibitor of an enzyme of DNA damage repair, a SYK inhibitor, or a MEK inhibitor. In this case, two separate pharmaceutical compositions – one comprising the Compound of the Disclosure and one comprising the Second Therapeutic Agent – are administered to a subject. The Second Therapeutic Agent may comprise a combination of two of a BTK inhibitor, an anti-CD20 monoclonal antibody, an alkylating agent, a topoisomerase II inhibitor, a vinca alkaloid, a platinum-based drug, a nucleoside anticancer agent, a PI3K inhibitor, a CDK4/6 inhibitor, a CARM1 inhibitor, an inhibitor of an enzyme of DNA damage repair, a SYK inhibitor, or a MEK inhibitor. In this case, three separate pharmaceutical compositions – one comprising the Compound of the Disclosure, one comprising the first Second Therapeutic Agent, and one comprising the second Second Therapeutic Agent – are administered to a subject. Likewise, if the Second Therapeutic Agent comprises a combination of, e.g., three or more of a BTK inhibitor, an anti-CD20 monoclonal antibody, a chemotherapeutic drug, a PI3K inhibitor, a CDK4/6 inhibitor, a CARM1 inhibitor, an inhibitor of an enzyme of DNA damage repair, a SYK inhibitor, or a MEK inhibitor, then three separate pharmaceutical compositions are administered to the subject. Separate pharmaceutical compositions can be administered to the subject, for example, at different periodicities, at different durations, and/or by different administration routes.

[0791] In some embodiments, a Compound of the Disclosure is administered to the patient prior to the Second Therapeutic Agent, e.g., 0.5, 1, 2, 3, 4, 5, 10, 12, or 18 hours, 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, or 4 weeks prior to the administration of the Second Therapeutic Agent.

[0792] In some embodiments, a Compound of the Disclosure is administered after the Second Therapeutic Agent, e.g., 0.5, 1, 2, 3, 4, 5, 10, 12, or 18 hours, 1, 2, 3, 4, 5, or 6 days, or 1, 2, 3, or 4 weeks after the administration of the Second Therapeutic Agent.

[0793] In some embodiments, a Compound of the Disclosure and the Second Therapeutic Agent are administered concurrently.

[0794] In some embodiments, a Compound of the Disclosure and the Second Therapeutic Agent are administered concurrently but on different schedules, e.g., a Compound of the Disclosure is administered daily while the Second Therapeutic Agent is administered, e.g., once a week, once every two weeks, once every three weeks, or once every four weeks.

[0795] A Compound of the Discloure, a Second Therapeutic Agent and a Third Therapeutic Agent can be administered in any order to a subject. For example, the Compound of the Discloure can be administered prior the the Second Therapeutic Agent and Third Therapeutic Agent, the Compound of the Discloure can be administered prior to the Second Therapeutic Agent and after the Third Therapeutic Agent, the Compound of the Discloure can be administered after the the Second Therapeutic Agent and Third Therapeutic Agent, and so on.

[0796] In practice, a physician determines the actual dosing regimen that is most suitable for an individual patient, which can vary with the age, weight, and response of the particular patient.

[0797] In another embodiment, the present disclosure provides kits which comprise a Compound of the Disclosure (or a composition comprising a Compound of the Disclosure) packaged in a manner that facilitates their use to practice methods of the present disclosure. In one embodiment, the kit includes a Compound of the Disclosure (or a composition comprising a Compound of the Disclosure) packaged in a container, such as a sealed bottle or vessel, with a label affixed to the container or included in the kit that describes use of the compound or composition to practice the method of the disclosure. In one embodiment, the compound or composition is packaged in a unit dosage form. The kit further can include a device suitable for administering the composition according to the intended route of administration. The kit further can include a Second Therapeutic Agent. In some embodiments, the kit comprises a Compound of the Disclosure and a Second Therapeutic Agent as separate pharmaceutical compositions.

V. Biomarkers

[0798] In another embodiment, present disclosure provides methods of treating a subject having cancer, e.g., multiple myeloma, comprising (a) determining whether a biomarker is present or absent in a biological sample taken from the subject; and (b) administering a therapeutically effective amount of a Compound of the Disclosure and a Second Therapeutic Agent to the subject if the biomarker is present in the biological sample. *See, e.g.*, Goossens *et al.*, *Transl Cancer Res. 4*:256-269 (2015); Kamel and Al-Amodi, *Genomics Proteomics Bioinformatics 15*:220-235 (2017); and Konikova and Kusenda, *Neoplasma 50*:31-40 (2003).

[0799] Biomarkers include, but are not limited to, chromosomal translocations in a cancer, e.g., mulitple myeloma, cell and WHSC1/NSD2/MMSET expression. In one embodiment, the measurable aspect of the biomarker is its expression status. In one embodiment, the measurable aspect of the biomarker is its mutation status.

[0800] In one embodiment, the biomarker is WHSC1/NSD2/MMSET expression which is differentially present in a subject of one phenotypic status, e.g., a subject having a hematological cancer, as compared with another phenotypic status, e.g., a normal undiseased subject or a patient having cancer without overexpression WHSC1/NSD2/MMSET. In one embodiment, the biomarker is overexpression of WHSC1/NSD2/MMSET.

[0801] Biomarker standards can be predetermined, determined concurrently, or determined after a biological sample is obtained from the subject. Biomarker standards for use with the methods described herein can, for example, include data from samples from subjects without cancer; data from samples from subjects with cancer, e.g., breast cancer, that is not metastatic; and data from samples from subjects with cancer, e.g., breast cancer, that metastatic. Comparisons can be made to establish predetermined threshold biomarker standards for different classes of subjects, e.g., diseased vs. non-diseased subjects. The standards can be run in the same assay or can be known standards from a previous assay.

[0802] A biomarker is differentially present between different phenotypic status groups if the mean or median expression or mutation levels of the biomarker is calculated to be different, i.e., higher or lower, between the groups. Thus, biomarkers provide an indication that a subject, e.g., a cancer patient, belongs to one phenotypic status or another.

[0803] The determination of the expression level or mutation status of a biomarker in a patient can be performed using any of the many methods known in the art. Any method known in the art for quantitating specific proteins and/or detecting WHSC1/NSD2/MMSET expression and/or chromosomal translocations, or the expression or mutation levels of any other biomarker in a patient or a biological sample may be used in the methods of the disclosure. Examples include, but are not limited to, PCR (polymerase chain reaction), or RT-PCR, flow cytometry, Northern blot, Western blot, ELISA (enzyme linked immunosorbent assay), RIA (radioimmunoassay), gene chip analysis of RNA expression, immunohistochemistry or immunofluorescence. *See, e.g.*, Slagle et al. Cancer 83:1401 (1998); Hudlebusch et al., *Clin Cancer Res 17*:2919-2933 (2011). Certain embodiments of the disclosure include methods wherein biomarker RNA expression (transcription) is determined. Other embodiments of the disclosure include methods wherein protein expression in the biological sample is determined. *See, e.g.*, Harlow *et al.*, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, (1988); Ausubel *et al.*, Current Protocols in Molecular Biology, John Wiley & Sons, New York 3rd Edition, (1995); Kamel and Al-Amodi, *Genomics Proteomics Bioinformatics 15*:220–235 (2017). For northern blot or RT-PCR analysis, RNA is isolated from the tumor tissue sample using RNAse free techniques. Such techniques are commonly known in the art.

[0804] In one embodiment of the disclosure, a biological sample is obtained from the patient and the biological sample is assayed for determination of a biomarker expression or mutation status.

[0805] In one embodiment, the present disclosure provides a method of treating a subject having cancer, e.g., multiple myeloma, the method comprising: (a) determining whether a chromosomal translocation is present or absent in a biological sample taken from the subject; and (b) administering a therapeutically effective amount of a Compound of the Disclosure, a Second Theraputic Agent and, optionally, a Third Therapeutic Agent to the subject if a chromosomal translocation is present in the biological sample.

[0806] In another embodiment, the present disclosure provides a method of treating a subject having cancer, e.g., multiple myeloma, the method comprising administering a therapeutically effective amount of a Compound of the Disclosure a Second Therapetuic Agent and, optionally, a Third Therapeutic Agent to the subject having a chromosomal translocation.

[0807] In another embodiment, the present disclosure provides a method, comprising administering a therapeutically effective amount of a Compound of the Disclosure, a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent, to a subject in need thereof, wherein: (a) the subject has multiple myeloma; and (b) the multiple myeloma is characterized as having a chromosomal translocation.

[0808] In any of the above embodiments, the chromosomal translocation is a t(4;14) translocation.

[0809] In one embodiment, the present disclosure provides a method of treating a subject having multiple myeloma, the method comprising: (a) determining whether an overexpression of WHSC1/NSD2/MMSET is present or absent in a biological sample taken from the subject; and (b) administering a therapeutically effective amount of a Compound of the Disclosure, a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent, to the subject if an overexpression of WHSC1/NSD2/MMSET is present in the biological sample.

[0810] In one embodiment, the present disclosure provides a method of treating a subject having multiple myeloma, the method comprising administering a therapeutically effective amount of a Compound of the Disclosure, a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent, to the subject if an overexpression of WHSC1/NSD2/MMSET is present in subject.

[0811] In another embodiment, the present disclosure provides a method, comprising administering a therapeutically effective amount of a Compound of the Disclosure, a Second Therapeutic Agent and, optionally, a Third Therapeutic Agent, to a subject in need thereof, wherein: (a) the subject has multiple myeloma; and (b) the multiple myeloma is characterized as having an overexpression of WHSC1/NSD2/MMSET.

VI. Definitions

[0812] The term "halo" as used herein by itself or as part of another group refers to -Cl, -F, -Br, or -I.

[0813] The term "nitro" as used herein by itself or as part of another group refers to $-NO_2$.

[0814] The term "cyano" as used herein by itself or as part of another group refers to -CN.

[0815] The term "hydroxy" as herein used by itself or as part of another group refers to -OH.

[0816] The term "alkyl" as used herein by itself or as part of another group refers to a straight- or branched-chain aliphatic hydrocarbon containing one to twelve carbon atoms, i.e., a C_1-C_{12} alkyl, or the number of carbon atoms designated, e.g., a C_1 alkyl such as methyl, a C_2 alkyl such as ethyl, etc. In one embodiment, the alkyl is a C_1-C_{10} alkyl. In another embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1-C_3 alkyl, i.e., methyl, ethyl, propyl, or isopropyl. Non-limiting exemplary C_1-C_{12} alkyl groups include methyl, ethyl, propyl, isopropyl, butyl, *sec*-butyl, *tert*-butyl, *iso*-butyl, 3-pentyl, hexyl, heptyl, octyl, nonyl, and decyl.

[0817] The term "optionally substituted alkyl" as used herein by itself or as part of another group refers to an alkyl group that is either unsubstituted or substituted with one, two, or three substituents, wherein each substituent is independently nitro, haloalkoxy, aryloxy, aralkyloxy, alkylthio, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carbamate, carboxy, alkoxycarbonyl, carboxyalkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, $-N(R^{56a})C(=N-R^{60})R^{61}$, $-N(R^{56a})C(=C-NO_2)R^{64}$, $-C(=N-R^{60})R^{61}$, or $-C(=C-NO_2)R^{64}$; wherein:

[0818] R^{56a} is hydrogen or alkyl;

[0819] R^{56b} is alkyl, haloalkyl, optionally substituted cycloalkyl, alkoxy, (alkoxy)alkyl, (aryl)alkyl, (heteroaryl)alkyl, (amino)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycle, optionally substituted C_6-C_{10} aryl, or optionally substituted heteroaryl;

[0820] R^{56c} is hydrogen or alkyl;

[0821] R^{56d} is alkyl, haloalkyl, optionally substituted cycloalkyl, alkoxy, (alkoxy)alkyl, (aryl)alkyl, (heteroaryl)alkyl, (amino)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycle, optionally substituted C_6-C_{10} aryl, or optionally substituted heteroaryl;

[0822] R^{56e} is alkyl, haloalkyl, optionally substituted cycloalkyl, alkoxy, (alkoxy)alkyl, (aryl)alkyl, (heteroaryl)alkyl, (amino)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally

substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycle, optionally substituted C_6-C_{10} aryl, or optionally substituted heteroaryl;

[0823] R^{57} is haloalkyl, amino, optionally substituted cycloalkyl, alkoxy, (alkoxy)alkyl, (aryl)alkyl, (heteroaryl)alkyl, (amino)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycle, optionally substituted heteroaryl, (C_3-C_6 cycloalkyl)oxy, or (4- to 8-membered heterocyclo)oxy;

[0824] R^{58} is haloalkyl, optionally substituted cycloalkyl, alkoxy, (alkoxy)alkyl, (aryl)alkyl, (heteroaryl)alkyl, (amino)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted cycloalkyl, optionally substituted heterocycle, or optionally substituted heteroaryl;

[0825] R^{60} is selected from the group consisting of cyano, nitro, hydroxy, C_1-C_6 alkoxy, $-C(=O)R^{62}$, and $-S(=O)_2R^{62}$;

[0826] R^{61} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and $-NR^{63a}R^{63b}$;

[0827] R^{62} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and $-NR^{63a}R^{63b}$;

[0828] R^{63a} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

[0829] R^{63b} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl; or

[0830] R^{63a} and R^{63b} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo;

R^{64} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and $-NR^{63c}R^{63d}$; and

[0831] R^{63c} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R^{63d} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl; or

[0832] R^{63c} and R^{63d} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo.

[0833] In one embodiment, the optionally substituted alkyl is either unsubstituted or substituted with one, two, or three substituents, wherein each substituent is independently nitro, haloalkoxy, aryloxy, aralkyloxy, alkylthio, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carbamate, carboxy, alkoxycarbonyl, carboxyalkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, or $-S(=O)_2R^{58}$.

[0834] In another embodiment, the optionally substituted alkyl is substituted with two substituents. In another embodiment, the optionally substituted alkyl is substituted with one substituent. In another embodiment, the optionally substituted alkyl is an optionally substituted C_1-C_6 alkyl. In another embodiment, the optionally substituted alkyl is an optionally substituted C_1-C_4 alkyl. In one embodiment, the optionally substituted alkyl is an optionally substituted is a C_1 or C_2 alkyl. Non-limiting exemplary optionally substituted alkyl groups include $-CH(CO_2Me)CH_2CO_2Me$ and $-CH(CH_3)CH_2N(H)C(=O)O(CH_3)_3$.

[0835] The term "alkenyl" as used herein by itself or as part of another group refers to an alkyl group containing one, two, or three carbon-to-carbon double bonds. In one embodiment, the alkenyl group is a C_2-C_6 alkenyl group. In another embodiment, the alkenyl group is a C_2-C_4 alkenyl group. In another embodiment, the alkenyl group has one carbon-to-carbon double bond. Non-limiting exemplary alkenyl groups include ethenyl, propenyl, isopropenyl, butenyl, *sec*-butenyl, pentenyl, and hexenyl.

[0836] The term "optionally substituted alkenyl" as used herein by itself or as part of another refers to an alkenyl group that is either unsubstituted or substituted with one, two or three substituents, wherein each substituent is independently halo, nitro, cyano, hydroxy, amino (e.g., alkylamino, dialkylamino), haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted heterocyclo. Non-limiting exemplary optionally substituted alkenyl groups include -CH=CHPh.

[0837] The term "alkynyl" as used herein by itself or as part of another group refers to an alkyl group containing one, two, or three carbon-to-carbon triple bonds. In one embodiment, the alkynyl has one carbon-to-carbon triple bond. In another embodiment, the alkynyl is a C_1-C_6 alkynyl. In another embodiment, the alkynyl is a C_2-C_4 alkynyl.

In another embodiment, the alkynyl has one carbon-to-carbon triple bond. Non-limiting exemplary alkynyl groups include ethynyl, propynyl, butynyl, 2-butynyl, pentynyl, and hexynyl groups.

[0838] The term "optionally substituted alkynyl" as used herein by itself or as part of another group refers to an alkynyl group that is either unsubstituted or substituted with one, two or three substituents, wherein each substituent is independently halo, nitro, cyano, hydroxy, amino (e.g., alkylamino, dialkylamino), haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted heterocyclo. Non-limiting exemplary optionally substituted alkynyl groups include -CH≡CHPh.

[0839] The term "haloalkyl" as used herein by itself or as part of another group refers to an alkyl group substituted by one or more fluorine, chlorine, bromine, and/or iodine atoms. In one embodiment, the alkyl is substituted by one, two, or three fluorine and/or chlorine atoms. In another embodiment, the alkyl is substituted by one, two, or three fluorine atoms. In another embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl group is a C_1 or C_2 alkyl. Non-limiting exemplary haloalkyl groups include fluoromethyl, difluoromethyl, trifluoromethyl, pentafluoroethyl, 1,1-difluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, 3,3,3-trifluoropropyl, 4,4,4-trifluorobutyl, and trichloromethyl groups.

[0840] The terms "hydroxyalkyl" or "(hydroxy)alkyl" as used herein by themselves or as part of another group refer to an alkyl group substituted with one, two, or three hydroxy groups. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. In another embodiment, the hydroxyalkyl is a monohydroxyalkyl group, i.e., substituted with one hydroxy group. In another embodiment, the hydroxyalkyl group is a dihydroxyalkyl group, i.e., substituted with two hydroxy groups. Non-limiting exemplary (hydroxyl)alkyl groups include hydroxymethyl, hydroxyethyl, hydroxypropyl and hydroxybutyl groups, such as 1-hydroxyethyl, 2-hydroxyethyl, 1,2-dihydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, 3-hydroxybutyl, 4-hydroxybutyl, 2-hydroxy-1-methylpropyl, and 1,3-dihydroxyprop-2-yl.

[0841] The term "alkoxy" as used herein by itself or as part of another group refers to an alkyl group attached to a terminal oxygen atom. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl group. Non-limiting exemplary alkoxy groups include methoxy, ethoxy, and *tert*-butoxy.

[0842] The term "haloalkoxy" as used herein by itself or as part of another group refers to a haloalkyl group attached to a terminal oxygen atom. In one embodiment, the haloalkyl is a C_1-C_6 alkyl. In another embodiment, the haloalkyl group is a C_1-C_4 haloalkyl group. Non-limiting exemplary haloalkoxy groups include fluoromethoxy, difluoromethoxy, trifluoromethoxy, and 2,2,2-trifluoroethoxy.

[0843] The term "alkylthio" as used herein by itself or as part of another group refers to an alkyl group attached to a terminal sulfur atom. In one embodiment, the alkyl group is a C_1-C_4 alkyl group. Non-limiting exemplary alkylthio groups include $-SCH_3$, and $-SCH_2CH_3$.

[0844] The terms "alkoxyalkyl" or "(alkoxy)alkyl" as used herein by themselves or as part of another group refers to an alkyl group substituted with one alkoxy group. In one embodiment, the alkoxy is a C_1-C_6 alkoxy. In another embodiment, the alkoxy is a C_1-C_4 alkoxy. In another embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. Non-limiting exemplary alkoxyalkyl groups include methoxymethyl, methoxyethyl, methoxypropyl, methoxybutyl, ethoxymethyl, ethoxyethyl, ethoxypropyl, ethoxybutyl, propoxymethyl, iso-propoxymethyl, propoxyethyl, propoxypropyl, butoxymethyl, tert-butoxymethyl, isobutoxymethyl, sec-butoxymethyl, and pentyloxymethyl.

[0845] The term "heteroalkyl" as used herein by itself or part of another group refers to a stable straight or branched chain hydrocarbon radical containing 1 to 10 carbon atoms and at least two heteroatoms, which can be the same or different, selected from O, N, or S, wherein the sulfur atom(s) can optionally be oxidized. The heteroatoms can be placed at any interior position of the heteroalkyl group or at a position at which the heteroalkyl group is attached to the remainder of the molecule. In one embodiment, the heteroalkyl contains two oxygen atoms. In another embodiment, the heteroalkyl contains one oxygen and one nitrogen atom. In another embodiment, the heteroalkyl contains two nitrogen atoms. Non-limiting exemplary heteroalkyl groups include $-OCH_2CH_2NH_2$, $-NHCH_2CH_2OCH_3$, and $-OCH_2CH_2OCH_3$.

[0846] The term "cycloalkyl" as used herein by itself or as part of another group refers to saturated and partially unsaturated, e.g., containing one or two double bonds, monocyclic, bicyclic, or tricyclic aliphatic hydrocarbons containing three to twelve carbon atoms, i.e., a C_{3-12} cycloalkyl, or the number of carbons designated, e.g., a C_3 cycloalkyl such a cyclopropyl, a C_4 cycloalkyl such as cyclobutyl, etc. In one embodiment, the cycloalkyl is bicyclic, i.e., it has two rings. In another embodiment, the cycloalkyl is monocyclic, i.e., it has one ring. In another embodiment, the cycloalkyl is a C_{3-8} cycloalkyl. In another embodiment, the cycloalkyl is a C_{3-6} cycloalkyl, i.e., cyclopropyl, cyclobutyl, cyclopentyl, or cyclohexyl. In another embodiment, the cycloalkyl is a C_5 cycloalkyl, i.e., cyclopentyl. In another embodiment, the cycloalkyl is a C_6 cycloalkyl, i.e., cyclohexyl. Non-limiting exemplary C_{3-12} cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, norbornyl, decalin, adamantyl, cyclohexenyl, and spiro[3.3]heptane.

[0847] The term "optionally substituted cycloalkyl" as used herein by itself or as part of another group refers to a cycloalkyl group is either unsubstituted or substituted with one, two, or three substituents, wherein each substituent is independently halo, nitro, cyano, hydroxy, amino (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, $-OR^{59}$, $-N(R^{56a})C(=N-R^{60})R^{61}$, $-N(R^{56a})C(=C-NO_2)R^{64}$, $-C(=N-R^{60})R^{61}$, or $-C(=C-NO_2)R^{64}$; wherein R^{56a}, R^{56b}, R^{56c}, R^{56d}, R^{56e}, R^{57}, R^{58}, R^{60}, R^{61}, and R^{64} are as defined in connection with the term "optionally substituted alkyl" and R^{59} is (hydroxy)alkyl or (amino)alkyl. Non-limiting exemplary optionally substituted cycloalkyl groups include 3-(4-acetylpiperazin-1-yl)cyclohexyl, 3-(3-(N-methylacetamido)pyrrolidin-1-yl)cyclohexyl, 3-morpholinocyclohexyl, and 3-(pyrimidin-5-yl)cyclohexyl. In one embodiment, the optionally substituted cycloalkyl is either unsubstituted or substituted with one, two, or three substituents, wherein each substituent is independently halo, nitro, cyano, hydroxy,

amino (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, and $-OR^{59}$.

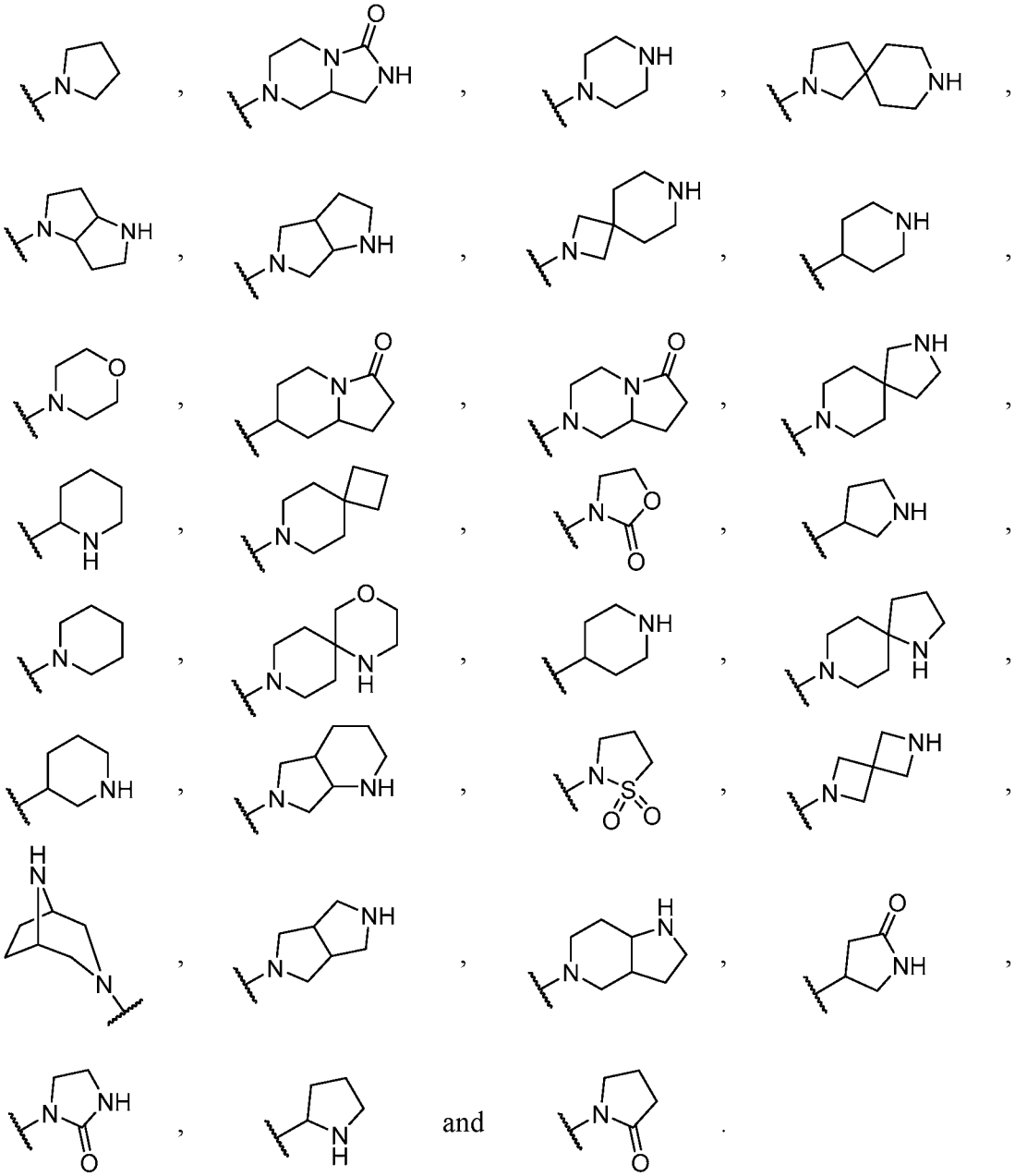
[0848] The term "heterocyclo" as used herein by itself or as part of another group refers to saturated and partially unsaturated, e.g., containing one or two double bonds, monocyclic, bicyclic, or tricyclic groups containing three to fourteen ring members, i.e., a 3- to 14-membered heterocyclo, comprising one, two, three, or four heteroatoms. Each heteroatom is independently oxygen, sulfur, or nitrogen. Each sulfur atom is independently oxidized to give a sulfoxide, i.e., S(=O), or sulfone, i.e., $S(=O)_2$.

[0849] The term heterocyclo includes groups wherein one or more $-CH_2-$ groups is replaced with one or more -C(=O)- groups, including cyclic ureido groups such as imidazolidinyl-2-one, cyclic amide groups such as pyrrolidin-2-one or piperidin-2-one, and cyclic carbamate groups such as oxazolidinyl-2-one.

[0850] The term heterocyclo also includes groups having fused optionally substituted aryl or optionally substituted heteroaryl groups such as indoline, indolin-2-one, 2,3-dihydro-1H-pyrrolo[2,3-c]pyridine, 2,3,4,5-tetrahydro-1H-benzo[d]azepine, or 1,3,4,5-tetrahydro-2H-benzo[d]azepin-2-one.

[0851] In one embodiment, the heterocyclo group is a 4- to 8-membered cyclic group containing one ring and one or two oxygen atoms, e.g., tetrahydrofuran or tetrahydropyran, or one or two nitrogen atoms, e.g., pyrrolidine, piperidine, or piperazine, or one oxygen and one nitrogen atom, e.g., morpholine, and, optionally, one $-CH_2-$ group is replaced with one -C(=O)- group, e.g., pyrrolidin-2-one or piperazin-2-one. In another embodiment, the heterocyclo group is a 5- to 8-membered cyclic group containing one ring and one or two nitrogen atoms and, optionally, one $-CH_2-$ group is replaced with one -C(=O)- group. In another embodiment, the heterocyclo group is a 5- or 6-membered cyclic group containing one ring and one or two nitrogen atoms and, optionally, one $-CH_2-$ group is replaced with one -C(=O)- group. In another embodiment, the

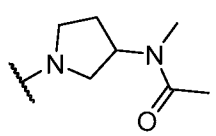
heterocyclo group is a 8- to12-membered cyclic group containing two rings and one or two nitrogen atoms. The heterocyclo can be linked to the rest of the molecule through any available carbon or nitrogen atom. Non-limiting exemplary heterocyclo groups include:



[0852] The term "optionally substituted heterocyclo" as used herein by itself or part of another group refers to a heterocyclo group that is either unsubstituted or substituted with one to four substituents, wherein each substituent is independently halo, nitro, cyano, hydroxy, amino, (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl,

alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, $-OR^{59}$, $-N(R^{56a})C(=N-R^{60})R^{61}$, $-N(R^{56a})C(=C-NO_2)R^{64}$, $-C(=N-R^{60})R^{61}$, or $-C(=C-NO_2)R^{64}$; wherein R^{56a}, R^{56b}, R^{56c}, R^{56d}, R^{56e}, R^{57}, R^{58}, R^{59}, R^{60}, R^{61}, and R^{64} are as defined in connection with the term "optionally substituted cycloalkyl." Substitution may occur on any available carbon or nitrogen atom of the heterocyclo group. In one embodiment, the optionally substituted heterocyclo is either unsubstituted or substituted with one to four substituents, wherein each substituent is independently halo, nitro, cyano, hydroxy, amino, (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, or $-OR^{59}$.

[0853] Non-limiting exemplary optionally substituted heterocyclo groups include: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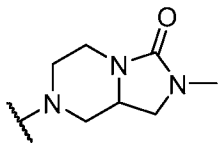
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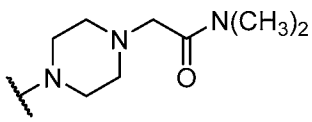
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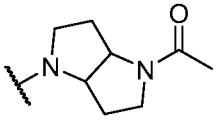
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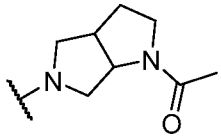
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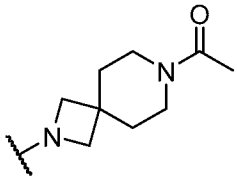
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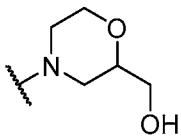
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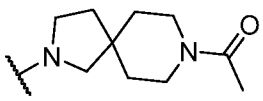
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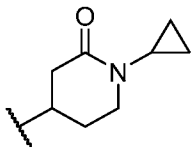
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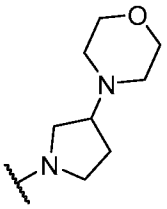
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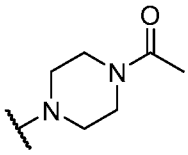
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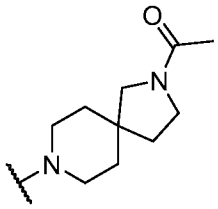
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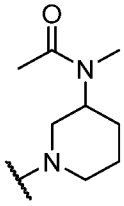
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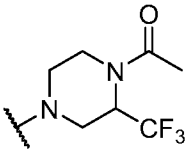
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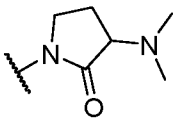
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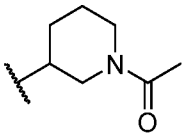
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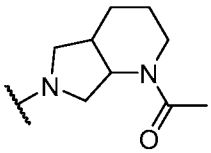
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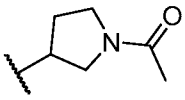
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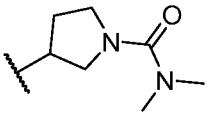
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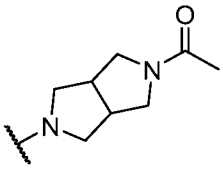
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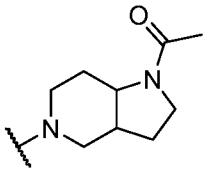
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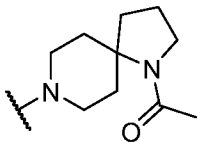
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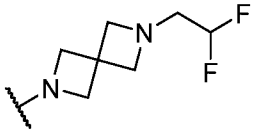
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[0854] The term "aryl" as used herein by itself or as part of another group refers to an aromatic ring system having six to fourteen carbon atoms, i.e., C_6-C_{14} aryl. Non-limiting exemplary aryl groups include phenyl (abbreviated as "Ph"), naphthyl, phenanthryl, anthracyl, indenyl, azulenyl, biphenyl, biphenylenyl, and fluorenyl groups. In one embodiment, the aryl group is phenyl or naphthyl. In another embodiment, the aryl group is phenyl.

[0855] The term "optionally substituted aryl" as used herein by itself or as part of another group refers to aryl that is either unsubstituted or substituted with one to five substituents, wherein the substituents are each independently halo, nitro, cyano, hydroxy, amino, (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl,

(heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, $-OR^{59}$, $-N(R^{56a})C(=N-R^{60})R^{61}$, $-N(R^{56a})C(=C-NO_2)R^{64}$, $-C(=N-R^{60})R^{61}$, or $-C(=C-NO_2)R^{64}$; wherein R^{56a}, R^{56b}, R^{56c}, R^{56d}, R^{56e}, R^{57}, R^{58}, R^{59}, R^{60}, R^{61}, and R^{64} are as defined in connection with the term "optionally substituted cycloalkyl." In one embodiment, the optionally substituted aryl is either unsubstituted or substituted with one to five substituents, wherein the substituents are each independently halo, nitro, cyano, hydroxy, amino, (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, or $-OR^{59}$.

[0856] In one embodiment, the optionally substituted aryl is an optionally substituted phenyl. In another embodiment, the optionally substituted phenyl has four substituents. In another embodiment, the optionally substituted phenyl has three substituents. In another embodiment, the optionally substituted phenyl has two substituents. In another embodiment, the optionally substituted phenyl has one substituent. Non-limiting exemplary optionally substituted aryl groups include 2-methylphenyl, 2-methoxyphenyl, 2-fluorophenyl, 2-chlorophenyl, 2-bromophenyl, 3-methylphenyl, 3-methoxyphenyl, 3-fluorophenyl, 3-chlorophenyl, 4-methylphenyl, 4-ethylphenyl, 4-methoxyphenyl, 4-fluorophenyl, 4-chlorophenyl, 2,6-di-fluorophenyl, 2,6-di-chlorophenyl, 2-methyl, 3-methoxyphenyl, 2-ethyl, 3-methoxyphenyl, 3,4-di-methoxyphenyl, 3,5-di-fluorophenyl 3,5-di-methylphenyl, 3,5-dimethoxy, 4-methylphenyl, 2-fluoro-3-chlorophenyl, 3-chloro-4-fluorophenyl, and 2-phenylpropan-2-amine. The term optionally substituted aryl includes aryl groups having fused optionally substituted cycloalkyl groups and fused optionally substituted heterocyclo groups. Non-limiting examples include: 2,3-dihydro-1H-inden-1-yl, 1,2,3,4-tetrahydronaphthalen-1-yl, 1,3,4,5-tetrahydro-2H-benzo[c]azepin-2-yl, 1,2,3,4-tetrahydroisoquinolin-1-yl, and 2-oxo-2,3,4,5-tetrahydro-1H-benzo[d]azepin-1-yl.

[0857] The term "heteroaryl" as used herein by itself or as part of another group refers to monocyclic and bicyclic aromatic ring systems having five to 14 fourteen ring members, i.e., a 5- to 14-membered heteroaryl, comprising one, two, three, or four heteroatoms. Each heteroatom is independently oxygen, sulfur, or nitrogen. In one embodiment, the heteroaryl has three heteroatoms. In another embodiment, the heteroaryl has two heteroatoms. In another embodiment, the heteroaryl has one heteroatom. In another embodiment, the heteroaryl is a 5- to 10-membered heteroaryl. In another embodiment, the heteroaryl has 5 ring atoms, e.g., thienyl, a 5-membered heteroaryl having four carbon atoms and one sulfur atom. In another embodiment, the heteroaryl has 6 ring atoms, e.g., pyridyl, a 6-membered heteroaryl having five carbon atoms and one nitrogen atom. Non-limiting exemplary heteroaryl groups include thienyl, benzo[b]thienyl, naphtho[2,3-b]thienyl, thianthrenyl, furyl, benzofuryl, pyranyl, isobenzofuranyl, benzooxazonyl, chromenyl, xanthenyl, 2*H*-pyrrolyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, isoindolyl, 3*H*-indolyl, indolyl, indazolyl, purinyl, isoquinolyl, quinolyl, phthalazinyl, naphthyridinyl, cinnolinyl, quinazolinyl, pteridinyl, 4a*H*-carbazolyl, carbazolyl, β-carbolinyl, phenanthridinyl, acridinyl, pyrimidinyl, phenanthrolinyl, phenazinyl, thiazolyl, isothiazolyl, phenothiazolyl, isoxazolyl, furazanyl, and phenoxazinyl. In one embodiment, the heteroaryl is chosen from thienyl (e.g., thien-2-yl and thien-3-yl), furyl (e.g., 2-furyl and 3-furyl), pyrrolyl (e.g., 1H-pyrrol-2-yl and 1H-pyrrol-3-yl), imidazolyl (e.g., 2H-imidazol-2-yl and 2H-imidazol-4-yl), pyrazolyl (e.g., 1H-pyrazol-3-yl, 1H-pyrazol-4-yl, and 1H-pyrazol-5-yl), pyridyl (e.g., pyridin-2-yl, pyridin-3-yl, and pyridin-4-yl), pyrimidinyl (e.g., pyrimidin-2-yl, pyrimidin-4-yl, and pyrimidin-5-yl), thiazolyl (e.g., thiazol-2-yl, thiazol-4-yl, and thiazol-5-yl), isothiazolyl (e.g., isothiazol-3-yl, isothiazol-4-yl, and isothiazol-5-yl), oxazolyl (e.g., oxazol-2-yl, oxazol-4-yl, and oxazol-5-yl) and isoxazolyl (e.g., isoxazol-3-yl, isoxazol-4-yl, and isoxazol-5-yl). The term heteroaryl also includes N-oxides. A non-limiting exemplary N-oxide is pyridyl N-oxide.

[0858] The term "optionally substituted heteroaryl" as used herein by itself or as part of another group refers to a heteroaryl that is either unsubstituted or substituted with one to four substituents, wherein the substituents are independently halo, nitro, cyano, hydroxy, amino, (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl,

arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, $-OR^{59}$, $-N(R^{56a})C(=N-R^{60})R^{61}$, $-N(R^{56a})C(=C-NO_2)R^{64}$, $-C(=N-R^{60})R^{61}$, or $-C(=C-NO_2)R^{64}$; wherein R^{56a}, R^{56b}, R^{56c}, R^{56d}, R^{56e}, R^{57}, R^{58}, R^{59}, R^{60}, R^{61}, and R^{64} are as defined in connection with the term "optionally substituted cycloalkyl." In one embodiment, optionally substituted heteroaryl is either unsubstituted or substituted with one to four substituents, wherein the substituents are independently halo, nitro, cyano, hydroxy, amino, (e.g., $-NH_2$, alkylamino, dialkylamino, aralkylamino, hydroxyalkylamino, or (heterocyclo)alkylamino), heteroalkyl, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, aralkyl, aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, ureido, guanidino, carboxy, carboxyalkyl, optionally substituted alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, $-N(R^{56a})C(=O)R^{56b}$, $-N(R^{56c})S(=O)_2R^{56d}$, $-C(=O)R^{57}$, $-S(=O)R^{56e}$, $-S(=O)_2R^{58}$, or $-OR^{59}$.

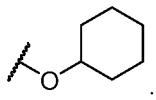
[0859] In one embodiment, the optionally substituted heteroaryl has two substituents. In another embodiment, the optionally substituted heteroaryl has one substituent. Any available carbon or nitrogen atom can be substituted.

[0860] The term "aryloxy" as used herein by itself or as part of another group refers to an optionally substituted aryl attached to a terminal oxygen atom. A non-limiting exemplary aryloxy group is PhO-.

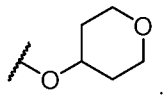
[0861] The term "heteroaryloxy" as used herein by itself or as part of another group refers to an optionally substituted heteroaryl attached to a terminal oxygen atom. A non-limiting exemplary aryloxy group is pyridyl-O-.

[0862] The term "aralkyloxy" as used herein by itself or as part of another group refers to an aralkyl attached to a terminal oxygen atom. A non-limiting exemplary aralkyloxy group is $PhCH_2O$-.

[0863] The term "(cycloalkyl)oxy" as used herein by itself or as part of another group refers to a cycloalkyl group attached to a terminal oxygen atom. A non-limiting exemplary cycloalkyloxy group is:

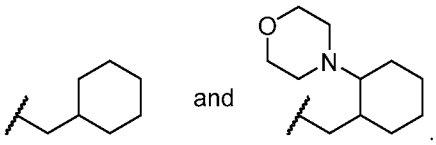


[0864] The term "(heterocyclo)oxy" as used herein by itself or as part of another group refers to a heterocyclo group attached to a terminal oxygen atom. A non-limiting exemplary (heterocyclo)oxy group is:



[0865] The term "(cyano)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one, two, or three cyano groups. In one embodiment, the alkyl is substituted with one cyano group. In another embodiment, the alkyl is a C_1-C_6 alkyl In another embodiment, the alkyl is a C_1-C_4 alkyl. Non-limiting exemplary (cyano)alkyl groups include $-CH_2CH_2CN$ and $-CH_2CH_2CH_2CN$.

[0866] The term "(cycloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one optionally substituted cycloalkyl group. In one embodiment, the cycloalkyl group is an optionally substituted C_3-C_6 cycloalkyl. In another embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. Non-limiting exemplary (cycloalkyl)alkyl groups include:



[0867] The term "sulfonamido" as used herein by itself or as part of another group refers to a radical of the formula $-SO_2NR^{50a}R^{50b}$, wherein R^{50a} and R^{50b} are each independently hydrogen, alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclo, optionally substituted aryl, or optionally substituted heteroaryl; or R^{50a} and R^{50b} taken together with the nitrogen to which they are attached form a 3- to 8-membered optionally substituted heterocyclo group. Non-limiting exemplary sulfonamido groups include $-SO_2NH_2$, $-SO_2N(H)CH_3$, and $-SO_2N(H)Ph$.

[0868] The term "alkylcarbonyl" as used herein by itself or as part of another group refers to a carbonyl group, i.e., -C(=O)-, substituted by an alkyl group. In one

embodiment, the alkyl is a C_1-C_4 alkyl. A non-limiting exemplary alkylcarbonyl group is $-COCH_3$.

[0869] The term "arylcarbonyl" as used herein by itself or as part of another group refers to a carbonyl group, i.e., -C(=O)-, substituted by an optionally substituted aryl group. A non-limiting exemplary arylcarbonyl group is -COPh.

[0870] The term "alkylsulfonyl" as used herein by itself or as part of another group refers to a sulfonyl group, i.e., $-SO_2-$, substituted by an alkyl group. A non-limiting exemplary alkylsulfonyl group is $-SO_2CH_3$.

[0871] The term "arylsulfonyl" as used herein by itself or as part of another group refers to a sulfonyl group, i.e., $-SO_2-$, substituted by an optionally substituted aryl group. A non-limiting exemplary arylsulfonyl group is $-SO_2Ph$.

[0872] The term "mercaptoalkyl" as used herein by itself or as part of another group refers to an alkyl substituted by a –SH group.

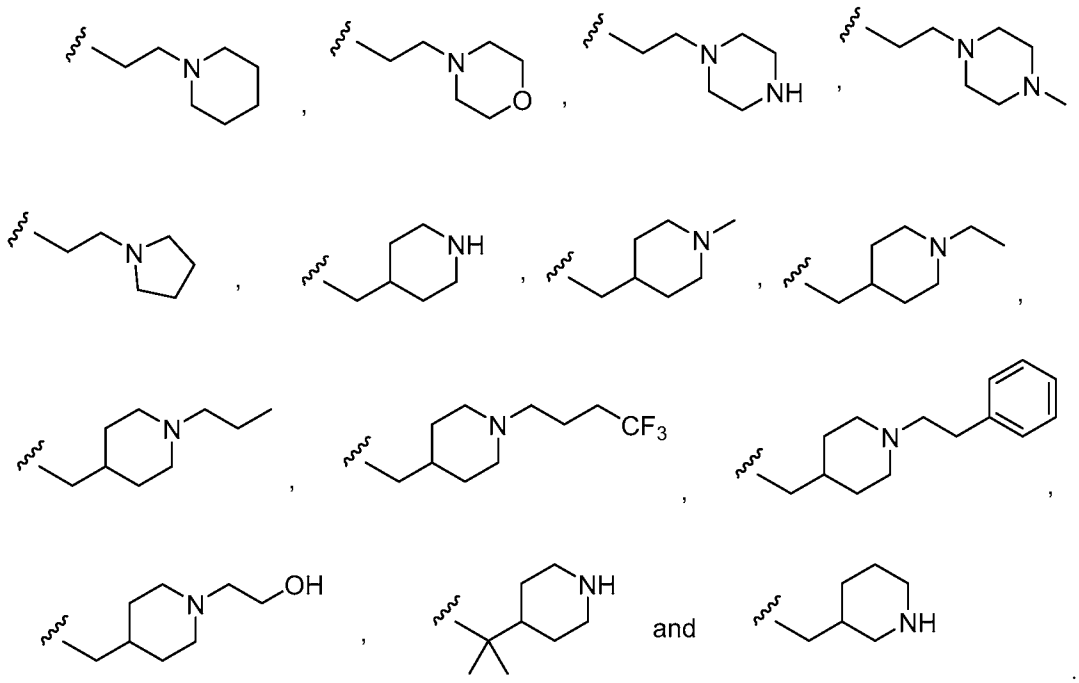
[0873] The term "carboxy" as used by itself or as part of another group refers to a radical of the formula -C(=O)OH.

[0874] The term "ureido" as used herein by itself or as part of another group refers to a radical of the formula $-NR^{51a}-C(=O)-NR^{51b}R^{51c}$, wherein R^{51a} is hydrogen or alkyl; and R^{51b} and R^{51c} are each independently hydrogen, alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclo, optionally substituted aryl, or optionally substituted heteroaryl, or R^{51b} and R^{51c} taken together with the nitrogen to which they are attached form a 4- to 8-membered optionally substituted heterocyclo group. Non-limiting exemplary ureido groups include $-NH-C(C=O)-NH_2$ and $-NH-C(C=O)-NHCH_3$.

[0875] The term "guanidino" as used herein by itself or as part of another group refers to a radical of the formula $-NR^{52a}-C(=NR^{53})-NR^{52b}R^{52c}$, wherein R^{52a} is hydrogen or alkyl; R^{52b} and R^{53c} are each independently hydrogen, alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclo, optionally substituted aryl, or optionally substituted heteroaryl; or R^{52b} and R^{52c} taken together with the nitrogen to which they are attached form a 4- to 8-membered optionally substituted heterocyclo group; and R^{53} is hydrogen, alkyl, cyano, alkylsulfonyl, alkylcarbonyl, carboxamido, or sulfonamido. Non-limiting exemplary guanidino groups include $-NH-C(C=NH)-NH_2$, $-NH-C(C=NCN)-NH_2$, and $-NH-C(C=NH)-NHCH_3$.

[0876] The term "(heterocyclo)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one, two, or three optionally substituted heterocyclo

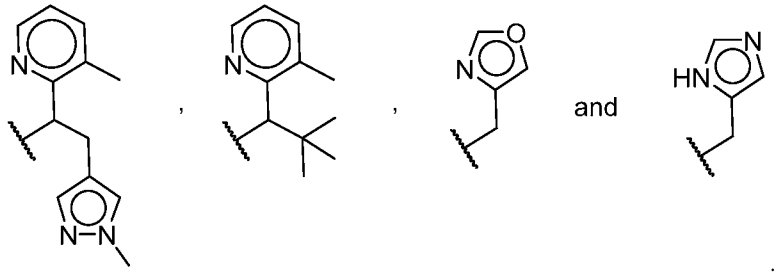
groups. In one embodiment, the alkyl is substituted with one optionally substituted 5- to 8-membered heterocyclo group. In another embodiment, alkyl is a C_1-C_6 alkyl. In another embodiment, alkyl is a C_1-C_4 alkyl. The heterocyclo group can be linked to the alkyl group through a carbon or nitrogen atom. Non-limiting exemplary (heterocyclo)alkyl groups include:



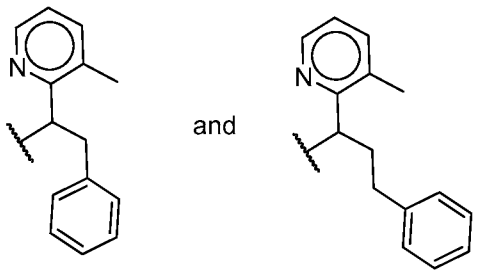
[0877] The term "carbamate" as used herein by itself or as part of another group refers to a radical of the formula $-NR^{54a}-C(=O)-OR^{54b}$, wherein R^{54a} is hydrogen or alkyl, and R^{54b} is hydrogen, alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclo, optionally substituted aryl, or optionally substituted heteroaryl. A non-limiting exemplary carbamate group is -NH-(C=O)-OtBu.

[0878] The term "(heteroaryl)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one or two optionally substituted heteroaryl groups. In one embodiment, the alkyl group is substituted with one optionally substituted 5- to 14-membered heteroaryl group. In another embodiment, the alkyl group is substituted with two optionally substituted 5- to 14-membered heteroaryl groups. In another embodiment, the alkyl group is substituted with one optionally substituted 5- to 9-membered heteroaryl group. In another embodiment, the alkyl group is substituted with two optionally substituted 5- to 9-membered heteroaryl groups. In another embodiment, the alkyl group is substituted with one optionally substituted 5- or 6-membered heteroaryl group. In another embodiment, the alkyl group is substituted

with two optionally substituted 5- or 6-membered heteroaryl groups. In one embodiment, the alkyl group is a C_1-C_6 alkyl. In another embodiment, the alkyl group is a C_1-C_4 alkyl. In another embodiment, the alkyl group is a C_1 or C_2 alkyl. Non-limiting exemplary (heteroaryl)alkyl groups include:

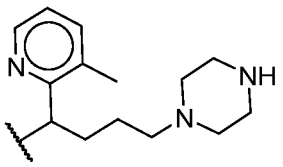


[0879] The term "(heteroaryl)(aryl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted heteroaryl group and one optionally substituted aryl group. In one embodiment, the heteroaryl is an optionally substituted 5- to 9-membered heteroaryl group. In another embodiment, the heteroaryl is an optionally substituted 5- or 6-membered heteroaryl group. In one embodiment, the aryl is an optionally substituted phenyl group or optionally substituted naphthyl group. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. Non-limiting exemplary (heteroaryl)(aryl)alkyl groups include:

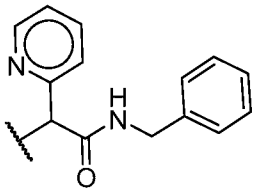
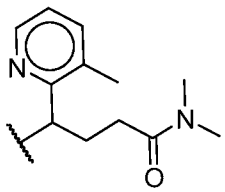
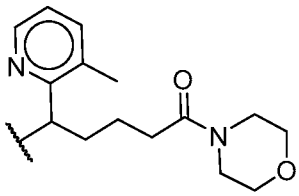


[0880] The term "(heteroaryl)(heterocyclo)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted heteroaryl group and one optionally substituted heterocyclo group. In one embodiment, the heteroaryl is an optionally substituted 5- to 9-membered heteroaryl group. In another embodiment, the heteroaryl is an optionally substituted 5- or 6-membered heteroaryl group. In one embodiment, the heterocyclo is an optionally substituted 5- to 8-membered heterocyclo. In another embodiment, the heterocyclo is an optionally substituted 5- or 6-membered heterocyclo. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another

embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (heteroaryl)(heterocyclo)alkyl group is:



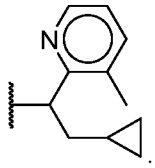
[0881] The term "(heteroaryl)(carboxamido)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted heteroaryl group and one carboxamido group. In one embodiment, the heteroaryl is an optionally substituted 5- to 9-membered heteroaryl group. In another embodiment, the heteroaryl is an optionally substituted 5- or 6-membered heteroaryl group. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1-C_3 alkyl. Non-limiting exemplary (heteroaryl)(carboxamido)alkyl groups include:


, 
and 

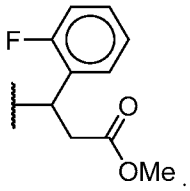
[0882] The term "carboxamido" as used herein by itself or as part of another group refers to a radical of formula $-C(=O)NR^{55a}R^{55b}$, wherein R^{55a} and R^{55b} are each independently hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, haloalkyl, (alkoxy)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclo, optionally substituted aryl, optionally substituted heteroaryl, (aryl)alkyl, (cycloalkyl)alkyl, (heterocyclo)alkyl, or (heteroaryl)alkyl; or R^{55a} and R^{55b} taken together with the nitrogen to which they are attached from a 4- to 8-membered optionally substituted heterocyclo group. Non-limiting exemplary carboxamido groups include: morpholine-4-carbonyl, N,N-dimethylaminocarbonyl, N-(1-methylpiperidin-4-yl)aminocarbonyl, 4-methylpiperazine-1-carbonyl, N-(3-aminocyclopentyl)aminocarbonyl, N-(pyridin-3-yl)aminocarbonyl, and N-(tetrahydrofuran-3-yl)aminocarbonyl.

[0883] The term "(heteroaryl)(cycloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted heteroaryl group and one optionally substituted cycloalkyl group. In one embodiment,

the heteroaryl is an optionally substituted 5- to 9-membered heteroaryl group. In another embodiment, the heteroaryl is an optionally substituted 5- or 6-membered heteroaryl group. In one embodiment, the cycloalkyl is an optionally substituted C_3-C_6 cycloalkyl. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1-C_3 alkyl. A non-limiting exemplary (heteroaryl)(C_3-C_6 cycloalkyl) alkyl group is:



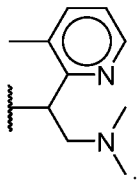
[0884] The term "(aryl)(alkoxycarbonyl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted aryl group and one alkoxycarbonyl group. In one embodiment, the aryl is an optionally substituted phenyl group or optionally substituted naphthyl group. In another embodiment, the aryl is an optionally substituted phenyl group. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (aryl)(alkoxycarbonyl)alkyl group is:



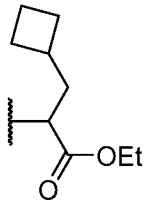
[0885] The term "alkoxycarbonyl" as used herein by itself or as part of another group refers to a carbonyl group, i.e., -C(=O)-, substituted by a C_1-C_6 alkoxy group. In one embodiment, the alkoxy group is a C_1-C_4 alkoxy. In another embodiment, the alkoxy group is a C_1-C_3 alkoxy. Non-limiting exemplary alkoxycarbonyl groups include $-CO_2$-Me and $-CO_2Et$.

[0886] The term "(heteroaryl)(amino)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted heteroaryl group and one amino group. In one embodiment, the heteroaryl is an optionally substituted 5- to 9-membered heteroaryl group. In another embodiment, the heteroaryl is an optionally substituted 5- or 6-membered heteroaryl group. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another

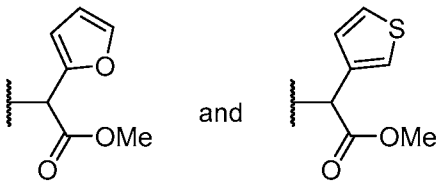
embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (heteroaryl)(amino)alkyl group is:



[0887] The term "(cycloalkyl)(alkoxycarbonyl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted cycloalkyl group and one alkoxycarbonyl group. In one embodiment, the cycloalkyl is an optionally substituted C_3-C_6 cycloalkyl. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (cycloalkyl)(alkoxycarbonyl)alkyl group is:

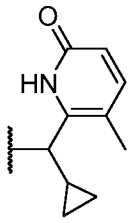


[0888] The term "(heteroaryl)(alkoxycarbonyl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted heteroaryl group and one alkoxycarbonyl group. In one embodiment, the heteroaryl is an optionally substituted 5- to 9-membered heteroaryl group. In another embodiment, the heteroaryl is an optionally substituted 5- or 6-membered heteroaryl group. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. Non-limiting exemplary (heteroaryl)(alkoxycarbonyl)alkyl groups include:

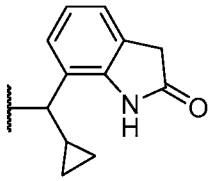


[0889] The term "(heterocyclo)(cycloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted heterocyclo group and one optionally substituted cycloalkyl group. In one embodiment, the heterocyclo is an optionally substituted 5- to 8-membered heterocyclo. In another embodiment, the heterocyclo is an optionally substituted 5- or 6-membered heterocyclo.

In one embodiment, the cycloalkyl is an optionally substituted C_3-C_6 cycloalkyl. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (heterocyclo)(cycloalkyl)alkyl group is:



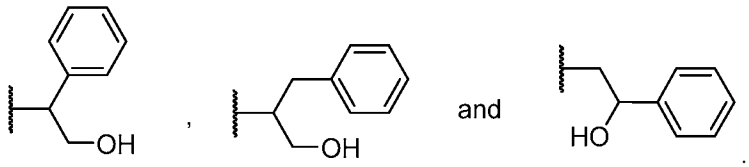
[0890] The term "(aryl)(cycloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted aryl group and one optionally substituted cycloalkyl group. In one embodiment, the aryl is an optionally substituted phenyl group or optionally substituted naphthyl group. In another embodiment, the aryl is an optionally substituted phenyl group. In one embodiment, the cycloalkyl is an optionally substituted C_3-C_6 cycloalkyl. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (aryl)(cycloalkyl)alkyl group is:



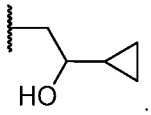
[0891] The terms "aralkyl" or "(aryl)alkyl" as used herein by themselves or as part of another group refers to an alkyl substituted with one, two, or three optionally substituted aryl groups. In one embodiment, the alkyl is substituted with one optionally substituted aryl group. In another embodiment, the alkyl is substituted with two optionally substituted aryl groups. In one embodiment, the aryl is an optionally substituted phenyl or optionally substituted naphthyl. In another embodiment, the aryl is an optionally substituted phenyl. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. Non-limiting exemplary (aryl)alkyl groups include benzyl, phenethyl, $-CHPh_2$, and $-CH(4\text{-}F\text{-}Ph)_2$.

[0892] The term "(aryl)(hydroxy)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one optionally substituted aryl group and one

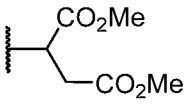
hydroxyl group. In one embodiment, the aryl is an optionally substituted phenyl group or optionally substituted naphthyl group. In another embodiment, the aryl is an optionally substituted phenyl group. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. Non-limiting exemplary (aryl)(hydroxy)alkyl groups include:



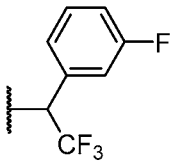
[0893] The term "(cycloalkyl)(hydroxy)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one optionally substituted cycloalkyl group and one hydroxyl group. In one embodiment, the cycloalkyl group is an optionally substituted C_3-C_6 cycloalkyl group. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (cycloalkyl)(hydroxy)alkyl group is:



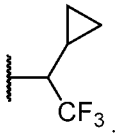
[0894] The term "(alkoxycarbonyl)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one or two alkoxycarbonyl groups. In one embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (alkoxycarbonyl)alkyl groups is:



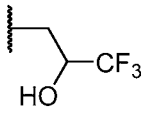
[0895] The term "(aryl)(haloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one optionally substituted aryl group and one haloalkyl group. In one embodiment, the aryl is an optionally substituted group or optionally substituted naphthyl. In another embodiment, the aryl is an optionally substituted phenyl. In one embodiment, the haloalkyl is a C_1-C_4 haloalkyl. In one embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (aryl)(haloalkyl)alkyl groups is:



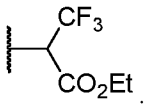
[0896] The term "(cycloalkyl)(haloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one optionally substituted cycloalkyl group and one haloalkyl group. In one embodiment, the cycloalkyl is an optionally substituted C_3-C_6 cycloalkyl. In one embodiment, the haloalkyl is a C_1-C_4 haloalkyl. In one embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (cycloalkyl)(haloalkyl) alkyl groups is:



[0897] The term "(hydroxy)(haloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one hydroxy group and one haloalkyl group. In one embodiment, the haloalkyl is a C_1-C_4 haloalkyl. In one embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (hydroxy)(haloalkyl)alkyl groups is:



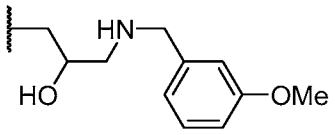
[0898] The term "(alkoxycarbonyl)(haloalkyl)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one alkoxycarbonyl group and one haloalkyl group. In one embodiment, the haloalkyl is a C_1-C_4 haloalkyl. In one embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (alkoxycarbonyl)(haloalkyl)alkyl groups is:



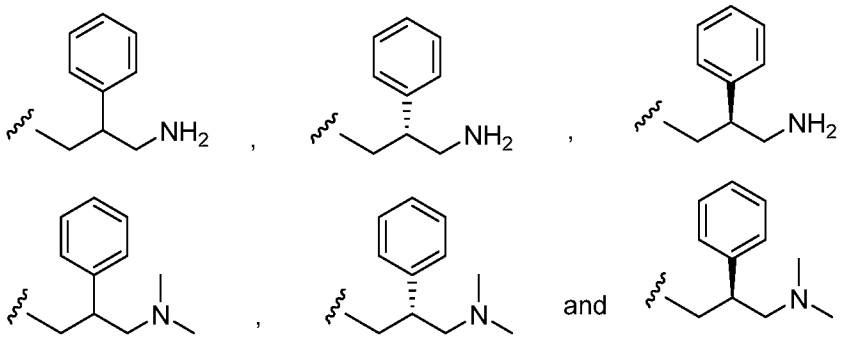
[0899] The term "(carboxamido)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with a carboxamido group. In one embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. Non-limiting exemplary (carboxamido)alkyl groups include $-CH_2C(=O)NH_2$, $-C(H)(CH_3)C(=O)NH_2$, $-CH_2C(=O)N(H)CH_3$, and $-CH_2C(=O)N(CH_3)_2$.

[0900] The term "(carboxy)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with -C(=O)OH. In one embodiment, the alkyl is a C_1-C_4 alkyl. In another embodiment, the alkyl is a C_1 or C_2 alkyl. A non-limiting exemplary (carboxy)alkyl group is $-CH_2CO_2H$.

[0901] The term "(amino)(hydroxy)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one hydroxy group and one amino group. In one embodiment, the alkyl is a C_1-C_4 alkyl. A non-limiting exemplary "(amino)(hydroxy)alkyl group is:



[0902] The term "(amino)(aryl)alkyl" as used herein by itself or as part of another group refers to an alkyl group substituted with one amino group and one optionally substituted aryl group. In one embodiment, the amino group is $-NH_2$, alkylamino, or dialkylamino. In one embodiment, the aryl group is an optionally substituted phenyl. In one embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. Non-limiting exemplary (amino)(aryl)alkyl groups include:



[0903] The term "amino" as used by itself or as part of another group refers to a radical of the formula $-NR^{55a}R^{55b}$, wherein R^{55a} and R^{55b} are independently hydrogen, optionally substituted alkyl, haloalkyl, (hydroxy)alkyl, (alkoxy)alkyl, (amino)alkyl, heteroalkyl, optionally substituted cycloalkyl, optionally substituted heterocyclo, optionally substituted aryl, optionally substituted heteroaryl, (aryl)alkyl, (cycloalkyl)alkyl, (heterocyclo)alkyl, or (heteroaryl)alkyl.

[0904] In one embodiment, the amino is $-NH_2$.

[0905] In another embodiment, the amino is an "alkylamino," i.e., an amino group wherein R^{55a} is C_{1-6} alkyl and R^{55b} is hydrogen. In one embodiment, R^{55a} is C_1-C_4 alkyl. Non-limiting exemplary alkylamino groups include $-N(H)CH_3$ and $-N(H)CH_2CH_3$.

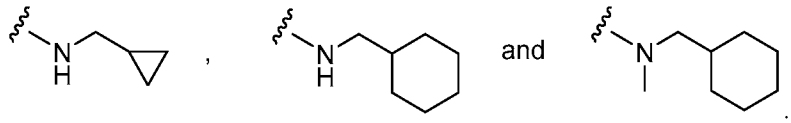
[0906] In another embodiment, the amino is a "dialkylamino," i.e., an amino group wherein R^{55a} and R^{55b} are each independently C_{1-6} alkyl. In one embodiment, R^{55a} and R^{55b} are each independently C_1-C_4 alkyl. Non-limiting exemplary dialkylamino groups include $-N(CH_3)_2$ and $-N(CH_3)CH_2CH(CH_3)_2$.

[0907] In another embodiment, the amino is a "hydroxyalkylamino," i.e., an amino group wherein R^{55a} is (hydroxyl)alkyl and R^{55b} is hydrogen or C_1-C_4 alkyl.

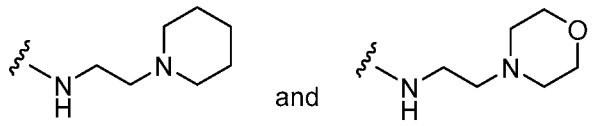
[0908] In another embodiment, the amino is a "cycloalkylamino," i.e., an amino group wherein R^{55a} is optionally substituted cycloalkyl and R^{55b} is hydrogen or C_1-C_4 alkyl.

[0909] In another embodiment, the amino is a "aralkylamino," i.e., an amino group wherein R^{55a} is aralkyl and R^{55b} is hydrogen or C_1-C_4 alkyl. Non-limiting exemplary aralkylamino groups include $-N(H)CH_2Ph$, $-N(H)CHPh_2$, and $-N(CH_3)CH_2Ph$.

[0910] In another embodiment, the amino is a "(cycloalkyl)alkylamino," i.e., an amino group wherein R^{55a} is (cycloalkyl)alkyl and R^{55b} is hydrogen or C_1-C_4 alkyl. Non-limiting exemplary (cycloalkyl)alkylamino groups include:



[0911] In another embodiment, the amino is a "(heterocyclo)alkylamino," i.e., an amino group wherein R^{55a} is (heterocyclo)alkyl and R^{55b} is hydrogen or C_1-C_4 alkyl. Non-limiting exemplary (heterocyclo)alkylamino groups include:



[0912] The term "(amino)alkyl" as used herein by itself or as part of another group refers to an alkyl substituted with one amino group. In one embodiment, the amino group is $-NH_2$. In one embodiment, the amino group is an alkylamino. In another embodiment, the amino group is a dialkylamino. In another embodiment, the alkyl is a C_1-C_6 alkyl. In another embodiment, the alkyl is a C_1-C_4 alkyl. Non-limiting exemplary (amino)alkyl groups include $-CH_2NH_2$, $CH_2CH_2N(H)CH_3$, $-CH_2CH_2N(CH_3)_2$, $CH_2N(H)$cyclopropyl, $-CH_2N(H)$cyclobutyl, and $-CH_2N(H)$cyclohexyl, and $-CH_2CH_2CH_2N(H)CH_2Ph$ and $-CH_2CH_2CH_2N(H)CH_2(4\text{-}CF_3\text{-}Ph)$.

[0913] The present disclosure encompasses any of the Compounds of the Disclosure being isotopically-labelled (i.e., radiolabeled) by having one or more atoms replaced by an atom having a different atomic mass or mass number. Examples of isotopes that can be incorporated into the disclosed compounds include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine and chlorine, such as ^{2}H (or deuterium (D)), ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{15}N, ^{18}O, ^{17}O, ^{31}P, ^{32}P, ^{35}S, ^{18}F, and ^{36}Cl, respectively, e.g., ^{3}H, ^{11}C, and ^{14}C. In one embodiment, provided is a composition wherein substantially all of the atoms at a position within the Compound of the Disclosure are replaced by an atom having a different atomic mass or mass number. In another embodiment, provided is a composition wherein a portion of the atoms at a position within the Compound of the disclosure are replaced, i.e., the Compound of the Disclosure is enriched at a position with an atom having a different atomic mass or mass number." Isotopically-labelled Compounds of the Disclosure can be prepared by methods known in the art.

[0914] Compounds of the Disclosure may contain one or more asymmetric centers and may thus give rise to enantiomers, diastereomers, and other stereoisomeric forms. The present disclosure encompasses the use of all such possible forms, as well as their racemic and resolved forms and mixtures thereof. The individual enantiomers can be separated according to methods known in the art in view of the present disclosure. When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that they include both E and Z geometric isomers. All tautomers are also encompassed by the present disclosure.

[0915] As used herein, the term "stereoisomers" is a general term for all isomers of individual molecules that differ only in the orientation of their atoms in space. It includes enantiomers and isomers of compounds with more than one chiral center that are not mirror images of one another (diastereomers).

[0916] The term "chiral center" or "asymmetric carbon atom" refers to a carbon atom to which four different groups are attached.

[0917] The terms "enantiomer" and "enantiomeric" refer to a molecule that cannot be superimposed on its mirror image and hence is optically active wherein the enantiomer rotates the plane of polarized light in one direction and its mirror image compound rotates the plane of polarized light in the opposite direction.

[0918] The term "racemic" refers to a mixture of equal parts of enantiomers and which mixture is optically inactive. In one embodiment, Compounds of the Disclosure are racemic.

[0919] The term "absolute configuration" refers to the spatial arrangement of the atoms of a chiral molecular entity (or group) and its stereochemical description, e.g., R or S.

[0920] The stereochemical terms and conventions used in the specification are meant to be consistent with those described in *Pure & Appl. Chem 68*:2193 (1996), unless otherwise indicated.

[0921] The term "enantiomeric excess" or "ee" refers to a measure for how much of one enantiomer is present compared to the other. For a mixture of *R* and *S* enantiomers, the percent enantiomeric excess is defined as $|R - S|*100$, where *R* and *S* are the respective mole or weight fractions of enantiomers in a mixture such that $R + S = 1$. With knowledge of the optical rotation of a chiral substance, the percent enantiomeric excess is defined as $([\alpha]_{obs}/[\alpha]_{max})*100$, where $[\alpha]_{obs}$ is the optical rotation of the mixture of enantiomers and $[\alpha]_{max}$ is the optical rotation of the pure enantiomer. Determination of enantiomeric excess is possible using a variety of analytical techniques, including NMR spectroscopy, chiral column chromatography or optical polarimetry.

[0922] In one embodiment, Compounds of the Disclosure having one or more chiral centers are enantiomerically enriched, e.g., the ee is about 5% or more. In another embodiment, the ee is about 10%. In another embodiment, the ee is about 20%. In another embodiment, the ee is about 30%. In another embodiment, the ee is about 40%. In another embodiment, the ee is about 50%. In another embodiment, the ee is about 60%. In another embodiment, the ee is about 70%. In another embodiment, the ee is about 80%. In another embodiment, the ee is about 85%. In another embodiment, the ee is about 90%. In another embodiment, the ee is about 91%. In another embodiment, the ee is about 92%. In another embodiment, the ee is about 93%. In another embodiment, the ee is about 94%. In another embodiment, the ee is about 95%. In another embodiment, the ee is about 96%. In another embodiment, the ee is about 97%. In another embodiment, the ee is about 98%. In another embodiment, the ee is about 99%.

[0923] The terms "a" and "an" refer to one or more.

[0924] The term "about," as used herein, includes the recited number ± 10%. Thus, "about 10" means 9 to 11.

[0925] The terms "treat," "treating," "treatment," and the like as used herein refer to eliminating, reducing, or ameliorating a disease or condition, and/or symptoms associated therewith. Although not precluded, treating a disease or condition does not require that the disease, condition, or symptoms associated therewith be completely eliminated. As used herein, the terms "treat," "treating," "treatment," and the like may include "prophylactic treatment," which refers to reducing the probability of redeveloping a disease or condition, or of a recurrence of a previously-controlled disease or condition, in a subject who does not have, but is at risk of or is susceptible to, redeveloping a disease or condition or a recurrence of the disease or condition. The term "treat" and synonyms contemplate administering a therapeutically effective amount of a Compound of the Disclosure to an individual in need of such treatment.

[0926] Within the meaning of the disclosure, "treatment" also includes relapse prophylaxis or phase prophylaxis, as well as the treatment of acute or chronic signs, symptoms and/or malfunctions. The treatment can be orientated symptomatically, for example, to suppress symptoms. It can be effected over a short period, be oriented over a medium term, or can be a long-term treatment, for example within the context of a maintenance therapy.

[0927] The term "therapeutically effective amount" or "effective dose" as used herein refers to an amount of the active ingredient(s) that is(are) sufficient, when administered by a method of the disclosure, to efficaciously deliver the active ingredient(s) for the treatment of condition or disease of interest to an individual in need thereof. In the case of a cancer or other proliferation disorder, the therapeutically effective amount of the agent may reduce (*i.e.*, retard to some extent and preferably stop) unwanted cellular proliferation; reduce the number of cancer cells; reduce the tumor size; inhibit (*i.e.*, retard to some extent and preferably stop) cancer cell infiltration into peripheral organs; inhibit (*i.e.*, retard to some extent and preferably stop) tumor metastasis; inhibit, to some extent, tumor growth; modulate protein methylation in the target cells; and/or relieve, to some extent, one or more of the symptoms associated with the cancer. To the extent the administered compound or composition prevents growth and/or kills existing cancer cells, it may be cytostatic and/or cytotoxic.

[0928] The term "container" means any receptacle and closure therefore suitable for storing, shipping, dispensing, and/or handling a pharmaceutical product.

[0929] The term "insert" means information accompanying a pharmaceutical product that provides a description of how to administer the product, along with the safety and efficacy data required to allow the physician, pharmacist, and patient to make an informed decision regarding use of the product. The package insert generally is regarded as the "label" for a pharmaceutical product.

[0930] The term "disease" or "condition" or "disorder" denotes disturbances and/or anomalies that as a rule are regarded as being pathological conditions or functions, and that can manifest themselves in the form of particular signs, symptoms, and/or malfunctions. Compounds of the Disclosure inhibit SETD2 protein and can be used in treating diseases and conditions such as proliferative diseases, wherein inhibition of SETD2 protein provides a benefit. *See, e.g.*, U.S. Provisional Appl. No. 62/545,353.

[0931] In some embodiments, the Compounds of the Disclosure can be used to treat a "SETD2 protein mediated disorder" A SETD2 protein mediated disorder is any pathological condition in which a SETD2 protein is known to play a role. In some embodiments, a SETD2 mediated disorder is a proliferative disease.

[0932] In some embodiments inhibiting SETD2 protein is the inhibition of the activity of one or more activities of SETD2 protein. In some embodiments, the activity of the SETD2 protein is the ability of the SETD2 protein to transfer a methyl group to a target protein, e.g., histone. It should be appreciated that the activity of SETD2 may be inhibited *in vitro* or *in vivo*. Exemplary levels of inhibition of the activity of SETD2 include at least 5% inhibition at least 10% inhibition, at least 20% inhibition, at least 30% inhibition, at least 40% inhibition, at least 50% inhibition, at least 60% inhibition, at least 70% inhibition, at least 80% inhibition, at least 90% inhibition, and up to about 100% inhibition.

[0933] The term "biological sample" as used herein refers any tissue or fluid from a subject that is suitable for detecting chromosomal translocations. Examples of useful biological samples include, but are not limited to, biopsied tissues and/or cells, e.g., solid tumor, lymph gland, inflamed tissue, tissue and/or cells involved in a condition or disease, blood, plasma, serous fluid, cerebrospinal fluid, saliva, urine, lymph, cerebral spinal fluid, and the like. Other suitable biological samples will be familiar to those of ordinary skill in the relevant arts. A biological sample can be analyzed for chromosomal translocations using any technique known in the art. Such techniques include, but are not limited to, polymerase chain reaction (PCR) methodology, reverse

transcription-polymerase chain reaction (RT-PCR) methodology, or cytoplasmic light chain immunofluorescence combined with fluorescence in situ hybridization (cIg-FISH). A biological sample can be obtained using techniques that are well within the scope of ordinary knowledge of a clinical practioner. In one embodiment of the disclosure, the biological sample comprises blood cells.

[0934] The phrase "in combination" as used in connection with the administration of a Compound of the Disclosure and a Second Therapeutic Agent to a subject means that the Compound of the Disclosure and the Second Therapeutic Agent can be administered to the subject together, e.g., as part of a single pharmaceutical composition or formulation, or separately, e.g., as part of two or more separate pharmaceutical compositions or formulations. The phrase "in combination" as used in connection with the administration of a Compound of the Disclosure and a Second Therapeutic Agent to a subject is thus intended to embrace administration of a Compound of the Disclosure and a Second Therapeutic Agent in a sequential manner, wherein the Compound of the Disclosure and the Second Therapeutic Agent are administered to the subject at a different time, as well as administration concurrently, or in a substantially simultaneous manner. Simultaneous administration can be accomplished, for example, by administering to the subject a single capsule having a fixed ratio of each of the Compound of the Disclosure and the Second Therapeutic Agent or in multiple, single capsules for each of the Compound of the Disclosure and the Second Therapeutic Agent. Sequential or substantially simultaneous administration of the Compound of the Disclosure and the Second Therapeutic Agent agent can be accomplished by any appropriate route including, but not limited to, oral routes, intravenous routes, intramuscular routes, and direct absorption through mucous membrane tissues. The Compound of the Disclosure and the Second Therapeutic Agent can be administered by the same route or by different routes. For example, the Second Therapeutic Agent of the combination may be administered by intravenous injection while the Compound of the Disclosure of the combination may be administered orally. Alternatively, for example, both the Compound of the Disclosure and the Second Therapeutic Agent may be administered orally or both the Compound of the Disclosure and the Second Therapeutic Agent may be administered by intravenous injection. The Compound of the Disclosure and the Second Therapeutic Agent may also be administered in alternation. In one embodiment, the Compound of the Disclosure and the Second Therapeutic Agent are administered to a subject separately, e.g., as part of two or

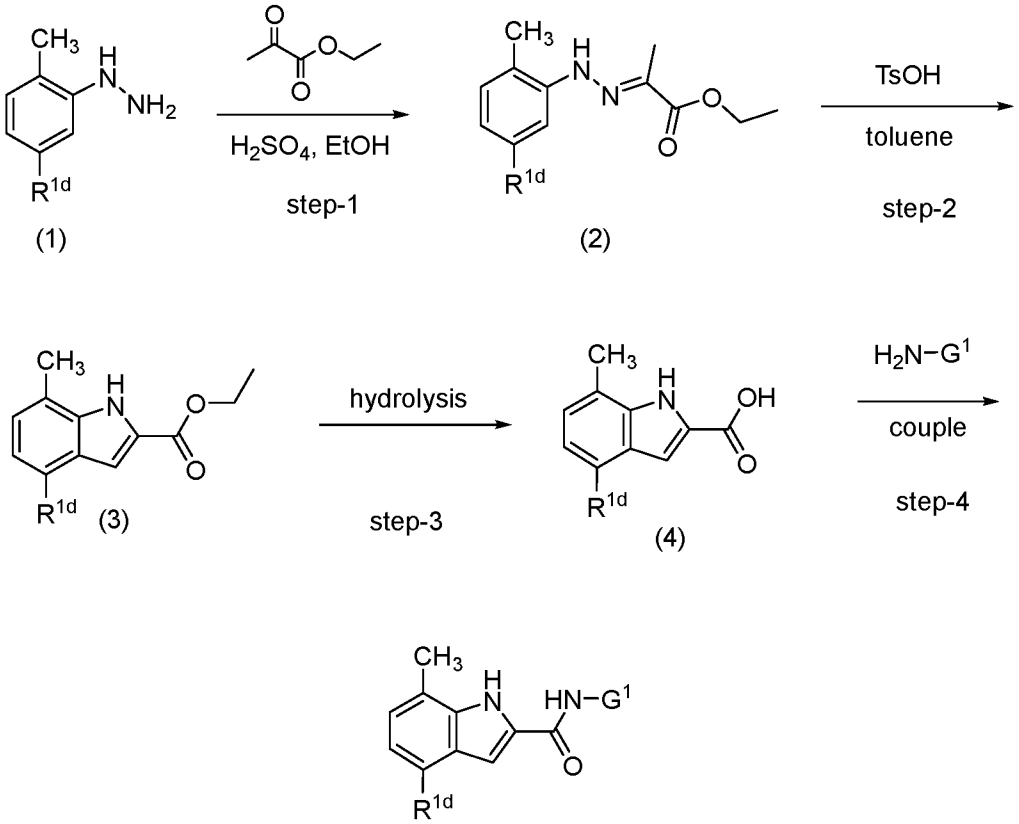
more separate pharmaceutical compositions or formulations. The same principles apply when a Compound of the Disclosure, a Second Therapeutic Agent, and a Third Therapeutic Agent are administered in combination to a subject. For example, the phrase in combination as used in connection with the administration of a Compound of the Disclosure, a Second Therapeutic Agent, and a Third Therapeutic Agent to a subject is intended to embrace administration of a Compound of the Disclosure, a Second Therapeutic Agent, and a Third Therapeutic agent in a sequential manner, wherein the Compound of the Disclosure, Second Therapeutic Agent, and Third Therapeutic Agent are administered to the subject at different times, as well as administration concurrently, or in a substantially simultaneous manner. In one embodiment, the Compound of the Disclosure, the Second Therapeutic Agent, and the Third Therapeutic Agent are each administered to a subject separately, e.g., as part of three or more separate pharmaceutical compositions or formulations.

[0935] General Synthesis of Compounds

[0936] Compounds of the Disclosure are prepared using methods disclosed in WO 2020/037079, or by the illustrative methods shown in the General Schemes below. In the General Schemes, R^{1d}, R^{2b}, R^{2d}, R^{2e}, A^1, A^2, R^{11a}, R^{14a}, R^{14b}, R^{19}, R^{20}, G, Z^4, and q are as defined in connection with Formulae **II**, **III**, **IV**, **V**, or **VI**, unless otherwise indicated. In any of the General Schemes, suitable protecting groups can be employed in the synthesis, for example, when Z is (amino)alkyl or any other group that may group that may require protection, or when R^8 is amino, (amino)alkyl, or any other group that may require protection. (See, Wuts, P. G. M.; Greene, T. W., "Greene's Protective Groups in Organic Synthesis", 4th Ed., J. Wiley & Sons, NY, 2007) unless otherwise indicated.

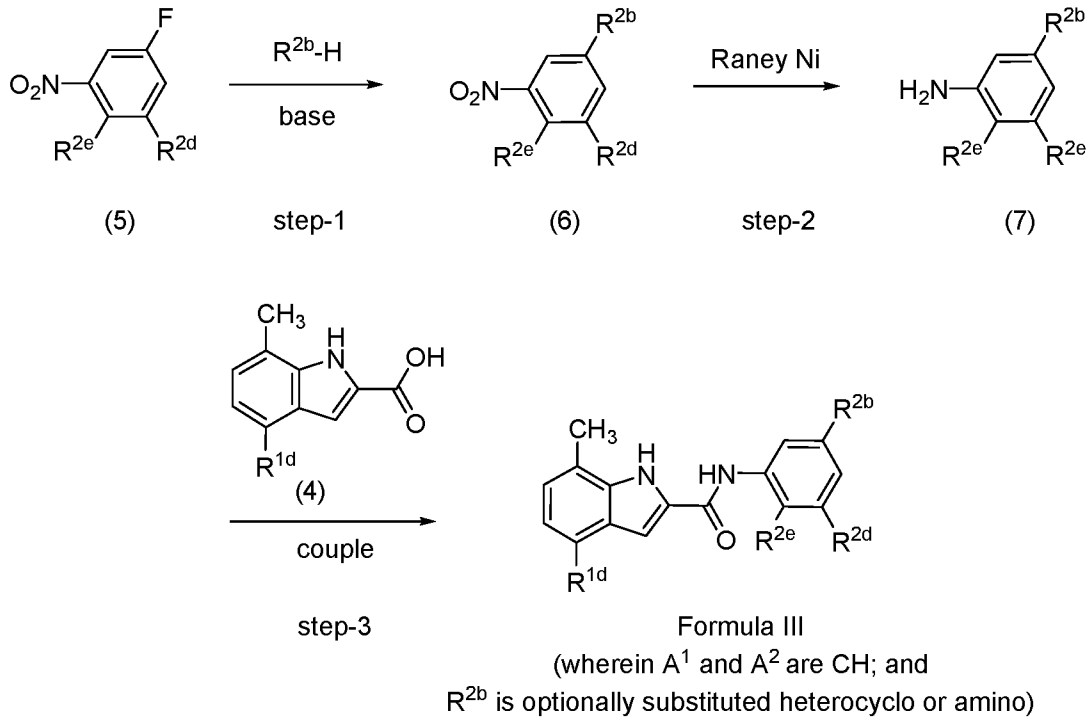
[0937] In General Scheme 1, the aryl hydrazine of Formula (1) is reacted with ethyl 2-oxopropanoate to give a compound of Formula (2). In step 2, the compound of Formula (2) is converted to the indole of Formula (3) under acidic conditions. In step 3, the compound of Formula (3) is hydrolyzed to give the indole-2-carboxylic acid of Formula (4). In step 4, a compound of Formula (4) is reacted with G^1NH_2 under standard coupling conditions to give a compound of Formula **II**.

General Scheme 1



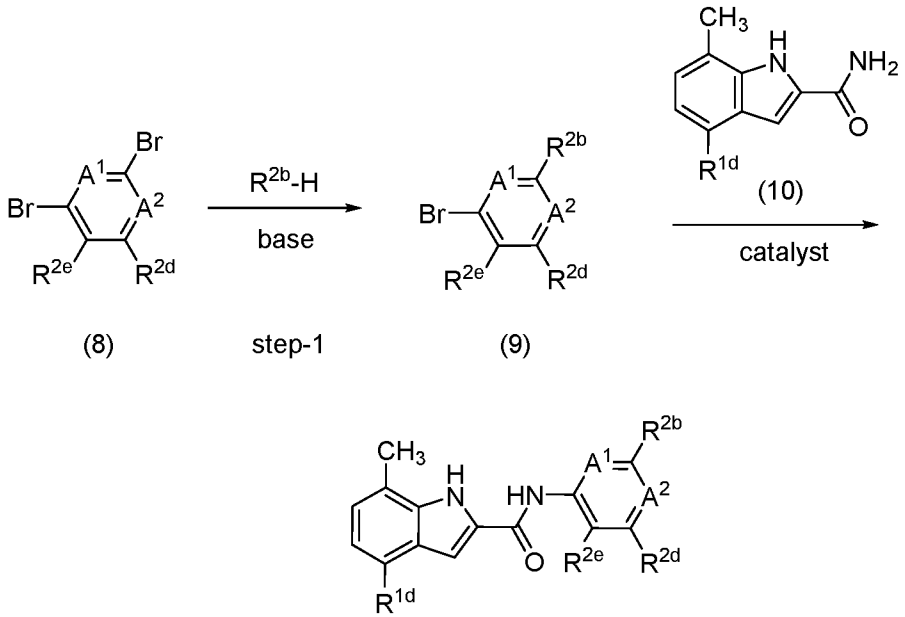
[0938] In General Scheme 2, a compound of Formula (5) is reacted with R^{2b}-H wherein R^{2b} is a heterocyclo, e.g., R^{2b}-H is piperidine, or an amine, e.g., R^{2b}-H is dimethyl amine, to give a compound of Formula (6). The nitro group of the compound of Formula (6) is reduced to give a compound of Formula (7). In step 3, the compound of Formula (7) is reacted with a compound of Formula (4), *see* General Scheme 1, under standard coupling conditions to give a compound of Formula **III**, wherein A^1 and A^2 are CH and R^{2b} is an optionally substituted heterocyclo or an amino group.

General Scheme 2



[0939] In General Scheme 3, a compound of Formula (8) is reacted with R^{2b}-H wherein R^{2b} is a heterocyclo, e.g., R^{2b}-H is piperidine, or an amine, e.g., R^{2b}-H is dimethyl amine, to give a compound of Formula (9). In step 2, the compound of Formula (9) is reacted with a compound of Formula (10) to give a compound of Formula **III**, wherein A^1 and/or A^2 are N and R^{2b} is an optionally substituted heterocyclo or an amino group.

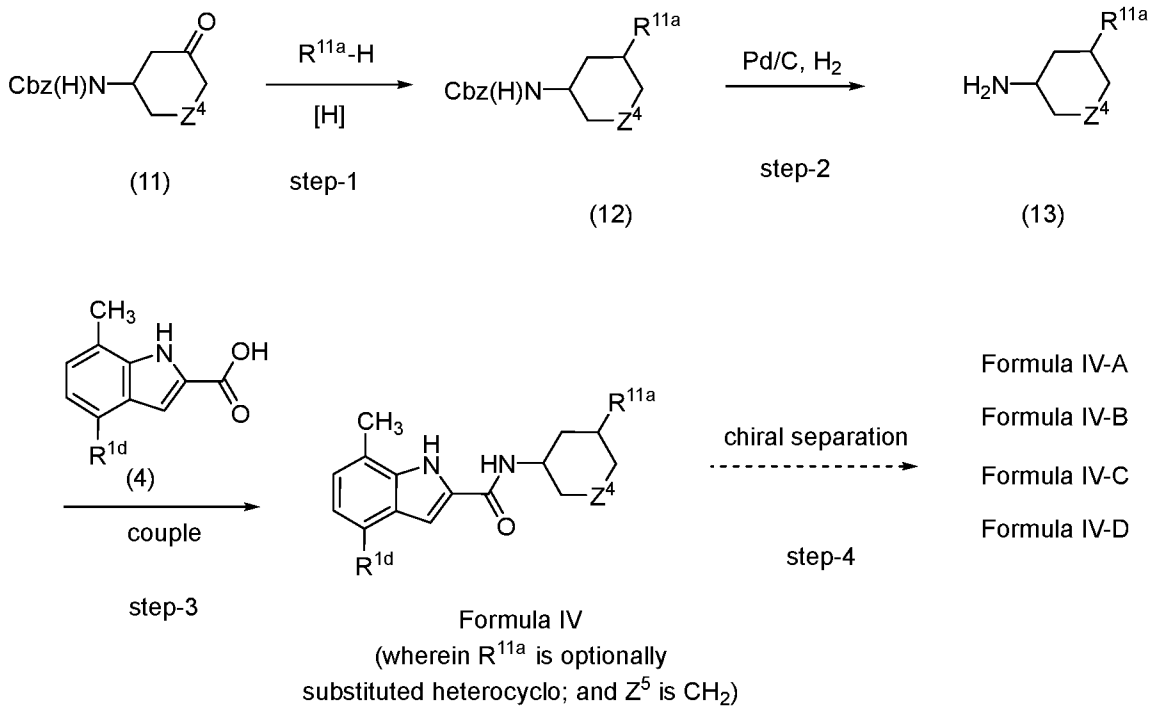
General Scheme 3



Formula III
(wherein A^1 and/or A^2 are N; and
R^{2b} is optionally substituted heterocyclo or amino)

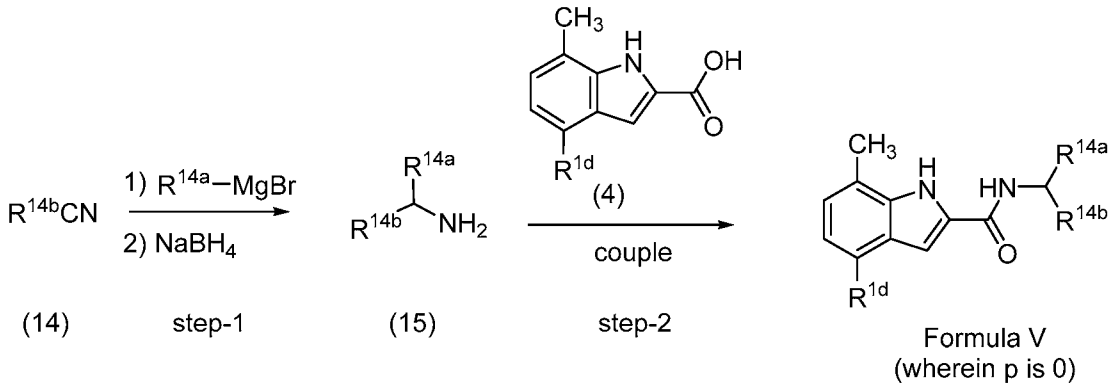
[0940] In General Scheme 4, a compound of Formula (11) is reacted with R^{11a}-H, wherein R^{11a} is a heterocyclo, e.g., R^{11a}-H is piperidine, to give a compound of Formula (12). In step 2, the Cbz group is removed to give a compound of Formula (13). The compound of Formula (13) is coupled with a compound of Formula (4) to give a compound of Formula IV, wherein R^{11a} is optionally substituted heterocyclo and Z^5 is $-CH_2-$.

General Scheme 4



[0941] In step 1 of General Scheme 5, a nitrile of Formula (14) is reacted with a Grignard reagent (R^{14a}-MgBr) and the resulting product is reduced to give a compound of Formula (15). The compound of Formula (15) is coupled with a compound of Formula (4) to give a compound of Formula V, wherein p is 0.

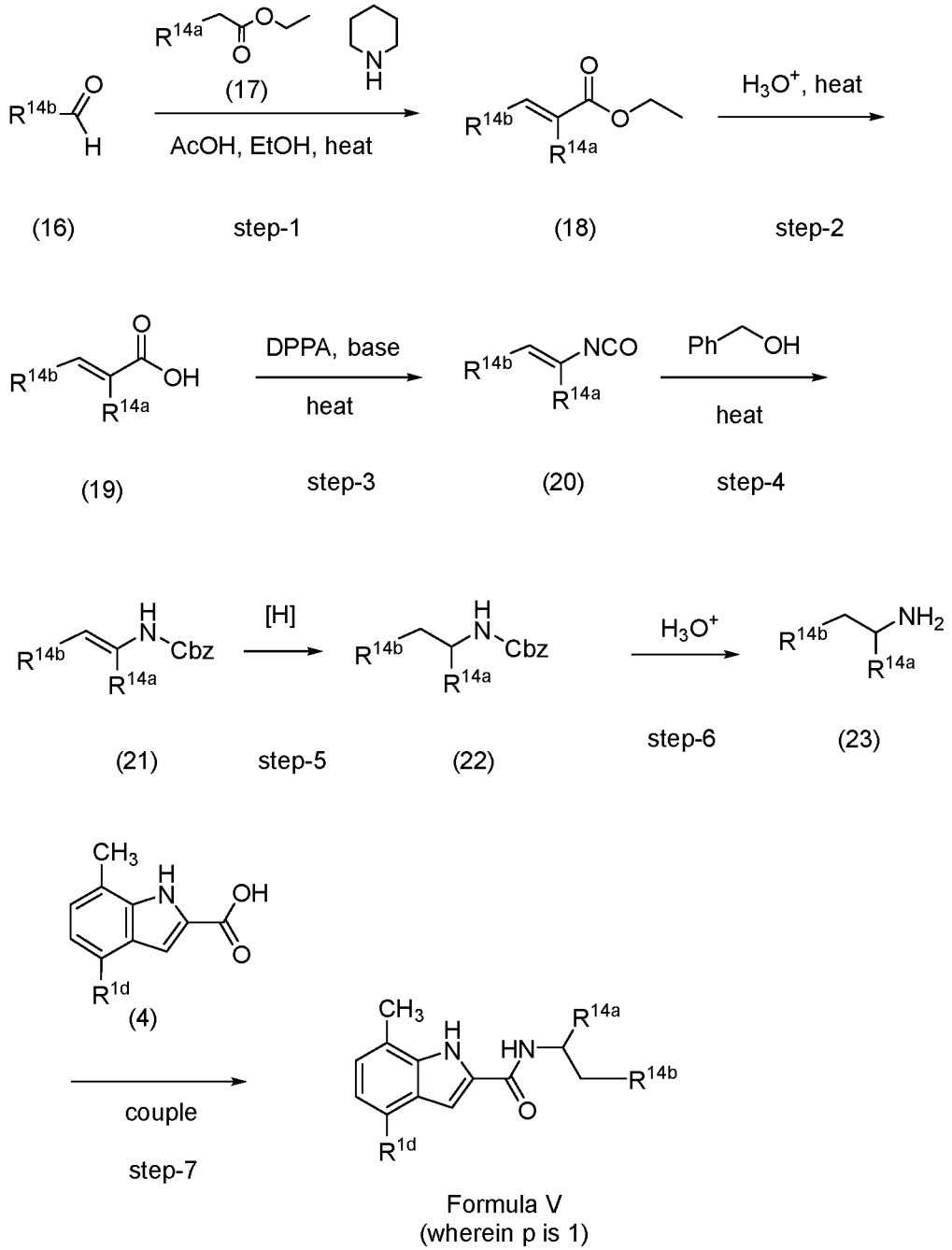
General Scheme 5



[0942] In General Scheme 6, an aldehyde of Formula (16) is reacted with an ester of Formula (17) to give a compound of Formula (18). In step 2, the compound of Formula (18) hydrolyzed to give a compound of Formula (19). In step 3, the compound of Formula (19) is converted to the isocyanate of Formula (20). The compound of Formula (20) is reacted with benzyl alcohol to give a compound of Formula (21). Hydrogenation of a compound of Formula (21) and removal of the Cbz groups gives an

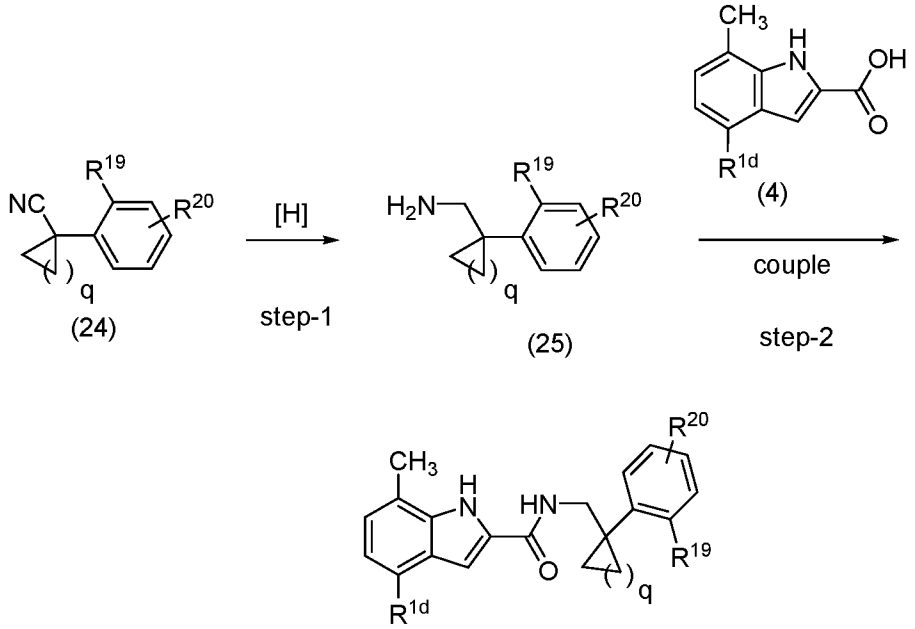
amine of Formula (23). Coupling a compound of Formula (23) with a compound of Formula (4) gives a compound of Formula V, wherein p is 1.

General Scheme 6



[0943] In General Scheme 7, the nitrile of Formula (24) is reduced to give an amine of Formula (25). The compound of Formula (25) is coupled with a compound of Formula (4) to give a compound of Formula VI.

General Scheme 7



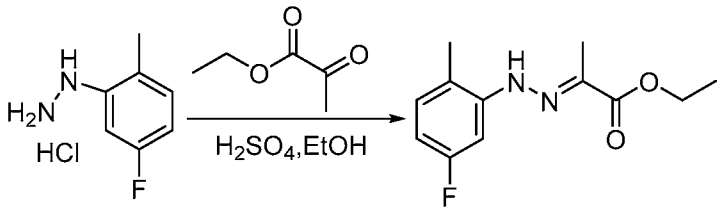
Formula VI

EXAMPLES

EXAMPLE 1

Synthesis of N-((1R,3S)-3-(4-acetylpiperazin-1-yl)cyclohexyl)-4-fluoro-7-methyl-1H-indole-2-carboxamide (Cpd. No. 15)

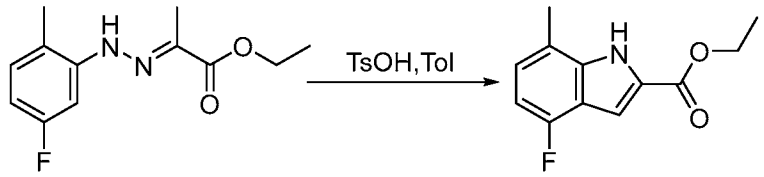
[0944] Step 1. Synthesis of ethyl (2E)-2-[2-(5-fluoro-2-methylphenyl)hydrazin-1-ylidene]propanoate



[0945] Into a 1000-mL round-bottom flask, was placed a solution of (5-fluoro-2-methylphenyl)hydrazine hydrochloride (100 g, 572.73 mmol, 1.00 equiv) in ethanol (400 mL), ethyl 2-oxopropanoate (66 g, 1.20 equiv), sulfuric acid (10 mL). The resulting solution was stirred for 2 h at 25 °C. The reaction progress was monitored by LCMS. The resulting mixture was concentrated under vacuum. The solids were collected by filtration. This resulted in 120 g (yield = 88%) of ethyl (2E)-2-[2-(5-fluoro-2-methylphenyl) hydrazin-1-ylidene]propanoate as a yellow solid. LCMS (Method A: ESI): RT = 1.399

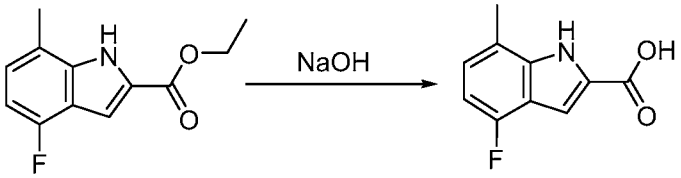
min, *m/z* = 239.0 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (d, *J* = 2.0 Hz, 1H), 7.15 (m, 2H), 6.62 (m, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 2.12 (d, *J* = 9.3 Hz, 6H), 1.29 (t, *J* = 7.1 Hz, 3H) ppm.

[0946] Step 2. Synthesis of ethyl 4-fluoro-7-methyl-1H-indole-2-carboxylate



[0947] Into a 1000-mL round-bottom flask, was placed a solution of ethyl (2E)-2-[2-(5-fluoro-2-methylphenyl)hydrazin-1-ylidene]propanoate (40 g, 167.89 mmol, 1.00 equiv) in Toluene (400 mL), 4-methylbenzene-1-sulfonic acid (50 g, 290.36 mmol, 1.70 equiv). The resulting solution was stirred for 18 h at 100 °C. The reaction progress was monitored by LCMS. The resulting solution was concentrated under vacuum, and the residue was dissolved by 100 ml of ethyl acetate. The resulting mixture was washed with 3x200 mL of saturated aqueous $NaHCO_3$. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:5). The resulting mixture was concentrated under vacuum. The solid was purified by recrystalization from ethanol. This resulted in 9.0 g (yield = 24%) of ethyl 4-fluoro-7-methyl-1H-indole-2-carboxylate as a yellow solid. LCMS (Method A, ESI): RT = 1.354 min,: *m/z* = 222.0 $[M+H]^+$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (s, 1H), 7.17 (d, *J* = 2.1 Hz, 1H), 7.00 (m, 1H), 6.77 (m, 7.8 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.49 (d, *J* = 1.0 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H) ppm.

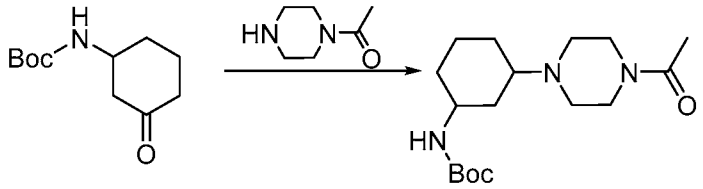
[0948] Step 3. Synthesis of 4-fluoro-7-methyl-1H-indole-2-carboxylic acid



[0949] Into a 500-mL round-bottom flask, was placed a solution of ethyl 4-fluoro-7-methyl-1H-indole-2-carboxylate (9.1 g, 41.13 mmol, 1.00 equiv) in tetrahydrofuran (150 mL), sodium hydroxide (8 g, 200.00 mmol, 5.00 equiv), water (50 mL), methanol (2 mL). The resulting solution was stirred for 6 h at 25 °C. The resulting mixture was concentrated under vacuum. The residue was diluted with water 50 ml, then adjusted to pH 5 with hydrogen chloride (3.0 mol/L). The resulting solution was extracted with 3x50

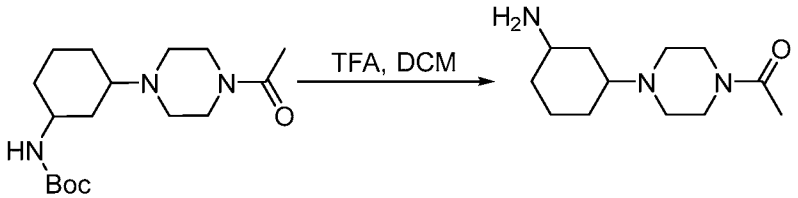
mL of ethyl acetate. The solid was collected by filtration. This resulted in 8.0 (yield = 81%) g of 4-fluoro-7-methyl-1H-indole-2-carboxylic acid as a brown solid. LCMS (Method C, ESI): RT = 0.989 min, *m/z* = 192.0 $[M-H]^+$. ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.10 (s, 1H), 11.94 (s, 1H), 7.09 (d, *J* = 2.1 Hz, 1H), 6.96 (m, 1H), 6.73 (m, 1H), 2.46 (d, *J* = 1.1 Hz, 3H) ppm.

[0950] Step 4. Synthesis of tert-butyl N-[3-(4-acetylpiperazin-1-yl)cyclohexyl]carbamate



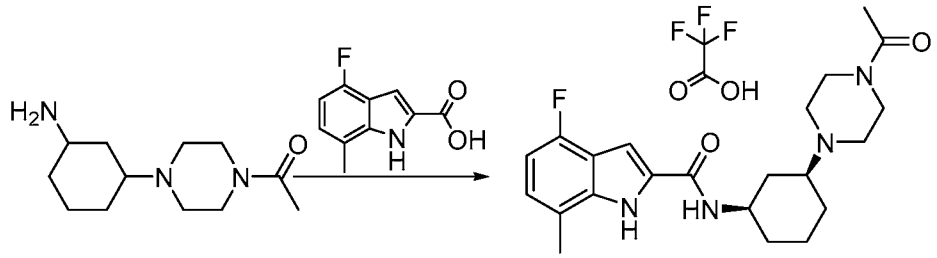
[0951] Into a 100-mL round-bottom flask, was placed tert-butyl N-(3-oxocyclohexyl)carbamate (800 mg, 3.75 mmol, 1.00 equiv), 1-(piperazin-1-yl)ethan-1-one (800 mg, 6.24 mmol, 1.66 equiv), methanol (10 mL), Pd/C (0.2 g), and to the above mixture, hydrogen was introduced. The resulting solution was stirred for 2 h at 25 °C. The reaction progress was monitored by LCMS. The solids were filtered out. The resulting mixture was concentrated under vacuum. The crude product (900 mg) was purified by Flash-Prep-HPLC with the following conditions: Column, C18 silica gel; mobile phase ; Detector, UV 254/220 nm. This resulted in 700 mg (yield = 57%) of tert butyl N-[3-(4-acetylpiperazin-1-yl)cyclohexyl]carbamate as colorless oil. LCMS (Method A, ESI): RT = 1.361 min, m/z = 325.9 $[M+H]^+$.

[0952] Step 5. Synthesis of 1-[4-(3-aminocyclohexyl)piperazin-1-yl]ethan-1-one



[0953] Into a 100-mL round-bottom flask, was placed tert-butyl N-[3-(4-acetylpiperazin-1-yl)cyclohexyl]carbamate (700 mg, 2.15 mmol, 1.00 equiv), dichloromethane (3 mL), trifluoroacetic acid (2 mL) was added by dropwise. The resulting solution was stirred for 2 h at 25 °C. The reaction progress was monitored by LCMS. The resulting mixture was concentrated under vacuum. This resulted in 700 mg of 1-[4-(3-aminocyclohexyl)piperazin-1-yl]ethan-1-one as a brown oil. LCMS (Method A, ES): RT = 0.647 min, m/z = 225.95 $[M+H]^+$.

[0954] Step 6. Synthesis of N-[(1R,3S)-3-(4-acetylpiperazin-1-yl)cyclohexyl]-4-fluoro-7-methyl-1H-indole-2-carboxamide (as the TFA salt)



Cpd. No. 15

[0955] Into a 100-mL round-bottom flask, was placed 4-fluoro-7-methyl-1H-indole-2-carboxylic acid (100 mg, 0.52 mmol, 1.00 equiv), 1-[4-(3-aminocyclohexyl)piperazin-1-yl]ethan-1-one (110 mg, 0.49 mmol, 0.94 equiv), N,N-dimethylformamide (4 mL), DIEA (200 mg, 1.55 mmol, 2.99 equiv), HATU (260 mg, 0.68 mmol, 1.32 equiv) was added batchwise. The resulting solution was stirred for 2 h at 25 °C. The reaction progress was monitored by LCMS, and the reaction solution was quenched by 10 ml of water. The resulting solution was extracted with 3x15 ml of ethyl acetate and the organic layers combined and concentrated under vacuum. The residue was applied onto a silica gel column with ethyl acetate/petroleum ether (1:1). The crude product was purified by Chiral-Prep-HPLC with the following conditions: Column, (R,R)-WHELK-014.6*50 mm, 3.5 μm:1-78220-30056749; mobile phase, Hexane (0.1%DEA):EtOH = 85:15; Detector, UV 254 nm/220 nm. The product thus obtained was further purified by Prep-HPLC with the following conditions: Column, XBridge Prep Phenyl OBD Column, 5 μm, 19*150 mm; mobile phase, Water with 10 mmol TFA and MeCN (20.0% MeCN up to 30.0% in 10 min, up to 95.0% in 1 min, hold 95.0% in 1 min, down to 20.0% in 2 min); Detector, UV 254/220 nm. This resulted in 30.5 mg (yield = 11%) of N-[(1R,3S)-3-(4-acetylpiperazin-1-yl)cyclohexyl]-4-fluoro-7-methyl-1H-indole-2-carboxamide trifluoroacetic acid salt as a white solid. LCMS (Method B, ES): RT = 1.138 min, m/z = 401.0 $[M-TFA]^+$. ^{1}H NMR (300 MHz, Methanol-d4) δ 7.18 (s, 1H), 6.94 – 6.92 (m, 1H), 6.64 – 6.62 (m, 1H), 4.03 – 3.88 (m, 1H), 3.57 – 3.55 (m, 4H), 2.65 (t, J = 16.4 Hz, 5H), 2.48 (t, J = 1.0 Hz, 3H), 2.23 (d, J = 12.0 Hz, 1H), 2.09 (s, 3H), 1.93 (d, J = 12.2 Hz, 3H), 1.53 – 1.18 (m, 4H) ppm.

EXAMPLE 2

Combination Studies

[0956] Mantle cell lymphoma (MCL) and diffuse large B-cell lymphoma (DLBCL) cell line cultures in log-linear growth rate were treated with combinations of Cpd. No. 15 and combination partners according to a co-treatment model. Assay-ready plates were prepared by dispensing the compounds with the HP-D300 nanoliter dispenser (Tecan, Mannedorf, Switzerland) onto 384-well white opaque plates (CulturPlate-384, White Opaque 384-well Microplate, Sterile and Tissue Culture Treated) to achieve either 2-fold or 3-fold serial dilutions in a concentration range bracketed around the IC_{50} of Cpd. No. 15 and the combination partner. Concentrations were matrixed in an 8x9 array (8 concentrations of Cpd. No. 15 and 9 concentrations of its combination partner). Each combination was tested in quadruplicate wells. The final concentration of DMSO (vehicle) in the assay was 0.1% v/v. Fifty microliters of cell line suspension were directly dispensed to the assay-ready plates with an automated multichannel dispenser on to 384-well assay-ready plates. Assay plates were incubated for seven days unless otherwise indicated in a humidified atmosphere of 5% CO_2 at 37°C. Quantification of the effect of single agents or combinations on cell viability was performed through measurement of cellular adenosine triphosphate (ATP) using a CellTiter-Glo® (Promega, Madison, WI) Luminescent Cell Viability Assay. Luminescence was detected using a SpectraMax M5 microplate reader (Molecular Devices, Sunnyvale, CA). Concentration response plots were generated in GraphPad Prism version 7.0 for Windows, GraphPad Software, (La Jolla, California) and curves fitted to a four-parameter logistic model with variable slope. Percent of inhibition was calculated at each treatment concentration. Quantification of synergy was performed using the Loewe Additivity model and by calculating the Loewe Volume (VLoewe) with the CHALICE software (Horizon Discovery, Cambridge, UK) (Lehar 2007) (VLoewe > 1: synergy, between 1 and -1: additivity, and < -1: antagonistic; if neither of the agents or the combination reached 50 percent inhibition of proliferation, it is deemed as "No Effect." *See* Loewe, *Arzneimittelforschung 3(6)*:285-290 (1953) and Lehar *et al.*, *Mol Syst Biol 3*:80 (2007). The cell lines used in these studies were purchased from commercial suppliers. For example, NCI-H929, MM1.S, MINO, REC1, MAVER1, Z138, JEKO1, JVM2, and RPMI-8226 cell lines were purchased from the American Type Culture Collection (ATCC, Manassas VA); KMS-11, KMS34, and KMS-28-BM were purchased from the Japanese Collection of Research Bioresources

(JCRB, Osaka, Japan); and L-363 and GRANTA519 were purchased from Leibniz Institute DSMZ-German Collection of Microorganisms and Cell Cultures.

[0957] The results of these combinations are summarized in Table A (mantle cell lymphoma cell lines) and Tables B-F (diffuse large B-cell lymphoma cell lines).

EXAMPLE 3

[0958] Diffuse large B-cell lymphoma (DLBCL) cell line cultures were tested with Cpd. No. 15 and combination partners according to a pre-treatment model. Cell lines in log-linear growth rate were seeded first into flasks and pre-treated with 5 concentrations of Compound 15 or DMSO for 7 days. On day 7 assay-ready plates were prepared by dispensing the compounds with the HP-D300 nanoliter dispenser (Tecan, Mannedorf, Switzerland) onto 384-well white opaque plates (CulturPlate-384, White Opaque 384-well Microplate, Sterile and Tissue Culture Treated) to achieve either 2-fold or 3-fold serial dilutions in a concentration range bracketed around the IC_{50} of Cpd. No. 15 and the combination partner. Concentrations were matrixed in an 5x9 array (5 concentrations of Cpd. No. 15 and 9 concentrations of its combination partner). Each combination was tested in triplicate wells. The final concentration of DMSO (vehicle) in the assay was 0.1% v/v. Fifty microliters of cell line suspension were directly dispensed to the assay-ready plates with an automated multichannel dispenser on to 384-well assay-ready plates. Assay plates were incubated for seven days unless otherwise indicated in a humidified atmosphere of 5% CO_2 at 37°C. Quantification of the effect of single agents or combinations on cell viability was performed through measurement of cellular adenosine triphosphate (ATP) using a CellTiter-Glo® (Promega, Madison, WI) Luminescent Cell Viability Assay. Luminescence was detected using a SpectraMax M5 microplate reader (Molecular Devices, Sunnyvale, CA). Concentration response plots were generated in GraphPad Prism version 7.0 for Windows, GraphPad Software, (La Jolla, California) and curves fitted to a four-parameter logistic model with variable slope. Percent of inhibition was calculated at each treatment concentration. Quantification of synergy was performed using the Loewe Additivity model and by calculating the Loewe Volume (VLoewe) with the CHALICE software (Horizon Discovery, Cambridge, UK) (Lehar 2007) (VLoewe > 1: synergy, between 1 and -1: additivity, and < -1: antagonistic; if neither of the agents or the combination reached 50 percent inhibition of proliferation, it is deemed as "No Effect." *See* Loewe, *Arzneimittelforschung 3(6)*:285-290 (1953) and Lehar *et al.*, *Mol*

Syst Biol 3:80 (2007). The cell lines used in these studies were purchased from commercial suppliers. The results of these combinations are summarized in Table G.

Table A

Drug Class	Combination Partner	MINO Cat. No. CRL-3000	REC1 Cat. No. CRL-3004	MAVER1 Cat. No. CRL-3008	Z138 Cat. No. CRL-3001	JEKO1 Cat. No. CRL-3006	JVM2 Cat. No. CRL-3002	GRANTA519 Cat. No. ACC 342
BTKi	Ibrutinib	Synergy	Additivity	Synergy	No Effect	Synergy	Additivity	Additivity
	Acalabrutinib	Synergy	Additivity	Synergy	No Effect	Synergy	Additivity	Additivity
	Zanubrutinib	Synergy	Additivity	Synergy	No Effect	Synergy	Additivity	Additivity
Anti CD20 Mab	Rituximab	No Effect	Additivity	Synergy	No Effect	Synergy	Additivity	Additivity
Alkylating agent	Mafosfamide	Additivity	Additivity	Additivity	Additivity	Additivity	Additivity	Additivity
Topoisomerase II inhibitor	Doxorubicin	Additivity	Additivity	Additivity	Additivity	Additivity	Additivity	Additivity
Vinca alkaloid	Vincristine	Additivity	Synergy	Synergy	Additivity	Additivity	Additivity	Additivity
nucleoside anticancer agents	Cytarabine	Additivity	Additivity	Additivity	Additivity	Additivity	Additivity	Additivity
PI3Ki	Copanlisib	Additivity	Additivity	Synergy	Additivity	Additivity	Additivity	Additivity
CDK4/6	Palbociclib	Additivity	Additivity	Synergy	Additivity	Synergy	Additivity	Additivity

Table B

Drug Class	Combination Partner	KARPAS422 Cat. No. 06101702-1VL	WSUDLCL2 Cat. No. ACC 575	SUDHL6 Cat. No. CRL-2956	SUDHL10* Cat. No. ACC 576
Anti CD20 Mab	Rituximab	No Effect	not tested	Synergy	Additivity
Alkylating agent	Mafosfamide	Additivity	Additivity	Synergy	Additivity
Topoisomerase II inhibitor	Doxorubicin	Additivity	Additivity	Synergy	Additivity
	Etoposide	Additivity	Additivity	Additivity	Additivity
Vinca alkaloid	Vincristine	Synergy	Synergy	Additivity	Additivity
platinum-based drug	Oxaliplatin	Additivity	Synergy	not tested	Additivity
	Carboplatin	Additivity	not tested	not tested	Additivity
nucleoside anticancer agent	Gemcitabine	Additivity	Additivity	Additivity	Additivity
BTKi	Ibrutinib	No Effect	Additivity	Synergy	No Effect
	Acalabrutinib	No Effect	Additivity	Synergy	No Effect
	Zanubrutinib	No Effect	Additivity	Synergy	No Effect
CARM1i	EPZ-2302	Synergy	Synergy	Synergy	No Effect

* SUDHL10 :5-Day Cotreatment

Table C

Drug Class	Combination Partner	SUDHL4 Cat. No. ACC 495	RL** Cat. No. CRL-2261	DB Cat. No. CRL-2289	Pfeiffer Cat. No. CRL-2632
Anti CD20 Mab	Rituximab	not tested	not tested	No Effect	No Effect
Alkylating agent	Mafosfamide	Additivity	Synergy	Additivity	Additivity
Topoisomerase II inhibitor	Doxorubicin	Additivity	Additivity	Additivity	Additivity
	Etoposide	Additivity	Synergy	Additivity	Additivity
Vinca alkaloid	Vincristine	Additivity	Synergy	Additivity	Additivity
nucleoside anticancer agent	Gemcitabine	Additivity	Additivity	Additivity	Additivity
platinum-based drug	Carboplatin	not tested	not tested	Additivity	Additivity
	Oxaliplatin	not tested	not tested	Additivity	Additivity
BTKi	Ibrutinib	Synergy	Additivity	No Effect	No Effect
	Acalabrutinib	No Effect	No Effect	No Effect	No Effect
	Zanubrutinib	Synergy	No Effect	No Effect	No Effect
CARM1i	EPZ-2302	Synergy	Synergy	No Effect	No Effect

**RL :6-Day Cotreatment

Table D

Drug Class	Combination Partner	DOHH2 Cat. No. ICLC HTL99022	TOLEDO Cat. No. ACC 576	HT Cat. No. CRL-2631	SUDHL5 Cat. No. ACC 571
Anti CD20 Mab	Rituximab	Synergy	Additivity	Additivity	not tested
Alkylating agent	Mafosfamide	Additivity	Synergy	Additivity	Additivity
Topoisomerase II inhibitor	Doxorubicin	Additivity	Synergy	Additivity	Additivity
	Etoposide	Additivity	Synergy	Synergy	Additivity
Vinca alkaloid	Vincristine	Synergy	Synergy	Synergy	Synergy
nucleoside anticancer agent	Gemcitabine	Additivity	Additivity	Additivity	Additivity
platinum-based drug	Carboplatin	Additivity	Additivity	Additivity	Additivity
	Oxaliplatin	Additivity	Additivity	Additivity	Additivity
BTKi	Ibrutinib	Synergy	No Effect	No Effect	No Effect
	Acalabrutinib	No Effect	No Effect	No Effect	No Effect
	Zanubrutinib	Synergy	Additivity	No Effect	No Effect
CARM1i	EPZ-2302	Synergy	Synergy	Synergy	Additivity

Table E

Drug Class	Combination Partner	WSUNHL Cat. No. ACC 58	SUDHL8 Cat. No. CRL-2961	WILL2 Cat. No. ACC 652	SUDHL2 Cat. No. CRL-2260
Anti CD20 Mab	Rituximab	Additivity	Additivity	Additivity	No Effect
Alkylating agent	Mafosfamide	Synergy	Additivity	Additivity	Additivity
Topoisomerase II inhibitor	Doxorubicin	Additivity	Additivity	Additivity	Additivity
	Etoposide	Synergy	Synergy	Additivity	Additivity
Vinca alkaloid	Vincristine	Synergy	Synergy	Additivity	Additivity
nucleoside anticancer agent	Gemcitabine	Additivity	Additivity	Additivity	Additivity
platinum-based drug	Carboplatin	Synergy	Synergy	Additivity	Additivity
	Oxaliplatin	Synergy	Additivity	Additivity	Additivity
BTKi	Ibrutinib	Additivity	No Effect	Additivity	No Effect
	Acalabrutinib	No Effect	No Effect	Additivity	No Effect
	Zanubrutinib	Additivity	No Effect	Additivity	No Effect
CARM1i	EPZ-022302-9	Synergy	No Effect	Synergy	Synergy

Table F

Drug Class	Combination Partner	TMD8 Cat. No. M-097	Ri1 Cat. No. 96090512-1VL	WILL1 Cat. No. ACC 651
Anti CD20 Mab	Rituximab	No Effect	Additivity	No Effect
Alkylating agent	Mafosfamide	Additivity	Additivity	No Effect
Topoisomerase II inhibitor	Doxorubicin	Additivity	Synergy	Additivity
	Etoposide	Synergy	Synergy	Additivity
Vinca alkaloid	Vincristine	Additivity	Synergy	not tested
nucleoside anticancer agent	Gemcitabine	Additivity	Additivity	Additivity
platinum-based drug	Oxaliplatin	Synergy	Additivity	Additivity
	Carboplatin	Additivity	Additivity	Additivity
BTKi	Ibrutinib	Synergy	Synergy	No Effect
	Acalabrutinib	Synergy	Synergy	No Effect
	Zanubrutinib	Synergy	Synergy	No Effect
CARM1i	EPZ-022302-9	Synergy	Synergy	Synergy

Table G

Drug Class	Drug	Cell Lines				
		WILL2	SUDHL4	HT	Farage	OCILY7
		Cat. No. ACC 652	Cat. No. ACC 495	Cat. No. CRL-2631	Cat. No. CRL-2630	Cat. No. ACC 688
ATM inhibitor	AZD0156	No Effect	Synergy	Synergy	Synergy	Synergy
ATR inhibitor	AZD6738	No Effect	Synergy	Additivity	Synergy	Additivity
Chk1 inhibitor	AZD7762	Additivity	Synergy	Additivity	Synergy	Additivity
Wee1 inhibitor	AZD1775	Synergy	Synergy	Additivity	Synergy	Additivity
RAD51 inhibitor	B02	Additivity	Synergy	Additivity	Synergy	Additivity
PARP inhibitor	Olaparib	Synergy	Synergy	Synergy	Synergy	Additivity
PARP inhibitor	Niraparib	Synergy	Synergy	Synergy	Synergy	Additivity
Alkylating agent	Mafosfamide (C)	not tested	Additivity	Additivity	Additivity	no effect
Topoisomerase II inhibitor	Doxorubicin (H)	Synergy	Synergy	Synergy	Synergy	Additivity
Topoisomerase II inhibitor	Etoposide	Synergy	Synergy	Synergy	Synergy	Additivity
BTK inhibitor	Ibrutinib	not tested	Synergy	no effect	Synergy	not tested
PI3Kdelta inhibitor	Idelalisib	not tested	Synergy	Synergy	Synergy	Additivity
AKT inhibitor	MK2206	Synergy	Synergy	Synergy	Synergy	Synergy
platinum-based drug	Carboplatin	Synergy		Synergy	Additivity	Additivity
Vinca alkaloid	Vincristine (O)	Synergy	Synergy	Synergy	Synergy	Additivity
Antimetabolite	Gemcitabine	Additivity	Additivity	Additivity	Additivity	Additivity
BTK inhibitor	Acalabrutinib	No Effect	No Effect	No Effect	Synergy	No Effect
BTK inhibitor	Zanubrutinib	not tested	Synergy	Synergy	Synergy	Synergy
SYK inhibitor	Tamatinib	Additivity	Synergy	Additivity	Synergy	Additivity
MEK inhibitor	Trametinib	not tested	Synergy	Synergy	Synergy	Synergy

[0959] Having now fully described this invention, it will be understood by those of ordinary skill in the art that the same can be performed within a wide and equivalent range of conditions, formulations, and other parameters without affecting the scope of the invention or any embodiment thereof.

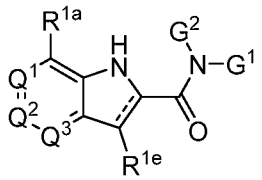
[0960] Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the invention being indicated by the following claims.

[0961] All patents, patent applications, e.g., WO 2020/037079, WO 2021/168313, and publications cited herein are fully incorporated by reference herein in their entirety.

What is Claimed Is:

1. A method of treating a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of:

(a) compound of Formula **I**:



I,

wherein:

R^{1a} is selected from the group consisting of halogen, alkyl, alkoxy, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

Q^1 is selected from the group consisting of -C(R^{1b})= and –N=;

Q^2 is selected from the group consisting of -C(R^{1c})= and –N=;

Q^3 is selected from the group consisting of -C(R^{1d})= and –N=;

provided that at least one of Q^1, Q^2, or Q^3 is -C(R^{1b})=, -C(R^{1c})=, or -C(R^{1d})=, respectively;

R^{1b}, R^{1c}, and R^{1d} are each independently selected from the group consisting of hydrogen, halogen, alkyl, alkenyl, (hydroxy)alkyl, and alkoxy;

R^{1e} is selected from the group consisting of hydrogen, halogen, alkyl, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

=== is a single or double bond;

G^1 is selected from the group consisting of: optionally substituted aryl; optionally substituted heteroaryl; optionally substituted heterocyclo; optionally substituted cycloalkyl; (aryl)alkyl; (heteroaryl)alkyl; (heterocyclo)alkyl; (amino)(aryl)alkyl; (heteroaryl)(aryl)alkyl; (heteroaryl)(heterocyclo)alkyl; (heteroaryl)(carboxamido)alkyl; (heteroaryl)(cycloalkyl)alkyl; (aryl)(alkoxycarbonyl)alkyl; (cycloalkyl)alkyl; (heteroaryl)(amino)alkyl; (cycloalkyl)(alkoxycarbonyl)alkyl; (heteroaryl)(alkoxycarbonyl)alkyl; (heterocyclo)(cycloalkyl)alkyl; (aryl)(cycloalkyl)alkyl; (aryl)(hydroxy)alkyl; (cycloalkyl)(hydroxy)alkyl; (hydroxy)alkyl; optionally substituted alkyl; (aryl)(haloalkyl)alkyl; (cycloalkyl)(haloalkyl)alkyl; (hydroxy)(haloalkyl)alkyl; and (alkoxycarbonyl)(haloalkyl)alkyl; and

G^2 is selected from the group consisting of hydrogen and alkyl; or

G^1 and G^2 taken together with the nitrogen atom to which they are attached form an optionally substituted heterocyclo,

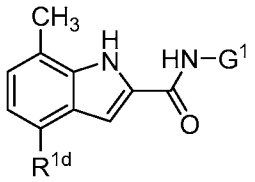
or a pharmaceutically acceptable salt or solvate thereof; and

(b) a Second Therapeutic Agent,

wherein:

the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof.

2. The method of claim 1, wherein the compound is a compound of Formula **II**:

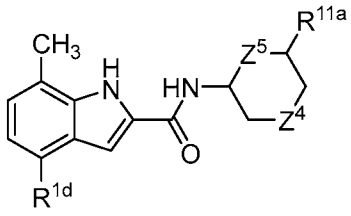


II,

or a pharmaceutically acceptable salt or solvate thereof.

3. The method of claims 1 or 2, wherein G^1 is selected from the group consisting of: optionally substituted C_6-C_{10} aryl; optionally substituted 5- to 9-membered heteroaryl; optionally substituted 3- to 10-membered heterocyclo; optionally substituted C_6-C_8 cycloalkyl; (5- to 9-membered heteroaryl)C_1-C_6 alkyl; (5- to 9-membered heteroaryl)(C_{6-10} aryl)C_1-C_4 alkyl; (5- to 9-membered heteroaryl heteroaryl)(C_3-C_6 cycloalkyl)C_1-C_4 alkyl; and (C_3-C_6 cycloalkyl)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

4. The method of claim 3, wherein the compound is a compound of of Formula **IV**:



IV,

wherein:

Z^4 is selected from the group consisting of -O-, -C(R^{28a})(R^{28b})-, and -N(R^{23})-; or Z^4 is absent;

Z^5 is selected from the group consisting of -CH_2- and -CH_2CH_2-;

R^{11a} is selected from the group consisting of optionally substituted alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, and -N(R^{12b})C(=O)R^{13c};

R^{12b} is selected from the group consisting of hydrogen, alkyl, cycloalkyl, and heterocyclo, (C_1-C_4 alkoxy)C_1-C_4 alkyl, and (hydroxy)C_1-C_4 alkyl; and

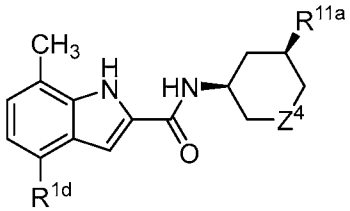
R^{13c} is selected from the group consisting of alkyl, haloalkyl, alkoxy, (alkoxy)alkyl, (hydroxy)alkyl, (cyano)alkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted cycloalkyl, and optionally substituted heterocycle, amino, (amino)alkyl, (C_3-C_6 cycloalkyl)oxy, and (4- to 8-membered heterocyclo)oxy;

R^{23} is selected from the group consisting of hydrogen and C_1-C_4 alkyl; and

R^{28a} and R^{28b} are independently selected from the group consisting of hydrogen, alkyl, and halo;,

or a pharmaceutically acceptable salt or solvate thereof.

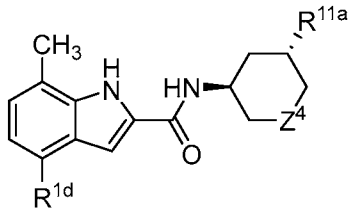
5. The method of claim 4, wherein the compound is a compound of Formula **IV-A**:



IV-A,

or a pharmaceutically acceptable salt or solvate thereof.

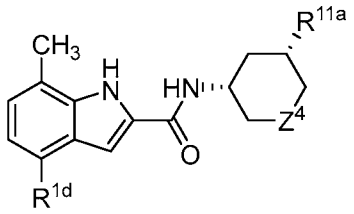
6. The method of claim 4, wherein the compound is a compound of Formula **IV-B**:



IV-B,

or a pharmaceutically acceptable salt or solvate thereof.

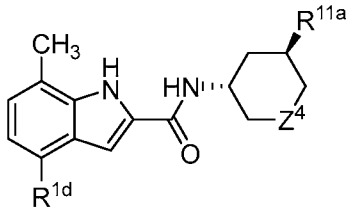
7. The method of claim 4, wherein the compound is a compound of Formula **IV-C**:



IV-C,

or a pharmaceutically acceptable salt or solvate thereof.

8. The method of claim 4, wherein the compound is a compound of Formula **IV-D**:



IV-D,

or a pharmaceutically acceptable salt or solvate thereof.

9. The method of any one of claims 4-8, wherein:

R^{11a} is selected from the group consisting of:

(A) unsubstituted 4- to 14-membered heterocyclo;

(B) substituted 4- to 14-membered heterocyclo having one, two or three substituents independently selected from the group consisting of:

(i) $-N(R^{12a})C(=O)R^{13a}$; (ii) $-C(=O)R^{13b}$; (iii) C_1-C_4 alkyl; (iv) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (v) (hydroxy)C_1-C_4 alkyl; (vi) C_1-C_4 haloalkyl; (vii) amino; (vii) hydroxy; (viii) $-N(R^{12a})S(=O)_2R^{24}$; (ix) $-S(=O)_2R^{24}$; (x) unsubstituted C_3-C_6 cycloalkyl; (xi) substituted

C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; (xii) unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (xiii) -C(=N-R^{60})R^{61}; and(xiv) -C(=C-NO_2)R^{64};

(C) unsubstituted 5- to 10-membered heteroaryl;

(D) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo and C_1-C_4 alkyl;

(E) C_1-C_6 alkyl; and

(F) -N(R^{12b})C(=O)R^{13c};

R^{12a} and R^{12b} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl, and (hydroxy)C_1-C_4 alkyl;

R^{13a}, R^{13b}, and R^{13c} are each independently selected from the group consisting of (A) C_1-C_6 alkyl; (B) C_1-C_6 haloalkyl; (C) unsubstituted C_3-C_6 cycloalkyl; (D) C_1-C_6 alkoxy; (E) (C_1-C_4 alkoxy)C_1-C_4 alkyl; (F) (hydroxy)C_1-C_4 alkyl; (G) (cyano)alkyl; (H) unsubstituted C_6-C_{10} aryl; (I) substituted C_6-C_{10} aryl, having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (J) unsubstituted 5- or 6-membered heteroaryl; (K) substituted 5- or 6-membered heteroaryl having one, two, three, or four substituents independently selected from the group consisting of halo, amino, hydroxy, and C_1-C_4 alkyl; (L) unsubstituted 4- to 14-membered heterocyclo; (M) substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (N) amino; (O) (amino)alkyl; (P) (C_3-C_6 cycloalkyl)oxy; and (Q) (4- to 8-membered heterocyclo)oxy; and

R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl;

R^{60} is selected from the group consisting of cyano, nitro, hydroxy, C_1-C_6 alkoxy, -C(=O)R^{62}, and -S(=O)$_2$$R^{62}$;

R^{61} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and -$NR^{63a}R^{63b}$;

R^{62} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and -$NR^{63a}R^{63b}$;

R^{63a} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R^{63b} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl; or

R^{63a} and R^{63b} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo;

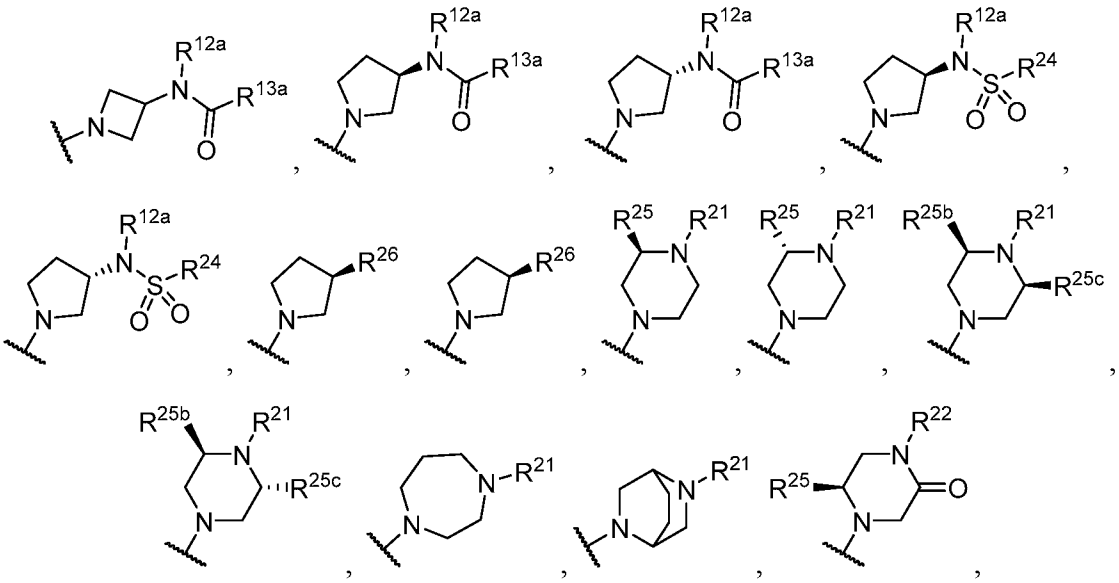
R^{64} is selected from the group consisting of C_1-C_6 alkyl, C_3-C_6 cycloalkyl, and $-NR^{63c}R^{63d}$;

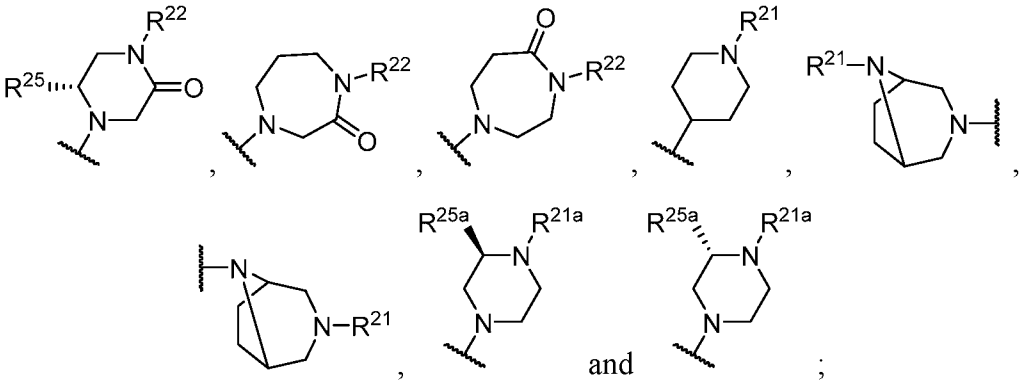
R^{63c} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R^{63d} is selected from the group consisting of hydrogen, C_1-C_6 alkyl, and C_3-C_6 cycloalkyl; or

R^{63c} and R^{63d} taken together with the nitrogen atom to which they are attached form a 4- to 6-membered optionally substituted heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

10. The method of claim 9, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:





R^{12a} is selected from the group consisting of hydrogen, C_1-C_3 alkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl; and (hydroxy)C_1-C_4 alkyl;

R^{13a} is selected from the group consisting of C_1-C_4 alkyl; amino; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (hydroxy)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl;

R^{13b} is selected from the group consisting of C_1-C_4 alkyl; amino; C_1-C_4 haloalkyl; C_1-C_4 alkoxy; (hydroxy)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (amino)alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy;

R^{21} is selected from the group consisting of hydrogen, $-C(=O)R^{13b}$, C_1-C_4 alkyl, C_1-C_4 haloalkyl, unsubstituted 4- to 14-membered heterocyclo, and $-S(=O)_2R^{24}$;

R^{22} is C_1-C_4 alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl;

R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl;

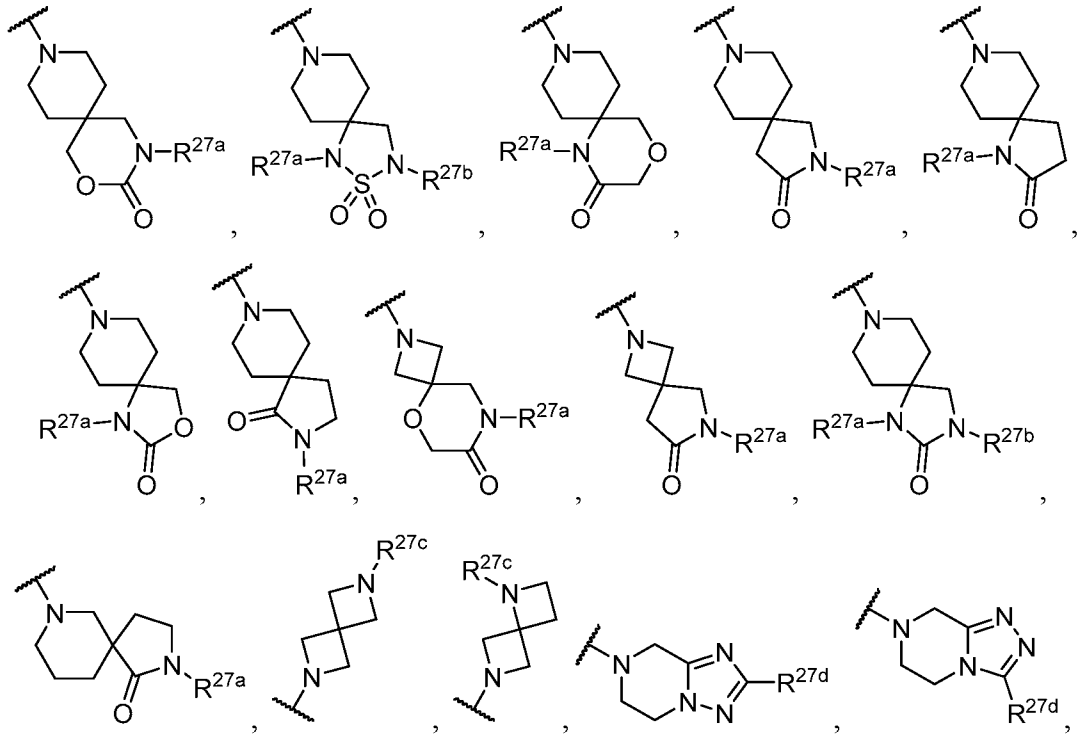
R^{25} is selected from the group consisting of hydrogen, C_1-C_4 alkyl, and C_1-C_4 haloalkyl;

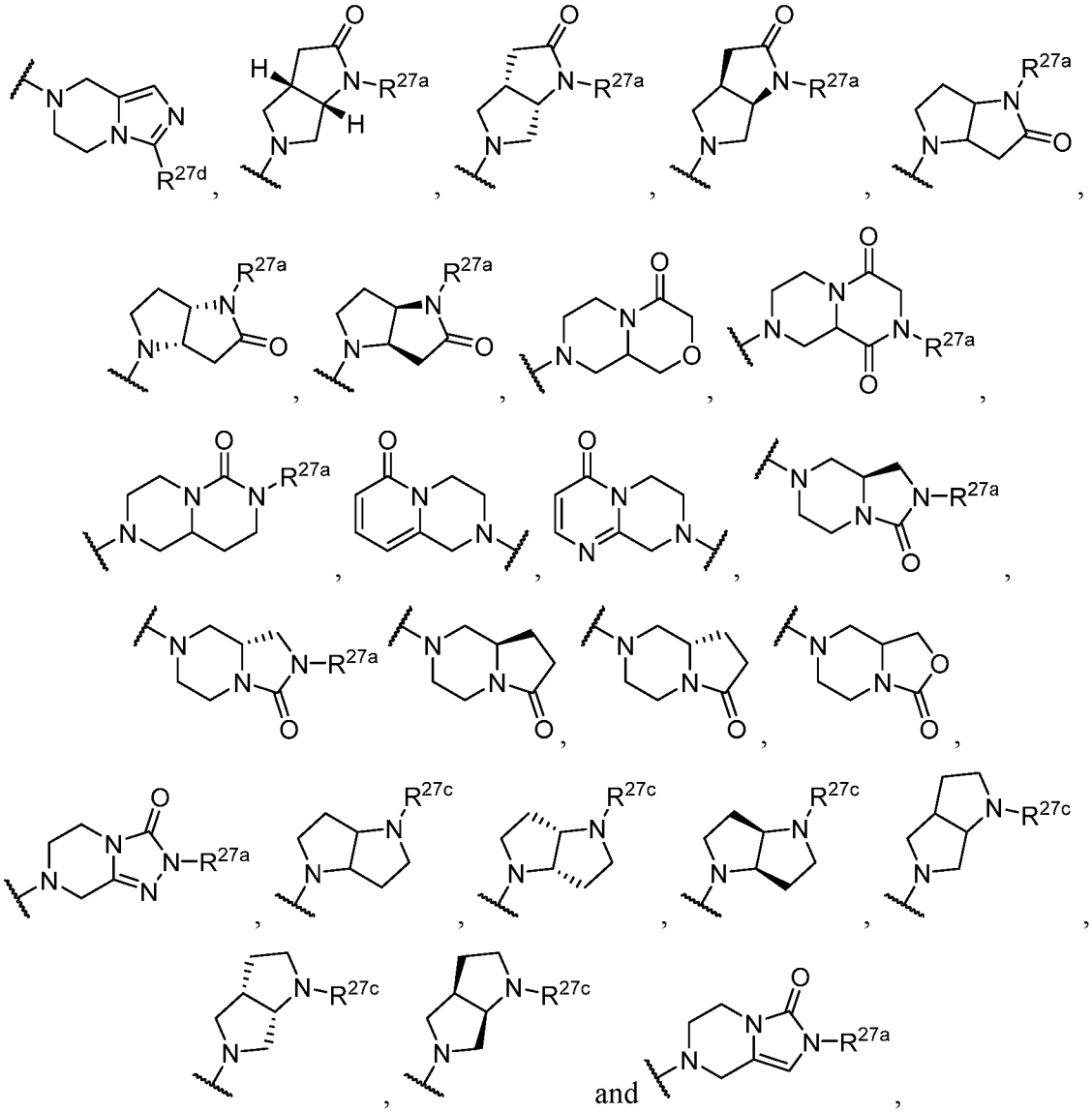
R^{25b} and R^{25c} are independently selected from the group consisting of C_1-C_4 alkyl and C_1-C_4 haloalkyl;

R^{26} is selected from the group consisting of unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; and

R^{21a} and R^{25a} taken together with the atoms to which they are attached form an optionally substituted 4- to 8-membered heterocyclo, or a pharmaceutically acceptable salt or solvate thereof.

11. The method of claim 9, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:





R^{27a} and R^{27b} are each independently selected from the group consisting of hydrogen, C_1-C_4 alkyl, C_1-C_4 haloalkyl, (C_1-C_4 alkoxy)C_1-C_4 alkyl; and (hydroxy)C_1-C_4 alkyl;

R^{27c} is selected from the group consisting of hydrogen; -C(=O)R^{13b}; C_1-C_4 alkyl; C_1-C_4 haloalkyl; unsubstituted 4- to 14-membered heterocyclo; and substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; and -S(=O)$_2R^{24}$;

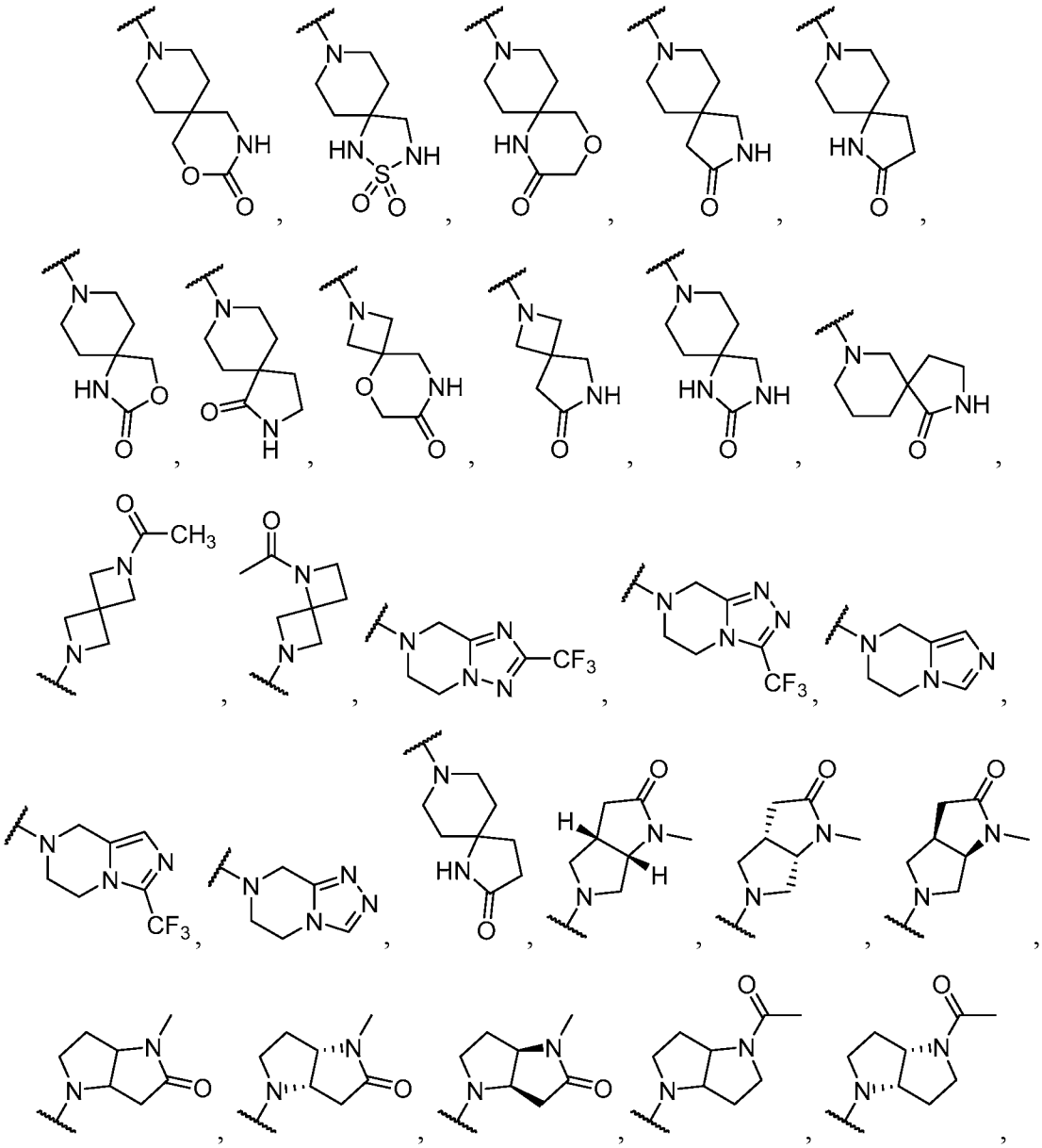
R^{27d} is selected from the group consisting of hydrogen; C_1-C_4 alkyl; and C_1-C_4 haloalkyl;

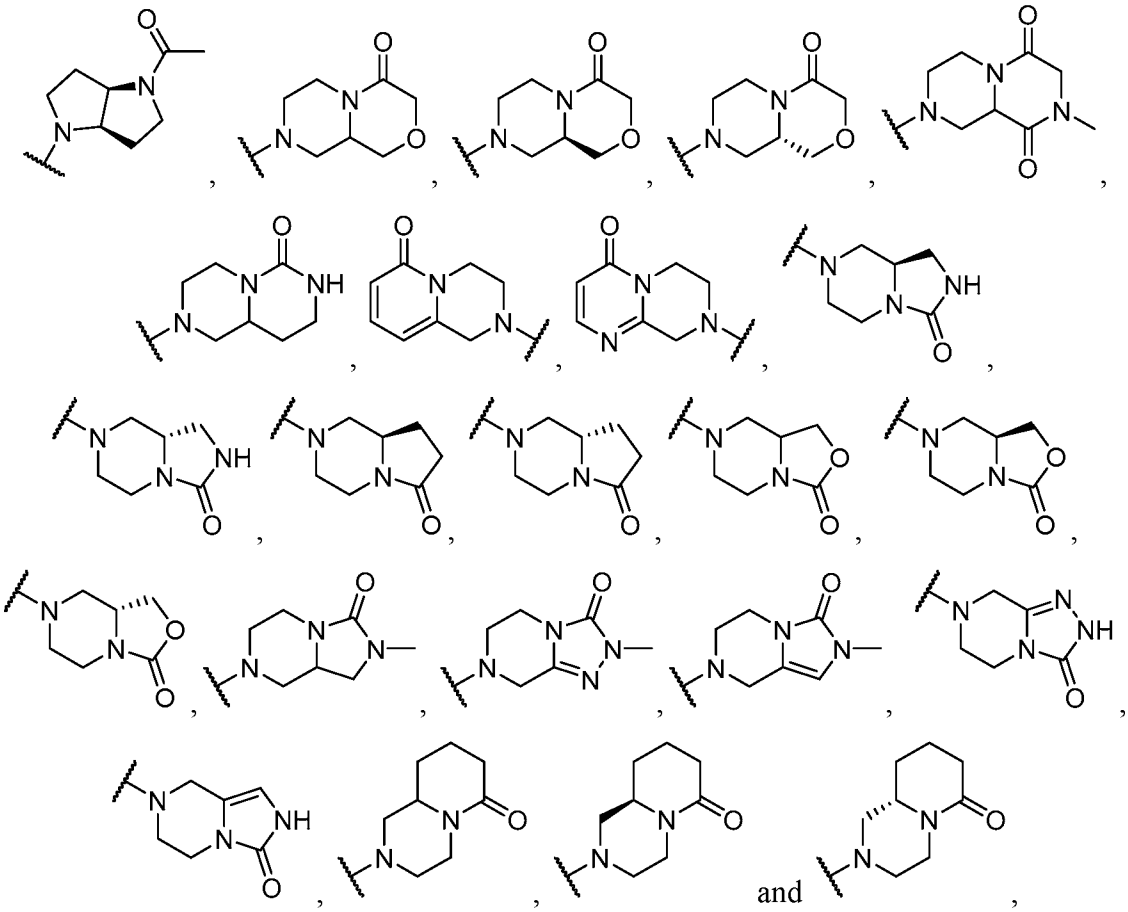
R^{13b} is selected from the group consisting of C_1-C_4 alkyl; aminoC_1-C_4 haloalkyl; C_1-C_4 alkoxy; (hydroxy)C_1-C_4 alkyl; (C_1-C_4 alkoxy)C_1-C_4 alkyl; (amino)alkyl; unsubstituted C_3-C_6 cycloalkyl; substituted C_3-C_6 cycloalkyl having one or two

substituents independently selected from the group consisting of halo, hydroxy, C_1-C_4 alkyl, amino, and (amino)C_1-C_4 alkyl; unsubstituted 4- to 14-membered heterocyclo; substituted 4- to 14-membered heterocyclo having one or two substituents independently selected from the group consisting of amino, hydroxy, and C_1-C_4 alkyl; (C_3-C_6 cycloalkyl)oxy; and (4- to 8-membered heterocyclo)oxy; and

R^{24} is selected from the group consisting of C_1-C_4 alkyl and (hydroxy)C_1-C_4 alkyl, or a pharmaceutically acceptable salt or solvate thereof.

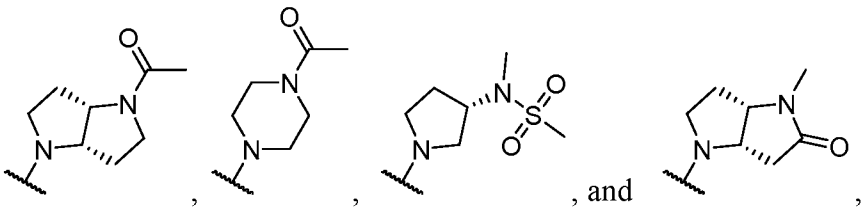
12. The method of claim 11, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:





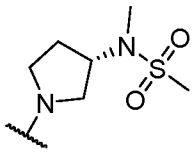
or a pharmaceutically acceptable salt or solvate thereof.

13. The method of claim 9, wherein R^{11a} is a substituted 4- to 14-membered heterocyclo selected from the group consisting of:



or a pharmaceutically acceptable salt or solvate thereof.

14. The method of claim 13, wherein R^{11a} is:



or a pharmaceutically acceptable salt or solvate thereof.

15. The method of any one of claims 4-14, wherein Z^4 is $-CH_2-$, or a pharmaceutically acceptable salt or solvate thereof.

16. The method of any one of claims 1-15, wherein R^{1d} is fluoro, or a pharmaceutically acceptable salt or solvate thereof.

17. The method of claim 1, wherein the compound is a compound of Table 1, or a pharmaceutically acceptable salt or solvate thereof.

18. The method of claim 1, wherein the compound is a compound of Table 1B, or a pharmaceutically acceptable salt or solvate thereof.

19. The method of any one of claims 1-18, wherein the Second Therapeutic Agent comprises a BTK inhibitor.

20. The method of claim 19, wherein the BTK inhibitor is ibrutinib, acalabrutinib, or zanubrutinib.

21. The method of any one of claims 1-20, wherein the Second Therapeutic Agent comprises an anti-CD20 monoclonal antibody.

22. The method of claim 21, wherein the anti CD20 monoclonal antibody is rituximab.

23. The method of any one of claims 1-22, wherein the Second Therapeutic Agent comprises a PI3K inhibitor.

24. The method of claim 23, wherein the PI3K inhibitor is copanlisib.

25. The method of any one of claims 1-24, wherein the Second Therapeutic Agent comprises a CDK4/6 inhibitor.

26. The method of claim 25, wherein the CDK4/6 inhibitor is palbociclib.

27. The method of any one of claims 1-26, wherein the Second Therapeutic Agent comprises a CARM1 inhibitor.

28. The method of claim 27, wherein the CARM1 inhibitor is EZM2302.

29. The method of any one of claims 1-28, wherein the Second Therapeutic Agent comprises an alkylating agent.

30. The method of claim 29, wherein the alkylating agent is mafosfamide.

31. The method of any one of claims 1-30, wherein the Second Therapeutic Agent comprises a topoisomerase II inhibitor.

32. The method of claim 29, wherein the topoisomerase II inhibitor is doxorubicin or etoposide.

33. The method of any one of claims 1-32, wherein the Second Therapeutic Agent comprises a vinca alkaloid.

34. The method of claim 33, wherein the vinca alkaloid is vincristine.

35. The method of any one of claims 1-34, wherein the Second Therapeutic Agent comprises a platinum-based drug.

36. The method of claim 33, wherein the platinum-based drug is carboplatin or oxaliplatin.

37. The method of any one of claims 1-36, wherein the Second Therapeutic Agent comprises a nucleoside anticancer agent.

38. The method of claim 37, wherein the nucleoside anticancer agent is gemcitabine.

39. The method of any one of claims 1-38, wherein the Second Therapeutic Agent comprises a DNA repair enzyme inhibitor.

40. The method of claim 39, wherein the DNA repair enzyme inhibitor is an ATM inhibitor, ATR inhibitor, Chk1 inhibitor, Wee1 inhibitor, RAD51 inhibitor, PARP inhibitor, or AKT inhibitor.

41. The method of claim 40, the ATM inhibitor is AZD0156, dactolisib, KU-55933, CP-466722, or AZD1390.

42. The method of claim 40, the ATR inhibitor is AZD6738 VX-803, or elimusertib.

43. The method of claim 40, the Chk1 inhibitor is AZD7762, rabusertib, MK-8776, CHIR-124, or PF-477736.

44. The method of claim 40, the Wee1 inhibitor is AZD1775.

45. The method of claim 40, the RAD51 inhibitor is B02 or RI-1.

46. The method of claim 40, the PARP inhibitor is olaparib, niraparib rucaparib, or talazoparib.

47. The method of claim 40, the AKT inhibitor is MK2206.

48. The method of any one of claims 1-47, wherein the Second Therapeutic Agent comprises a SYK inhibitor.

49. The method of claim 48, the SYK inhibitor is tamatinib, fostamatinib, R406, MNS, lanraplenib, TAK-659, entospletinib, or BAY-61-3606.

50. The method of any one of claims 1-49, wherein the Second Therapeutic Agent comprises a MEK inhibitor.

51. The method of claim 50, the MEK inhibitor is trametinib, selumetinib, or merdametinib.

52. The method of any one of claims 18-51, wherein the compound of Table 1B is Cpd. No. 15, or a pharmaceutically acceptable salt or solvate thereof.

53. The method of any one of claims 1-52 further comprising administering a therapeutically effective amount of a Third Therapeutic Agent to the subject, wherein the Third Therapeutic Agent comprises one or more glucocorticoid receptor agonists, one or more immunomodulatory drugs, one or more proteasome inhibitors, one or more Bcl-2 inhibitors, one or more pleiotropic pathway modulators, one or more XPO1 inhibitors, one or more histone deacetylase inhibitors, one or more EZH2 inhibitors, or a combination thereof.

54. The method claim 53, wherein the Third Therapeutic Agent comprises a glucocorticoid receptor agonist.

55. The method of claim 54, wherein the glucocorticoid receptor agonist is dexamethasone.

59. The method of any one of claims 53-55, wherein the Third Therapeutic Agent comprises an immunomodulatory drug.

60. The method of claim 59, wherein the immunomodulatory drug is pomalidomide or lenalidomide.

61. The method of any one of claims 53-60, wherein the Third Therapeutic Agent comprises a proteasome inhibitor.

62. The method of claim 61, wherein the proteasome inhibitor is bortezomib.

63. The method of any one of claims 53-62, wherein the Third Therapeutic Agent comprises a Bcl-2 inhibitor.

64. The method of claim 63, wherein the Bcl-2 inhibitor is venetoclax.

65. The method of any one of claims 53-64, wherein the Third Therapeutic Agent comprises a pleiotropic pathway modulator.

66. The method of claim 65, wherein the pleiotropic pathway modulator is CC-122.

67. The method of any one of claims 53-66, wherein the Third Therapeutic Agent comprises a XPO1 inhibitor.

68. The method of claim 67, wherein the XPO1 inhibitor is selinexor.

69. The method of any one of claims 53-68, wherein the Third Therapeutic Agent comprises a histone deacetylase inhibitor.

70. The method of claim 69, wherein the histone deacetylase inhibitor is panobinostat.

71. The method of any one of claims 53-70, wherein the Third Therapeutic Agent is an EZH2 inhibitor.

72. The method of claim 71, wherein the EZH2 inhibitor is tazemetostat.

73. The method of any one of claims 1-52, wherein the compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and the Second Therapeutic Agent are administered to the subject separately.

74. The method of any one of claims 53-73, wherein the compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, the Second Therapeutic Agent, and the Third Therapeutic Agent are administered to the subject separately

75. The method of any one of claims 1-74, wherein the subject in need thereof has cancer.

76. The method of claim 75, wherein the cancer is any one or more of the cancers of Table 2.

77. The method of claim 75, wherein the cancer is a hematological cancer.

78. The method of claim 77, wherein the hematological cancer is any one or more of the cancers of Table 3.

79. The method of claim 78, wherein the hematological cancer is multiple myeloma, mantle cell lymphoma, or diffuse large B-cell lymphoma.

80. The method of claim 79, wherein the hematological cancer is mantle cell lymphoma.

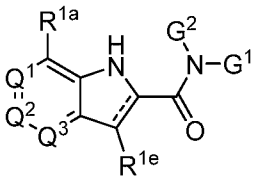
81. The method of claim 79, wherein the hematological cancer is diffuse large B-cell lymphoma.

82. The method of claim 79, wherein the hematological cancer is multiple myeloma.

83. The method of claim 82, wherein the the hematological cancer is t(4;14) multiple myeloma.

84. A kit for carrying out the method of any one of claims 1-83, the kit comprising:

(a) compound of Formula **I**:



I,

or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^{1a} is selected from the group consisting of halogen, alkyl, alkoxy, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

Q^1 is selected from the group consisting of -C(R^{1b})= and –N=;

Q^2 is selected from the group consisting of -C(R^{1c})= and –N=;

Q^3 is selected from the group consisting of -C(R^{1d})= and –N=;

provided that at least one of Q^1, Q^2, or Q^3 is -C(R^{1b})=, -C(R^{1c})=, or -C(R^{1d})=, respectively;

R^{1b}, R^{1c}, and R^{1d} are each independently selected from the group consisting of hydrogen, halogen, alkyl, alkenyl, (hydroxy)alkyl, and alkoxy;

R^{1e} is selected from the group consisting of hydrogen, halogen, alkyl, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

--- is a single or double bond;

G^1 is selected from the group consisting of: optionally substituted aryl;

optionally substituted heteroaryl; optionally substituted heterocyclo; optionally substituted cycloalkyl; (aryl)alkyl; (heteroaryl)alkyl; (heterocyclo)alkyl; (amino)(aryl)alkyl; (heteroaryl)(aryl)alkyl; (heteroaryl)(heterocyclo)alkyl; (heteroaryl)(carboxamido)alkyl; (heteroaryl)(cycloalkyl)alkyl; (aryl)(alkoxycarbonyl)alkyl; (cycloalkyl)alkyl; (heteroaryl)(amino)alkyl; (cycloalkyl)(alkoxycarbonyl)alkyl; (heteroaryl)(alkoxycarbonyl)alkyl; (heterocyclo)(cycloalkyl)alkyl; (aryl)(cycloalkyl)alkyl; (aryl)(hydroxy)alkyl; (cycloalkyl)(hydroxy)alkyl; (hydroxy)alkyl; optionally substituted alkyl; (aryl)(haloalkyl)alkyl; (cycloalkyl)(haloalkyl)alkyl; (hydroxy)(haloalkyl)alkyl; and (alkoxycarbonyl)(haloalkyl)alkyl; and

G^2 is selected from the group consisting of hydrogen and alkyl; or

G^1 and G^2 taken together with the nitrogen atom to which they are attached form an optionally substituted heterocyclo,

wherein:

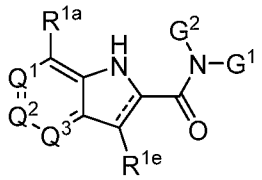
the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of

enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof; and

(c) instructions for administering the compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and the Second Therapeutic Agent to the subject.

85. A kit comprising:

(a) compound of Formula **I**:



I,

or a pharmaceutically acceptable salt or solvate thereof, wherein:

R^{1a} is selected from the group consisting of halogen, alkyl, alkoxy, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

Q^1 is selected from the group consisting of -C(R^{1b})= and –N=;

Q^2 is selected from the group consisting of -C(R^{1c})= and –N=;

Q^3 is selected from the group consisting of -C(R^{1d})= and –N=;

provided that at least one of Q^1, Q^2, or Q^3 is -C(R^{1b})=, -C(R^{1c})=, or -C(R^{1d})=, respectively;

R^{1b}, R^{1c}, and R^{1d} are each independently selected from the group consisting of hydrogen, halogen, alkyl, alkenyl, (hydroxy)alkyl, and alkoxy;

R^{1e} is selected from the group consisting of hydrogen, halogen, alkyl, cycloalkyl, (hydroxy)alkyl, and (cycloalkyl)alkyl;

--- is a single or double bond;

G^1 is selected from the group consisting of: optionally substituted aryl;

optionally substituted heteroaryl; optionally substituted heterocyclo; optionally substituted cycloalkyl; (aryl)alkyl; (heteroaryl)alkyl; (heterocyclo)alkyl; (amino)(aryl)alkyl; (heteroaryl)(aryl)alkyl; (heteroaryl)(heterocyclo)alkyl; (heteroaryl)(carboxamido)alkyl; (heteroaryl)(cycloalkyl)alkyl; (aryl)(alkoxycarbonyl)alkyl; (cycloalkyl)alkyl; (heteroaryl)(amino)alkyl; (cycloalkyl)(alkoxycarbonyl)alkyl; (heteroaryl)(alkoxycarbonyl)alkyl; (heterocyclo)(cycloalkyl)alkyl; (aryl)(cycloalkyl)alkyl; (aryl)(hydroxy)alkyl;

(cycloalkyl)(hydroxy)alkyl; (hydroxy)alkyl; optionally substituted alkyl; (aryl)(haloalkyl)alkyl; (cycloalkyl)(haloalkyl)alkyl; (hydroxy)(haloalkyl)alkyl; and (alkoxycarbonyl)(haloalkyl)alkyl; and

G^2 is selected from the group consisting of hydrogen and alkyl; or

G^1 and G^2 taken together with the nitrogen atom to which they are attached form an optionally substituted heterocyclo,

(b) a Second Therapeutic Agent,

wherein the Second Therapeutic Agent comprises one or more BTK inhibitors, one or more anti-CD20 monoclonal antibodies, one or more alkylating agents, one or more topoisomerase II inhibitors, one or more vinca alkaloids, one or more platinum-based drugs, one or more nucleoside anticancer agents, one or more PI3K inhibitors, one or more CDK4/6 inhibitors, one or more CARM1 inhibitors, one or more inhibitors of enzymes of DNA damage repair, one or more SYK inhibitors, or one or more MEK inhibitors, or a combination thereof; and

(c) instructions for administering the compound of Formula **I**, or a pharmaceutically acceptable salt or solvate thereof, and the Second Therapeutic Agent to a subject.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/32718

A. CLASSIFICATION OF SUBJECT MATTER

IPC - INV. A61K 31/165, A61K 31/404, C07D 209/42; ADD. A61P 35/00 (2022.01)

CPC - INV. A61K 31/165, A61K 31/404, C07D 209/42, A61K 2300/00; ADD. A61P 35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2020/037079 A1 (EPIZYME, INC.) 20 February 2020 (20.02.2020) para [0361], Table 1; para [0377]-[0382], [0398], [0399], [0404]	1-8, 17-18, 85
Y	US 2017/0232030 A1 (EPIZYME, INC. et al.) 17 August 2017 (17.08.2017) para [0016]-[0020], [0033]-[0034], [0097], [0225], [0302]-[0309], [0333]	1-8, 17-18, 85
A	US 9,446,064 B2 (EPIZYME, INC.) 20 September 2016 (20.09.2016) Entire Document	1-8, 17-18, 85
A	US 2017/0281810 A1 (ZHEJIANG DTRM BIOPHARMA CO. LTD.) 05 October 2017 (05.10.2017) Entire Document	1-8, 17-18, 85
A,P	WO 2021/168313 A1 (EPIZYME, INC.) 26 August 2021 (26.08.2021) Entire Document	1-8, 17-18, 85

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2022	SEP 12 2022
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Authorized officer Kari Rodriquez Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 22/32718

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 9-16, 19-55 and 59-84
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.