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(71) Applicant(s)
Sloan-Kettering Institute for Cancer Research

(72) Inventor(s)
Sun, Weilin;Taldone, Tony;Patel, Pallav;Chiosis, Gabriela

(74) Agent / Attorney
Davies Collison Cave Pty Ltd, Level 15 1 Nicholson Street, MELBOURNE, VIC, 3000, AU

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(71) Applicant *(for all designated States except US)*: **SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH** [US/US]; 1275 York Avenue, New York, New York 10065 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **SUN, Weilin** [CN/US]; 475 Main Street, Apartment 2B, New York, New York 10044 (US). **TALDONE, Tony** [US/US]; 425 Main Street, Apartment 12F, New York, New York 10044 (US). **PATEL, Pallav** [IN/US]; 4040 Presidential Blvd., Apartment 2915, Philadelphia, Pennsylvania 19131 (US). **CHIOSIS, Gabriela** [US/US]; c/o Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, New York 10065 (US).

(74) Agent: **LARSON, Marina**; Larson & Anderson, LLC, P.O. Box 4928, Dillon, Colorado 80435 (US).

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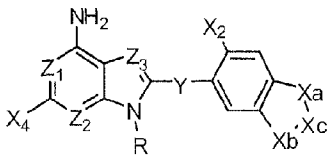
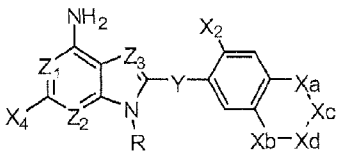
(54) **Title**: HSP90 INHIBITORS



(IA)



(IB)

(57) **Abstract**: The disclosure relates to Compounds of Formulae (IA) and (IB), and pharmaceutically acceptable salts thereof wherein Z_1, Z_2, Z_3, Xa, Xb, Xc, Xd, Y, X_2, and X_4 are as defined herein, compositions comprising an effective amount of a Compound of Formula (IA) and/or (IB), and methods to treat or prevent a condition, such cancer which overexpresses Her-kinases, comprising administering to an patient in need thereof a therapeutically effective amount of a Compound of Formula (IA) or (IB). The disclosure further relates to compounds of Formulae (IA) and (IB) in which X_2 is a leaving for introducing a radiolabeled atom, such as ^{124}I or ^{131}I and to methods of using such compounds in the preparation of radiolabeled compounds, particularly for use in imaging.

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HSP90 INHIBITORS

This application claims the benefit of and priority from US provisional application no. 61/472,061, filed April 5, 2011, the contents of which are incorporated herein by reference.

1. BACKGROUND

This application relates to compounds that inhibit heat shock protein 90 (Hsp90).

The Hsp90 family of proteins has four recognized members in mammalian cells: Hsp90 α and β, Grp94 and Trap-1. Hsp90 α and β exist in the cytosol and the nucleus in association with a number of other proteins. Hsp90 in its various forms is the most abundant cellular chaperone, and has been shown in experimental systems to be required for ATP-dependent refolding of denatured or "unfolded" proteins. It has therefore been proposed to function as part of the cellular defense against stress. When cells are exposed to heat or other environmental stresses, the aggregation of unfolded proteins is prevented by pathways that catalyze their refolding or degradation. This process depends on the association of the unfolded protein in an ordered fashion with multiple chaperones (Hsp60, Hsp90, Hsp70 and p23), forming a "refoldosome" and ultimately the ATP-dependent release of the chaperones from the refolded protein.

Hsp90 can also play a role in maintaining the stability and function of mutated proteins. It seems to be required for expression of mutated p53 and v-src to a much greater extent than for their wild-type counterparts. It has been suggested that this occurs as a result of Hsp90-mediated suppression of the phenotypes of mutations that lead to protein unfolding.

Hsp90 is also necessary to the conformational maturation of several key proteins involved in the growth response of the cell to extracellular factors. These include the steroid receptors as well as certain kinases (*i.e.*, Raf serine kinase, v-src and Her2). The mechanism whereby Hsp90 affects these proteins is not fully understood, but appears to be similar to its role in protein refolding. In the case of the progesterone receptor, it has been shown that binding and release of Hsp90 from the receptor occurs in a cyclic fashion in concert with release of other chaperones and immunophilins and is required for high affinity binding of the steroid to the receptor. Thus, Hsp90 could function as a physiologic regulator of signaling pathways, even in the absence of stress.

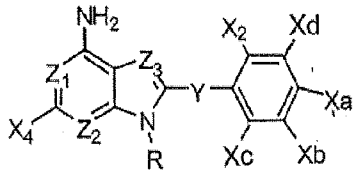
Hsp90 has been shown to be overexpressed in multiple tumor types and as a function of oncogenic transformation. Whether it plays a necessary role in maintaining transformation is unknown, but it could have at least three functions in this regard. Cancer cells grow in an environment of hypoxia, low pH and low nutrient concentration. They also rapidly adapt to or are selected to become resistant to radiation and cytotoxic chemotherapeutic agents. Thus, the general role of Hsp90 in maintaining the stability of proteins under stress may be necessary for cell viability

under these conditions. Secondly, cancer cells harbor mutated oncogenic proteins. Some of these are gain-of-function mutations which are necessary for the transformed phenotype. Hsp90 may be required for maintaining the folded, functionally-active conformation of these proteins. Thirdly, activation of signaling pathways mediated by steroid receptors, Raf and other Hsp90 targets is necessary for the growth and survival of many tumors which thus probably also require functional Hsp90.

Hsp90 has been recognized as a viable target for therapeutic agents. Hsp90 family members possess a unique pocket in their N-terminal region that is specific to and conserved among all Hsp90s from bacteria to mammals, but which is not present in other molecular chaperones. The endogenous ligand for this pocket is not known, but it binds ATP and ADP with low affinity and has weak ATPase activity. The ansamycin antibiotics geldanamycin (GM) and herbimycin (HA) have been shown to bind to this conserved pocket, and this binding affinity has been shown for all members of the Hsp90 family. International Patent Publication No. WO98/51702 discloses the use of ansamycin antibiotics coupled to a targeting moiety to provide targeted delivery of the ansamycin leading to the degradation of proteins in and death of the targeted cells. International Patent Publication No. WO00/61578 relates to bifunctional molecules having two moieties which interact with the chaperone protein Hsp90, including in particular homo- and heterodimers of ansamycin antibiotics. These bifunctional molecules act to promote degradation and/or inhibition of HER-family tyrosine kinases and are effective for treatment of cancers which overexpress Her-kinases.

Exemplary small molecule therapeutics that bind to the same binding pocket of Hsp90 as ATP and the ansamycin antibiotics are disclosed in PCT Publication Nos. WO02/36075, WO2006/084030, WO2009/042646, WO2009/065035, and WO2011/044394; U.S. Patent No. 7,834,181; and U.S. Patent Publication Nos. 2005/0113339, 2005/0004026, 2005/0049263, 2005/0256183, 2005/0119292, 2005/0113340, 2005/0107343, 2008/0096903, 2008/0234297, 2008/0234314, 2008/0253865, and 2009/0298857, all of which are incorporated herein by reference.

In particular, certain small molecule therapeutics that bind to the same binding pocket of Hsp90 can be described by the following general structural formula where Z_1, Z_2, and Z_3 are selected from CH and N and the variable substituents are selected from a number of options :

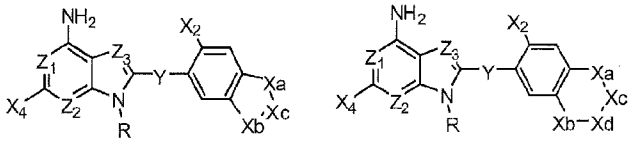


While these compounds can be active as inhibitors of Hsp90, their level of activity is extremely variable with measured values for EC_{50} and IC_{50} being reported in anywhere from the micromolar to nanomolar ranges.

2. SUMMARY

In one aspect of the disclosure, new compounds that inhibit Hsp90 are described.

Compounds of Formula (IA) or (IB) are herein disclosed:



(IA) (IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is independently CH or N;

(b) Y is CH_2, O, or S;

(c) Xa, Xb, Xc and Xd are independently selected from CH, CH_2, O, N, NH, S, carbonyl, fluoromethylene, and difluoromethylene selected so as to satisfy valence, wherein each bond to an X group is either a single bond or a double bond;

(d) X_2 is halogen, aryl, alkynyl, or amino;

(e) X_4 is hydrogen or halogen; and

(f) R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkylwherein

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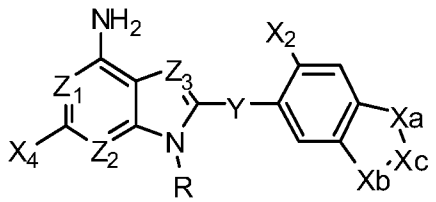
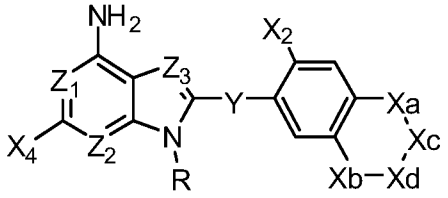
the R group is interrupted by 1, 2, or 3 groups selected from -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -$NR_A$$SO_2$-, -C(O)N($R_A$)-, and -$NR_A$C(O)-, and/or terminated by –S(O)NR_AR_B, -NR_AS(O)R_B, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -C(O)NR_AR_B, or -NR_AC(O)R_B, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

In one aspect of the invention, there is provided a Compound of Formula (IA) or (IB):



(IA)



(IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is N;

(b) Y is S;

(c) Xa, Xb, Xc and Xd are O, O, CH_2, and CH_2, respectively ;

(d) X_4 is hydrogen or halogen; and

(e) X_2 and R are a combination selected from the following:

(i) in formula (IA):

(a) X_2 is NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -$NR_A$$SO_2$-, -C(O)N($R_A$)-, or -$NR_A$C(O)- groups, and/or terminated by an -S(O)NR_AR_B, -NR_AS(O)R_B,

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$-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(b) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, or $-C(O)N(R_A)-$ groups, and/or terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(c) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-NR_AC(O)-$ groups, and/or terminated by an $-NR_AC(O)R_B$ group, wherein each R_A is independently selected from C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(d) X_2 is aryl or alkynyl, R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or

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unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, or -NR_AC(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -N$R_A$$SO_2$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(e) X_2 is aryl or alkynyl, R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -N$R_A$$SO_2$- or -C(O)N($R_A$)- groups, and/or terminated by an -SO_2N$R_A$$R_B$ or -C(O)N$R_A$$R_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl;

(f) X_2 is halogen, aryl, alkynyl, or N$R_1$$R_2$, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl; and R is straight-chain- substituted or unsubstituted alkyl, straight-chain- substituted or unsubstituted alkenyl, straight-chain- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein R_A is independently selected from hydrogen, C_2-C_6 alkenyl,

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C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

(ii) in formula (IB):

(g) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, or $-SO_2N(R_A)-$ groups, and/or terminated by an $-S(O)NR_AR_B$ or $-NR_AS(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(h) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-NR_ASO_2$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$ groups, and/or terminated by an $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6

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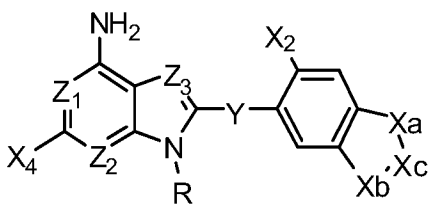
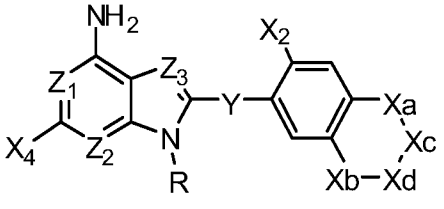
alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(i) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl; and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is independently selected from C_2-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

In another aspect of the invention, there is provided a Compound of Formula (IA) or (IB):



(IA)



(IB)

or a pharmaceutically acceptable salt thereof, wherein:

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(a) each of Z_1, Z_2 and Z_3 is N;

(b) Y is CH_2;

(c) Xa, Xb, Xc and Xd are O, O, CH_2, and CH_2, respectively;

(d) X_4 is hydrogen or halogen; and

(e) X_2 and R are a combination selected from the following:

(i) in formula (IA):

(a) X_2 is NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -NR_ASO_2-, -C(O)N(R_A)-, or -NR_AC(O)- groups, and/or terminated by an -S(O)NR_AR_B, -NR_AS(O)R_B, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -C(O)NR_AR_B, or -NR_AC(O)R_B group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(b) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -NR_ASO_2-, -C(O)N(R_A)-, or -NR_AC(O)- groups, and/or terminated by an -S(O)NR_AR_B, -NR_AS(O)R_B, -$NR_ASO_2R_B$, -C(O)NR_AR_B, or -NR_AC(O)R_B group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl,

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heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(c) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by a $-SO_2NR_AR_B$ group, wherein R_A is selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(d) X_2 is aryl or alkynyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$ groups, and/or terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(e) X_2 is aryl or alkynyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-SO_2NR_AR_B$ or $-C(O)NR_AR_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl,

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aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

(ii) in formula (IB),

(a) X_2 is NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$,-N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(b) X_2 is halogen, aryl, or alkynyl, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -N$R_A$$SO_2$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A

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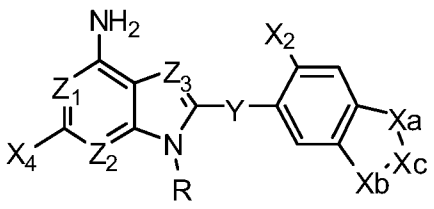
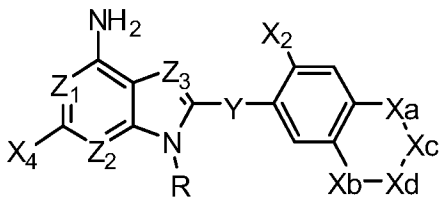
and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(c) X_2 is halogen, aryl, or alkynyl, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-SO_2NR_AR_B$ or $-C(O)NR_AR_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

In yet another aspect of the invention, there is provided a Compound of Formula (IA) or (IB):



(IA)



(IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is N;

(b) Y is O;

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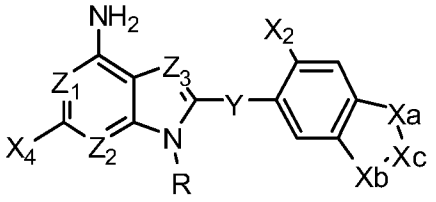
(c) Xa, Xb, Xc and Xd are independently selected from CH, CH_2, O, N, NH, S, carbonyl, fluoromethylene, and difluoromethylene selected so as to satisfy valence, wherein each bond to an X group is either a single bond or a double bond;

(d) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl;

(e) X_4 is hydrogen or halogen; and

(f) R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

In a further aspect of the invention, there is provided a Compound of Formula (IA)



or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is N;

(b) Y is S or CH_2;

(c) Xa-Xc-Xb are -CH_2-CH_2-CH_2-, -O-CH_2-CH_2-, or -CH_2-CH_2-O-;

(d) X_4 is hydrogen or halogen;

(e) X_2 is halogen or alkynyl; and

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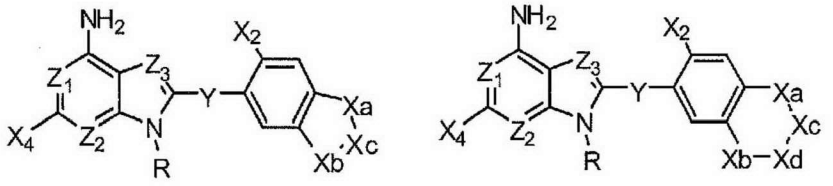
(f) R is straight-chain- C1-C6 alkyl, which is terminated by a $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, or cycloalkyl.

3. DETAILED DESCRIPTION

The invention includes the following:

(1) A Compound of Formula (IA) or (IB):



(IA) (IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is independently CH or N;

(b) Y is CH_2, O, or S;

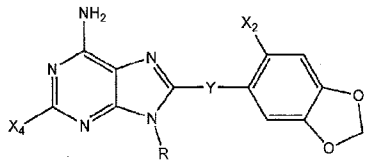
(c) Xa, Xb, Xc and Xd are independently selected from CH, CH_2, O, N, NH, S, carbonyl, fluoromethylene, and difluoromethylene selected so as to satisfy valence, wherein each bond to an X group is either a single bond or a double bond;

(d) X_2 is halogen, aryl, alkynyl, or amino;

(e) X_4 is hydrogen or halogen; and

(f) R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or -NRAC(O)-, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

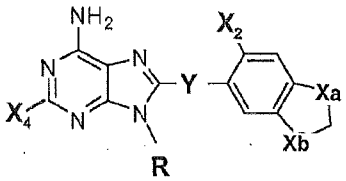
(2) The compound as in the above (1) which is a Compound of Formula (1):



(1)

or a pharmaceutically acceptable salt thereof, wherein Y is CH_2 or S.

(3) The compound as in the above (1) which is a Compound of Formula (2):



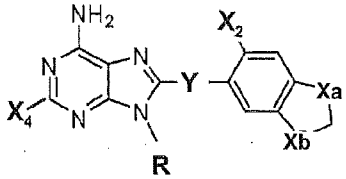
(2)

or a pharmaceutically acceptable salt thereof, wherein:

one of Xa and Xb is O and the other is CH_2; and

Y is CH_2 or S.

(4) The compound as in the above (1) which is a Compound of Formula (3):



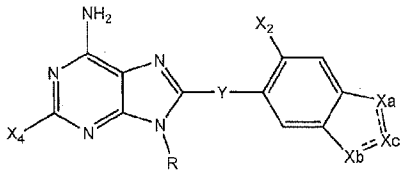
(3)

or a pharmaceutically acceptable salt thereof, wherein:

one of Xa and Xb is C(=O) and the other is CH_2; and

Y is CH_2 or S.

(5) The compound as in the above (1) which is a Compound of Formula (4):



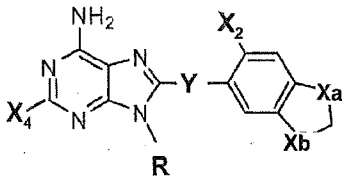
(4)

or a pharmaceutically acceptable salt thereof, wherein:

Xa-Xc-Xb is CH_2-CH_2-CH_2, CH=CH-CH_2, or CH_2-CH=CH; and

Y is CH_2 or S.

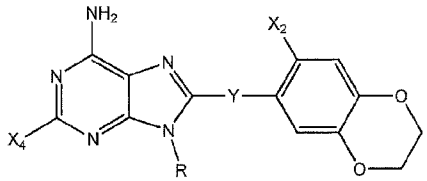
(6) The compound as the above (1) which is a Compound of Formula (5):



(5)

or a pharmaceutically acceptable salt thereof, wherein at least one of Xa and Xb is CHF or CF_2 and the other is CHF, CF_2, or CH_2.

(7) The compound as in the above (1) which is Compound of Formula (6):



(6)

or a pharmaceutically acceptable salt thereof.

(8) The compound as in the above (1), wherein Z_1 is CH or Z_2 is CH or Z_3 is CH.

(9) The compound as in the above (1), wherein Z_1 and Z_2 are each CH or Z_1 and Z_3 are each CH or Z_2 and Z_3 are each CH.

(10) The compound as in the above (1), wherein Z_1, Z_2, and Z_3 are each CH.

(11) The compound as in the above (1) to (10), wherein R is interrupted by one or more -$S(O)N(R_A)$-, -$NR_AS(O)$-, -$SO_2N(R_A)$-, -NR_ASO_2-, -$C(O)N(R_A)$-, or -$NR_AC(O)$- groups.

(12) The compound as in the above (1) to (11), wherein R is terminated by an -$S(O)NR_AR_B$, -$NR_AS(O)R_B$, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -$C(O)NR_AR_B$, or -$NR_AC(O)R_B$ group.

(13) The compound as in one of the above (1) to (12), wherein R is 2-ethanesulfonic acid isopropylamide, 2-ethanesulfonic acid ethylamide, 2-ethanesulfonic acid methylamide, 2-ethanesulfonic acid amide, 2-ethanesulfonic acid t-butylamide, 2-ethanesulfonic acid isobutylamide, 2-ethanesulfonic acid cyclopropylamide, isopropanesulfonic acid 2-ethylamide, ethanesulfonic acid 2-ethylamide, N-2 ethyl methanesulfonamide, 2-methyl-propane-2-sulfonic acid 2-ethylamide, 2-methyl-propane-2-sulfinic acid 2-ethylamide, 2-methyl-propane-1-sulfonic acid 2-ethylamide, cyclopropanesufonic acid 2-ethylamide, 3-propane-1-sulfonic acid isopropylamide, 3-propane-1-sulfonic acid ethylamide, 3-propane-1-sulfonic acid methylamide, 3-propane-1-sulfonic acid amide, 3-propane-1-sulfonic acid t-butylamide, 3-propane-1-sulfonic acid isobutylamide, 3-propane-1-sulfonic acid cyclopropylamide, propane-2-sulfonic acid 3-propylamide, ethanesulfonic acid 3-propylamide, N-3-propyl methanesulfonamide, 2-methyl-propane-2-sulfonic acid 3-propylamide, 2-methyl-propane-2-sulfinic acid 3-propylamide, 2-methyl-propane-1-sulfonic acid 3-propylamide, cyclopropanesulfonic acid 3-propylamide, 3-N-isopropyl propionamide, 3-N-ethyl propionamide, 3-N-methyl propionamide, 3-propionamide, 3-N-t-butyl propionamide, 3-N-isobutyl propionamide, 3-N-cyclopropyl propionamide, N-2-ethyl isobutyramide, N-2-ethyl propionamide, N-2-ethyl acetamide, N-2-ethyl formamide, N-2-ethyl 2,2-dimethyl-propionamide, N-2-ethyl 3-methylbutyramide, or cyclopropane carboxylic acid 2-ethyl-amide.

(14) The compound as in one of the above (1) to (12), wherein R is cyclopropane carboxylic acid 3-propyl-amide, N-3-propyl 2,2-dimethyl-propionamide, N-propyl-2-methyl-propane-2-sulfinamide, t-butanesulfonic acid 3-propylamide, or cyclopropanesulfonic acid 3-propylamide.

(15) The compound as in one of the above (1) to (14), wherein X_4 is H or F.

(16) The compound as in one of the above (1) to (15), wherein Y is S.

(17) The compound as in one of the above (1) to (15), wherein Y is CH_2.

(18) The compound as in one of the above (1) to (17), wherein X_2 is optionally substituted heteroaryl.

(19) The compound as in one of the above (1) to (18), wherein X_2 is furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, or 5-methyloxazol-2-yl.

(20) The compound as in one of the above (1) to (17), wherein X_2 is alkynyl.

(21) The compound as in one of the above (1) to (17) or (20), wherein X_2 is ethynyl.

(22) The compound as in one of the above (1) to (17), wherein X_2 is halo.

(23) The compound as in one of the above (1) to (17) or (22), wherein X_2 is I.

(24) The compound as in one of the above (1) to (17), wherein X_2 is amino.

(25) The compound as in one of the above (1) to (17) or (24), wherein X_2 is dimethylamino.

(26) The compound as in one of the above (1) to (11) or (13) to (25), wherein Z_1 is N or Z_2 is N or Z_3 is N.

(27) The compound as in one of the above (1) to (10) or (13) to (25), wherein Z_1 and Z_2 are each N or Z_1 and Z_3 are each N or Z_2 and Z_3 are each N.

(28) A pharmaceutical composition comprising the compound as in one of the above (1) to (27) and a pharmaceutically acceptable carrier.

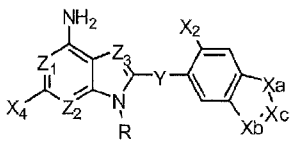
(29) A method for treating or preventing cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a compound as in one of the above (1) to (27).

(30) Use of a compound as in one of the above (1) to (27) in formulating a pharmaceutical composition for the treatment or prevention of cancer or a neurodegenerative disorder.

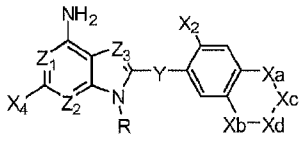
(31) A method for the inhibition of Hsp90, comprising contacting Hsp90 with an Hsp90 function inhibiting amount of a compound as in one of the above (1) to (27).

(32) Use of a compound as in one of the above (1) to (27) in formulating a pharmaceutical composition for the inhibition of Hsp90.

(34) A Compound of Formula (IA) or (IB):



(IA)



(IB)

or a salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is independently CH or N;

(b) Y is CH_2, O, or S;

(c) Xa, Xb, Xc and Xd are independently selected from CH, CH_2, O, N, NH, S, carbonyl, fluoromethylene, and difluoromethylene selected so as to satisfy valence, wherein each bond to an X group is either a single bond or a double bond;

(d) X_2 is a leaving group for introduction of a a radiolabeled atom to the structure;

(e) X_4 is hydrogen or halogen; and

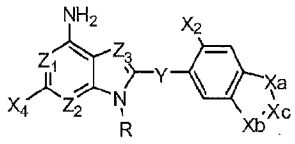
(f) R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$ groups, and/or terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

(35) A compound as in (34) above, or a salt thereof, wherein X_2 is trialkyl tin or $-Sn(CH_2CH_2(CF_2)_5CF_3)_3$.

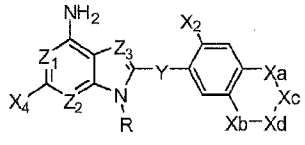
(36) Use of a compound as in (34) or (35) above, or a salt thereof, as a precursor for the formation of a radiolabeled compound.

A. Compounds of Formulae (IA) and (IB)

As stated above, the disclosure encompasses Compounds of Formulae (IA) and (IB):



(IA)



(IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is independently CH or N;

(b) Y is CH_2, O, or S;

(c) Xa, Xb, Xc and Xd are independently selected from CH, CH_2, O, N, NH, S, carbonyl, fluoromethylene, and difluoromethylene selected so as to satisfy valence, wherein each bond to an X group is either a single bond or a double bond;

(d) X_2 is halogen, aryl, alkynyl, or amino;

(e) X_4 is hydrogen or halogen; and

(f) R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched-substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkylwherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, and $-NR_AC(O)-$, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

In certain embodiments, there may be 1, 2 or 3 interrupting and/or terminating groups, which may be the same or different. In general, the R groups of these compounds can be described as sulfonamido groups, sulfinamido groups, or amido groups.

In certain embodiments, specific R groups include without limitation: 2-ethanesulfonic acid isopropylamide, 2-ethanesulfonic acid ethylamide, 2-ethanesulfonic acid methylamide, 2-ethanesulfonic acid amide, 2-ethanesulfonic acid t-butylamide, 2-ethanesulfonic acid isobutylamide, 2-ethanesulfonic acid cyclopropylamide, isopropanesulfonic acid 2-ethylamide, ethanesulfonic acid 2-ethylamide, N-2 ethyl methanesulfonamide, 2-methyl-propane-2-sulfonic acid 2-ethylamide, 2-methyl-propane-2-sulfinic acid 2-ethylamide, 2-methyl-propane-1-sulfonic acid 2-ethylamide, cyclopropanesufonic acid 2-ethylamide, 3-propane-1-sulfonic acid isopropylamide, 3-propane-1-sulfonic acid ethylamide, 3-propane-1-sulfonic acid methylamide, 3-propane-1-sulfonic acid amide, 3-propane-1-sulfonic acid t-butylamide, 3-propane-1-sulfonic acid

isobutylamide, 3-propane-1-sulfonic acid cyclopropylamide, propane-2-sulfonic acid 3-propylamide, ethanesulfonic acid 3-propylamide, N-3-propyl methanesulfonamide, 2-methyl-propane-2-sulfonic acid 3-propylamide, 2-methyl-propane-2-sulfinic acid 3-propylamide, 2-methyl-propane-1-sulfonic acid 3-propylamide, cyclopropanesulfonic acid 3-propylamide, 3-N-isopropyl propionamide, 3-N-ethyl propionamide, 3-N-methyl propionamide, 3-propionamide, 3-N-t-butyl propionamide, 3-N-isobutyl propionamide, 3-N-cyclopropyl propionamide, N-2-ethyl isobutyramide, N-2-ethyl propionamide, N-2-ethyl acetamide, N-2-ethyl formamide, N-2-ethyl 2,2-dimethyl-propionamide, N-2-ethyl 3-methylbutyramide, and cyclopropane carboxylic acid 2-ethyl-amide.

In certain embodiments, specific R groups include without limitation: cyclopropane carboxylic acid 3-propyl-amide, N-3-propyl 2,2-dimethyl-propionamide, N-propyl-2-methyl-propane-2-sulfinamide, t-butanesulfonic acid 3-propylamide, and cyclopropanesulfonic acid 3-propylamide.

In another embodiment, Z_1 is CH. In another embodiment, Z_2 is CH. In another embodiment, Z_3 is CH. In another embodiment, Z_1 is N. In another embodiment, Z_2 is N. In another embodiment, Z_3 is N.

In another embodiment, Z_1 and Z_2 are each CH. In another embodiment, Z_1 and Z_3 are each CH. In another embodiment, Z_2 and Z_3 are each CH. In another embodiment, Z_1 and Z_2 are each N. In another embodiment, Z_1 and Z_3 are each N. In another embodiment, Z_2 and Z_3 are each N.

In another embodiment, Z_1 and Z_2 are each CH and Z_3 is N. In another embodiment, Z_1 and Z_3 are each CH and Z_2 is N. In another embodiment, Z_2 and Z_3 are each CH and Z_1 is N. In another embodiment, Z_1 and Z_2 are each N and Z_3 is CH. In another embodiment, Z_1 and Z_3 are each N and Z_2 is CH. In another embodiment, Z_2 and Z_3 are each N and Z_1 is CH. In another embodiment, Z_1, Z_2, and Z_3 are each CH. In another embodiment, Z_1, Z_2, and Z_3 are each N.

In the structures set forth in Formulae (1) through (6) below, embodiments are provided in which Z_1, Z_2, and Z_3 are each N. These embodiments are intended as exemplary, and are not intended to exclude the above embodiments in which one, two, or three of Z_1, Z_2, and Z_3 is CH with the same substituents or other substituent combinations within the scope of Formulae (IA) and (IB) as set forth above. In particular, embodiments in which Z_2 or Z_3 are each CH are considered to be within the scope of this disclosure.

B. Definitions

As used in connection with the present disclosure, the terms used herein have the following meaning:

The terms "alkyl" and "substituted alkyl" are interchangeable unless otherwise specifically noted and refer to substituted and unsubstituted C_1-C_{10} straight-chain saturated aliphatic hydrocarbon groups, *i.e.*, groups having 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms, and substituted and unsubstituted C_3-C_{10} branched saturated aliphatic hydrocarbon groups, *i.e.*, groups having 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms. For example, "alkyl" includes but is not limited to: methyl (Me), ethyl (Et), propyl (Pr), isopropyl, butyl (Bu), tert-butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, and the like. In one embodiment, an alkyl is a C_1-C_6 alkyl, *i.e.*, a group having 1, 2, 3, 4, 5, or 6 carbon atoms. An alkyl can be substituted with 1, 2, or 3 substituents or optionally substituted with 1, 2, or 3 substituents. Illustrative examples of substituted C_1-C_6 alkyl groups include $-CH_2OH$, $-CF_2OH$, $-CH_2C(CH_3)_2C(O)OCH_3$, $-CF_3$, $-C(O)CF_3$, $-C(O)CH_3$, $-(CH_2)_4SCH_3$, $-CH(C(O)OH)CH_2CH_2C(O)N(CH_3)_2$, $-(CH_2)_5NHC(O)NH_2$, $-CH_2CH_2$-(4-fluorophenyl), $-CH(OCH_3)CH_2CH_3$, $-CH_2SO_2NH_2$, and $-CH(CH_3)CH_2CH_2OC(O)CH_3$.

The terms "alkenyl" and "substituted alkenyl" are interchangeable unless otherwise specifically noted and refer to substituted and unsubstituted C_2-C_{10} straight-chain aliphatic hydrocarbon groups having 1, 2, or 3 carbon-carbon double bonds, *i.e.*, groups having 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms, and substituted and unsubstituted C_3-C_{10} branched aliphatic hydrocarbon groups having 1, 2, or 3 carbon-carbon double bonds, *i.e.*, groups having 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms. For example, "alkenyl" includes but is not limited to: ethenyl, 1-prop-1-enyl, 1-prop-2-enyl, 2-prop-1-enyl, 1-but-3-enyl, 2-pent-2-enyl, 1-hex-6-enyl, 1-hept-7-enyl, 1-oct-8-enyl, and the like. In one embodiment, an alkenyl is a C_2-C_6 alkenyl, *i.e.*, a group having 2, 3, 4, 5, or 6 carbon atoms and 1 or 2 carbon-carbon double bonds. An alkenyl can be substituted with 1, 2, or 3 substituents or optionally substituted with 1, 2, or 3 substituents. Illustrative examples of substituted C_2-C_6 alkenyl groups include $-C(H)=CHCH_2OH$, $-C(H)=CF_2$, $-CH_2C(H)=CH(CH_2)_2CF_2OH$, $-CH_2C(=CH_2)C(O)OCH_3$, $-C(H)=CHCF_3$, $-CH_2CH_2C(H)=CHC(O)CH_3$, $-C(H)=C(CH_3)SCH_3$, $-C(H)=CHC(H)=C(CH_3)C(O)OCH_3$, and $-C(H)=C=CHOC(O)CH_3$.

The terms "alkynyl" and "substituted alkynyl" are interchangeable unless otherwise specifically noted and refer to substituted and unsubstituted C_2-C_{10} straight-chain aliphatic hydrocarbon groups having 1, 2, or 3 carbon-carbon triple bonds, *i.e.*, groups having 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms, and substituted and unsubstituted C_3-C_{10} branched aliphatic hydrocarbon groups having 1, 2, or 3 carbon-carbon triple bonds, *i.e.*, groups having 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms. For example, "alkynyl" includes but is not limited to: ethynyl, 1-prop-1-ynyl, 1-prop-2-ynyl, 2-prop-1-ynyl, 3-prop-1-ynyl, 1-but-3-ynyl, 2-pent-2-ynyl, 1-hex-6-ynyl, 1-hept-7-ynyl, 1-oct-8ynyl, and the like. In one embodiment, an alkynyl is a C_2-C_6 alkynyl, *i.e.*, a group having 2, 3, 4, 5, or 6 carbon atoms and 1 or 2 carbon-carbon triple bonds. An alkynyl can be substituted with 1, 2, or 3 substituents or optionally substituted with 1, 2, or 3 substituents.

Illustrative examples of substituted C_2-C_6 alkynyl groups include -C≡CCH_2OH, -C≡CF, -CH_2C≡$C(CH_2)_2CF_2OH$, -C≡$CCH_2C(O)OCH_3$, -CH_2C≡CCF_3, -CH_2CH_2C≡$CC(O)CH_3$, -C≡$CSCH_3$, and -C≡$CC(O)OC(O)CH_3$.

The terms "cycloalkyl" and "substituted cycloalkyl" are interchangeable unless otherwise specifically noted and refer to a mono- or multi-ringed carbocycle wherein each ring contains 3, 4, 5, 6, 7, 8, 9, or 10 carbon atoms, and wherein any ring can contain 1, 2, or 3 carbon-carbon double or triple bonds. For example, "cycloalkyl" includes but is not limited to: cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloalkenyl, cycloalkynyl, and cycloheptyl. A cycloalkyl can be substituted with 1, 2, or 3 substituents or optionally substituted with 1, 2, or 3 substituents.

The term "amino" refers to the group -NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl. Optionally the amino group can be protonated to provide a compound in salt form. A protonated amino group, being positively charged, is usually associated with an anion known to those in the art, such as OH^-, Cl^-, Br^-, $CH_3C(O)O^-$, $H_2PO_4^-$, or HSO_4^-.

The terms "aryl" and "substituted aryl" are interchangeable unless otherwise specifically noted and refer to a monocyclic, polycyclic, biaryl aromatic groups covalently attached at any ring position capable of forming a stable covalent bond, certain preferred points of attachment being apparent to those in the art (*e.g.*, 3-phenyl, 4-naphthyl, and the like). An aryl can be substituted with 1, 2, or 3 substituents or optionally substituted with 1, 2, or 3 substituents. The definition of "aryl" includes but is not limited to heteroaryl. Illustrative examples of aryl groups include phenyl, biphenyl, naphthyl, dihydronaphthyl, tetrahydronaphthyl, indenyl, indanyl, azulenyl, anthryl, phenanthryl, fluorenyl, pyrenyl, anthracenyl, pyridyl, pyrimidyl, pyridizinyl, thiadiazolyl, and the like.

The term "heteroalkyl" refers to an alkyl group where one or more of the carbon atoms or hydrogen atoms present is replaced, independently, with a nitrogen, oxygen, sulfur, or halogen heteroatom. If the heteroatom does not have the same number of valence sites as the carbon atom it replaces, the number of hydrogens bonded to the replacement heteroatom may need to be increased or decreased to match the number of valence sites of the heteroatom. For example, if a carbon atom (with a valence of four) is replaced by a nitrogen atom (valence of three), one of the hydrogen atoms formerly attached to the replaced carbon is deleted. Likewise, if a carbon atom is replaced by a halogen atom (valence of one), three of the hydrogen atoms formerly attached to the replaced carbon is deleted. The term "heteroalkyl" also refers to (1) an alkyl group where at least one of the hydrogen atoms attached to a carbon or (2) to a heteroalkyl group where at least one of the

hydrogen atoms attached to a heteroatom of the heteroalkyl can be substituted with at least one of the following: alkyl, aryl, and heteroalkyl.

The terms "heteroaryl" and "substituted heteroaryl" are interchangeable unless otherwise specifically noted and the terms "heterocyclo" and "substituted heterocyclo" are interchangeable unless otherwise specifically noted and these terms refer to a monovalent unsaturated group having a single ring or multiple condensed rings, from 1 to 8 carbon atoms, and from 1 to 4 heteroatoms within the ring, each heteroatom being independently selected from nitrogen, sulfur, or oxygen. In either heteroaryl or heterocyclo, the point of attachment to the molecule can be at a heteroatom or elsewhere within the ring. A heteroaryl or heterocyclo can be substituted with 1, 2, or 3 substituents or optionally substituted with 1, 2, or 3 substituents.

Illustrative examples of heteroaryl groups include thienyl, benzothienyl, isobenzothienyl, 2,3-dihydrobenzothienyl, furyl, pyranyl, benzofuranyl, isobenzofuranyl, 2,3-dihydrobenzofuranyl, pyrrolyl, pyrrol-3-yl, pyrrol-1-yl, indolyl, isoindolyl, 3H-indolyl, indolinyl, indolizinyl, indazolyl, imidazolyl, imidazol-4-yl, 2H-imidazolinyl, benzimidazolyl, pyridyl, pyrazinyl, pyradazinyl, pyrimidinyl, pyrimidin-2-yl, triazinyl, quinolyl, isoquinolyl, 4H-quinolizinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, chromanyl, benzodioxolyl, piperonyl, purinyl, pyrazolyl, pyrazol-3-yl, triazolyl, 1,2,4-triazol-1-yl, tetrazolyl, tetrazol-1-yl, thiazolyl, thiazol-4-yl, isothiazolyl, benzthiazolyl, oxazolyl, oxazol-2-yl, isoxazolyl, isoxazol-3-yl, benzoxazolyl, oxadiazolyl, 1,2,4-oxadiazol-3-yl, thiadiazolyl, pyridazin-4-yl, pyrazin-2-yl, thiophen-2-yl, furan-2-yl, pyridin-2-yl, pyridin-4-yl, pyrimidin-2-yl, and the like.

When any group is substituted with 1, 2, or 3 substituents or optionally substituted with 1, 2, or 3 substituents, each substituent is independently selected from the group comprising halo, -OH, -SH, -CN, $-NO_2$,$-NH_2$, trihalomethyl, pentahaloethyl, C_1-C_{10}alkyl, arylC_0-C_{10}alkyl, C_0-C_{10}alkyloxyC_0-C_{10}alkyl, arylC_0-C_{10}alkyloxyC_0-C_{10}alkyl, C_0-C_{10}alkylthioC_0-C_{10}alkyl, arylC_0-C_{10}alkylthioC_0-C_{10}alkyl, C_0-C_{10}alkylaminoC_0-C_{10}alkyl, arylC_0-C_{10}alkylaminoC_0-C_{10}alkyl, N-aryl-N-C_0-C_{10}alkylaminoC_0-C_{10}alkyl, C_1-C_{10}alkylcarbonylC_0-C_{10}alkyl, arylC_1-C_{10}alkylcarbonylC_0-C_{10}alkyl, C_1-C_{10}alkylcarboxyC_0-C_{10}alkyl, arylC_1-C_{10}alkylcarboxyC_0-C_{10}alkyl, C_1-C_{10}alkylcarbonylaminoC_0-C_{10}alkyl, arylC_1-C_{10}alkylcarbonylaminoC_0-C_{10}alkyl, -C_0-C_{10}alkylC(O)OR_X, and -C_0-C_{10}alkylC(O)NR_YR_Z wherein R_X, R_Y and R_Z are independently selected from hydrogen, alkyl, and aryl or R_Y and R_Z are taken together with the nitrogen to which they are attached to form a saturated cyclic or unsaturated cyclic system having 3, 4, 5, 6, 7, or 8 carbon atoms with at least one substituent as defined above. A "C_0alkyl," as in C_0-C_{10}alkyl, is a covalent bond.

The term "C_0-C_{10}alkyloxy" refers to an alkyl group having the indicated number of carbon atoms and attached to the molecule through an oxygen atom. In one embodiment, a C_0-C_{10}alkyloxy

is a C_1-C_6alkyloxy, *i.e.*, a group having 1, 2, 3, 4, 5, or 6 carbon atoms. Illustrative examples of alkyloxy groups include methoxy, ethoxy, n-propyloxy, and isopropyloxy. Thus, the term "C_0-C_{10}alkyloxyC_0-C_{10}alkyl" refers to a C_0-C_{10}alkyloxy attached through an oxygen atom to a C_0-C_{10}alkyl which is attached to the molecule. Likewise, the term "arylC_0-C_{10}alkyloxyC_0-C_{10}alkyl" refers to a C_0-C_{10}alkyloxy, which is substituted by aryl, attached through an oxygen atom to a C_0-C_{10}alkyl which is attached to the molecule. A "C_6alkyloxy" is -OH.

The term "C_0-C_{10}alkylthio" refers to an alkyl group having the indicated number of carbon atoms and attached to the molecule through a sulfur atom. In one embodiment, a C_0-C_{10}alkylthio is a C_1-C_6alkylthio, *i.e.*, a group having 1, 2, 3, 4, 5, or 6 carbon atoms. Illustrative examples of alkyloxy groups include methylthio, ethylthio, n-propylthio, and isopropylthio. Thus, the term "C_0-C_{10}alkylthioC_0-C_{10}alkyl" refers to a C_0-C_{10}alkylthio attached through a sulfur atom to a C_0-C_{10}alkyl which is attached to the molecule. Likewise, the term "arylC_0-C_{10}alkylthioC_0-C_{10}alkyl" refers to a C_0-C_{10}alkylthio, which is substituted by aryl, attached through a sulfur atom to a C_0-C_{10}alkyl which is attached to the molecule. A "C_6alkylthio" is -SH.

The term "C_1-C_{10}alkylcarbonyl" refers to an alkyl group having the indicated number of carbon atoms and attached to the molecule through the carbon atom of a carbonyl group. In one embodiment, a C_1-C_{10}alkylcarbonyl is a C_1-C_6alkylcarbonyl, *i.e.*, a group having 1, 2, 3, 4, 5, or 6 carbon atoms, including the carbonyl carbon atom. Thus, the term "C_1-C_{10}alkylcarbonylC_0-C_{10}alkyl" refers to a C_1-C_{10}alkylcarbonyl attached through the carbon atom of a carbonyl group to a C_0-C_{10}alkyl which is attached to the molecule. Likewise, the term "arylC_1-C_{10}alkylcarbonylC_0-C_{10}alkyl" refers to a C_1-C_{10}alkylcarbonyl, which is substituted by aryl, attached through the carbon atom of a carbonyl group to a C_0-C_{10}alkyl which is attached to the molecule.

The term "C_1-C_{10}alkylcarboxy" refers to an alkyl group having the indicated number of carbon atoms, including the carboxy's carbon atom, and attached to the molecule through the carboxy group, wherein the carboxy group has either a -C(=O)-O- or a -O-C(=O)- orientation. In one embodiment, a C_1-C_{10}alkylcarboxy is a C_1-C_6alkylcarboxy, *i.e.*, a group having 2, 3, 4, 5, or 6 carbon atoms, including the carboxy's carbon atom. Thus, the term "C_1-C_{16}alkylcarboxyC_0-C_{10}alkyl" refers to a C_1-C_{10}alkylcarboxy attached through the carboxy group to a C_0-C_{10}alkyl which is attached to the molecule. Likewise, the term "arylC_1-C_{10}alkylcarboxyC_0-C_{10}alkyl" refers to a C_1-C_{10}alkylcarboxy, which is substituted by aryl, attached through the carboxy group to a C_0-C_{10}alkyl which is attached to the molecule.

The term "C_0-C_{10}alkylamino" refers to an alkyl group having the indicated number of carbon atoms and attached to the molecule through the nitrogen atom of the amino group -N(R_W)-, wherein R_W is H, C_1-C_6alkyl, or aryl. A "C_0alkylamino" is -NHR_W. In one embodiment, a C_0-C_{10}alkylamino is a C_1-C_6alkylamino, *i.e.*, a group having 1, 2, 3, 4, 5, or 6 carbon atoms in the alkyl

group and 0, 1, 2, 3, 4, 5, or 6 carbon atoms in the R_W group. Thus, the term "C_0-C_{10}alkylaminoC_0-C_{10}alkyl" refers to a C_0-C_{10}alkylamino attached through the nitrogen atom of an amino group to a C_0-C_{10}alkyl which is attached to the molecule. Likewise, the term "arylC_0-C_{10}alkylaminoC_0-C_{10}alkyl" refers to a C_0-C_{10}alkylamino, which is substituted by aryl, attached through the nitrogen atom of an amino group to a C_0-C_{10}alkyl which is attached to the molecule. The term "N-aryl-N-C_0-C_{10}alkylaminoC_0-C_{10}alkyl" refers to an amine nitrogen atom substituted by aryl and C_0-C_{10}alkyl, that nitrogen atom being further attached to a C_0-C_{10}alkyl which is attached to the molecule.

The term "C_1-C_{10}alkylcarbonylamino" refers to an alkyl group having the indicated number of carbon atoms, including the carbonylamino's (*i.e.*, amide's) carbon atom, and attached to the molecule through the amide, group, wherein the amide group has either a -C(=O)N(R_V)- or a -N(R_V)C(=O)- orientation and wherein R_V is H or C_1-C_6alkyl. In one embodiment, a C_1-C_{10}alkylcarbonylamino is a C_1-C_6alkylcarbonylamino, *i.e.*, a group having 2, 3, 4, 5, or 6 carbon atoms, including the amide's carbon atom, in the alkyl group and 0, 1, 2, 3, 4, 5, or 6 carbon atoms in the R_V group. Thus, the term "C_1-C_{10}alkylcarbonylaminoC_0-C_{10}alkyl" refers to a C_1-C_{10}alkylcarbonylamino attached through the amide group to a C_0-C_{10}alkyl which is attached to the molecule. Likewise, the term "arylC_1-C_{10}alkylcarbonylaminoC_0-C_{10}alkyl" refers to a C_1-C_{10}alkylcarbonylamino, which is substituted by aryl, attached through the amide group to a C_0-C_{10}alkyl which is attached to the molecule.

The term "alkylaryl" refers to an aryl group as defined above that is substituted with 1, 2, or 3 alkyl groups as defined above; a tolyl group is an exemplary alkylaryl. In one embodiment, an alkylaryl group is a "lower alkylaryl" group having 1, 2, or 3 alkyl groups attached to an aryl group, each alkyl group having, independently, 1, 2, 3, 4, 5, or 6 carbon atoms.

The term "arylalkyl" refers to an alkyl group as defined above that is substituted with 1, 2, or 3 aryl groups as defined above; a benzyl group is an exemplary arylalkyl. In one embodiment, an arylalkyl group is a "lower arylalkyl" group having 1, 2, or 3 aryl groups attached to an alkyl group having 1, 2, 3, 4, 5, or 6 carbon atoms.

The term "heterocycloalkyl" refers to an alkyl group as defined above that is substituted with 1, 2, or 3 heterocyclo groups as defined above. In one embodiment, a heterocycloalkyl group is a "lower heterocycloalkyl" group having 1, 2, or 3 heterocyclo groups attached to an alkyl group having 1, 2, 3, 4, 5, or 6 carbon atoms.

The term "alkylheteroaryl" refers to a heteroaryl group as defined above that is substituted with 1, 2, or 3 alkyl groups as defined above. In one embodiment, a alkylheteroaryl group is a "lower alkylheteroaryl" group having 1, 2, or 3 alkyl groups attached to a heteroaryl group, each alkyl group having, independently, 1, 2, 3, 4, 5, or 6 carbon atoms.

The term "heteroarylalkyl" refers to an alkyl group as defined above that is substituted with 1, 2, or 3 heteroaryl groups as defined above. In one embodiment, a heteroarylalkyl group is a "lower heteroarylalkyl" group having 1, 2, or 3 heteroaryl groups attached to an alkyl group having 1, 2, 3, 4, 5, or 6 carbon atoms.

The term "alkylheteroarylalkyl" refers to a heteroarylalkyl group as defined above that is substituted with 1, 2, or 3 alkyl groups as defined above. In one embodiment, an alkylheteroarylalkyl group is a "lower alkylheteroarylalkyl" group with each alkyl portion having, independently, 1, 2, 3, 4, 5, or 6 carbon atoms.

The terms "halogen" and "halo" refer to fluorine, chlorine, bromine, and iodine.

An R group disclosed to be " interrupted by -S(O)N(R_A)-, -$NR_AS(O)$-, -$SO_2N(R_A)$-, -NR_ASO_2-, -C(O)N(R_A)-, and -$NR_AC(O)$-, and/or terminated by -$S(O)NR_AR_B$, -$NR_AS(O)R_B$, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -$C(O)NR_AR_B$, or -$NR_AC(O)R_B$", means said R group is (1) interrupted by one or more (for example1, 2, or 3) -S(O)N(R_A)-, -$NR_AS(O)$-, -$SO_2N(R_A)$-, -NR_ASO_2-, -C(O)N(R_A)-, or -$NR_AC(O)$- groups, (2) terminated by -$S(O)NR_AR_B$, -$NR_AS(O)R_B$, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -$C(O)NR_AR_B$, or -$NR_AC(O)R_B$ groups, or (3) interrupted by one or more (for example 1, 2, or 3) -S(O)N(R_A)-, -$NR_AS(O)$-, -$SO_2N(R_A)$-, -NR_ASO_2-, -C(O)N(R_A)-, or -$NR_AC(O)$- groups and terminated by an -$S(O)NR_AR_B$, -$NR_AS(O)R_B$, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -$C(O)NR_AR_B$, or -$NR_AC(O)R_B$ group. In one embodiment, there are two interruptions and no terminations of an alkyl R group as described above. In another embodiment, there is one interruption and no terminations of an alkyl R group as described above. In another embodiment, there is no interruption and a termination of an alkyl R group as described above. In another embodiment, there is one interruption and a termination of an alkyl R group as described above.

Should there be doubt as to the agreement of a depicted chemical structure and a chemical name, the depicted chemical structure governs.

The term "pharmaceutically acceptable salt" refers to those salts which retain the biological effectiveness and properties of the "free" compounds of Formulae (IA) and (IB). A pharmaceutically acceptable salt can be obtained from the reaction of the free base of a Compound of Formulae (IA) or (IB) with an inorganic acid, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like, or an organic acid, for example, sulfonic acid, carboxylic acid, organic phosphoric acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, citric acid, fumaric acid, maleic acid, succinic acid, benzoic acid, salicylic acid, lactic acid, tartaric acid (*e.g.*, (+)-tartaric acid or (-)-tartaric acid or mixtures thereof), and the like. Certain compounds of Formulae (IA) and (IB) have acidic substituents and can exist as pharmaceutically acceptable salts with pharmaceutically acceptable bases. The present disclosure includes such salts. Examples of such salts include metal counterion salts, such as sodium,

potassium, lithium, magnesium, calcium, iron, copper, zinc, tin, silver, or aluminum salts, and organic amine salts, such as methylamine, dimethylamine, trimethylamine, diethylamine, triethylamine, n-propylamine, 2-propylamine, or dimethylisopropylamine salts, and the like. The term "pharmaceutically acceptable salt" includes mono-salts and compounds in which a plurality of salts is present, *e.g.*, di-salts and/or tri-salts. Pharmaceutically acceptable salts can be prepared by methods known to those in the art.

Certain compounds of Formulae (IA) and (IB) and/or their pharmaceutically acceptable salts can exist in more than one crystal form and the present disclosure encompasses each crystal form and mixtures thereof. These crystal forms can be prepared by methods known to those in the art.

The term "solvate" refers to a complex or aggregate formed by one or more molecules of a solute, *e.g.*, a Compound of Formulae (IA) or (IB) or its pharmaceutically acceptable salt, and one or more molecules of a solvent, which is present in stoichiometric or non-stoichiometric amount. Suitable solvents include but are not limited to water, acetic acid, ethanol, methanol, isopropanol, and n-propanol. Where the solvent is water, the solvate is a hydrate. Exemplary hydrates include but are not limited to a hemihydrate, a monohydrate, a dihydrate, a trihydrate, and a tetrahydrate. In one embodiment, the solvent is pharmaceutically acceptable. In another embodiment, the complex or aggregate is in a crystalline form. In another embodiment, the complex or aggregate is in a noncrystalline form. The present disclosure encompasses each solvate and mixtures thereof. These solvates can be prepared by methods known to those in the art.

Certain compounds of Formulae (IA) and (IB) may exist in different tautomeric forms or as different geometric isomers, and the present disclosure includes each tautomer and/or geometric isomer of compounds of Formulae (IA) and (IB) and mixtures thereof.

Certain compounds of Formulae (IA) and (IB) may contain one or more chiral centers and exist in different optically active forms, and the present disclosure includes each optically active form of compounds of Formulae (IA) and (IB) and mixtures thereof. When compounds of Formulae (IA) and (IB) contain one chiral center, the compounds exist in two enantiomeric forms and the present disclosure includes both enantiomers and mixtures of enantiomers, such as racemic mixtures. The enantiomers may be resolved by methods known to the art, for example, by formation of diastereoisomeric salts which may be separated, *e.g.*, by crystallization or liquid chromatography. Alternatively, specific enantiomers may be synthesized by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting one enantiomer into the other by asymmetric transformation. When a Compound of Formulae (IA) or (IB) contains more than one chiral center, it may exist in diastereoisomeric forms. The diastereoisomeric compounds may be separated by methods known to the art, for example, by chromatography or

crystallization, and the individual enantiomers may be separated as described above. The present disclosure includes each diastereoisomer of compounds of Formulae (IA) and (IB) and mixtures thereof.

The term "isotopically enriched" refers to a Compound of Formulae (IA) or (IB) that contains an unnatural proportion of an isotope at one or more of the atoms constituting the compound, and the present disclosure includes each isotopically enriched form of compounds of Formulae (IA) and (IB) and mixtures thereof. In certain embodiments, an isotopically enriched compound contains unnatural proportions of one or more isotopes, including but not limited to hydrogen (^{1}H), deuterium (^{2}H), tritium (^{3}H), carbon-11 (^{11}C), carbon-12 (^{12}C), carbon-13 (^{13}C), carbon-14 (^{14}C), nitrogen-13 (^{13}N), nitrogen-14 (^{14}N), nitrogen-15 (^{15}N), oxygen-14 (^{14}O), oxygen-15 (^{15}O), oxygen-16 (^{16}O), oxygen-17 (^{17}O), oxygen-18 (^{18}O), fluorine-17 (^{17}F), fluorine-18 (^{18}F), sulfur-32 (^{32}S), sulfur-33 (^{33}S), sulfur-34 (^{34}S), sulfur-35 (^{35}S), sulfur-36 (^{36}S), chlorine-35 (^{35}Cl), chlorine-36 (^{36}Cl), chlorine-37 (^{37}Cl), bromine-79 (^{79}Br), bromine-81 (^{81}Br), iodine-123 (^{123}I), iodine-125 (^{125}I), iodine-127 (^{127}I), iodine-129 (^{129}I), and iodine-131 (^{131}I). In another embodiment, an isotopically enriched compound contains unnatural proportions of one or more isotopes, including but not limited to ^{1}H, ^{2}H, ^{12}C, ^{13}C, ^{14}N, ^{15}N, ^{16}O, ^{17}O, ^{18}O, ^{17}F, ^{32}S, ^{33}S, ^{34}S, ^{36}S, ^{35}Cl, ^{37}Cl, ^{79}Br, ^{81}Br, and ^{127}I. In another embodiment, an isotopically enriched compound is radioactive. In another embodiment, an isotopically enriched compound contains unnatural proportions of one or more isotopes, including but not limited to ^{3}H, ^{11}C, ^{4}C, ^{13}N, ^{14}O, ^{15}O, ^{18}F, ^{35}S, ^{36}Cl, ^{123}I, ^{125}I, ^{129}I, and ^{131}I. In another embodiment, an isotopically enriched compound contains unnatural proportions of ^{123}I, ^{124}I, or ^{131}I and another isotope selected from ^{3}H, ^{11}C, ^{4}C, ^{13}N, ^{14}O, ^{15}O, ^{18}F, ^{35}S, and ^{36}Cl. In another embodiment, an isotopically enriched compound contains an unnatural proportion of ^{123}I, ^{124}I, and/or ^{131}I. In another embodiment, an isotopically enriched compound contains an unnatural proportion of ^{123}I. In another embodiment, an isotopically enriched compound contains an unnatural proportion of ^{124}I. In another embodiment, an isotopically enriched compound contains an unnatural proportion of ^{131}I.

The term "isotopically enriched" refers to the percentage of incorporation of a less prevalent isotope (*e.g.*, deuterium for hydrogen) of an element at a given location in a molecule in place of a more prevalent isotope (*e.g.*, ^{1}H for hydrogen) of that element. When an atom at a particular location in a molecule is designated as a particular less prevalent isotope, it is understood that the abundance of that isotope at that location is substantially greater than its natural abundance.

The term "therapeutically effective amount" refers to an amount of a Compound of Formulae (IA) or (IB) or a combination of two or more such compounds that inhibits, totally or partially, the progression of the treated condition or alleviates, at least partially, one or more symptoms of the condition. A therapeutically effective amount can also be an amount which is prophylactically effective. The amount which is therapeutically effective depends on the patient's

gender and size, the condition to be treated, the condition's severity, and the result sought. For a given patient, a therapeutically effective amount can be determined by methods known to those in the art.

The term "patient" refers to an animal, including but not limited to a mammal, a primate (*e.g.*, a human), cow, pig, sheep, goat, horse, dog, cat, rabbit, rat, or mouse.

The term "cancer" or "neoplastic disorder" refers to a tumor resulting from abnormal or uncontrolled cellular growth. Examples of cancers include but are not limited to breast cancers, colon cancers, colorectal cancers, prostate cancers, ovarian cancers, pancreatic cancers, lung cancers, gastric cancers, esophageal cancers, glioma cancers, and hematologic malignancies. Examples of neoplastic disorders include but are not limited to hematopoietic disorders, such as the myeloproliferative disorders, essential thrombocytosis, thrombocythemia, angiogenic myeloid metaplasia, polycythemia vera, myelofibrosis, myelofibrosis with myeloid metaplasia, chronic idiopathic myelofibrosis, the cytopenias, and pre-malignant myelodysplastic syndromes.

The term "hematologic malignancy" refers to cancer of the bone marrow and lymphatic tissue - body's blood-forming and immune system. Examples of hematological malignancies include but are not limited to myelodysplasia, lymphomas, leukemias, lymphomas (non-Hodgkin's lymphoma), Hodgkin's disease (also known as Hodgkin's lymphoma), and myeloma, such as acute lymphocytic leukemia (ALL), adult T-cell ALL, acute myeloid leukemia (AML), AML with trilineage myelodysplasia, acute promyelocytic leukemia, acute undifferentiated leukemia, anaplastic large-cell lymphoma, chronic lymphocytic leukemia, chronic myeloid leukemia, chronic neutrophilic leukemia, juvenile myelomonocytic leukemia, mixed lineage leukemia, myeloproliferative disorders, myelodysplastic syndromes, multiple myeloma, and prolymphocytic leukemia.

The term "leukemia" refers to malignant neoplasms of the blood-forming tissues including but not limited to acute lymphoblastic leukemia, acute myeloid leukemia, acute myeloblastic leukemia, chronic lymphocytic leukemia, and chronic myelocytic leukemia. The leukemia can be relapsed, refractory, or resistant to conventional therapy.

The term "neurodegenerative disorder" refers to a disorder in which progressive loss of neurons occurs either in the peripheral nervous system or in the central nervous system. Examples of neurodegenerative disorders include but are not limited to chronic neurodegenerative diseases such as diabetic peripheral neuropathy, Alzheimer's disease, Pick's disease, diffuse Lewy body disease, progressive supranuclear palsy (Steel-Richardson syndrome), multisystem degeneration (Shy-Drager syndrome), motor neuron diseases including amyotrophic lateral sclerosis ("ALS"), degenerative ataxias, cortical basal degeneration, ALS-Parkinson's-Dementia complex of Guam, subacute sclerosing panencephalitis, Huntington's disease, Parkinson's disease, multiple sclerosis,

synucleinopathies, primary progressive aphasia, striatonigral degeneration, Machado-Joseph disease/spinocerebellar ataxia type 3 and olivopontocerebellar degenerations, Gilles De La Tourette's disease, bulbar and pseudobulbar palsy, spinal and spinobulbar muscular atrophy (Kennedy's disease), primary lateral sclerosis, familial spastic paraplegia, Wernicke-Korsakoff's related dementia (alcohol induced dementia), Werdnig-Hoffmann disease, Kugelberg-Welander disease, Tay-Sach's disease, Sandhoff disease, familial spastic disease, Wohifart-Kugelberg-Welander disease, spastic paraparesis, progressive multifocal leukoencephalopathy, and prion diseases (including Creutzfeldt-Jakob, Gerstmann-Straussler-Scheinker disease, Kuru and fatal familial insomnia). Other conditions also included within the methods of the present disclosure include age-related dementia and other dementias, and conditions with memory loss including vascular dementia, diffuse white matter disease (Binswanger's disease), dementia of endocrine or metabolic origin, dementia of head trauma and diffuse brain damage, dementia pugilistica, and frontal lobe dementia. Also other neurodegenerative disorders resulting from cerebral ischemia or infarction including embolic occlusion and thrombotic occlusion as well as intracranial hemorrhage of any type (including but not limited to epidural, subdural, subarachnoid, and intracerebral), and intracranial and intravertebral lesions (including but not limited to contusion, penetration, shear, compression, and laceration). Thus, the term "neurodegenerative disorder" also encompasses acute neurodegenerative disorders such as those involving stroke, traumatic brain injury, schizophrenia, peripheral nerve damage, hypoglycemia, spinal cord injury, epilepsy, anoxia, and hypoxia.

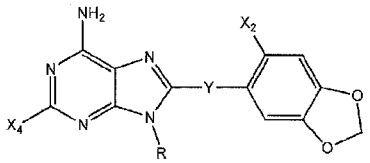
In certain embodiments, the neurodegenerative disorder is selected from Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, age-related memory loss, senility, and age-related dementia. In another embodiment, the neurodegenerative disorder is Alzheimer's disease, also characterized as an amyloidosis. Thus, other embodiments of the disclosure relate to the treatment or prevention of other amyloidosis disorders which share features, includin, but not limited to, hereditary cerebral angiopathy, normeuropathic hereditary amyloid, Down's syndrome, macroglobulinemia, secondary familial Mediterranean fever, Muckle-Wells syndrome, multiple myeloma, pancreatic- and cardiac-related amyloidosis, chronic hemodialysis arthropathy, Finnish amyloidosis, and Iowa amyloidosis.

The term "pharmaceutically acceptable carrier" refers to a pharmaceutically-acceptable material, composition, or vehicle, such as a liquid or solid filler, diluent, solvent, or encapsulating material. In one embodiment, each component is "pharmaceutically acceptable" in the sense of being compatible with the other ingredients of a pharmaceutical formulation, and suitable for use in contact with the tissue or an organ of a patient without excessive toxicity, irritation, allergic response, immunogenicity, or other problems or complications, commensurate with a reasonable benefit/risk ratio. Pharmaceutically acceptable carriers are known in the art; *see, e.g.*, *Pharmaceutical Preformulation and Formulation* (Gibson, ed., 2nd Ed., CRC Press, Boca Raton,

FL, 2009); *Handbook of Pharmaceutical Additives* (Ash and Ash, eds., 3rd Ed., Gower Publishing Co., Aldershot, UK, 2007); *Remington's Pharmaceutical Sciences* (Gennaro, ed., 19th Ed., Mack Publishing, Easton, PA, 1995); and *Handbook of Pharmaceutical Excipients* (Amer. Pharmaceutical Ass'n, Washington, DC, 1986).

C. Compounds of Formula (IA) in Which Xa and Xb are Each O

In accordance with an embodiment of the disclosure, the compounds are of Formula (IA) in which Xa and Xb are each O and Xc is CH_2. In certain embodiments, the compounds of this embodiment can be represented by Formula (1):



(1)

or a pharmaceutically acceptable salt thereof, wherein:

Y is CH_2 or S;

X_4 is hydrogen or halogen;

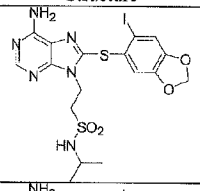
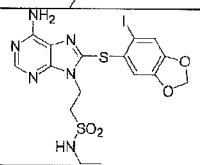
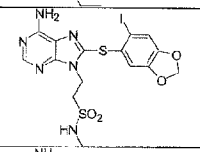
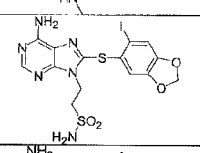
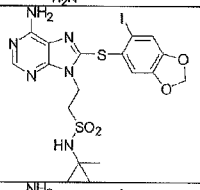
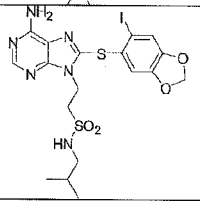
R is a is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, hetercaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

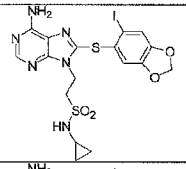
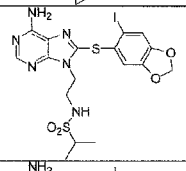
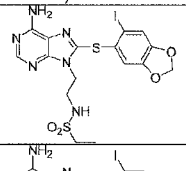
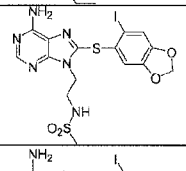
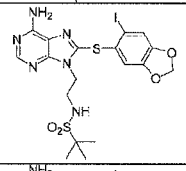
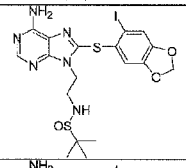
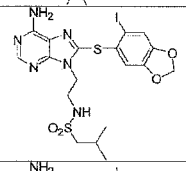
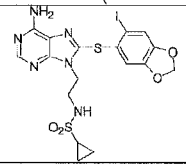
X_2 is as disclosed below.

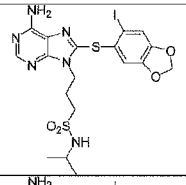
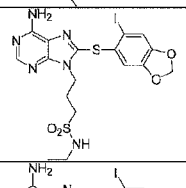
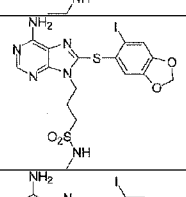
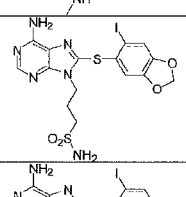
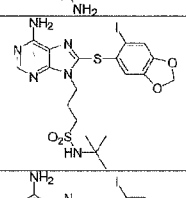
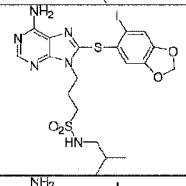
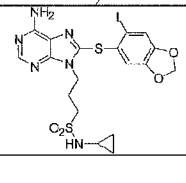
C-I. In some embodiments of the disclosure, X_2 is halogen. Table 1A lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is I and X_4 is H. However, corresponding structures in which X_2 is F, Cl, or Br are within the scope of the disclosure. In each of the structures in Table 1A, Y is S. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally,

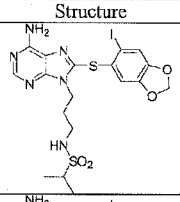
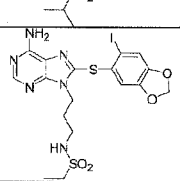
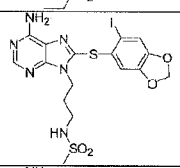
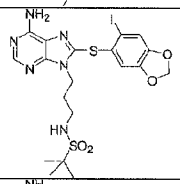
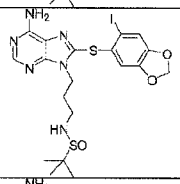
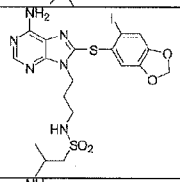
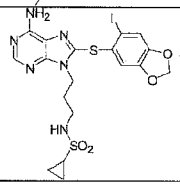
in connection with each of the structures in Table 1A, corresponding structures in which X_2 is F, Cl, or Br and Y is CH_2 are also within the scope of the disclosure.

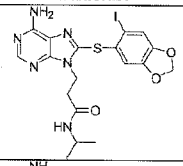
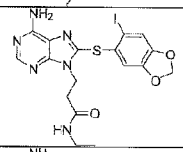
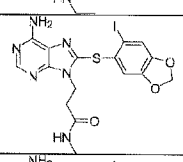
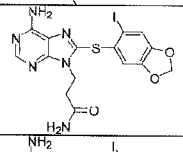
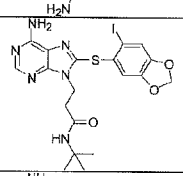
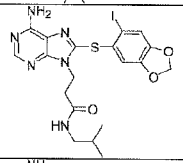
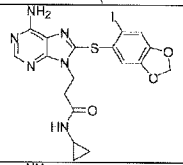
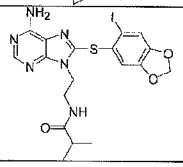
Table 1A

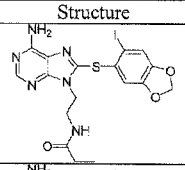
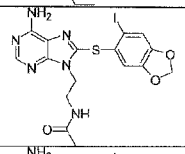
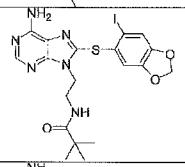
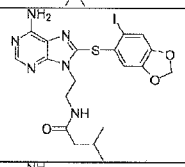
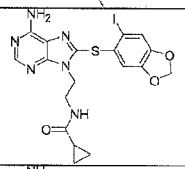
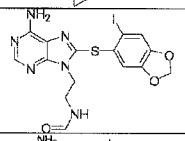
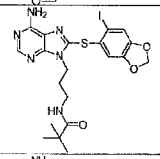
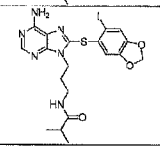
Compound No.	Structure	Name
1A-1		2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isopropylamide
1A-2		2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid ethylamide
1A-3		2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid methylamide
1A-4		2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid amide
1A-5		2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid tert-butylamide
1A-6		2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isobutyl-amide

Compound No.	Structure	Name
1A-7		2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid cyclopropylamide
1A-8		Propane-2-sulfonic acid {2-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1A-9		Ethanesulfonic acid {2-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1A-10		N-{2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-methanesulfonamide
1A-11		2-Methyl-propane-2-sulfonic acid {2-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1A-12		2-Methyl-propane-2-sulfinic acid {2-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1A-13		2-Methyl-propane-1-sulfonic acid {2-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1A-14		Cyclopropanesulfonic acid {2-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide

Compound No.	Structure	Name
1A-15		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isopropylamide
1A-16		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid ethylamide
1A-17		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid methylamide
1A-18		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid amide
1A-19		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid tert-butylamide
1A-20		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isobutyl-amide
1A-21		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid cyclopropylamide

Compound No.	Structure	Name
1A-22		Propane-2-sulfonic acid {3-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1A-23		Ethanesulfonic acid {3-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1A-24		N-{3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-methanesulfonamide
1A-25		2-Methyl-propane-2-sulfonic acid {3-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1A-26		2-Methyl-propane-2-sulfinic acid {3-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1A-27		2-Methyl-propane-1-sulfonic acid {3-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1A-28		Cyclopropanesulfonic acid {3-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide

Compound No.	Structure	Name
1A-29		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-isopropyl-propionamide
1A-30		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-ethyl-propionamide
1A-31		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-methyl-propionamide
1A-32		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propionamide
1A-33		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-tert-butyl-propionamide
1A-34		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-isobutyl-propionamide
1A-35		3-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-cyclopropyl-propionamide
1A-36		N-{2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-isobutyramide

Compound No.	Structure	Name
1A-37		N-{2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide
1A-38		N-{2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-acetamide
1A-39		N-{2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-2,2-dimethyl-propionamide
1A-40		N-{2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-3-methyl-butyramide
1A-41		Cyclopropanecarboxylic acid {2-[6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1A-42		N-{2-[6-Amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-formamide
1A-43		*N*-(3-(6-amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)pivalamide
1A-44		*N*-(3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)isobutyramide

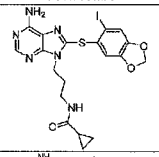
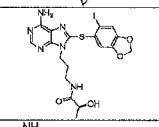
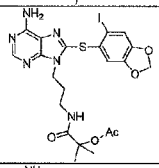
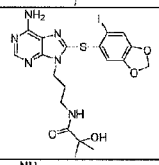
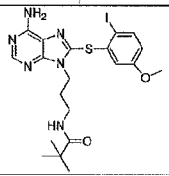
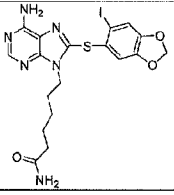
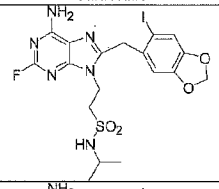
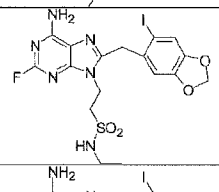
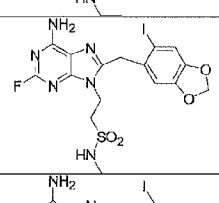
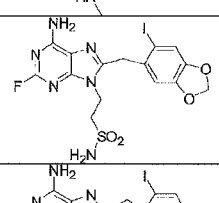
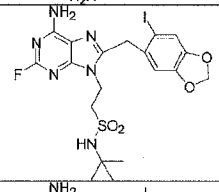
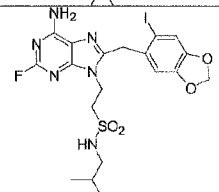
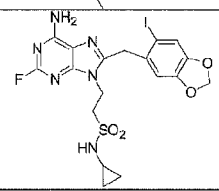
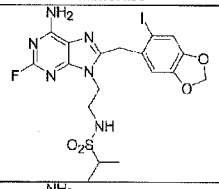
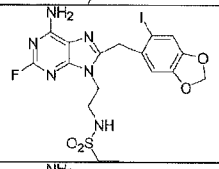
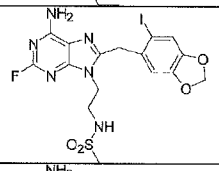
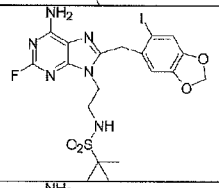
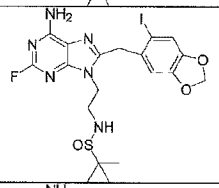
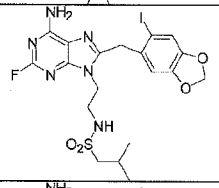
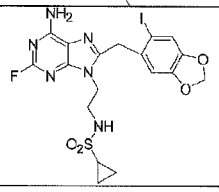
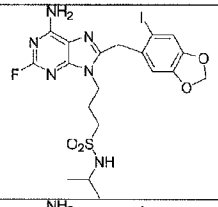
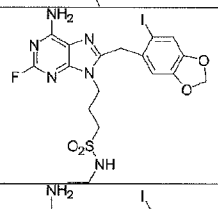
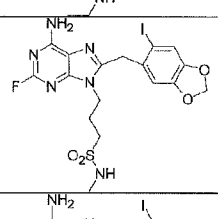
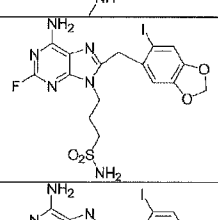
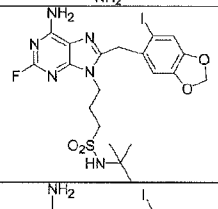
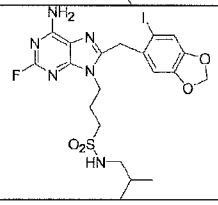
Compound No.	Structure	Name
1A-45		*N*-3-(6-amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)cyclopropane carboxamide
1A-46		*N*-(3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)isobutyramide
1A-47		1-((3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)amino)-2-methyl-1-oxopropan-2-yl acetate
1A-48		*N*-(3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)-2-hydroxy-2-methylpropanamide
1A-49		N-(3-(6-amino-8-((2-iodo-5-methoxyphenyl)thio)-9H-purin-9-yl)propyl)pivalamide
1A-50		6-(6-amino-8-((6-iodobenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)hexanamide

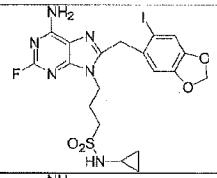
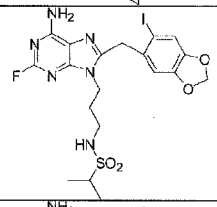
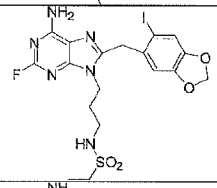
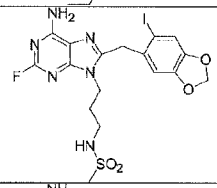
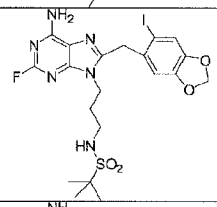
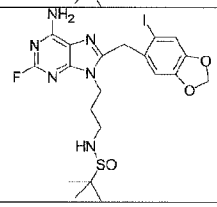
Table 4A lists specific examples in which X_2 is halogen and X_4 is halogen. In each of the structures as drawn, X_2 is I and X_4 is F. However, corresponding structures in which X_4 is H, Cl, Br, or I are within the scope of the disclosure. In each of the structures in Table 4A, Y is CH_2. However, corresponding structures in which Y is S and/or X_2 is F, Cl, or Br are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 4A, corresponding structures in which X_4 is H, Cl, Br, or I and Y is S are also within the scope of the disclosure.

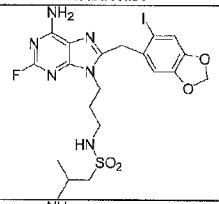
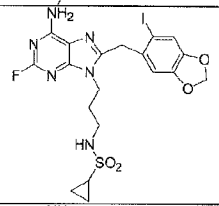
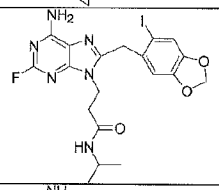
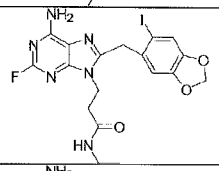
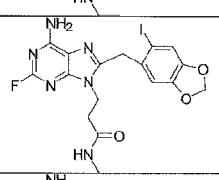
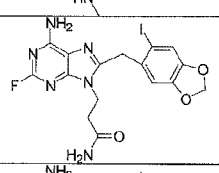
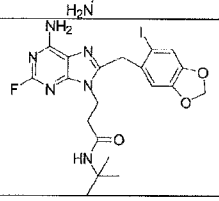
Table 4A

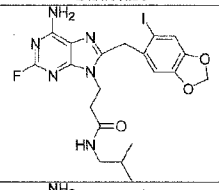
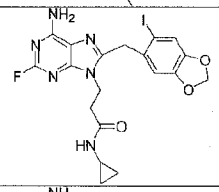
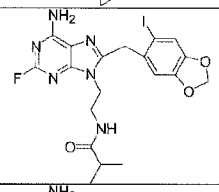
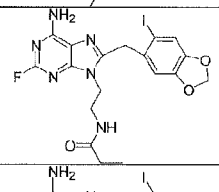
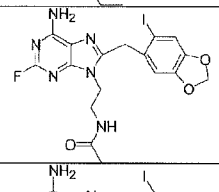
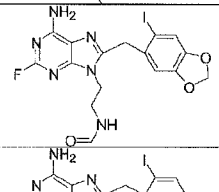
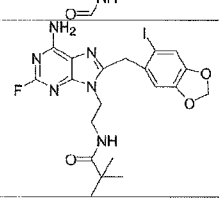
Compound No.	Structure	Name
4A-1		2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-isopropyl-ethanesulfonamide
4A-2		2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-ethylethanesulfonamide
4A-3		2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-methylethanesulfonamide
4A-4		2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethanesulfonamide
4A-5		2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
4A-6		2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-isobutylethanesulfonamide
4A-7		2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide

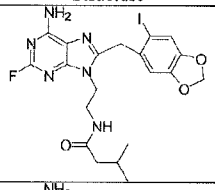
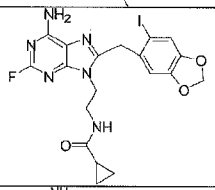
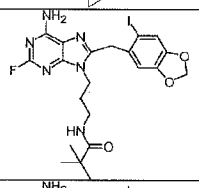
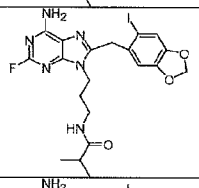
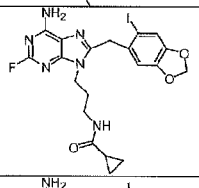
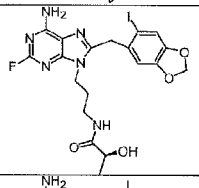
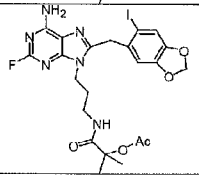
Compound No.	Structure	Name
4A-8		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
4A-9		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)ethanesulfonamide
4A-10		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)methane-sulfonamide
4A-11		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
4A-12		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
4A-13		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
4A-14		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide

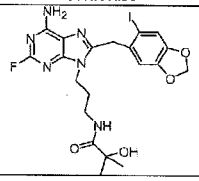
Compound No.	Structure	Name
4A-15		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
4A-16		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
4A-17		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
4A-18		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propane-1-sulfonamide
4A-19		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide
4A-20		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide

Compound No.	Structure	Name
4A-21		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
4A-22		N-(3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)propane-2-sulfonamide
4A-23		N-(3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)ethane-sulfonamide
4A-24		N-(3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)methane-sulfonamide
4A-25		N-(3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide
4A-26		N-(3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide

Compound No.	Structure	Name
4A-27		N-(3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide
4A-28		N-(3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
4A-29		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropanamide
4A-30		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropanamide
4A-31		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-methylpropanamide
4A-32		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propanamide
4A-33		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propanamide

Compound No.	Structure	Name
4A-34		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropanamide
4A-35		3-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropanamide
4A-36		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)isobutyramide
4A-37		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)propionamide
4A-38		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)acetamide
4A-39		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)formamide
4A-40		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)pivalamide

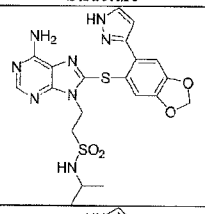
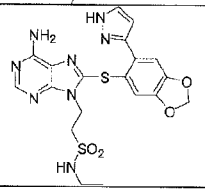
Compound No.	Structure	Name
4A-41		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)-3-methylbutanamide
4A-42		N-(2-(6-amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropanecarboxamide
4A-43		N-{3-[6-Amino-2-fluoro-8-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
4A-44		N-{3-[6-Amino-2-fluoro-8-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)-purin-9-yl]-propyl}-isobutyramide
4A-45		Cyclopropanecarboxylic acid {3-[6-amino-2-fluoro-8-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)-purin-9-yl]-propyl}-amide
4A-46		N-{3-[6-Amino-2-fluoro-8-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
4A-47		Acetic acid 1-{3-[6-amino-2-fluoro-8-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester

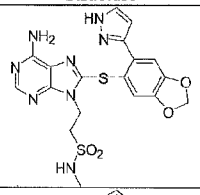
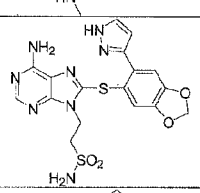
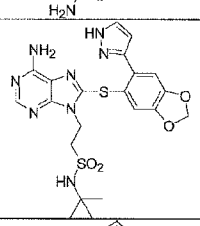
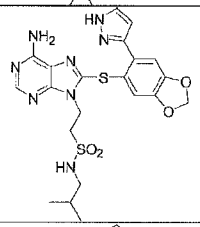
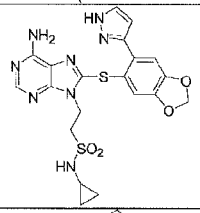
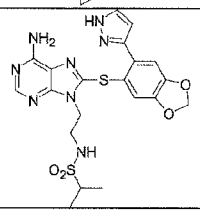
Compound No.	Structure	Name
4A-48		N-{3-[6-Amino-2-fluoro-8-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide

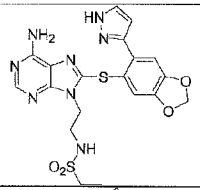
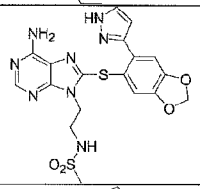
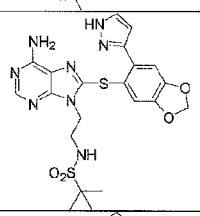
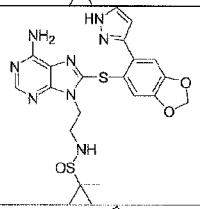
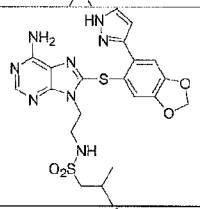
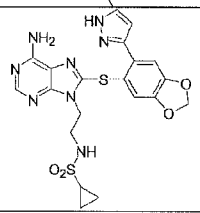
Hsp90 binding results are presented for Compounds 1A-5. 1A-10, 1A-11, 1A-12, 1A-15, 1A-19, 1A-22 , 1A-24, 1A-25 to1A-28, 1A-43 to 1A-50, 4A-26, 4A-28, 4A-43, and 4A-45in Table 12 below. As can be noted therefrom, all compounds showed a high level of binding affinity.

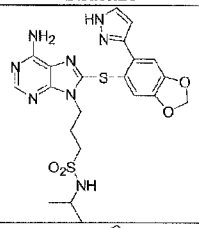
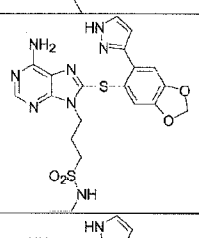
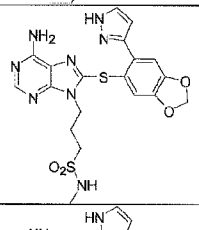
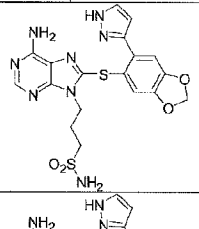
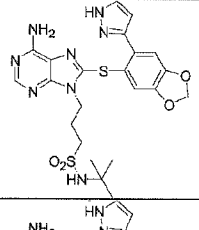
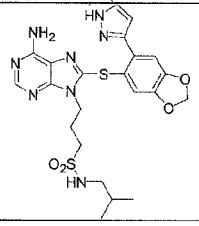
C-II. In some embodiments of the disclosure, X_2 is an optionally substituted aryl. Table 1C lists specific examples of compounds within this embodiment. In each of the structures as drawn therein, X_2 is a nitrogen-containing heteroaryl group, specifically a pyrazolyl group, and X_4 is H. Corresponding structures in which X_2 is a different nitrogen-containing optionally substituted aryl group are within the scope of the disclosure. In each of the structures in Table 1C, Y is S and X_4 is H. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 1C, corresponding structures in which X_2 is a nitrogen-containing optionally substituted aryl group different from optionally substituted pyrazolyl, Y is CH_2, and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure.

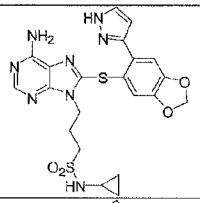
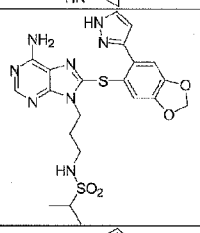
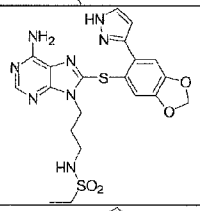
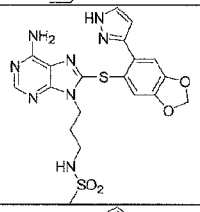
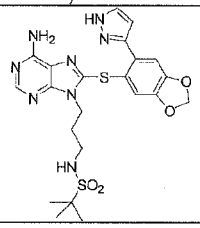
Table 1C

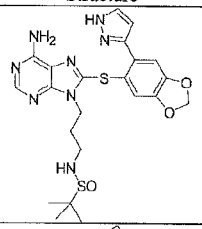
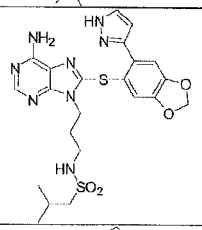
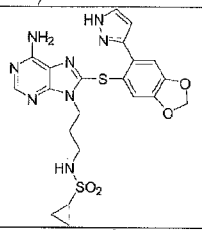
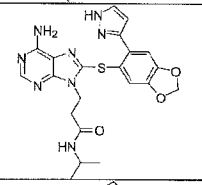
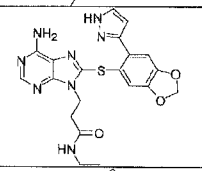
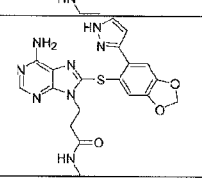
Compound No.	Structure	Name
1C-1		2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethanesulfonic acid isopropylamide
1C-2		2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethanesulfonic acid ethylamide

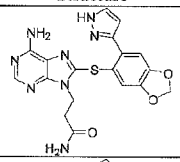
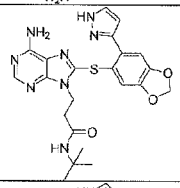
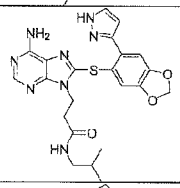
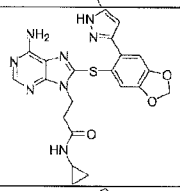
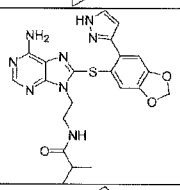
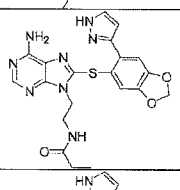
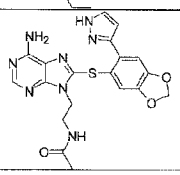
Compound No.	Structure	Name
1C-3		2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethanesulfonic acid methylamide
1C-4		2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethanesulfonic acid amide
1C-5		2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethanesulfonic acid tert-butylamide
1C-6		2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethanesulfonic acid isobutyl-amide
1C-7		2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethanesulfonic acid cyclopropylamide
1C-8		Propane-2-sulfonic acid (2-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-amide

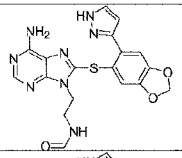
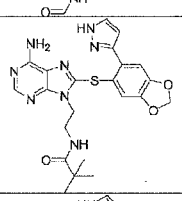
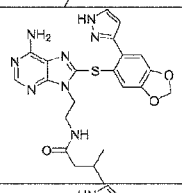
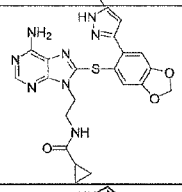
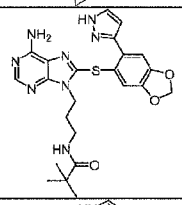
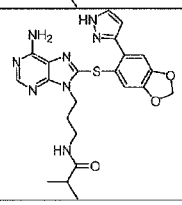
Compound No.	Structure	Name
1C-9		Ethanesulfonic acid (2-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-amide
1C-10		N-(2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-methanesulfonamide
1C-11		2-Methyl-propane-2-sulfonic acid (2-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-amide
1C-12		2-Methyl-propane-2-sulfinic acid (2-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-amide
1C-13		2-Methyl-propane-1-sulfonic acid (2-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-amide
1C-14		Cyclopropanesulfonic acid (2-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-amide

Compound No.	Structure	Name
1C-15		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propane-1-sulfonic acid isopropylamide
1C-16		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propane-1-sulfonic acid ethylamide
1C-17		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propane-1-sulfonic acid methylamide
1C-18		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propane-1-sulfonic acid amide
1C-19		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propane-1-sulfonic acid tert-butylamide
1C-20		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propane-1-sulfonic acid isobutyl-amide

Compound No.	Structure	Name
1C-21		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propane-1-sulfonic acid cyclopropylamide
1C-22		Propane-2-sulfonic acid (3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide
1C-23		Ethanesulfonic acid (3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide
1C-24		N-(3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-methanesulfonamide
1C-25		2-Methyl-propane-2-sulfonic acid (3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide

Compound No.	Structure	Name
1C-26		2-Methyl-propane-2-sulfinic acid (3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide
1C-27		2-Methyl-propane-1-sulfonic acid (3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide
1C-28		Cyclopropanesulfonic acid (3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide
1C-29		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-N-isopropyl-propionamide
1C-30		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-N-ethyl-propionamide
1C-31		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-N-methyl-propionamide

Compound No.	Structure	Name
1C-32		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propionamide
1C-33		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-N-tert-butyl-propionamide
1C-34		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-N-isobutyl-propionamide
1C-35		3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-N-cyclopropyl-propionamide
1C-36		N-(2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-isobutyramide
1C-37		N-(2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-propionamide
1C-38		N-(2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-acetamide

Compound No.	Structure	Name
1C-39		N-(2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-formamide
1C-40		N-(2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-2,2-dimethyl-propionamide
1C-41		N-(2-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-3-methyl-butyramide
1C-42		Cyclopropanecarboxylic acid (2-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-ethyl)-amide
1C-43		N-(3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-2,2-dimethyl-propionamide
1C-44		N-(3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-isobutyramide

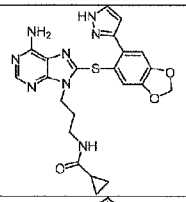
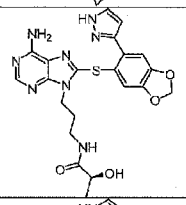
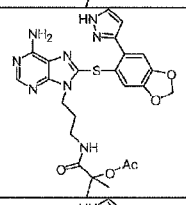
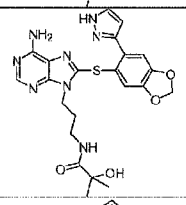
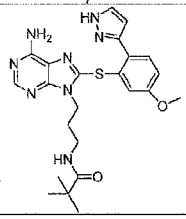
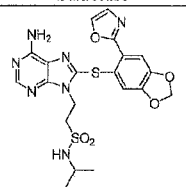
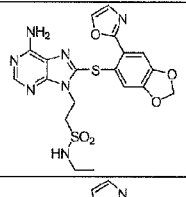
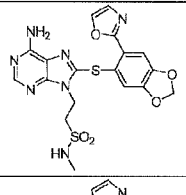
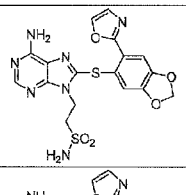
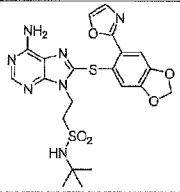
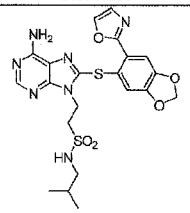
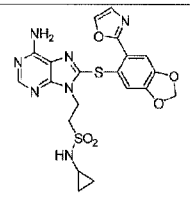
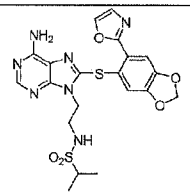
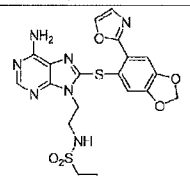
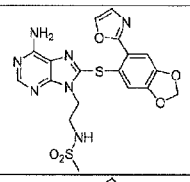
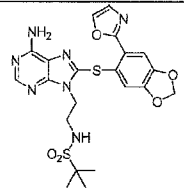
Compound No.	Structure	Name
1C-45		Cyclopropanecarboxylic acid (3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide
1C-46		N-(3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-2-hydroxy-propionamide
1C-47		Acetic acid 1-(3-{6-amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propylcarbamoyl)-1-methyl-ethyl ester
1C-48		N-(3-{6-Amino-8-[6-(1H-pyrazol-3-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-2-hydroxy-2-methyl-propionamide
1C-49		N-(3-(6-amino-8-((5-methoxy-2-(1H-pyrazol-3-yl)phenyl)thio)-9H-purin-9-yl)propyl)pivalamide

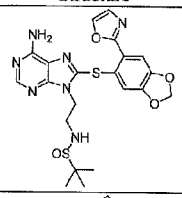
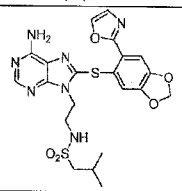
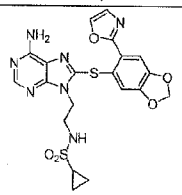
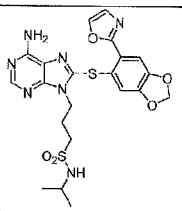
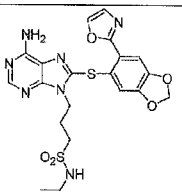
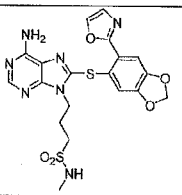
Table 1D lists specific examples of additional compounds within this embodiment. In each of the structures as drawn therein, X_2 is a nitrogen and oxygen-containing heteroaryl group, specifically an oxazolyl group, and X_4 is H. Corresponding structures in which X_2 is a different nitrogen and oxygen-containing optionally substituted aryl group are within the scope of the disclosure. In each of the structures in Table 1D, Y is S and X_4 is H. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure.

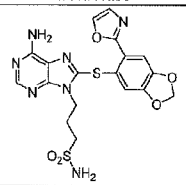
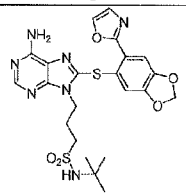
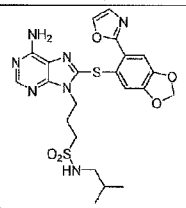
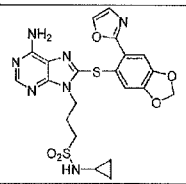
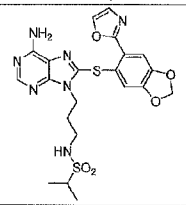
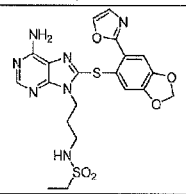
Additionally, in connection with each of the structures in Table 1D, corresponding structures in which X_2 is a nitrogen and oxygen-containing optionally substituted aryl group different from optionally substituted oxazolyl, Y is CH_2, and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure.

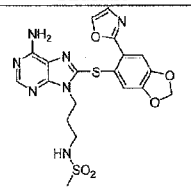
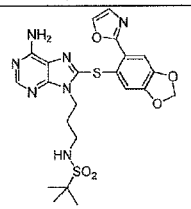
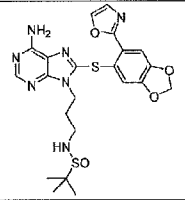
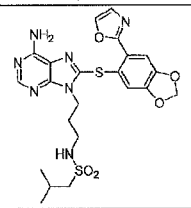
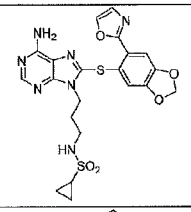
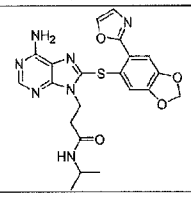
Table 1D

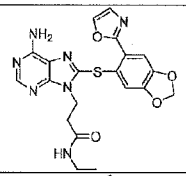
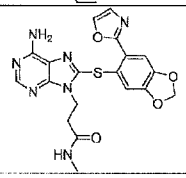
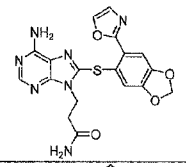
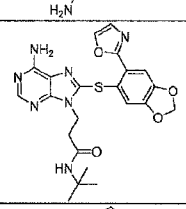
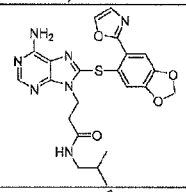
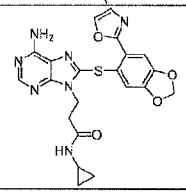
Compound No.	Structure	Name
1D-1		2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropyl-ethanesulfonamide
1D-2		2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylethanesulfonamide
1D-3		2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylethanesulfonamide
1D-4		2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethanesulfonamide
1D-5		2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide

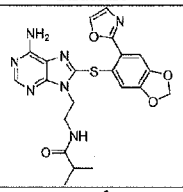
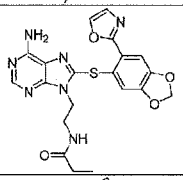
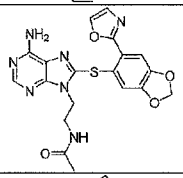
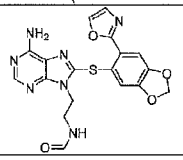
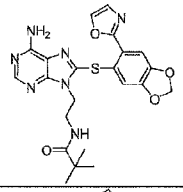
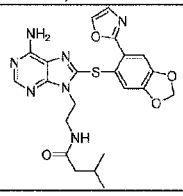
Compound No.	Structure	Name
1D-6		2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylethanesulfonamide
1D-7		2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
1D-8		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
1D-9		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)ethane-2-sulfonamide
1D-10		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)methane-2-sulfonamide
1D-11		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide

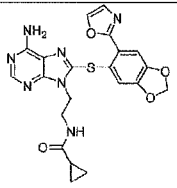
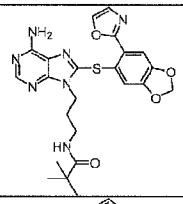
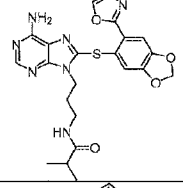
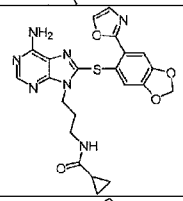
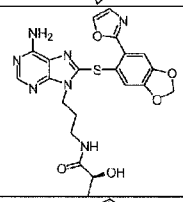
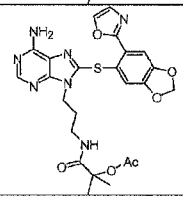
Compound No.	Structure	Name
1D-12		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
1D-13		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
1D-14		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
1D-15		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
1D-16		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
1D-17		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide

Compound No.	Structure	Name
1D-18		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propane-1-sulfonamide
1D-19		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide
1D-20		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
1D-21		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
1D-22		N-(3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfonamide
1D-23		N-(3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)ethane-sulfonamide

Compound No.	Structure	Name
1D-24		N-(3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)methane-2-sulfonamide
1D-25		N-(3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide
1D-26		N-(3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide
1D-27		N-(3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide
1D-28		N-(3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
1D-29		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropanamide

Compound No.	Structure	Name
1D-30		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropanamide
1D-31		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropanamide
1D-32		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propionamide
1D-33		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propanamide
1D-34		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropanamide
1D-35		3-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropanamide

Compound No.	Structure	Name
1D-36		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)isobutyramide
1D-37		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propionamide
1D-38		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)acetamide
1D-39		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)formamide
1D-40		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)pivalamide
1D-41		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-3-methylbutanamide

Compound No.	Structure	Name
1D-42		N-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-carboxamide
1D-43		N-{3-[6-Amino-8-(6-oxazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
1D-44		N-{3-[6-Amino-8-(6-oxazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-isobutyramide
1D-45		Cyclopropanecarboxylic acid {3-[6-amino-8-(6-oxazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1D-46		N-{3-[6-Amino-8-(6-oxazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
1D-47		Acetic acid 1-{3-[6-amino-8-(6-oxazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester

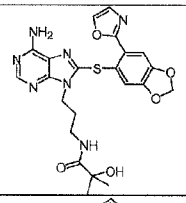
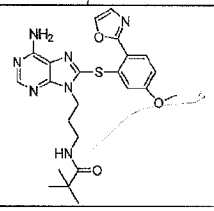
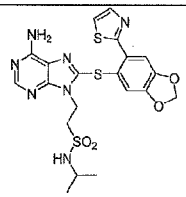
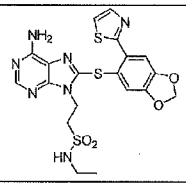
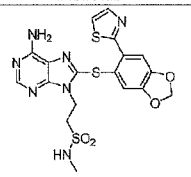
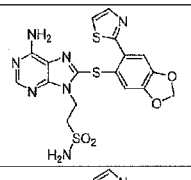
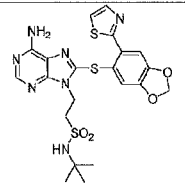
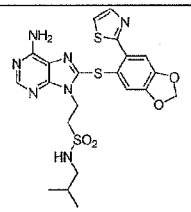
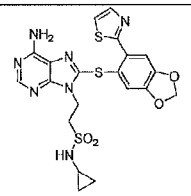
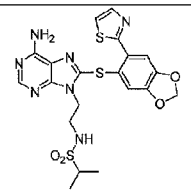
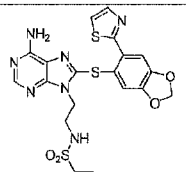
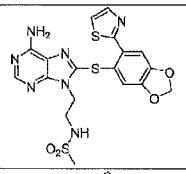
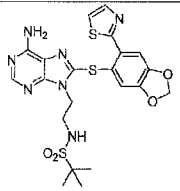
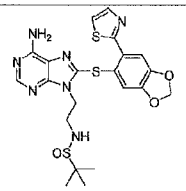
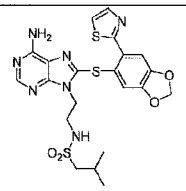
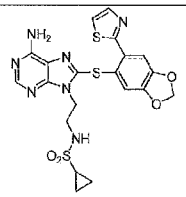
Compound No.	Structure	Name
1D-48		N-{3-[6-Amino-8-(6-oxazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide
1D-49		N-(3-(6-amino-8-((5-methoxy-2-(oxazol-2-yl)phenyl)thio)-9H-purin-9-yl)propyl)pivalamide

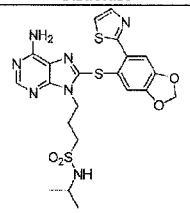
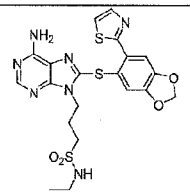
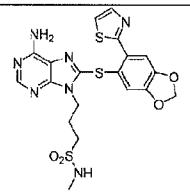
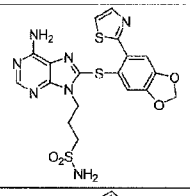
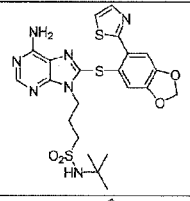
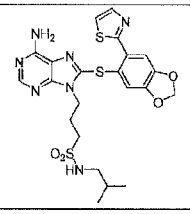
Table 1E lists specific examples of additional compounds within this embodiment. In each of the structures as drawn therein, X_2 is a nitrogen and sulfur-containing heteroaryl group, specifically a thiazolyl group, and X_4 is H. Corresponding structures in which X_2 is a different nitrogen and sulfur-containing optionally substituted aryl group are within the scope of the disclosure. In each of the structures in Table 1E, Y is S and X_4 is H. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 1E, corresponding structures in which X_2 is a nitrogen and sulfur-containing optionally substituted aryl group different from optionally substituted thiazolyl, Y is CH_2, and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure.

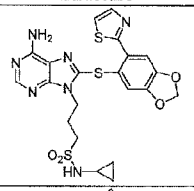
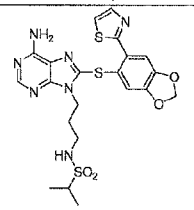
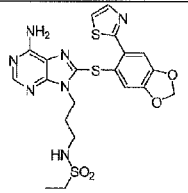
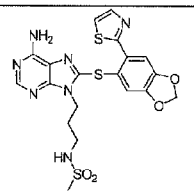
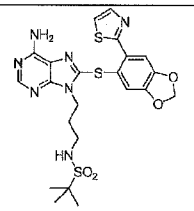
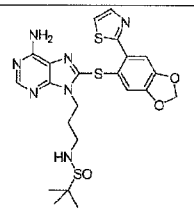
Table 1E

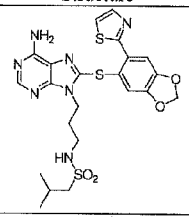
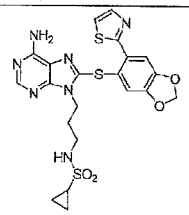
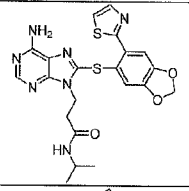
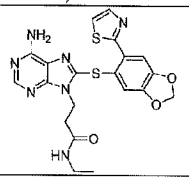
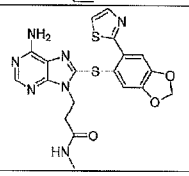
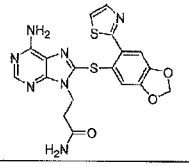
Compound No.	Structure	Name
1E-1		2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylethanesulfonamide
1E-2		2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylethanesulfonamide

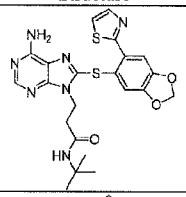
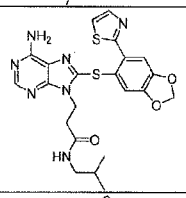
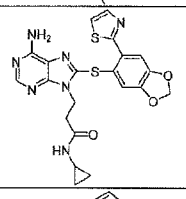
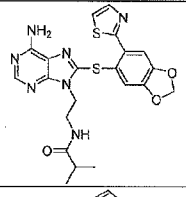
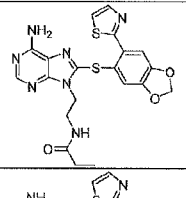
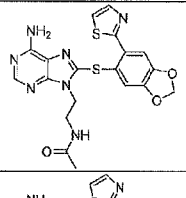
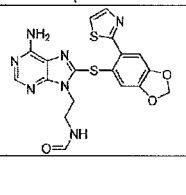
Compound No.	Structure	Name
1E-3		2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylethanesulfonamide
1E-4		2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethanesulfonamide
1E-5		2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
1E-6		2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylethanesulfonamide
1E-7		2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
1E-8		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propane-2-sulfonamide

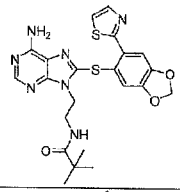
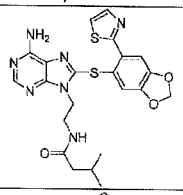
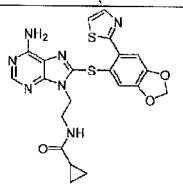
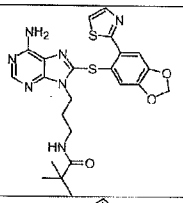
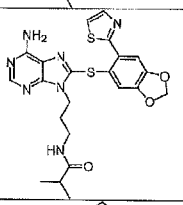
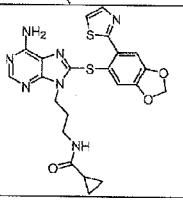
Compound No.	Structure	Name
1E-9		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)ethane-2-sulfonamide
1E-10		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)methane-2-sulfonamide
1E-11		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
1E-12		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
1E-13		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
1E-14		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide

Compound No.	Structure	Name
1E-15		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
1E-16		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
1E-17		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
1E-18		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propane-1-sulfonamide
1E-19		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide
1E-20		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide

Compound No.	Structure	Name
1E-21		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
1E-22		N-(3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfonamide
1E-23		N-(3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)ethane-2-sulfonamide
1E-24		N-(3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)methane-2-sulfonamide
1E-25		N-(3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methypropane-2-sulfonamide
1E-26		N-(3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methypropane-2-sulfinamide

Compound No.	Structure	Name
1E-27		N-(3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methypropane-1-sulfonamide
1E-28		N-(3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
1E-29		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropanamide
1E-30		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropanamide
1E-31		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropanamide
1E-32		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propanamide

Compound No.	Structure	Name
1E-33		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propanamide
1E-34		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropanamide
1E-35		3-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropanamide
1E-36		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)isobutyramide
1E-37		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propionamide
1E-38		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)acetamide
1E-39		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)formamide

Compound No.	Structure	Name
1E-40		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)pivalamide
1E-41		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-3-methylbutanamide
1E-42		N-(2-(6-amino-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-carboxamide
1E-43		N-{3-[6-Amino-8-(6-thiazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
1E-44		N-{3-[6-Amino-8-(6-thiazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-isobutyramide
1E-45		Cyclopropanecarboxylic acid {3-[6-amino-8-(6-thiazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide

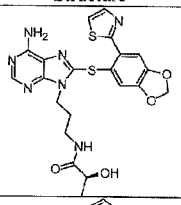
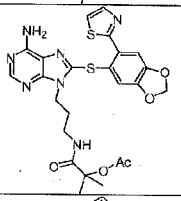
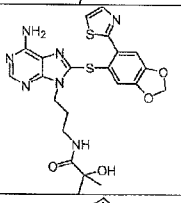
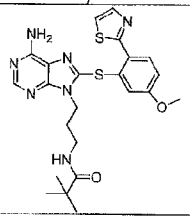
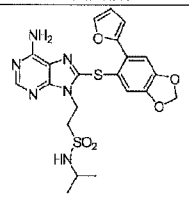
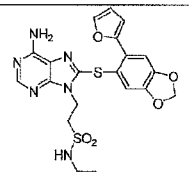
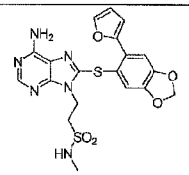
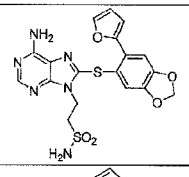
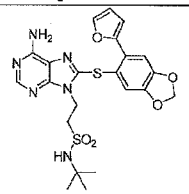
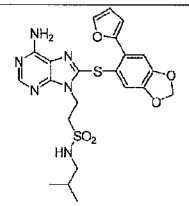
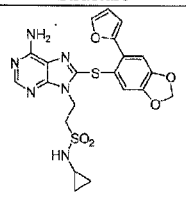
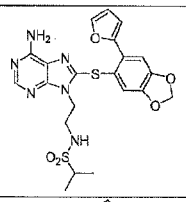
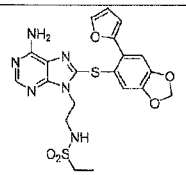
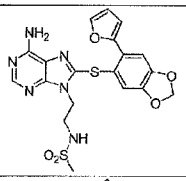
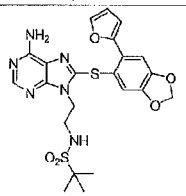
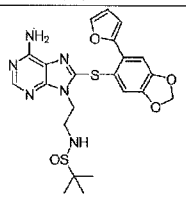
Compound No.	Structure	Name
1E-46		N-{3-[6-Amino-8-(6-thiazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
1E-47		Acetic acid 1-{3-[6-amino-8-(6-thiazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester
1E-48		N-{3-[6-Amino-8-(6-thiazol-2-yl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide
1E-49		N-(3-(6-amino-8-((5-methoxy-2-(thiazol-2-yl)phenyl)thio)-9H-purin-9-yl)propyl)pivalamide

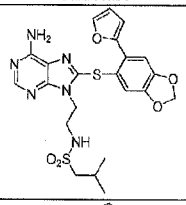
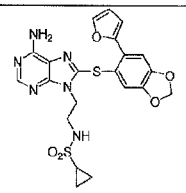
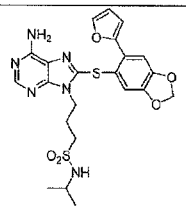
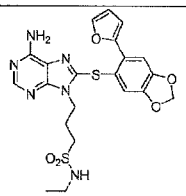
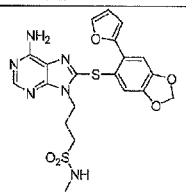
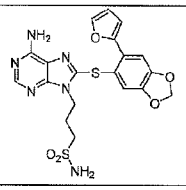
Table 1F lists specific examples of additional compounds within this embodiment. In each of the structures as drawn therein, X_2 is an oxygen-containing heteroaryl group, specifically a furanyl group, and X_4 is H. Corresponding structures in which X_2 is a different oxygen-containing optionally substituted aryl group are within the scope of the disclosure. In each of the structures in Table 1F, Y is S and X_4 is H. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 1F, corresponding structures in which X_2 is an oxygen-containing optionally substituted aryl group different from optionally substituted furanyl, Y is CH_2, and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure.

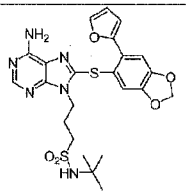
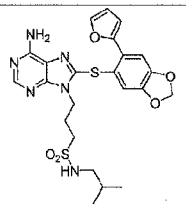
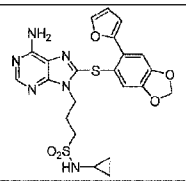
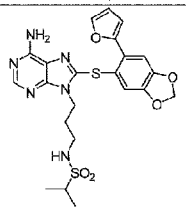
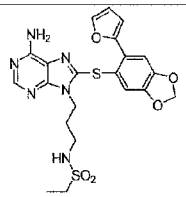
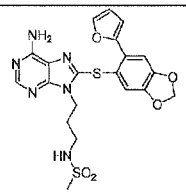
Table 1F

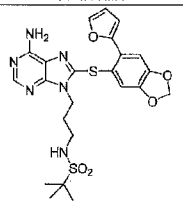
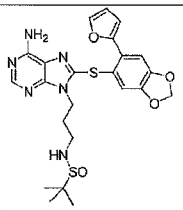
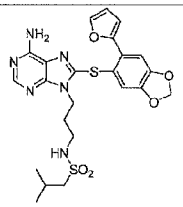
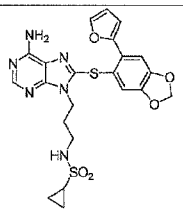
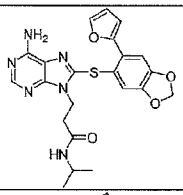
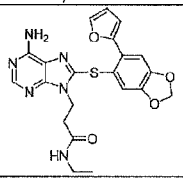
Compound No.	Structure	Name

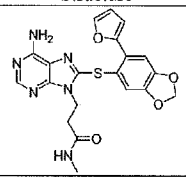
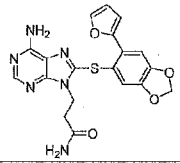
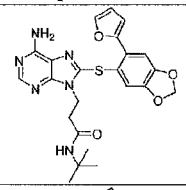
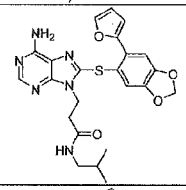
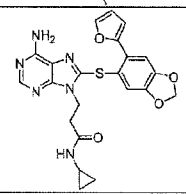
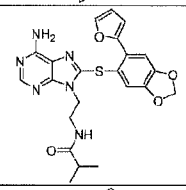
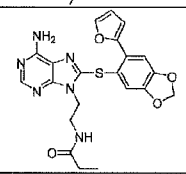
Compound No.	Structure	Name
1F-1		2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropyl-ethanesulfonamide
1F-2		2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylethanesulfonamide
1F-3		2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylethanesulfonamide
1F-4		2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethanesulfonamide
1F-5		2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
1F-6		2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylethanesulfonamide

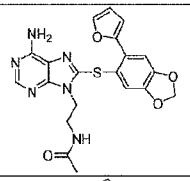
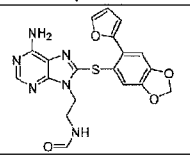
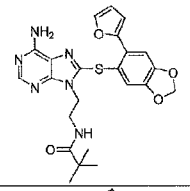
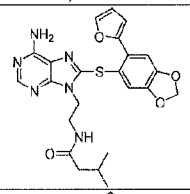
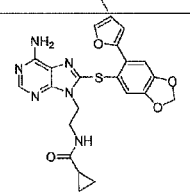
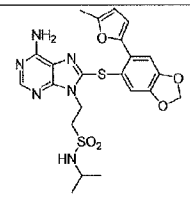
Compound No.	Structure	Name
1F-7		2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
1F-8		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
1F-9		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)ethane-2-sulfonamide
1F-10		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)methane-2-sulfonamide
1F-11		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
1F-12		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide

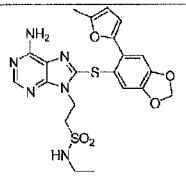
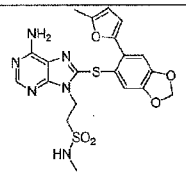
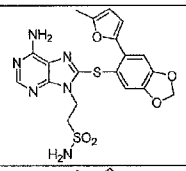
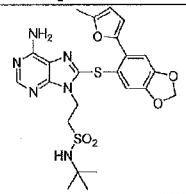
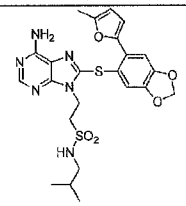
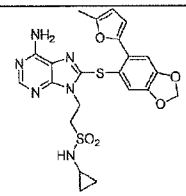
Compound No.	Structure	Name
1F-13		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
1F-14		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
1F-15		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
1F-16		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
1F-17		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
1F-18		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propane-1-sulfonamide

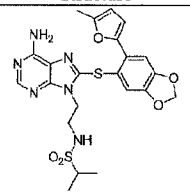
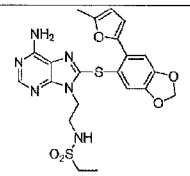
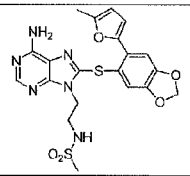
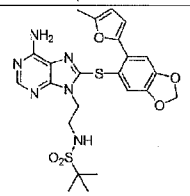
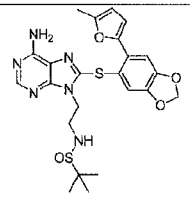
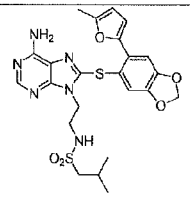
Compound No.	Structure	Name
1F-19		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide
1F-20		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
1F-21		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
1F-22		N-(3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfonamide
1F-23		N-(3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)ethane-2-sulfonamide
1F-24		N-(3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)methane-2-sulfonamide

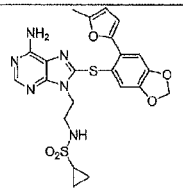
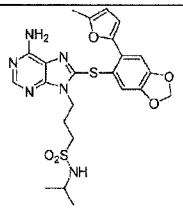
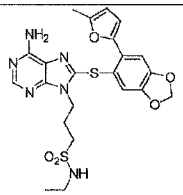
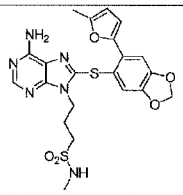
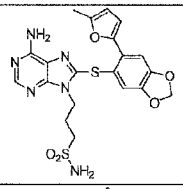
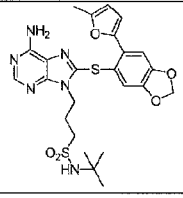
Compound No.	Structure	Name
1F-25		N-(3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide
1F-26		N-(3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfinamide
1F-27		N-(3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)2-methylpropane-1-sulfonamide
1F-28		N-(3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
1F-29		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropanamide
1F-30		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropanamide

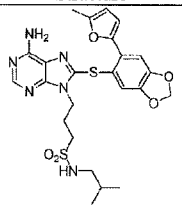
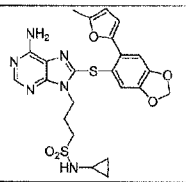
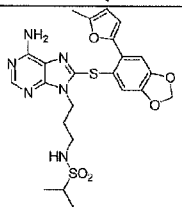
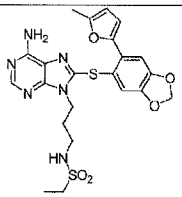
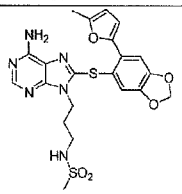
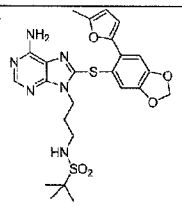
Compound No.	Structure	Name
1F-31		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropanamide
1F-32		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propanamide
1F-33		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propanamide
1F-34		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropanamide
1F-35		3-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropanamide
1F-36		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)isobutyramide
1F-37		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propanamide

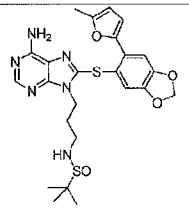
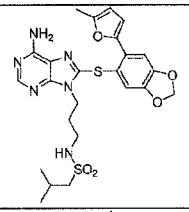
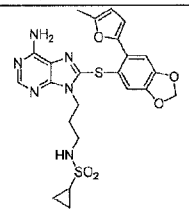
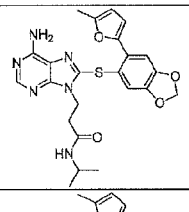
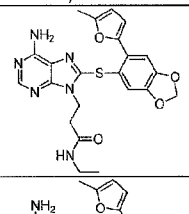
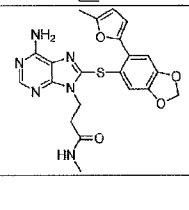
Compound No.	Structure	Name
1F-38		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)acetamide
1F-39		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)formamide
1F-40		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)pivalamide
1F-41		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-3-methylbutanamide
1F-42		N-(2-(6-amino-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-carboxamide
1F-43		2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropyl-ethanesulfonamide

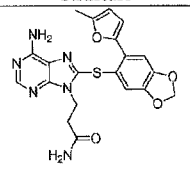
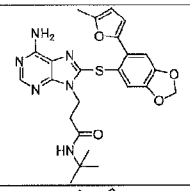
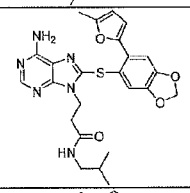
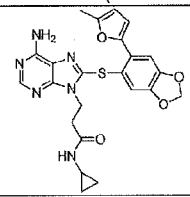
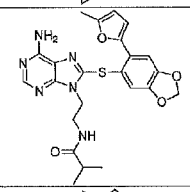
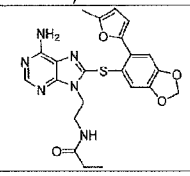
Compound No.	Structure	Name
1F-44		2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylethanesulfonamide
1F-45		2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylethanesulfonamide
1F-46		2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethanesulfonamide
1F-47		2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
1F-48		2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylethanesulfonamide
1F-49		2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide

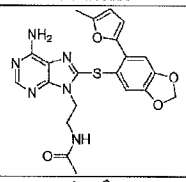
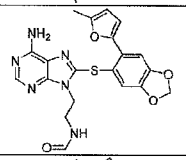
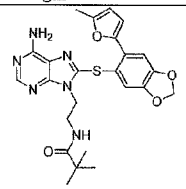
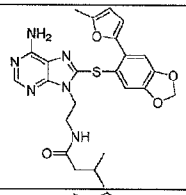
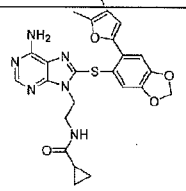
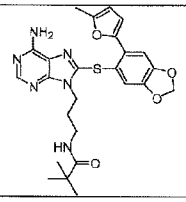
Compound No.	Structure	Name
1F-50		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
1F-51		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)ethane-2-sulfonamide
1F-52		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)methane-2-sulfonamide
1F-53		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
1F-54		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
1F-55		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide

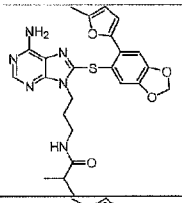
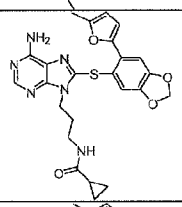
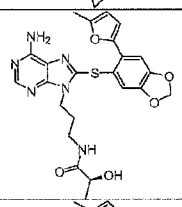
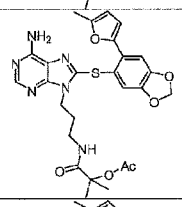
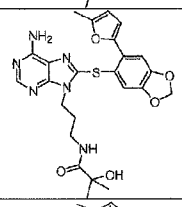
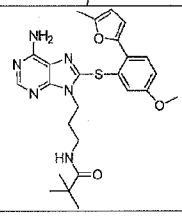
Compound No.	Structure	Name
1F-56		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
1F-57		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
1F-58		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
1F-59		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
1F-60		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propane-1-sulfonamide
1F-61		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide

Compound No.	Structure	Name
1F-62		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
1F-63		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
1F-64		N-(3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfonamide
1F-65		N-(3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)ethane-2-sulfonamide
1F-66		N-(3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)methane-2-sulfonamide
1F-67		N-(3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide

Compound No.	Structure	Name
1F-68		N-(3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfinamide
1F-69		N-(3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)2-methylpropane-1-sulfonamide
1F-70		N-(3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
1F-71		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropanamide
1F-72		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropanamide
1F-73		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropanamide

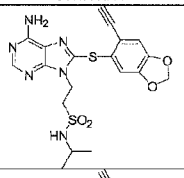
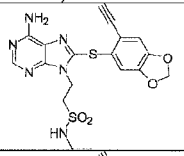
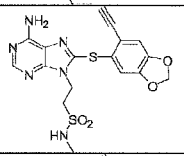
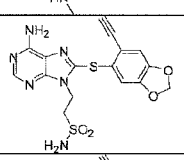
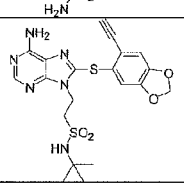
Compound No.	Structure	Name
1F-74		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propanamide
1F-75		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propanamide
1F-76		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropanamide
1F-77		3-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropanamide
1F-78		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)isobutyramide
1F-79		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propanamide

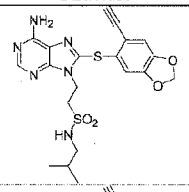
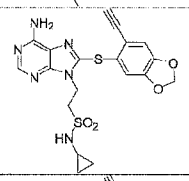
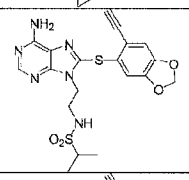
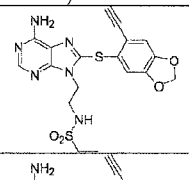
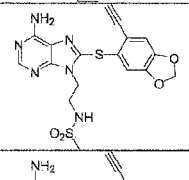
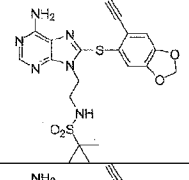
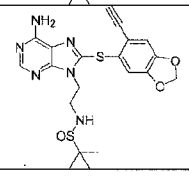
Compound No.	Structure	Name
1F-80		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)acetamide
1F-81		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)formamide
1F-82		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)pivalamide
1F-83		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-3-methylbutanamide
1F-84		N-(2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-carboxamide
1F-85		N-(3-{6-Amino-8-[6-(5-methyl-furan-2-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-2,2-dimethyl-propionamide

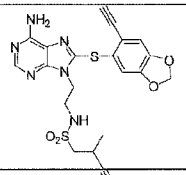
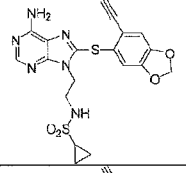
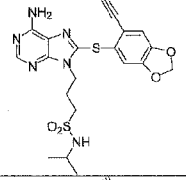
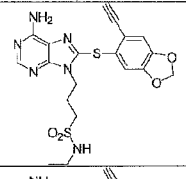
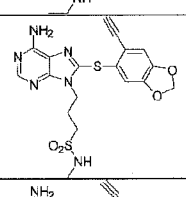
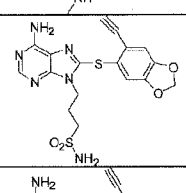
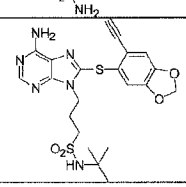
Compound No.	Structure	Name
1F-86		N-(3-{6-Amino-8-[6-(5-methyl-furan-2-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-isobutyramide
1F-87		Cyclopropanecarboxylic acid (3-{6-amino-8-[6-(5-methyl-furan-2-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-amide
1F-88		N-(3-{6-Amino-8-[6-(5-methyl-furan-2-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-2-hydroxy-propionamide
1F-89		Acetic acid 1-(3-{6-amino-8-[6-(5-methyl-furan-2-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propylcarbamoyl)-1-methyl-ethyl ester
1F-90		N-(3-{6-Amino-8-[6-(5-methyl-furan-2-yl)-benzo[1,3]dioxol-5-ylsulfanyl]-purin-9-yl}-propyl)-2-hydroxy-2-methyl-propionamide
1F-91		N-(3-(6-amino-8-((5-methoxy-2-(5-methylfuran-2-yl)phenyl)thio)-9H-purin-9-yl)propyl)pivalamide

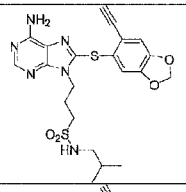
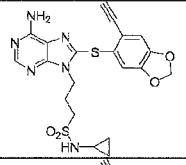
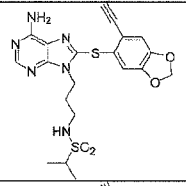
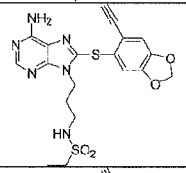
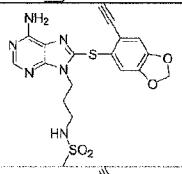
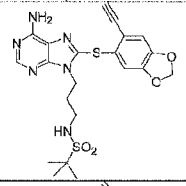
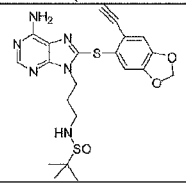
C-III. In some embodiments of the disclosure, X_2 is an alkynyl group, *e.g.*, ethynyl, 1-prop-1-ynyl, and 3-prop-1-ynyl. Table 1B lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is ethynyl and X_4 is H. However, corresponding structures in which X_2 is another alkynyl group, including specifically for example propynyl or butynyl, are within the scope of the disclosure. In each of the structures in Table 1B, Y is S. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 1B, corresponding structures in which X_2 is another alkynyl group, including specifically for example propynyl or butynyl, and Y is CH_2 are also within the scope of the disclosure.

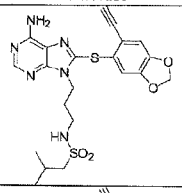
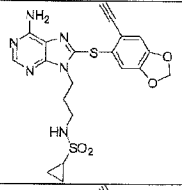
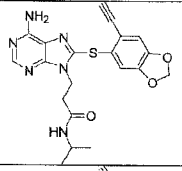
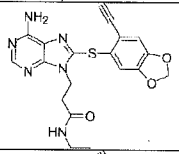
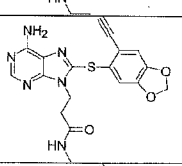
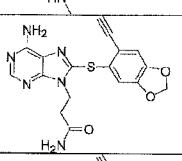
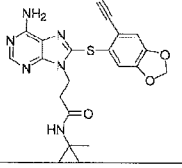
Table 1B

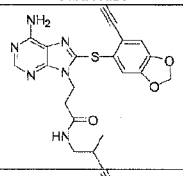
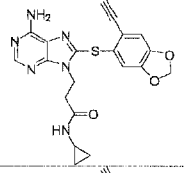
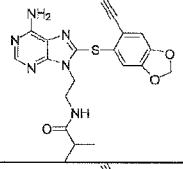
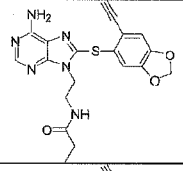
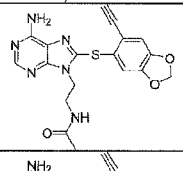
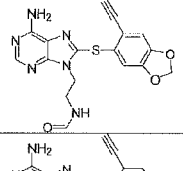
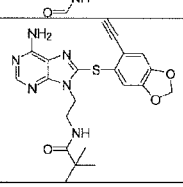
Compound No.	Structure	Name
1B-1		2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isopropylamide
1B-2		2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid ethylamide
1B-3		2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid methylamide
1B-4		2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid amide
1B-5		2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid tert-butylamide

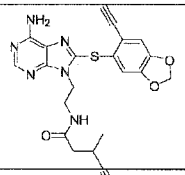
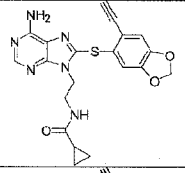
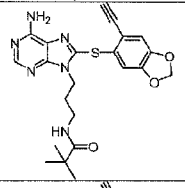
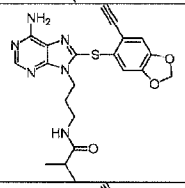
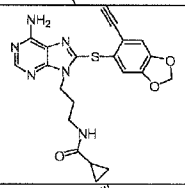
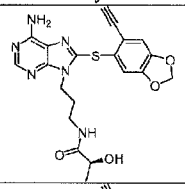
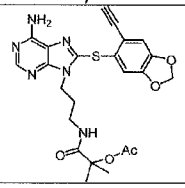
Compound No.	Structure	Name
1B-6		2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isobutyl-amide
1B-7		2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid cyclopropylamide
1B-8		Propane-2-sulfonic acid {2-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1B-9		Ethanesulfonic acid {2-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1B-10		N-{2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-methanesulfonamide
1B-11		2-Methyl-propane-2-sulfonic acid {2-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1B-12		2-Methyl-propane-2-sulfinic acid {2-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide

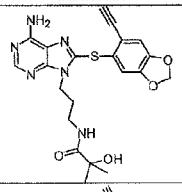
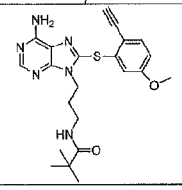
Compound No.	Structure	Name
1B-13		2-Methyl-propane-1-sulfonic acid {2-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1B-14		Cyclopropanesulfonic acid {2-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1B-15		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isopropylamide
1B-16		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid ethylamide
1B-17		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid methylamide
1B-18		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid amide
1B-19		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid tert-butylamide

Compound No.	Structure	Name
1B-20		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isobutyl-amide
1B-21		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid cyclopropylamide
1B-22		Propane-2-sulfonic acid {3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1B-23		Ethanesulfonic acid {3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1B-24		N-{3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-methanesulfonamide
1B-25		2-Methyl-propane-2-sulfonic acid {3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1B-26		2-Methyl-propane-2-sulfinic acid {3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide

Compound No.	Structure	Name
1B-27		2-Methyl-propane-1-sulfonic acid {3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1B-28		Cyclopropanesulfonic acid {3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1B-29		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-isopropyl-propionamide
1B-30		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-ethyl-propionamide
1B-31		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-methyl-propionamide
1B-32		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propionamide
1B-33		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-tert-butyl-propionamide

Compound No.	Structure	Name
1B-34		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-isobutyl-propionamide
1B-35		3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-N-cyclopropyl-propionamide
1B-36		N-{2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-isobutyramide
1B-37		N-{2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide
1B-38		N-{2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-acetamide
1B-39		N-{2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-formamide
1B-40		N-{2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-2,2-dimethyl-propionamide

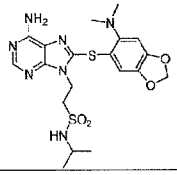
Compound No.	Structure	Name
1B-41		N-{2-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-3-methyl-butyramide
1B-42		Cyclopropanecarboxylic acid {2-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
1B-43		N-{3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
1B-44		N-{3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-isobutyramide
1B-45		Cyclopropanecarboxylic acid {3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
1B-46		N-{3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
1B-47		Acetic acid 1-{3-[6-amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester

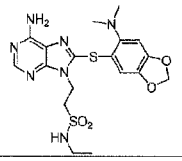
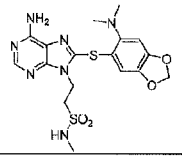
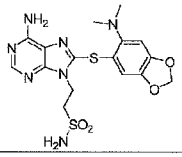
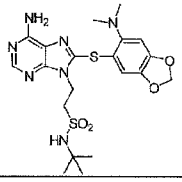
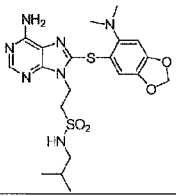
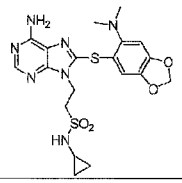
Compound No.	Structure	Name
1B-48		N-{3-[6-Amino-8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide
1B-49		N-(3-(6-amino-8-((2-ethynyl-5-methoxyphenyl)thio)-9H-purin-9-yl)propyl)pivalamide

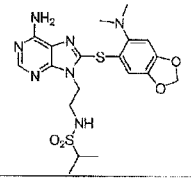
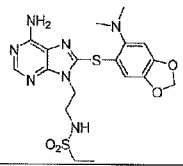
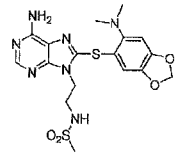
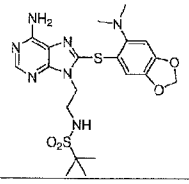
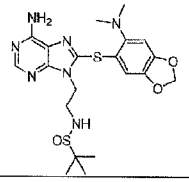
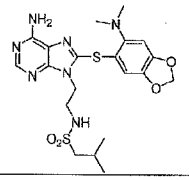
Hsp90 binding results are presented for Compounds 1B-28, 1B-43, and 1B-45 in Table 12 below. As can be noted therefrom, all compounds showed a high level of binding affinity.

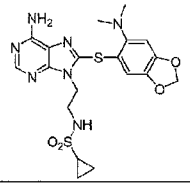
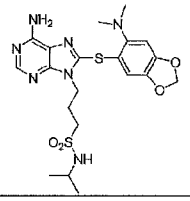
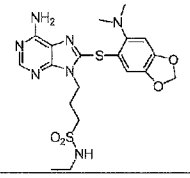
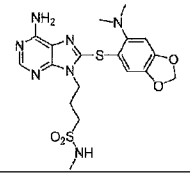
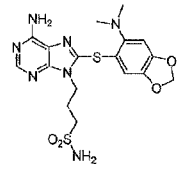
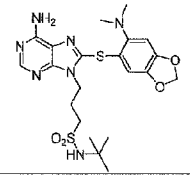
C-IV. In some embodiments of the disclosure, X_2 is an amino group, *i.e.*, $-NR_1R_2$, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl. Table 1G lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is dimethylamino and X_4 is H. However, corresponding structures in which X_3 is another amino group, including specifically for example diethylamino, methylethylamino or cyclopropylamino, are within the scope of the disclosure. In each of the structures in Table 1G, Y is S. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 1G, corresponding structures in which X_2 is another amino group, including specifically for example diethylamino, methylethylamino or cyclopropylamino, and Y is CH_2 are also within the scope of the disclosure.

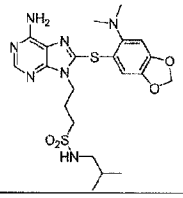
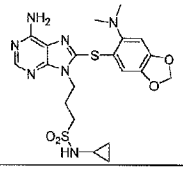
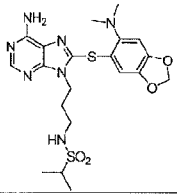
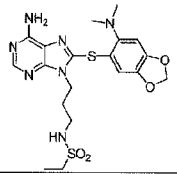
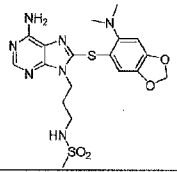
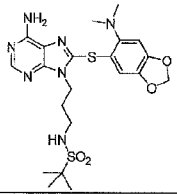
Table 1G

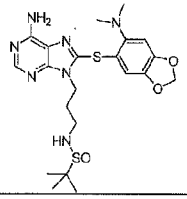
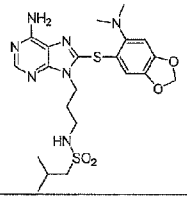
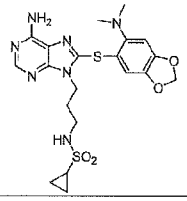
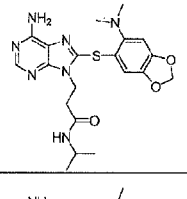
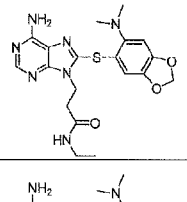
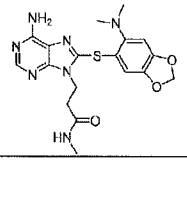
Compound No.	Structure	Name
1G-1		2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropyl-ethanesulfonamide

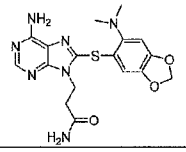
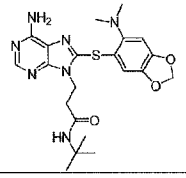
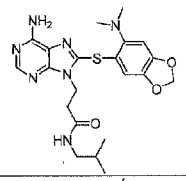
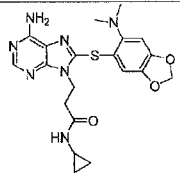
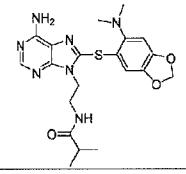
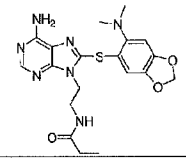
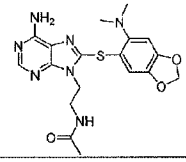
Compound No.	Structure	Name
1G-2		2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylethanesulfonamide
1G-3		2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylethanesulfonamide
1G-4		2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethanesulfonamide
1G-5		2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
1G-6		2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylethanesulfonamide
1G-7		2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide

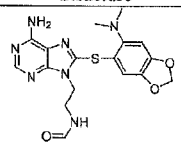
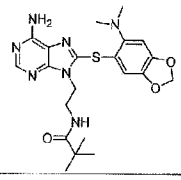
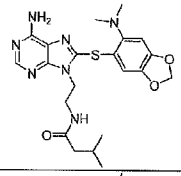
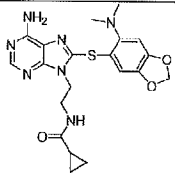
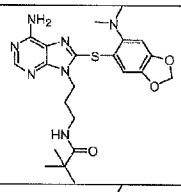
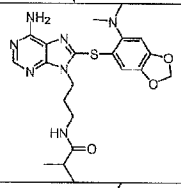
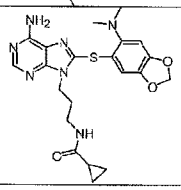
Compound No.	Structure	Name
1G-8		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
1G-9		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)ethane-2-sulfonamide
1G-10		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)methane-2-sulfonamide
1G-11		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
1G-12		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
1G-13		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2methylpropane-1-sulfonamide

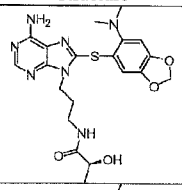
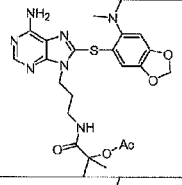
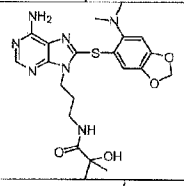
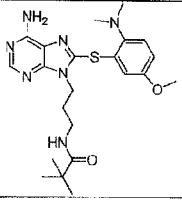
Compound No.	Structure	Name
1G-14		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropanesulfonamide
1G-15		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
1G-16		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
1G-17		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
1G-18		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propane-1-sulfonamide
1G-19		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide

Compound No.	Structure	Name
1G-20		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
1G-21		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
1G-22		N-(3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfonamide
1G-23		N-(3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)ethane-2-sulfonamide
1G-24		N-(3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)methane-2-sulfonamide
1G-25		N-(3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide

Compound No.	Structure	Name
1G-26		N-(3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide
1G-27		N-(3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide
1G-28		N-(3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
1G-29		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropanamide
1G-30		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-ethylpropanamide
1G-31		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-methylpropanamide

Compound No.	Structure	Name
1G-32		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)propanamide
1G-33		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propanamide
1G-34		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-isobutylpropanamide
1G-35		3-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropanamide
1G-36		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)isobutyramide
1G-37		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)propanamide
1G-38		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)acetamide

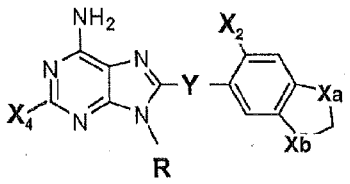
Compound No.	Structure	Name
1G-39		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)formamide
1G-40		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)pivalamide
1G-41		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-3-methylbutanamide
1G-42		N-(2-(6-amino-8-((6-(dimethylamino)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropanecarboxamide
1G-43		N-{3-[6-Amino-8-(6-dimethylamino-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
1G-44		N-{3-[6-Amino-8-(6-dimethylamino-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-isobutyramide
1G-45		Cyclopropanecarboxylic acid {3-[6-amino-8-(6-dimethylamino-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-amide

Compound No.	Structure	Name
1G-46		N-{3-[6-Amino-8-(6-dimethylamino-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
1G-47		Acetic acid 1-{3-[6-amino-8-(6-dimethylamino-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester
1G-48		N-{3-[6-Amino-8-(6-dimethylamino-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide
1G-49		N-(3-(6-amino-8-((2-(dimethylamino)-5-methoxyphenyl)thio)-9H-purin-9-yl)propyl)pivalamide

Hsp90 binding results are presented for Compounds 1G-28. 1G-43, and 1G-45 in Table 12 below. As can be noted therefrom, all compounds showed a high level of binding affinity.

D. Compounds of Formula (IA) in Which Xa or Xb is O

In accordance with another embodiment of the disclosure, the compounds are of Formula (IA) in which one of Xa and Xb is O and Xc and the other of Xa and Xb is CH_2. Thus, the compounds of this embodiment can be represented by Formula (2):



(2)

or a pharmaceutically acceptable salt thereof, wherein:

one of Xa and Xb is O and the other is CH_2;

Y is CH_2 or S;

X_4 is hydrogen or halogen;

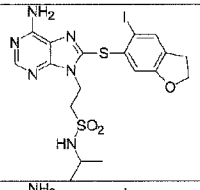
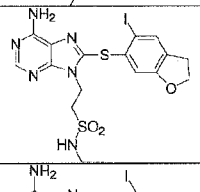
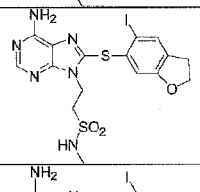
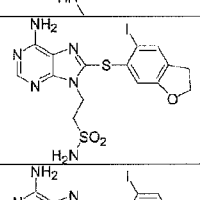
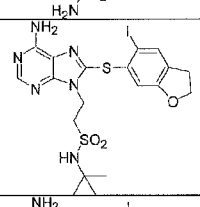
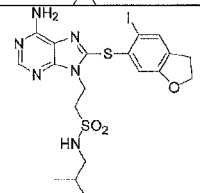
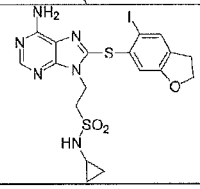
R is a is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

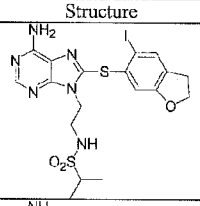
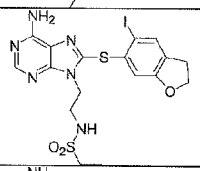
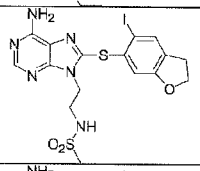
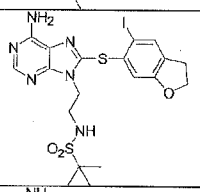
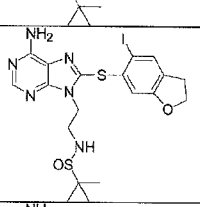
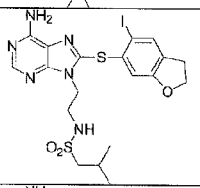
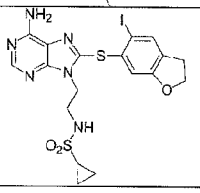
X_2 is as disclosed below.

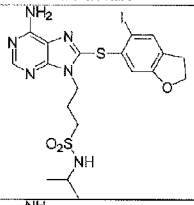
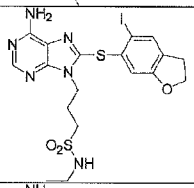
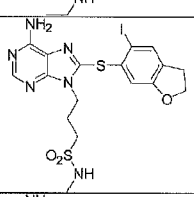
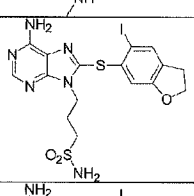
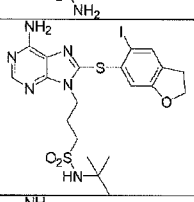
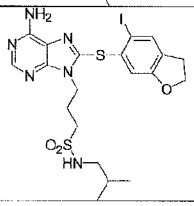
D-I. In some embodiments of the disclosure, X_2 is halogen. Table 2A lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is I and X_4 is H. However, corresponding structures in which X_2 is F, Cl, or Br are within the scope of the disclosure. In each of the structures in Table 2A, Y is S. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 2A, corresponding structures in which X_2 is F, Cl, or Br and Y is CH_2 are also within the scope of the disclosure.

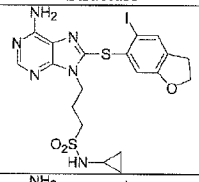
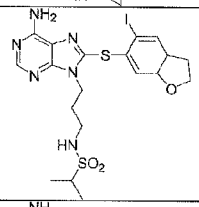
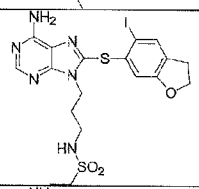
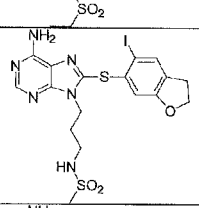
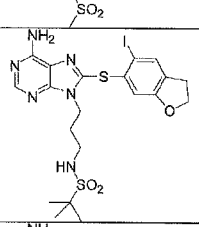
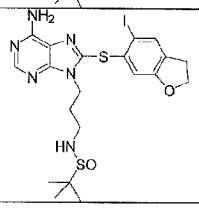
Table 2A

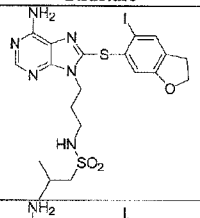
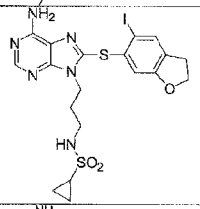
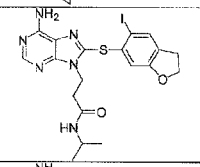
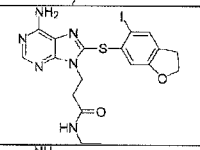
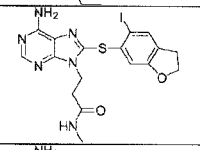
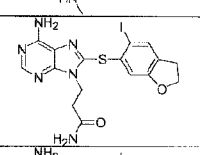
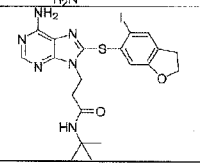
Compound No.	Structure	Name

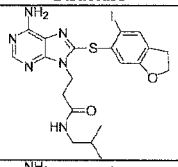
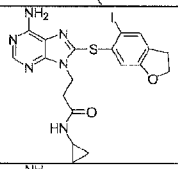
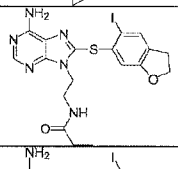
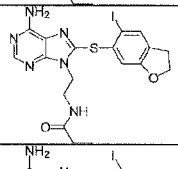
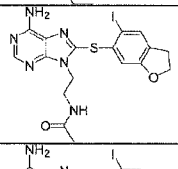
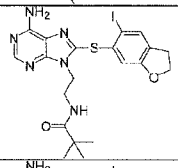
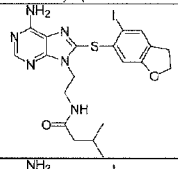
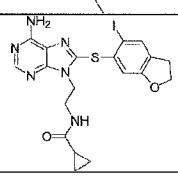
Compound No.	Structure	Name
2A-1		2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isopropylamide
2A-2		2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid ethylamide
2A-3		2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid methylamide
2A-4		2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid amide
2A-5		2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid tert-butylamide
2A-6		2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isobutyl-amide
2A-7		2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid cyclopropylamide

Compound No.	Structure	Name
2A-8		Propane-2-sulfonic acid {2-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-amide
2A-9		Ethanesulfonic acid {2-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-amide
2A-10		N-(2-(6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl)-ethyl)-methanesulfonamide
2A-11		2-Methyl-propane-2-sulfonic acid {2-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-amide
2A-12		2-Methyl-propane-2-sulfinic acid {2-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-amide
2A-13		2-Methyl-propane-1-sulfonic acid {2-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-amide
2A-14		Cyclopropanesulfonic acid {2-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-amide

Compound No.	Structure	Name
2A-15		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isopropylamide
2A-16		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid ethylamide
2A-17		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid methylamide
2A-18		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid amide
2A-19		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid tert-butylamide
2A-20		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isobutyl-amide

Compound No.	Structure	Name
2A-21		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid cyclopropylamide
2A-22		Propane-2-sulfonic acid {3-[6-amino-8-(5-iodo-2,3,3a,7a-tetrahydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-amide
2A-23		Ethanesulfonic acid {3-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-amide
2A-24		N-{3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-methanesulfonamide
2A-25		2-Methyl-propane-2-sulfonic acid {3-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-amide
2A-26		2-Methyl-propane-2-sulfinic acid {3-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-amide

Compound No.	Structure	Name
2A-27		2-Methyl-propane-1-sulfonic acid {3-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-amide
2A-28		Cyclopropanesulfonic acid {3-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-amide
2A-29		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-N-isopropyl-propionamide
2A-30		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-N-ethyl-propionamide
2A-31		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-N-methyl-propionamide
2A-32		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propionamide
2A-33		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-N-tert-butyl-propionamide

Compound No.	Structure	Name
2A-34		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-N-isobutyl-propionamide
2A-35		3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-N-cyclopropyl-propionamide
2A-36		N-{2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide
2A-37		N-{2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide
2A-38		N-{2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-acetamide
2A-39		N-{2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-2,2-dimethyl-propionamide
2A-40		N-{2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-3-methyl-butyramide
2A-41		Cyclopropanecarboxylic acid {2-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-amide

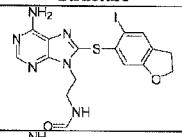
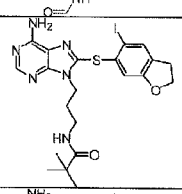
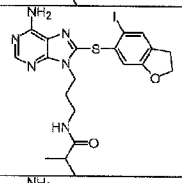
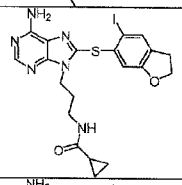
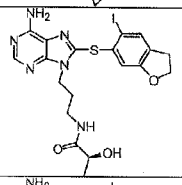
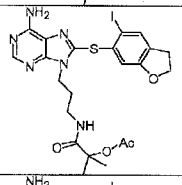
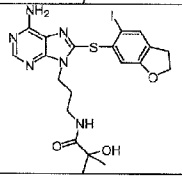
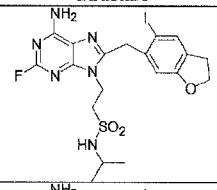
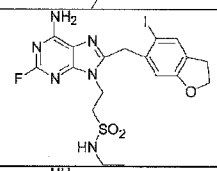
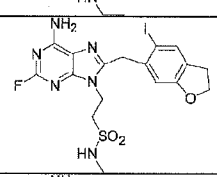
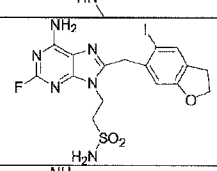
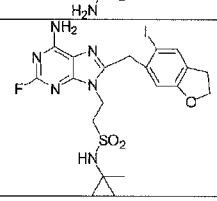
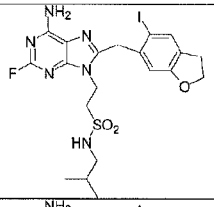
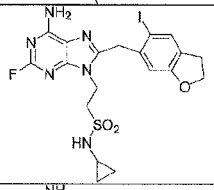
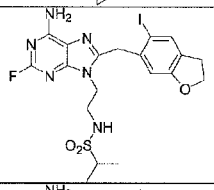
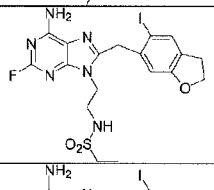
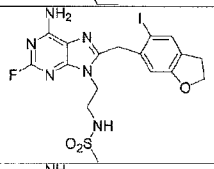
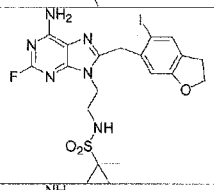
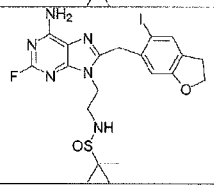
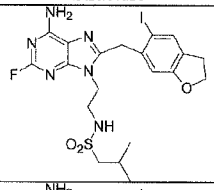
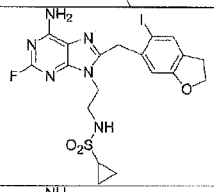
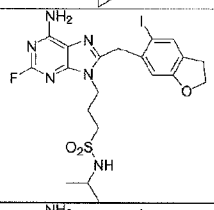
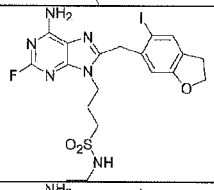
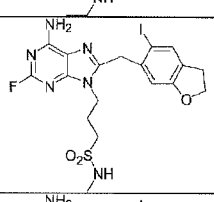
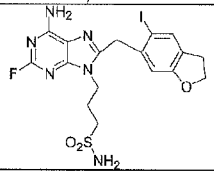
Compound No.	Structure	Name
2A-42		N-{2-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-ethyl}-formamide
2A-43		N-{3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
2A-44		N-{3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-isobutyramide
2A-45		Cyclopropanecarboxylic acid {3-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-amide
2A-46		N-{3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
2A-47		Acetic acid 1-{3-[6-amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester
2A-48		N-{3-[6-Amino-8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide

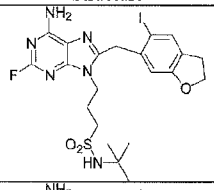
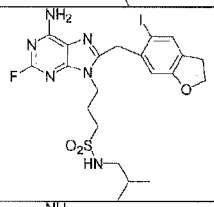
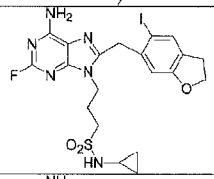
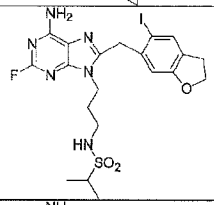
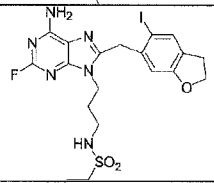
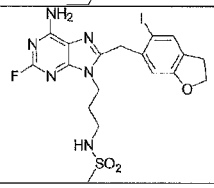
Table 5A lists specific examples in which X_2 is halogen and X_4 is halogen. In each of the structures as drawn, X_2 is I and X_4 is F. However, corresponding structures in which X_4 is H, Cl, Br, or I are within the scope of the disclosure. In each of the structures in Table 5A, Y is CH_2. However, corresponding structures in which Y is S and/or X_2 is F, Cl, or Br are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 5A, corresponding structures in which X_4 is H, Cl, Br, or I and Y is S are also within the scope of the disclosure.

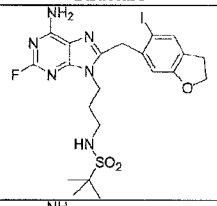
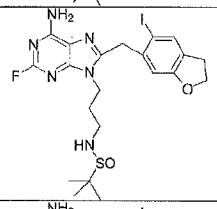
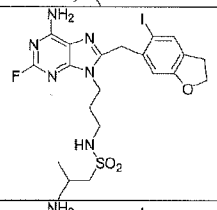
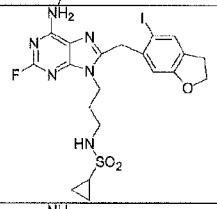
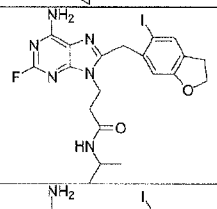
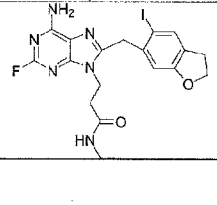
Table 5A

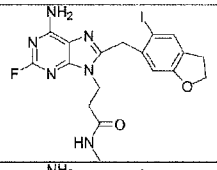
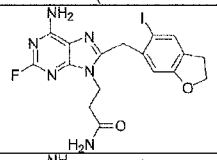
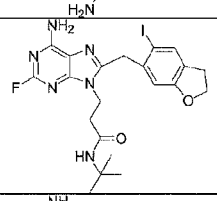
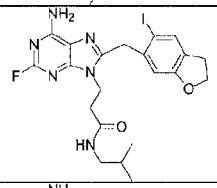
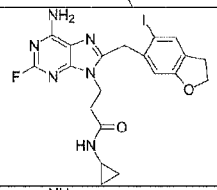
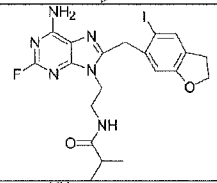
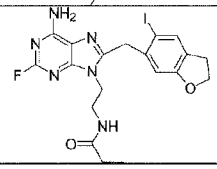
Compound No.	Structure	Name
5A-1		2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-isopropyl-ethanesulfonamide
5A-2		2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-ethylethanesulfonamide
5A-3		2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-methylethanesulfonamide
5A-4		2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)sulfonamide
5A-5		2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide

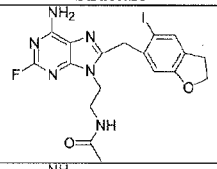
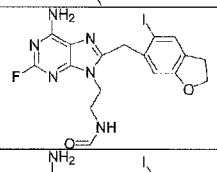
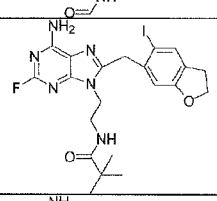
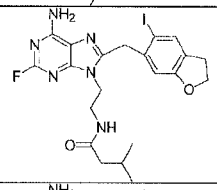
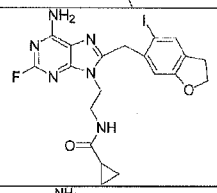
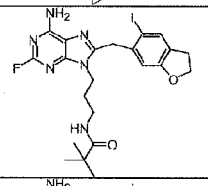
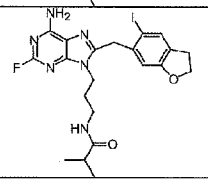
Compound No.	Structure	Name
5A-6		2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-isobutylethanesulfonamide
5A-7		2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
5A-8		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
5A-9		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)ethanesulfonamide
5A-10		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)methane-sulfonamide
5A-11		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
5A-12		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide

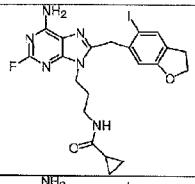
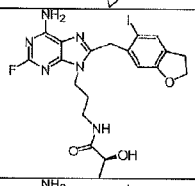
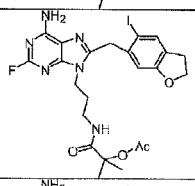
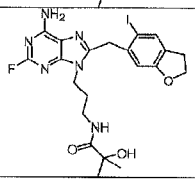
Compound No.	Structure	Name
5A-13		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
5A-14		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
5A-15		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
5A-16		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
5A-17		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
5A-18		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propane-1-sulfonamide

Compound No.	Structure	Name
5A-19		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide
5A-20		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
5A-21		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
5A-22		N-(3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propyl)propane-2-sulfonamide
5A-23		N-(3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propyl)ethane-sulfonamide
5A-24		N-(3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propyl)methane-sulfonamide

Compound No.	Structure	Name
5A-25		N-(3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide
5A-26		N-(3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide
5A-27		N-(3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide
5A-28		N-(3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
5A-29		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-isopropylpropanamide
5A-30		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-ethylpropanamide

Compound No.	Structure	Name
5A-31		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-methylpropanamide
5A-32		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)propanamide
5A-33		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propanamide
5A-34		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-isobutylpropanamide
5A-35		3-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropanamide
5A-36		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)isobutyramide
5A-37		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)propionamide

Compound No.	Structure	Name
5A-38		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)acetamide
5A-39		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)formamide
5A-40		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)pivalamide
5A-41		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)-3-methylbutanamide
5A-42		N-(2-(6-amino-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropanecarboxamide
5A-43		N-{3-[6-Amino-2-fluoro-8-(5-iodo-2,3-dihydrobenzofuran-6-ylmethyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
5A-44		N-{3-[6-Amino-2-fluoro-8-(5-iodo-2,3-dihydrobenzofuran-6-ylmethyl)-purin-9-yl]-propyl}-isobutyramide

Compound No.	Structure	Name
5A-45		Cyclopropanecarboxylic acid {3-[6-amino-2-fluoro-8-(5-iodo-2,3-dihydro-benzofuran-6-ylmethyl)-purin-9-yl]-propyl}-amide
5A-46		N-{3-[6-Amino-2-fluoro-8-(5-iodo-2,3-dihydro-benzofuran-6-ylmethyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
5A-47		Acetic acid 1-{3-[6-amino-2-fluoro-8-(5-iodo-2,3-dihydro-benzofuran-6-ylmethyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester
5A-48		N-{3-[6-Amino-2-fluoro-8-(5-iodo-2,3-dihydro-benzofuran-6-ylmethyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide

In each of the structures Xb is O and Xa is CH_2. However, corresponding structures in which Xb is CH_2 and Xa is O are also within the scope of the disclosure.

Hsp90 binding results are presented for Compounds 2A-11, 2A-12, 2A-26 and 2A-45 in Table 12 below. As can be noted therefrom, the compounds showed a high level of binding affinity.

D-II. In some embodiments of the disclosure, X_2 is an optionally substituted aryl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 2A and 5A, or variations thereof as described in A. and D-I. above, in which X_2 is an optionally substituted aryl, including but not limited to pyrazolyl, 1H-pyrazol-3-yl, oxazolyl, oxazol-2-yl, thiazolyl, thiazol-2-yl, furanyl, furan-2-yl, and 5-methylfuran-2-yl.

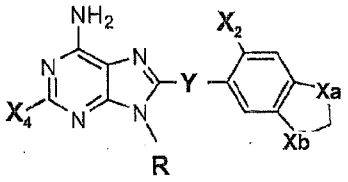
D-III. In some embodiments of the disclosure, X_2 is an alkynyl group, *e.g.*, ethynyl, 1-prop-1-ynyl, and 3-prop-1-ynyl. Specific examples of compounds within the scope of this aspect of

the disclosure correspond to the compounds disclosed in Tables 2A and 5A, or variations thereof as described in A. and D-I. above, in which X_2 is an alkynyl group.

D-IV. In some embodiments of the disclosure, X_2 is an amino group, *i.e.*, $-NR_1R_2$, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 2A and 5A, or variations thereof as described in A. and D-I. above, in which X_2 is an amino group.

E. Compounds of Formula (IA) in Which Xa or Xb is C(=O)

In accordance with another embodiment of the disclosure, the compounds are of Formula (IA) in which one of Xa and Xb is C(=O) and Xc and the other of Xa and Xb is CH_2. Thus, the compounds of this embodiment can be represented by Formula (3):



(3)

or a pharmaceutically acceptable salt thereof, wherein:

one of Xa and Xb is a carbonyl group, *i.e.*, C(=O), and the other is CH_2;

Y is CH_2 or S;

X_4 is hydrogen or halogen;

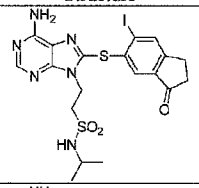
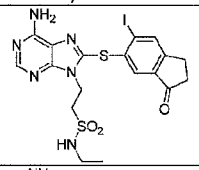
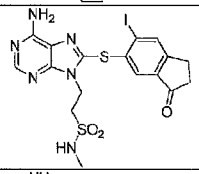
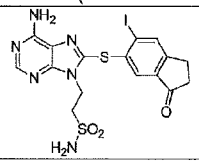
R is a is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6

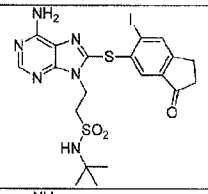
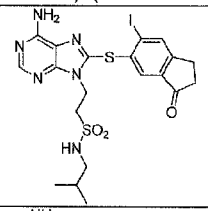
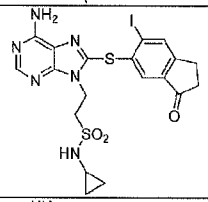
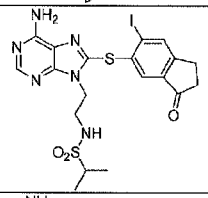
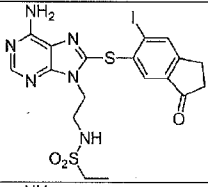
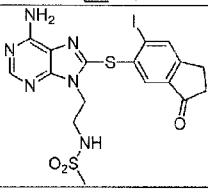
alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

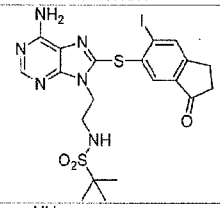
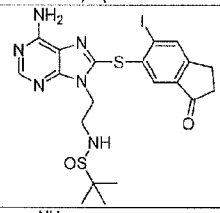
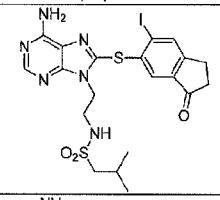
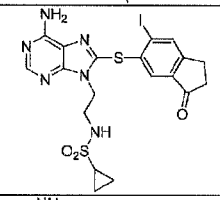
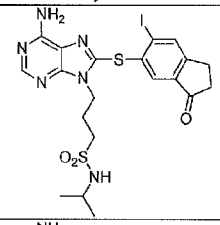
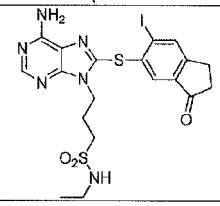
X_2 is as disclosed below.

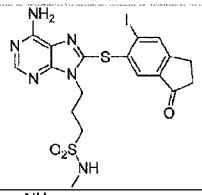
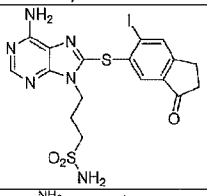
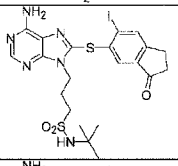
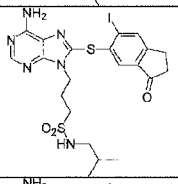
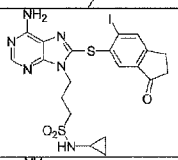
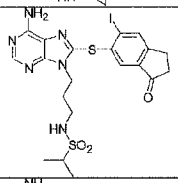
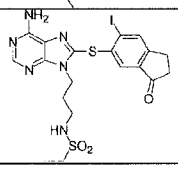
E-I. In some embodiments of the disclosure, X_2 is halogen. Table 7A lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is I and X_4 is H. However, corresponding structures in which X_2 is F, Cl, or Br are within the scope of the disclosure. In each of the structures in Table 7A, Y is S. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. In each of the structures in Table 7A, Xb is C(=O) and Xa is CH_2. However, corresponding structures where Xa is C(=O) and Xb is CH_2 are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 7A, corresponding structures in which X_2 is F, Cl, or Br, Y is CH_2, Xa is C(=O), and Xb is CH_2 are also within the scope of the disclosure.

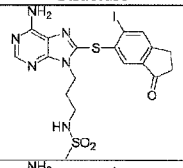
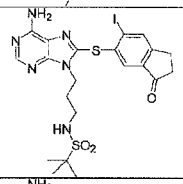
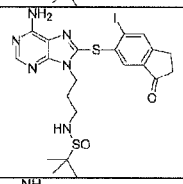
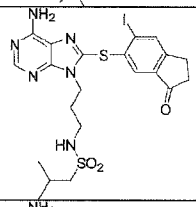
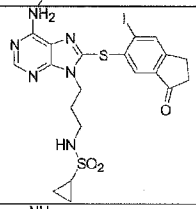
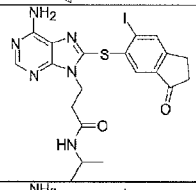
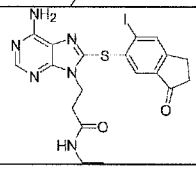
Table 7A

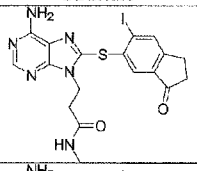
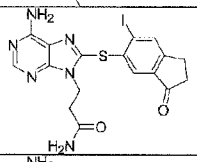
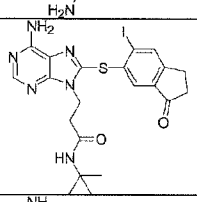
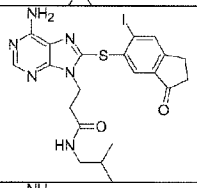
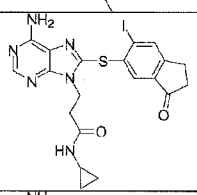
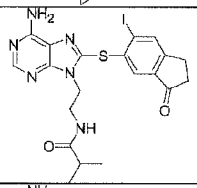
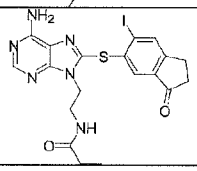
Compound No.	Structure	Name
7A-1		2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-isopropylethanesulfonamide
7A-2		2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-ethylethanesulfonamide
7A-3		2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-methylethanesulfonamide
7A-4		2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethanesulfonamide

Compound No.	Structure	Name
7A-5		2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
7A-6		2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-isobutylethanesulfonamide
7A-7		2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
7A-8		N-(2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
7A-9		N-(2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)ethanesulfonamide
7A-10		N-(2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)methane-sulfonamide

Compound No.	Structure	Name
7A-11		N-(2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
7A-12		N-(2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
7A-13		N-(2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
7A-14		N-(2-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
7A-15		3-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
7A-16		3-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide

Compound No.	Structure	Name
7A-17		3-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
7A-18		3-(6-amino-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)propane-1-sulfonamide
7A-19		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid tert-butylamide
7A-20		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isobutyl-amide
7A-21		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid cyclopropylamide
7A-22		Propane-2-sulfonic acid {3-[6-amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
7A-23		Ethanesulfonic acid {3-[6-amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide

Compound No.	Structure	Name
7A-24		N-{3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-methanesulfonamide
7A-25		2-Methyl-propane-2-sulfonic acid {3-[6-amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
7A-26		2-Methyl-propane-2-sulfinic acid {3-[6-amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
7A-27		2-Methyl-propane-1-sulfonic acid {3-[6-amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
7A-28		Cyclopropanesulfonic acid {3-[6-amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
7A-29		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-N-isopropyl-propionamide
7A-30		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-N-ethyl-propionamide

Compound No.	Structure	Name
7A-31		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-N-methyl-propionamide
7A-32		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-propionamide
7A-33		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-N-tert-butyl-propionamide
7A-34		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-N-isobutyl-propionamide
7A-35		3-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-N-cyclopropyl-propionamide
7A-36		N-{2-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-isobutyramide
7A-37		N-{2-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide

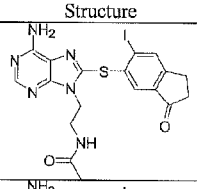
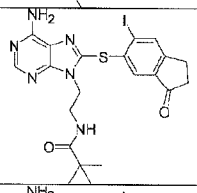
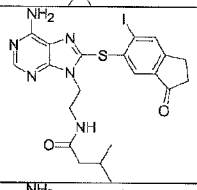
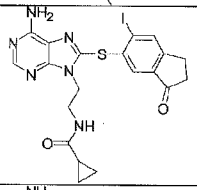
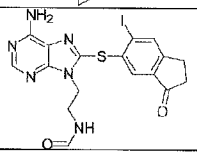
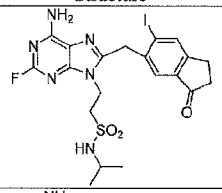
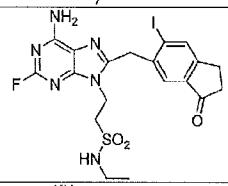
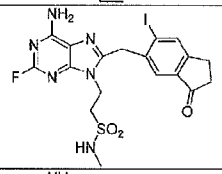
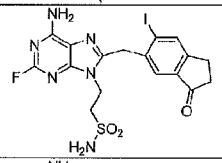
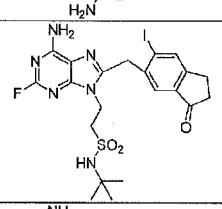
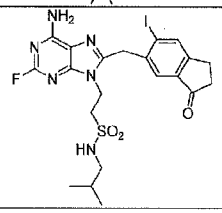
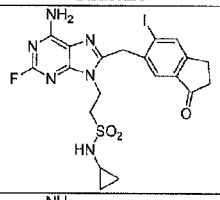
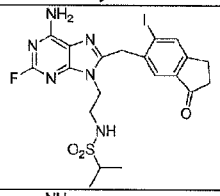
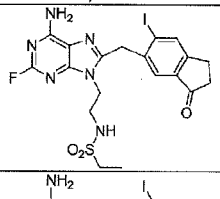
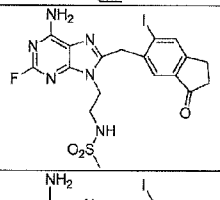
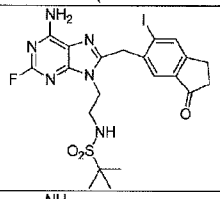
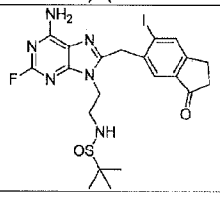
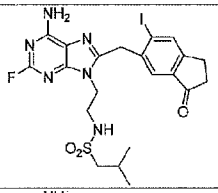
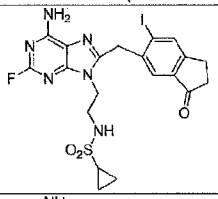
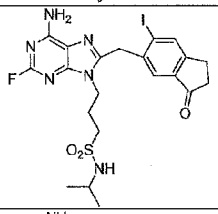
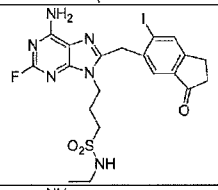
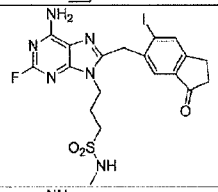
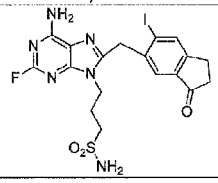
Compound No.	Structure	Name
7A-38		N-{2-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-acetamide
7A-39		N-{2-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-2,2-dimethyl-propionamide
7A-40		N-{2-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-3-methyl-butyramide
7A-41		Cyclopropanecarboxylic acid {2-[6-amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
7A-42		N-{2-[6-Amino-8-(6-iodo-3-oxo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-formamide

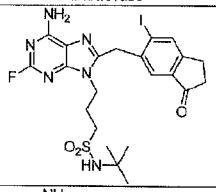
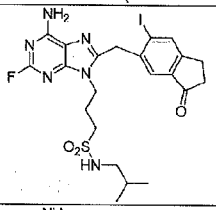
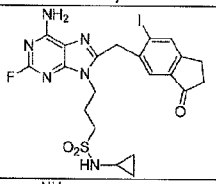
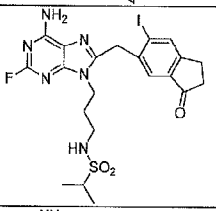
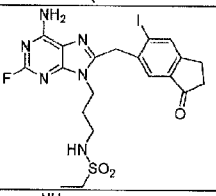
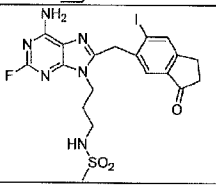
Table 9A lists specific examples in which X_2 is halogen and X_4 is halogen. In each of the structures as drawn, X_2 is I and X_4 is F. However, corresponding structures in which X_4 is H, Cl, Br, or I are within the scope of the disclosure. In each of the structures in Table 9A, Y is CH_2. However, corresponding structures in which Y is S and/or X_2 is F, Cl, or Br are also within the scope of the disclosure. In each of the structures in Table 9A, Xb is C(=O) and Xa is CH_2. However, corresponding structures where Xa is C(=O) and Xb is CH_2 are also within the scope of the disclosure. However, corresponding structures in which Y is S are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 9A, corresponding structures in which X_4 is H, Cl, Br, or I, Y is S, Xa is C(=O), and Xb is CH_2 are also within the scope of the disclosure.

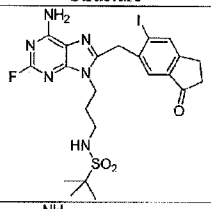
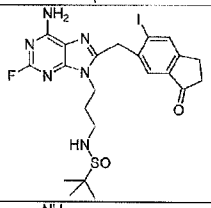
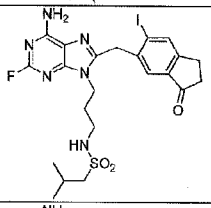
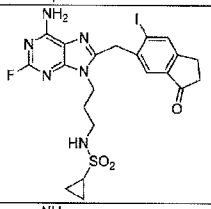
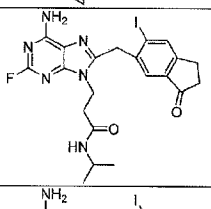
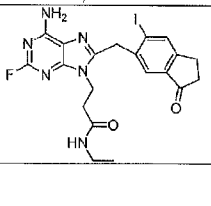
Table 9A

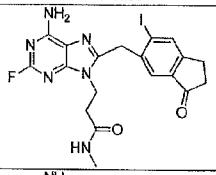
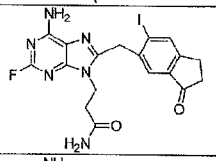
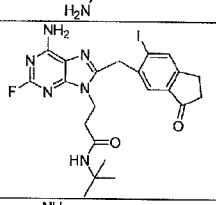
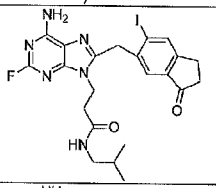
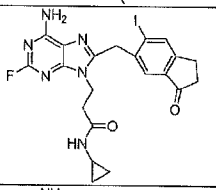
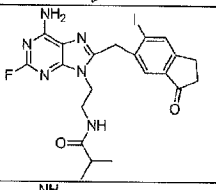
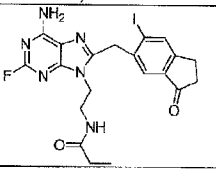
Compound No.	Structure	Name
9A-1		2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylethanesulfonamide
9A-2		2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylethanesulfonamide
9A-3		2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylethanesulfonamide
9A-4		2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethanesulfonamide
9A-5		2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
9A-6		2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylethanesulfonamide

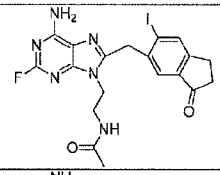
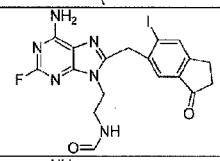
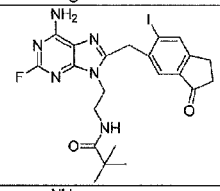
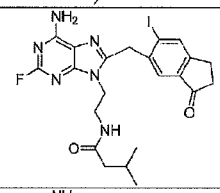
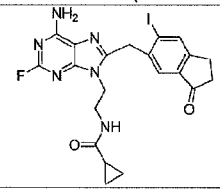
Compound No.	Structure	Name
9A-7		2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
9A-8		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
9A-9		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)ethanesulfonamide
9A-10		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)methane-sulfonamide
9A-11		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
9A-12		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide

Compound No.	Structure	Name
9A-13		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
9A-14		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
9A-15		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
9A-16		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
9A-17		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
9A-18		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propane-1-sulfonamide

Compound No.	Structure	Name
9A-19		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide
9A-20		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
9A-21		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
9A-22		N-(3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)propane-2-sulfonamide
9A-23		N-(3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)ethane-sulfonamide
9A-24		N-(3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)methane-sulfonamide

Compound No.	Structure	Name
9A-25		N-(3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide
9A-26		N-(3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide
9A-27		N-(3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide
9A-28		N-(3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
9A-29		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropanamide
9A-30		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropanamide

Compound No.	Structure	Name
9A-31		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylpropan-amide
9A-32		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propanamide
9A-33		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propanamide
9A-34		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropanamide
9A-35		3-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropanamide
9A-36		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)isobutyramide
9A-37		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)propionamide

Compound No.	Structure	Name
9A-38		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)acetamide
9A-39		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)formamide
9A-40		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)pivalamide
9A-41		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-3-methylbutanamide
9A-42		N-(2-(6-amino-2-fluoro-8-((6-iodo-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropanecarboxamide

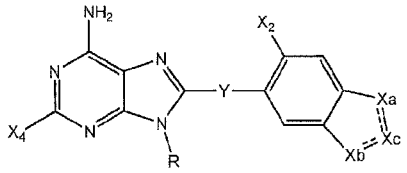
E-II. In some embodiments of the disclosure, X_2 is an optionally substituted aryl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 7A and 9A, or variations thereof as described in A. and E-I. above, in which X_2 is an optionally substituted aryl, including but not limited to pyrazolyl, 1H-pyrazol-3-yl, oxazolyl, oxazol-2-yl, thiazolyl, thiazol-2-yl, furanyl, furan-2-yl, and 5-methylfuran-2-yl.

E-III. In some embodiments of the disclosure, X_2 is an alkynyl group, *e.g.*, ethynyl, 1-prop-1-ynyl, and 3-prop-1-ynyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 7A and 9A, or variations thereof as described in A. and E-I. above, in which X_2 is an alkynyl group.

E-IV. In some embodiments of the disclosure, X_2 is an amino group, *i.e.*, $-NR_1R_2$, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 7A and 9A, or variations thereof as described in A. and E-I. above, in which X_2 is an amino group.

F. Compounds of Formula (IA) in Which Xa and Xb Each Comprise Hydrocarbon

In accordance with another embodiment of the disclosure, the compounds are of Formula (IA) in which Xa, Xb and Xc all comprise hydrocarbon and are connected by two single bonds or one single bond and one double bond. Thus, the compounds of this embodiment can be represented by Formula (4):



(4)

or a pharmaceutically acceptable salt thereof, wherein:

Xa-Xc-Xb is CH_2-CH_2-CH_2, CH=CH-CH_2, or CH_2-CH=CH;

Y is CH_2 or S;

X_4 is hydrogen or halogen;

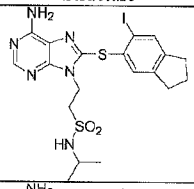
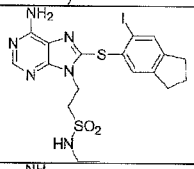
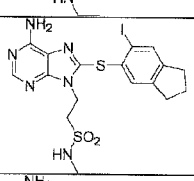
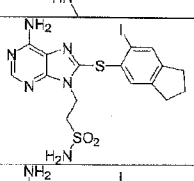
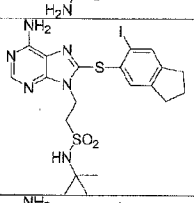
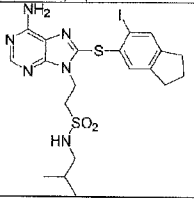
R is a is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

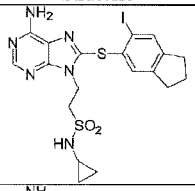
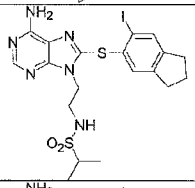
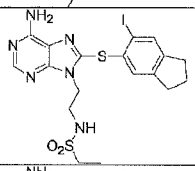
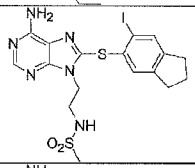
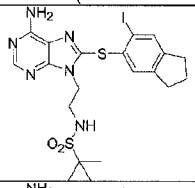
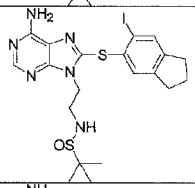
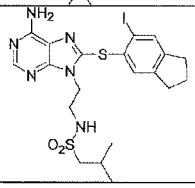
X_2 is as disclosed below.

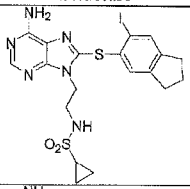
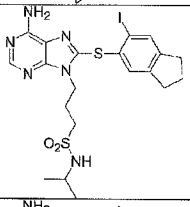
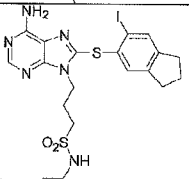
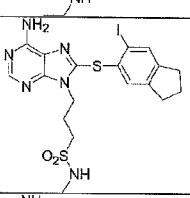
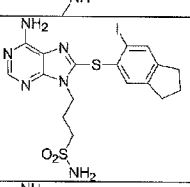
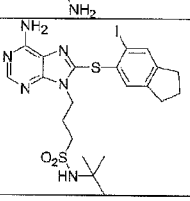
F-I. In some embodiments of the disclosure, X_2 is halogen. Table 3A lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is I and X_4

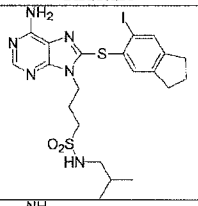
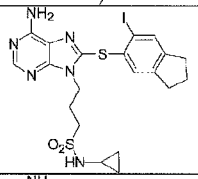
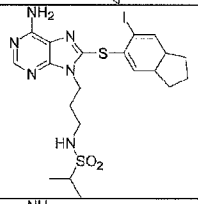
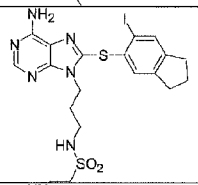
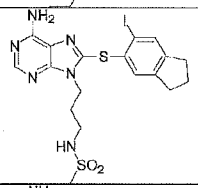
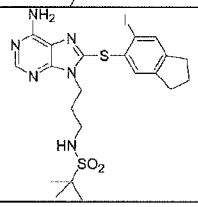
is H. However, corresponding structures in which X_2 is F, Cl, or Br are within the scope of the disclosure. In each of the structures in Table 3A, Y is S. However, corresponding structures in which Y is CH_2 and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 3A, corresponding structures in which X_2 is F, Cl, or Br and Y is CH_2 are also within the scope of the disclosure.

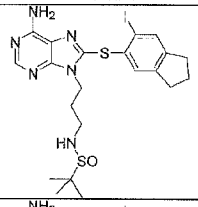
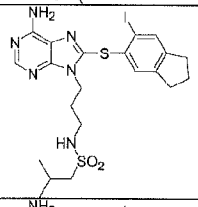
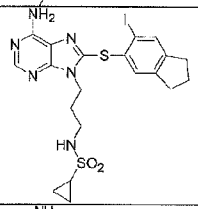
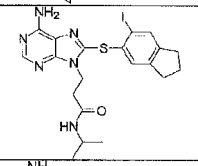
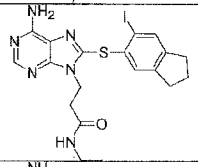
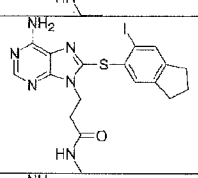
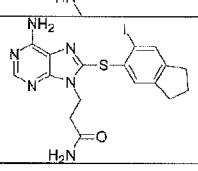
Table 3A

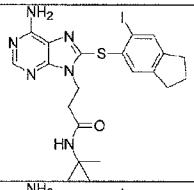
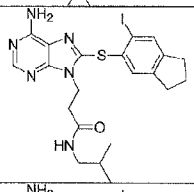
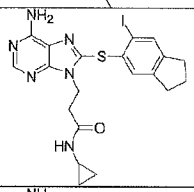
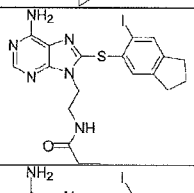
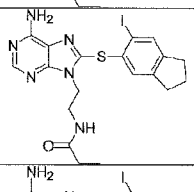
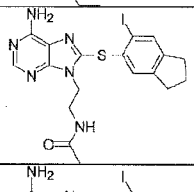
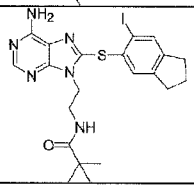
Compound No.	Structure	Name
3A-1		2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isopropylamide
3A-2		2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid ethylamide
3A-3		2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid methylamide
3A-4		2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid amide
3A-5		2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid tert-butylamide
3A-6		2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isobutyl-amide

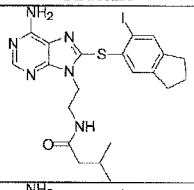
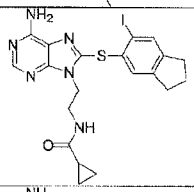
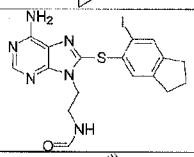
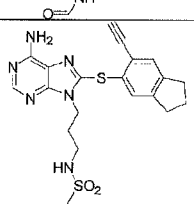
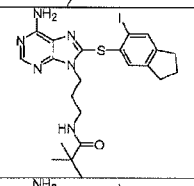
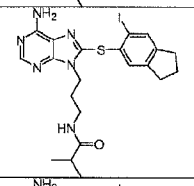
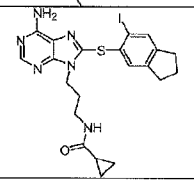
Compound No.	Structure	Name
3A-7		2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid cyclopropylamide
3A-8		Propane-2-sulfonic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
3A-9		Ethanesulfonic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
3A-10		N-{2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-methanesulfonamide
3A-11		2-Methyl-propane-2-sulfonic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
3A-12		2-Methyl-propane-2-sulfinic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
3A-13		2-Methyl-propane-1-sulfonic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide

Compound No.	Structure	Name
3A-14		Cyclopropanesulfonic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
3A-15		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isopropylamide
3A-16		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid ethylamide
3A-17		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid methylamide
3A-18		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid amide
3A-19		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid tert-butylamide

Compound No.	Structure	Name
3A-20		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isobutyl-amide
3A-21		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid cyclopropylamide
3A-22		Propane-2-sulfonic acid {3-[6-amino-8-(6-iodo-2,3,3a,7a-tetrahydro-1H-inden-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
3A-23		Ethanesulfonic acid {3-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
3A-24		N-{3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-methanesulfonamide
3A-25		2-Methyl-propane-2-sulfonic acid {3-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide

Compound No.	Structure	Name
3A-26		2-Methyl-propane-2-sulfinic acid {3-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
3A-27		2-Methyl-propane-1-sulfonic acid {3-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
3A-28		Cyclopropanesulfonic acid {3-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
3A-29		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-isopropyl-propionamide
3A-30		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-ethyl-propionamide
3A-31		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-methyl-propionamide
3A-32		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propionamide

Compound No.	Structure	Name
3A-33		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-tert-butyl-propionamide
3A-34		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-isobutyl-propionamide
3A-35		3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-cyclopropyl-propionamide
3A-36		N-{2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide
3A-37		N-{2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide
3A-38		N-{2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-acetamide
3A-39		N-{2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-2,2-dimethyl-propionamide

Compound No.	Structure	Name
3A-40		N-{2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-3-methyl-butyramide
3A-41		Cyclopropanecarboxylic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
3A-42		N-{2-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-formamide
3A-43		N-{3-[6-Amino-8-(6-ethynyl-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-methanesulfonamide
3A-44		N-{3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-2,2-dimethyl-propionamide
3A-45		N-{3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-isobutyramide
3A-46		Cyclopropanecarboxylic acid {3-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide

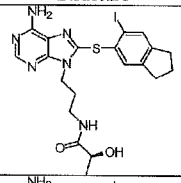
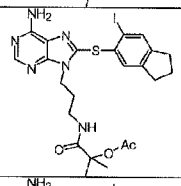
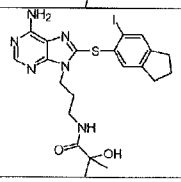
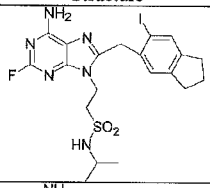
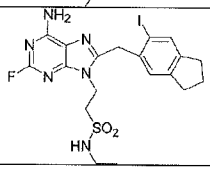
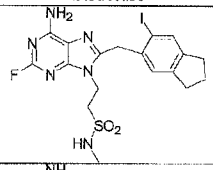
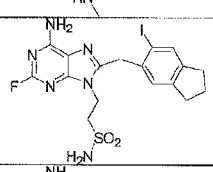
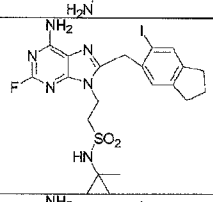
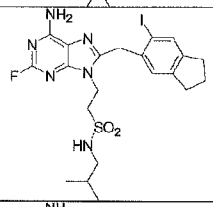
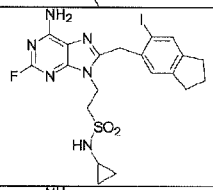
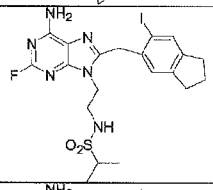
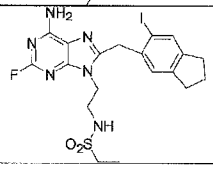
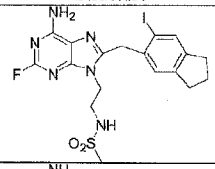
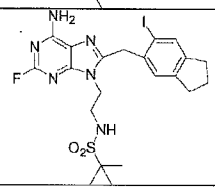
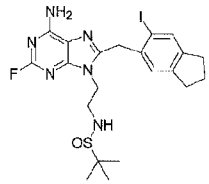
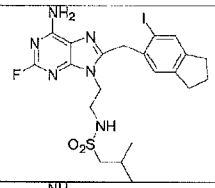
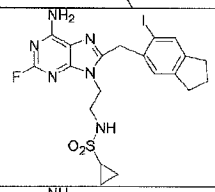
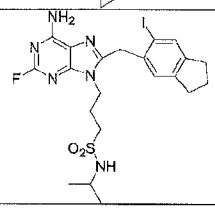
Compound No.	Structure	Name
3A-47		N-{3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-propionamide
3A-48		Acetic acid 1-{3-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propylcarbamoyl}-1-methyl-ethyl ester
3A-49		N-{3-[6-Amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-2-hydroxy-2-methyl-propionamide

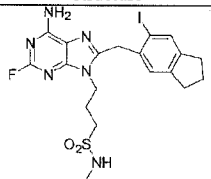
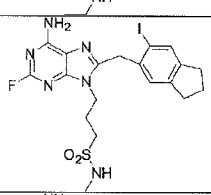
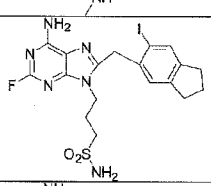
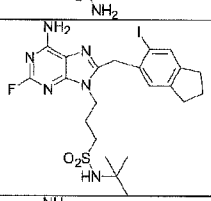
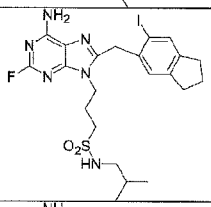
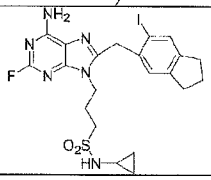
Table 6A lists specific examples in which X_2 is halogen and X_4 is halogen. In each of the structures as drawn, X_2 is I and X_4 is F. However, corresponding structures in which X_4 is H, Cl, Br, or I are within the scope of the disclosure. In each of the structures in Table 6A, Y is CH_2. However, corresponding structures in which Y is S and/or X_2 is F, Cl, or Br are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 6A, corresponding structures in which X_4 is H, Cl, Br, or I and Y is S are also within the scope of the disclosure.

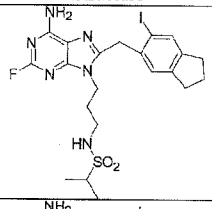
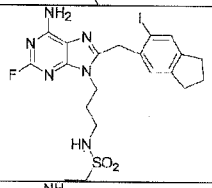
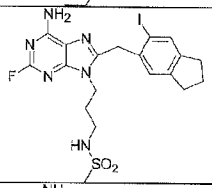
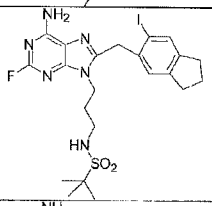
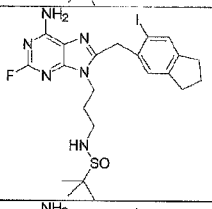
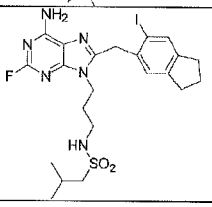
Table 6A

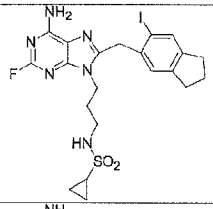
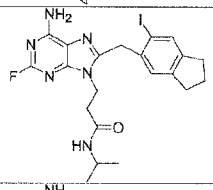
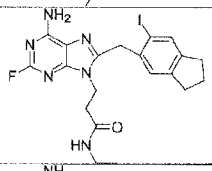
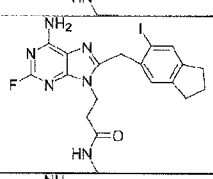
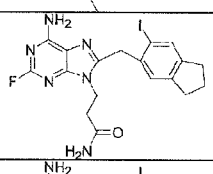
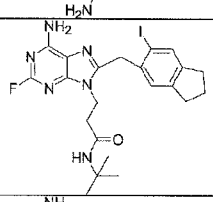
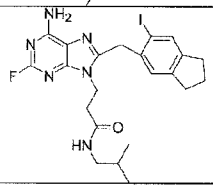
Compound No.	Structure	Name
6A-1		2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylethanesulfonamide
6A-2		2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ehtylethanesulfonamide

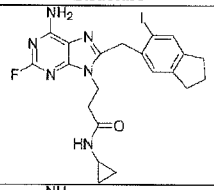
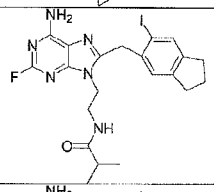
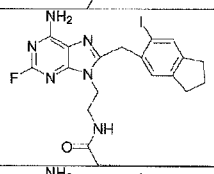
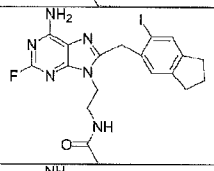
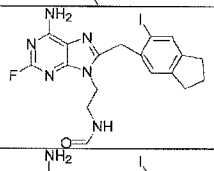
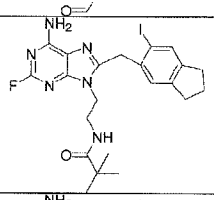
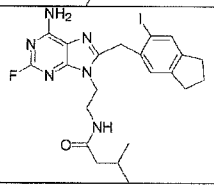
Compound No.	Structure	Name
6A-3		2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylethanesulfonamide
6A-4		2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethanesulfonamide
6A-5		2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
6A-6		2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylethanesulfonamide
6A-7		2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
6A-8		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
6A-9		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)ethanesulfonamide

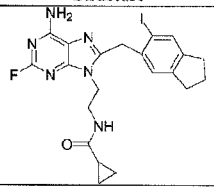
Compound No.	Structure	Name
6A-10		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)methanesulfonamide
6A-11		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
6A-12		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
6A-13		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide
6A-14		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
6A-15		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide

Compound No.	Structure	Name
6A-16		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
6A-17		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
6A-18		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-propanesulfonamide
6A-19		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide
6A-20		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
6A-21		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide

Compound No.	Structure	Name
6A-22		N-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)propane-2-sulfonamide
6A-23		N-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)ethanesulfonamide
6A-24		N-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)methane-sulfonamide
6A-25		N-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide
6A-26		N-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide
6A-27		N-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide

Compound No.	Structure	Name
6A-28		N-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)cyclopropanesulfonamide
6A-29		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropanamide
6A-30		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropanamide
6A-31		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylpropanamide
6A-32		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-propanamide
6A-33		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propanamide
6A-34		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropanamide

Compound No.	Structure	Name
6A-35		3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropanamide
6A-36		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)isobutyramide
6A-37		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)propionamide
6A-38		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)acetamide
6A-39		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)formamide
6A-40		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)pivalamide
6A-41		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-3-methylbutanamide

Compound No.	Structure	Name
6A-42		N-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropane-carboxamide

Hsp90 binding results are presented for Compounds 3A-10, 3A-11, 3A-12, 3A-24 and 3A-26 in Table 12 below. As can be noted therefrom, all compounds showed a high level of binding affinity.

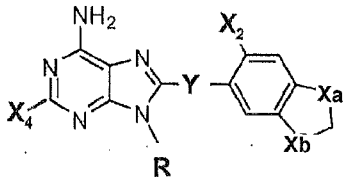
F-II. In some embodiments of the disclosure, X_2 is an optionally substituted aryl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 3A and 6A, or variations thereof as described in A. and F-I. above, in which X_2 is an optionally substituted aryl, including but not limited to pyrazolyl, 1H-pyrazol-3-yl, oxazolyl, oxazol-2-yl, thiazolyl, thiazol-2-yl, furanyl, furan-2-yl, and 5-methylfuran-2-yl.

F-III. In some embodiments of the disclosure, X_2 is an alkynyl group, *e.g.*, ethynyl, 1-prop-1-ynyl, and 3-prop-1-ynyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 3A and 6A, or variations thereof as described in A. and F-I. above, in which X_2 is an alkynyl group. Hsp90 binding results are presented for Compound 3A-43 in Table 12 below. As can be noted therefrom, the compound showed a high level of binding affinity.

F-IV. In some embodiments of the disclosure, X_2 is an amino group, *i.e.*, $-NR_1R_2$, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 3A and 6A, or variations thereof as described in A. and F-I. above, in which X_2 is an amino group.

G. Compounds of Formula (IA) in Which at Least one of Xa and Xb is CHF or CF_2

In accordance with another embodiment of the disclosure, the compounds are of Formula (IA) in which at least one of Xa and Xb is CHF or CF_2, the other of Xa and Xb is CHF, CF_2, or CH_2, and Xc is CH_2. Thus, the compounds of this embodiment can be represented by Formula (5):



(5)

or a pharmaceutically acceptable salt thereof, wherein:

at least one of Xa and Xb is CHF or CF_2 and the other is CHF, CF_2, or CH_2;

Y is CH_2, O, or S;

X_4 is hydrogen or halogen;

R is a is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

X_2 is as disclosed below.

In one embodiment, Y is O.

In another embodiment, Y is CH_2 or O

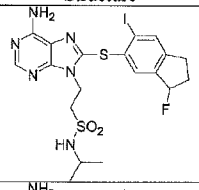
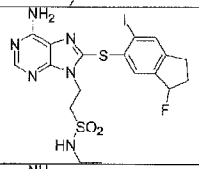
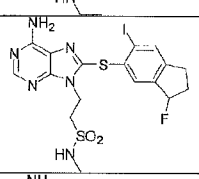
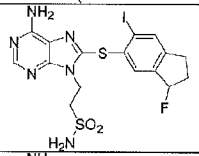
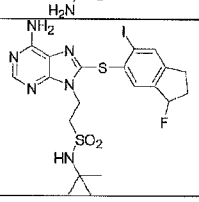
In another embodiment, Y is CH_2 or S.

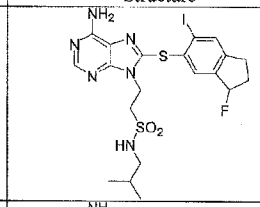
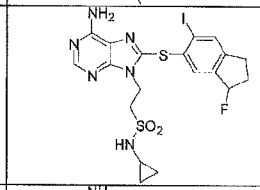
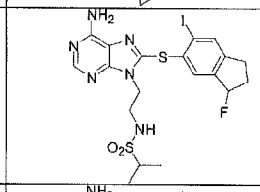
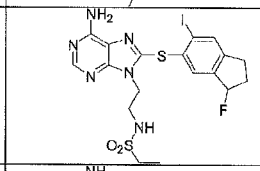
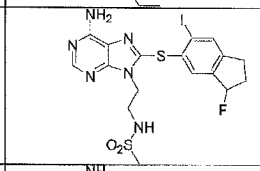
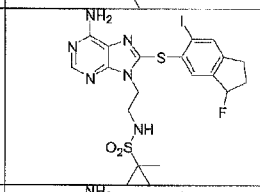
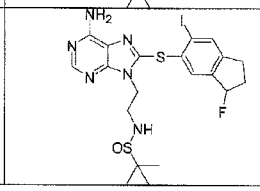
In another embodiment, Y is O or S.

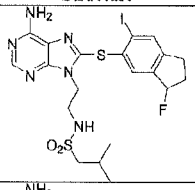
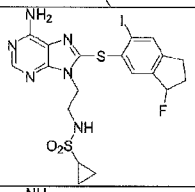
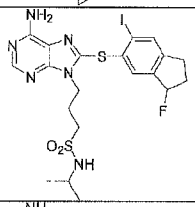
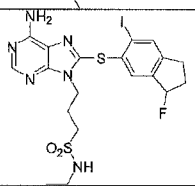
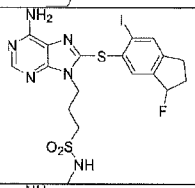
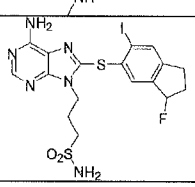
G-I. In some embodiments of the disclosure, X_2 is halogen. Table 8A lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is I and X_4 is H. However, corresponding structures in which X_2 is F, Cl, or Br are within the scope of the disclosure. In each of the structures in Table 8A, Y is S. However, corresponding structures in which Y is CH_2 or O and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. In each of the structures in Table 8A, Xb is CHF and Xa is CH_2. However, corresponding structures in

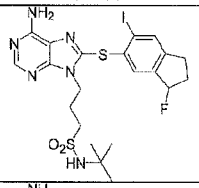
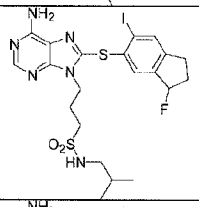
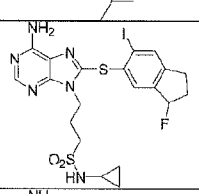
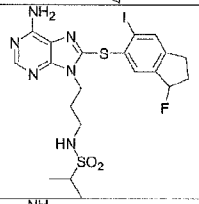
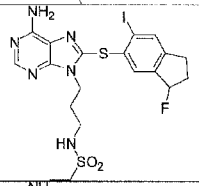
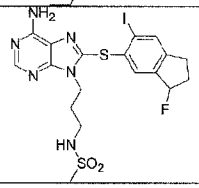
which Xa is CHF and Xb is CH_2, Xa is CF_2 and Xb is CH_2, Xb is CF_2 and Xa is CH_2, Xa is CHF and Xb is CF_2, Xb is CHF and Xa is CF_2, Xa is CHF and Xb is CHF, or Xa is CF_2 and Xb is CF_2 are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 8A, corresponding structures in which X_2 is F, Cl, or Br, Y is CH_2 or O, and Xa is CHF and Xb is CH_2, Xa is CF_2 and Xb is CH_2, Xb is CF_2 and Xa is CH_2, Xa is CHF and Xb is CF_2, Xb is CHF and Xa is CF_2, Xa is CHF and Xb is CHF, or Xa is CF_2 and Xb is CF_2 are also within the scope of the disclosure.

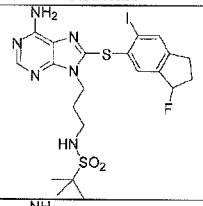
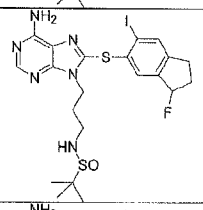
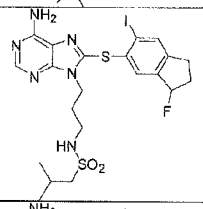
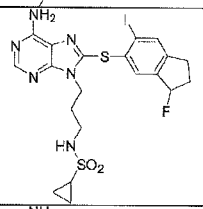
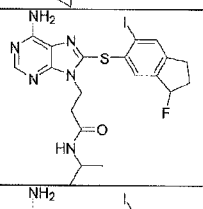
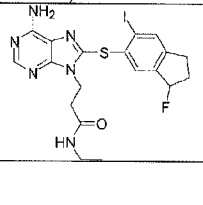
Table 8A

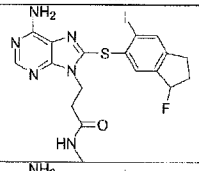
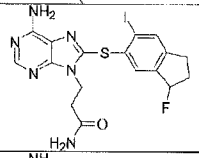
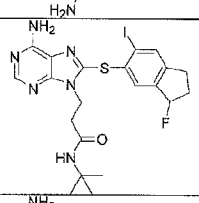
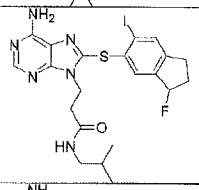
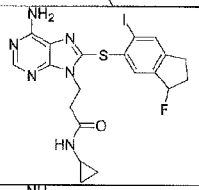
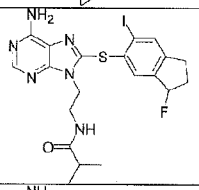
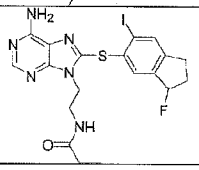
Compound No.	Structure	Name
8A-1		2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isopropylamide
8A-2		2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid ethylamide
8A-3		2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid methylamide
8A-4		2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid amide
8A-5		2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid tert-butylamide

Compound No.	Structure	Name
8A-6		2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid isobutyl-amide
8A-7		2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethanesulfonic acid cyclopropylamide
8A-8		Propane-2-sulfonic acid {2-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
8A-9		Ethanesulfonic acid {2-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
8A-10		N-{2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-methanesulfonamide
8A-11		2-Methyl-propane-2-sulfonic acid {2-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
8A-12		2-Methyl-propane-2-sulfinic acid {2-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide

Compound No.	Structure	Name
8A-13		2-Methyl-propane-1-sulfonic acid {2-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
8A-14		Cyclopropanesulfonic acid {2-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
8A-15		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isopropylamide
8A-16		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid ethylamide
8A-17		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid methylamide
8A-18		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid amide

Compound No.	Structure	Name
8A-19		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid tert-butylamide
8A-20		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid isobutyl-amide
8A-21		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propane-1-sulfonic acid cyclopropylamide
8A-22		Propane-2-sulfonic acid {3-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
8A-23		Ethanesulfonic acid {3-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
8A-24		N-{3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-methanesulfonamide

Compound No.	Structure	Name
8A-25		2-Methyl-propane-2-sulfonic acid {3-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
8A-26		2-Methyl-propane-2-sulfinic acid {3-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
8A-27		2-Methyl-propane-1-sulfonic acid {3-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
8A-28		Cyclopropanesulfonic acid {3-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propyl}-amide
8A-29		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-isopropyl-propionamide
8A-30		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-ethyl-propionamide

Compound No.	Structure	Name
8A-31		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-methyl-propionamide
8A-32		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-propionamide
8A-33		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-tert-butyl-propionamide
8A-34		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-isobutyl-propionamide
8A-35		3-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-N-cyclopropyl-propionamide
8A-36		N-{2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-isobutyramide
8A-37		N-{2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-propionamide

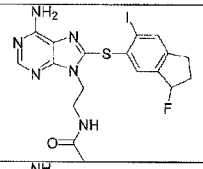
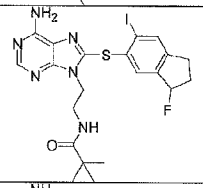
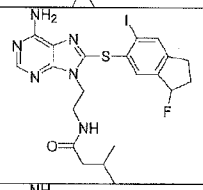
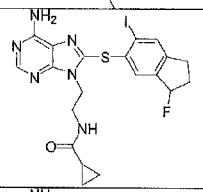
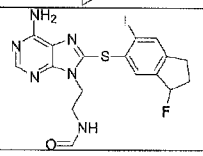
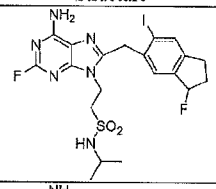
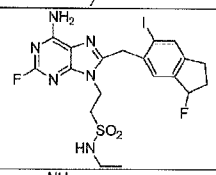
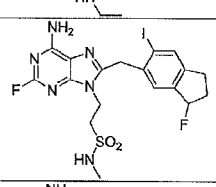
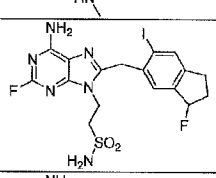
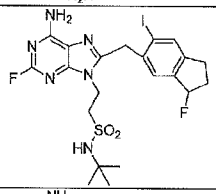
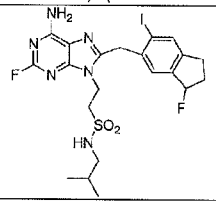
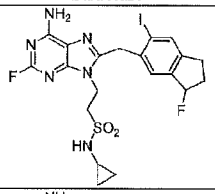
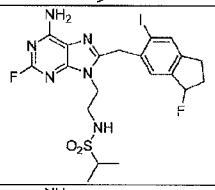
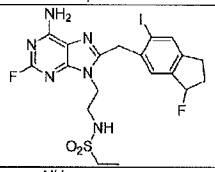
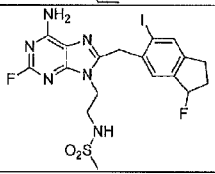
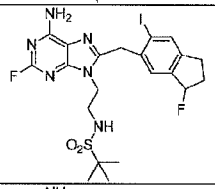
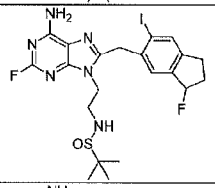
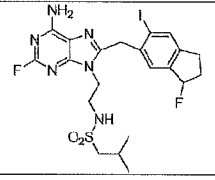
Compound No.	Structure	Name
8A-38		N-{2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-acetamide
8A-39		N-{2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-2,2-dimethyl-propionamide
8A-40		N-{2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-3-methyl-butyramide
8A-41		Cyclopropanecarboxylic acid {2-[6-amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide
8A-42		N-{2-[6-Amino-8-(3-fluoro-6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-formamide

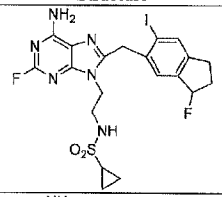
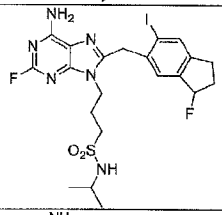
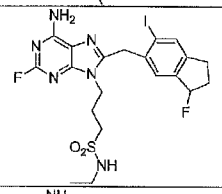
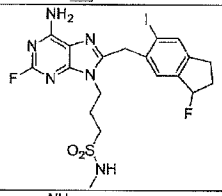
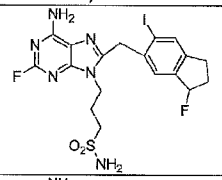
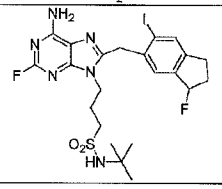
Table 10A lists specific examples in which X_2 is halogen and X_4 is halogen. In each of the structures as drawn, X_2 is I and X_4 is F. However, corresponding structures in which X_4 is H, Cl, Br, or I are within the scope of the disclosure. In each of the structures in Table 10A, Y is CH_2. However, corresponding structures in which Y is S or O and/or X_2 is F, Cl, or Br are also within the scope of the disclosure. In each of the structure in Table 10A, Xb is CHF and Xa is CH_2. However, corresponding structures in which Xa is CHF and Xb is CH_2, Xa is CF_2 and Xb is CH_2, Xb is CF_2 and Xa is CH_2, Xa is CHF and Xb is CF_2, Xb is CHF and Xa is CF_2, Xa is CHF and Xb is CHF, or Xa is CF_2 and Xb is CF_2 are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 10A, corresponding structures in which X_4 is H, Cl, Br, or I, Y is S or O, and Xa is CHF and Xb is CH_2, Xa is CF_2 and Xb is CH_2, Xb is CF_2 and Xa is

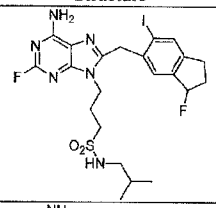
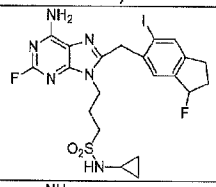
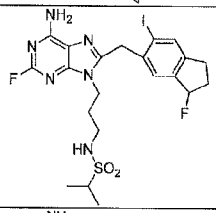
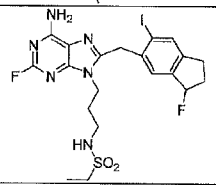
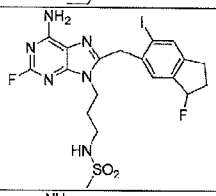
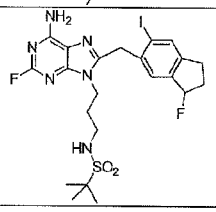
CH_2, Xa is CHF and Xb is CF_2, Xb is CHF and Xa is CF_2, Xa is CHF and Xb is CHF, or Xa is CF_2 and Xb is CF_2 are also within the scope of the disclosure.

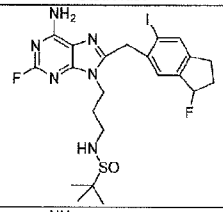
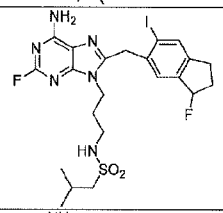
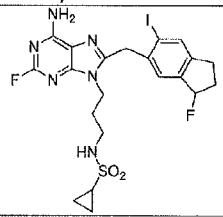
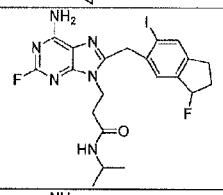
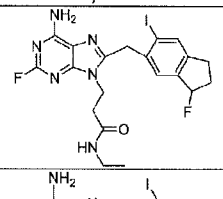
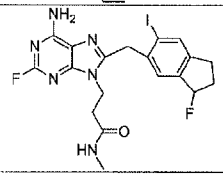
Table 10A

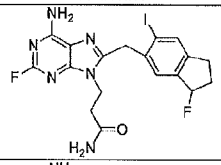
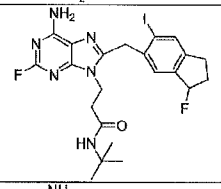
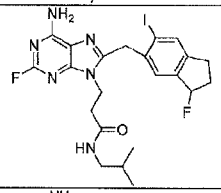
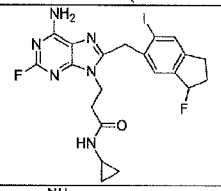
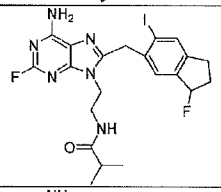
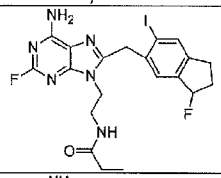
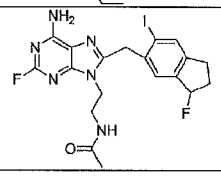
Compound No.	Structure	Name
10A-1		2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylethanesulfonamide
10A-2		2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylethanesulfonamide
10A-3		2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylethanesulfonamide
10A-4		2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethanesulfonamide
10A-5		2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
10A-6		2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylethanesulfonamide

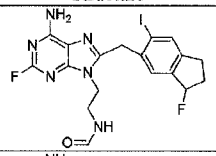
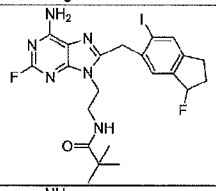
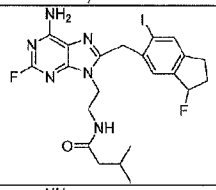
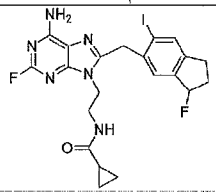
Compound No.	Structure	Name
10A-7		2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
10A-8		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
10A-9		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)ethanesulfonamide
10A-10		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)methanesulfonamide
10A-11		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
10A-12		NN-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
10A-13		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide

Compound No.	Structure	Name
10A-14		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
10A-15		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
10A-16		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
10A-17		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
10A-18		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propane-1-sulfonamide
10A-19		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide

Compound No.	Structure	Name
10A-20		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
10A-21		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
10A-22		N-(3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)propane-2-sulfonamide
10A-23		N-(3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)ethanesulfonamide
10A-24		N-(3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)methanesulfonamide
10A-25		N-(3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide

Compound No.	Structure	Name
10A-26		N-(3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide
10A-27		N-(3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide
10A-28		N-(3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
10A-29		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isopropylpropanamide
10A-30		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-ethylpropanamide
10A-31		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylpropanamide

Compound No.	Structure	Name
10A-32		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propanamide
10A-33		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-(tert-butyl)propanamide
10A-34		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-isobutylpropanamide
10A-35		3-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-cyclopropylpropanamide
10A-36		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)isobutyramide
10A-37		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)propionamide
10A-38		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)acetamide

Compound No.	Structure	Name
10A-39		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)formamide
10A-40		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)pivalamide
10A-41		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)-3-methylbutanamide
10A-42		N-(2-(6-amino-2-fluoro-8-((3-fluoro-6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)cyclopropane-carboxamide

G-II. In some embodiments of the disclosure, X_2 is an optionally substituted aryl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 8A and 10A, or variations thereof as described in A., G. and G-I. above, in which X_2 is an optionally substituted aryl, including but not limited to pyrazolyl, 1H-pyrazol-3-yl, oxazolyl, oxazol-2-yl, thiazolyl, thiazol-2-yl, furanyl, furan-2-yl, and 5-methylfuran-2-yl.

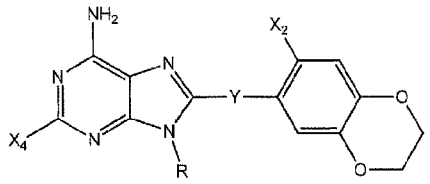
G-III. In some embodiments of the disclosure, X_2 is an alkynyl group, *e.g.*, ethynyl, 1-prop-1-ynyl, and 3-prop-1-ynyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Tables 8A and 10A, or variations thereof as described in A., G. and G-I. above, in which X_2 is an alkynyl group.

G-IV. In some embodiments of the disclosure, X_2 is an amino group, *i.e.*, $-NR_1R_2$, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl. Specific examples of compounds within the scope of this aspect of the

disclosure correspond to the compounds disclosed in Tables 8A and 10A, or variations thereof as described in A., G. and G-I. above, in which X_2 is an amino group.

H. Compounds of Formula (IB) in which Xa and Xb are Each O

In accordance with another embodiment of the disclosure, the compounds are of Formula (IB) in which each of Xa and Xb are O and each of Xc and Xd are CH_2. Thus, the compounds of this embodiment can be represented by Formula (6):



(6)

or a pharmaceutically acceptable salt thereof, wherein:

Y is CH_2, O, or S;

X_4 is hydrogen or halogen;

R is a is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$, and/or terminated by $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_5 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

X_2 is as disclosed below.

In one embodiment, Y is O.

In another embodiment, Y is CH_2 or O

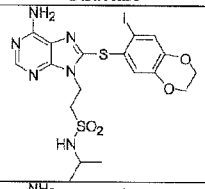
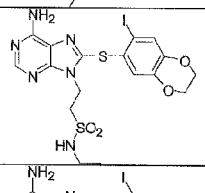
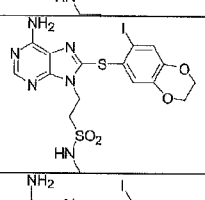
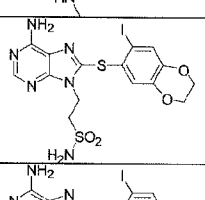
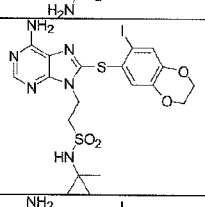
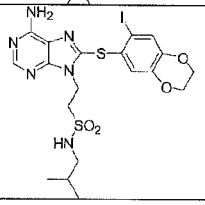
In another embodiment, Y is CH_2 or S.

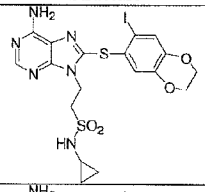
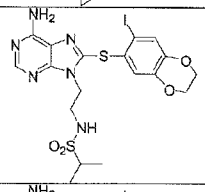
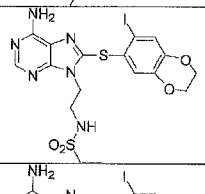
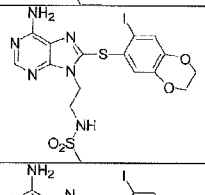
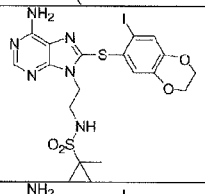
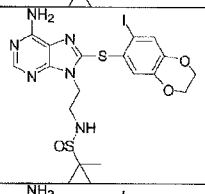
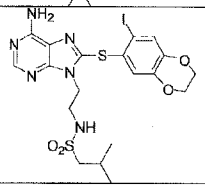
In another embodiment, Y is O or S.

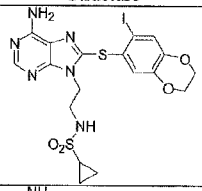
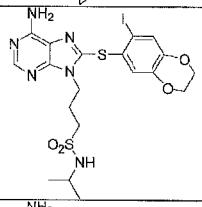
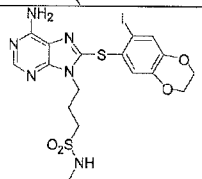
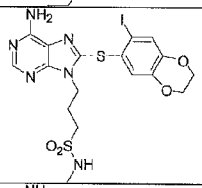
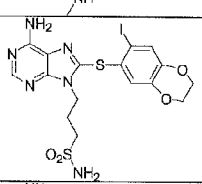
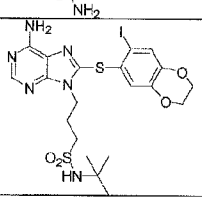
H-I. In some embodiments of the disclosure, X_2 is halogen. Table 11A lists specific examples of compounds within this embodiment. In each of the structures as drawn, X_2 is I and X_4

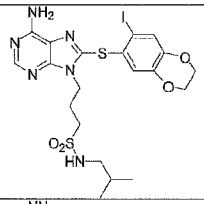
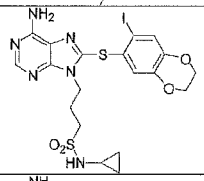
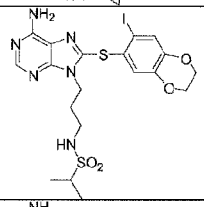
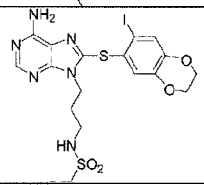
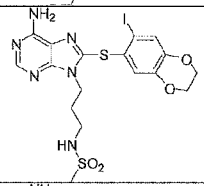
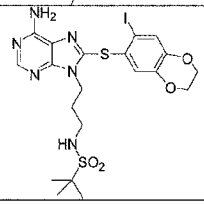
is H. However, corresponding structures in which X_2 is F, Cl, or Br are within the scope of the disclosure. In each of the structures in Table 11A, Y is S. However, corresponding structures in which Y is CH_2 or O and/or X_4 is F, Cl, Br, or I are also within the scope of the disclosure. Additionally, in connection with each of the structures in Table 11A, corresponding structures in which X_2 is F, Cl, or Br and Y is CH_2 or O are also within the scope of the disclosure.

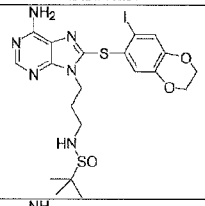
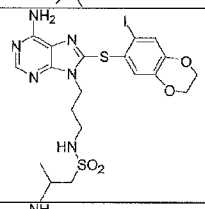
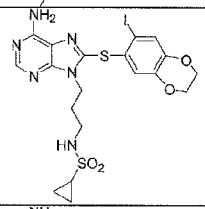
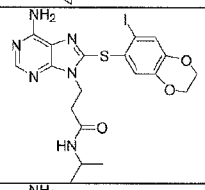
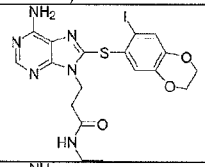
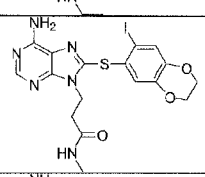
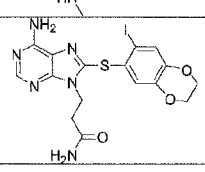
Table 11A

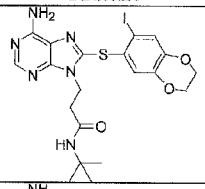
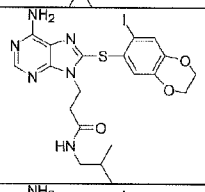
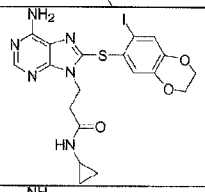
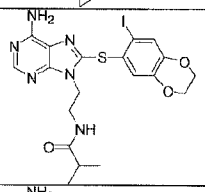
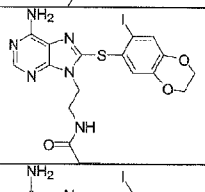
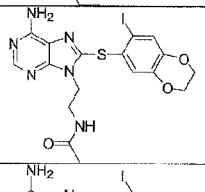
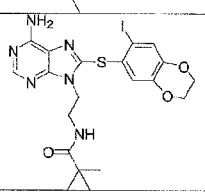
Compound No.	Structure	Name
11A-1		2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-isopropylethanesulfonamide
11A-2		2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-ethylethanesulfonamide
11A-3		2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-methylethanesulfonamide
11A-4		2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethanesulfonamide
11A-5		2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)ethanesulfonamide
11A-6		2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-isobutylethanesulfonamide

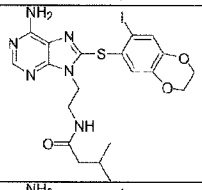
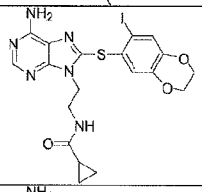
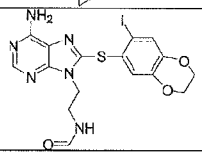
Compound No.	Structure	Name
11A-7		2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-cyclopropyl-ethanesulfonamide
11A-8		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)propane-2-sulfonamide
11A-9		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)ethanesulfonamide
11A-10		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)methanesulfonamide
11A-11		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide
11A-12		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide
11A-13		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-1-sulfonamide

Compound No.	Structure	Name
11A-14		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)cyclopropane-sulfonamide
11A-15		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-isopropylpropane-1-sulfonamide
11A-16		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-ethylpropane-1-sulfonamide
11A-17		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-methylpropane-1-sulfonamide
11A-18		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propane-1-sulfonamide
11A-19		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propane-1-sulfonamide

Compound No.	Structure	Name
11A-20		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-isobutylpropane-1-sulfonamide
11A-21		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropane-1-sulfonamide
11A-22		N-(3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)propane-2-sulfonamide
11A-23		N-(3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)ethanesulfonamide
11A-24		N-(3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)methane-sulfonamide
11A-25		N-(3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide

Compound No.	Structure	Name
11A-26		N-(3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide
11A-27		N-(3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide
11A-28		N-(3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)cyclopropane-sulfonamide
11A-29		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-isopropylpropanamide
11A-30		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-ethylpropanamide
11A-31		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-methylpropanamide
11A-32		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propanamide

Compound No.	Structure	Name
11A-33		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-(tert-butyl)propanamide
11A-34		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-isobutylpropanamide
11A-35		3-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-N-cyclopropylpropanamide
11A-36		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)isobutyramide
11A-37		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)propionamide
11A-38		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)acetamide
11A-39		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)pivalamide

Compound No.	Structure	Name
11A-40		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)-3-methylbutanamide
11A-41		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)cyclopropanecarboxamide
11A-42		N-(2-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)formamide

H-II. In some embodiments of the disclosure, X_2 is an optionally substituted aryl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Table 11A, or variations thereof as described in A., H. and H-I. above, in which X_2 is an optionally substituted aryl, including but not limited to pyrazolyl, 1H-pyrazol-3-yl, oxazolyl, oxazol-2-yl, thiazolyl, thiazol-2-yl, furanyl, furan-2-yl, and 5-methylfuran-2-yl.

H-III. In some embodiments of the disclosure, X_2 is an alkynyl group, *e.g.*, ethynyl, 1-prop-1-ynyl, and 3-prop-1-ynyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Table 11A, or variations thereof as described in A., H. and H-I. above, in which X_2 is an alkynyl group.

H-IV. In some embodiments of the disclosure, X_2 is an amino group, *i.e.*, $-NR_1R_2$, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl. Specific examples of compounds within the scope of this aspect of the disclosure correspond to the compounds disclosed in Table 11A, or variations thereof as described in A., H. and H-I. above, in which X_2 is an amino group.

J. Additional Embodiments

Each of the following embodiments relates to the compounds of Formulae (IA) and (IB) and, particularly, to each of the appropriate embodiments C-1 through H-IV of the compounds of Formulae (1) through (6).

In one embodiment, Y is CH_2. In another embodiment, Y is S.

In another embodiment, X_4 is H. In another embodiment, X_4 is halogen. In another embodiment, X_4 is F, Cl, or Br. In another embodiment, X_4 is F, Cl, or I. In another embodiment, X_4 is F, Br, or I. In another embodiment, X_4 is Cl, Br, or I. In another embodiment, X_4 is F or I. In another embodiment, X_4 is F or Br. In another embodiment, X_4 is F or Cl. In another embodiment, X_4 is Cl or I. In another embodiment, X_4 is Cl or Br. In another embodiment, X_4 is Br or I. In another embodiment, X_4 is F. In another embodiment, X_4 is Cl. In another embodiment, X_4 is Br. In another embodiment, X_4 is I. In another embodiment, X_4 is H, F, Cl, or Br. In another embodiment, X_4 is H, F, Cl, or I. In another embodiment, X_4 is H, F, Br, or I. In another embodiment, X_4 is H, Cl, Br, or I. In another embodiment, X_4 is H, F, or I. In another embodiment, X_4 is H, F, or Br. In another embodiment, X_4 is H, F, or Cl. In another embodiment, X_4 is H, Cl, or I. In another embodiment, X_4 is H, Cl, or Br. In another embodiment, X_4 is H, Br, or I. In another embodiment, X_4 is H or F. In another embodiment, X_4 is H or Cl. In another embodiment, X_4 is H or Br. In another embodiment, X_4 is H or I.

In another embodiment, X_2 is halogen, aryl, or alkynyl. In another embodiment, X_2 is halogen, aryl, or amino. In another embodiment, X_2 is halogen, alkynyl, or amino. In another embodiment, X_2 is aryl, alkynyl, or amino. In another embodiment, X_2 is halogen or amino. In another embodiment, X_2 is halogen or alkynyl. In another embodiment, X_2 is halogen or aryl. In another embodiment, X_2 is halogen. In another embodiment, X_2 is aryl. In another embodiment, X_2 is alkynyl. In another embodiment, X_2 is amino. In another embodiment, X_2 is halogen, heteroaryl, alkynyl, or amino. In another embodiment, X_2 is halogen, heteroaryl, or alkynyl. In another embodiment, X_2 is halogen, heteroaryl, or amino. In another embodiment, X_2 is heteroaryl, alkynyl, or amino. In another embodiment, X_2 is halogen or heteroaryl. In another embodiment, X_2 is heteroaryl. In another embodiment, X_2 is alkyl-substituted heteroaryl. In another embodiment, X_2 is C_1-C_6 alkyl-substituted heteroaryl. In another embodiment, X_2 is methyl-, ethyl-, n-propyl-, or isopropyl-substituted heteroaryl. In another embodiment, X_2 is methyl- or ethyl-substituted heteroaryl. In another embodiment, X_2 is methyl-substituted heteroaryl. In another embodiment, X_2 is ethyl-substituted heteroaryl.

In another embodiment, X_2 is F, Cl, or Br. In another embodiment, X_2 is F, Cl, or I. In another embodiment, X_2 is F, Br, or I. In another embodiment, X_2 is Cl, Br, or I. In another embodiment, X_2 is F or I. In another embodiment, X_2 is F or Br. In another embodiment, X_2 is F or

Cl. In another embodiment, X_2 is Cl or I. In another embodiment, X_2 is Cl or Br. In another embodiment, X_2 is Br or I. In another embodiment, X_2 is F. In another embodiment, X_2 is Cl. In another embodiment, X_2 is Br. In another embodiment, X_2 is I.

In another embodiment, X_2 is optionally substituted heteroaryl. In another embodiment, X_2 is unsubstituted heteroaryl. In another embodiment, X_2 is furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, 5-methyloxazol-2-yl, thiophene-2-yl, thiophene-3-yl, 1H-imidazo-2-yl, 1H-imidazo-4-yl, or 1H-imidazo-5-yl. In another embodiment, X_2 is furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, or 5-methyloxazol-2-yl. In another embodiment, X_2 is furan-2-yl, furan-3-yl, or 5-methylfuran-2-yl. In another embodiment, X_2 is 1H-pyrazol-2-yl or 1H-pyrazol-3-yl. In another embodiment, X_2 is thiazol-2-yl or 5-methylthiazol-2-yl. In another embodiment, X_2 is oxazol-2-yl or 5-methyloxazol-2-yl. In another embodiment, X_2 is thiophene-2-yl, thiophene-3-yl, 1H-imidazo-2-yl, 1H-imidazo-4-yl, or 1H-imidazo-5-yl. In another embodiment, X_2 is thiophene-2-yl or thiophene-3-yl. In another embodiment, X_2 is 1H-imidazo-2-yl, 1H-imidazo-4-yl, or 1H-imidazo-5-yl.

In another embodiment, X_2 is ethynyl, propynyl, or butynyl. In another embodiment, X_2 is ethynyl or propynyl. In another embodiment, X_2 is ethynyl or butynyl. In another embodiment, X_2 is propynyl or butynyl. In another embodiment, X_2 is ethynyl. In another embodiment, X_2 is propynyl. In another embodiment, X_2 is butynyl.

In another embodiment, X_2 is dimethylamino, diethylamino, methylethylamino, or cyclopropylamino. In another embodiment, X_2 is dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is dimethylamino, diethylamino, or cyclopropylamino. In another embodiment, X_2 is dimethylamino, methylethylamino, or cyclopropylamino. In another embodiment, X_2 is diethylamino, methylethylamino, or cyclopropylamino. In another embodiment, X_2 is dimethylamino or diethylamino. In another embodiment, X_2 is dimethylamino or methylethylamino. In another embodiment, X_2 is dimethylamino or cyclopropylamino. In another embodiment, X_2 is diethylamino or methylethylamino. In another embodiment, X_2 is diethylamino or cyclopropylamino. In another embodiment, X_2 is methylethylamino or cyclopropylamino. In another embodiment, X_2 is dimethylamino. In another embodiment, X_2 is diethylamino. In another embodiment, X_2 is methylethylamino. In another embodiment, X_2 is cyclopropylamino.

In another embodiment, X_2 is Br, I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, propynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or

methylethylamino. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino.

In another embodiment, X_2 is halogen, aryl, or alkynyl and Y is S. In another embodiment, X_2 is halogen, aryl, or amino and Y is S. In another embodiment, X_2 is halogen, alkynyl, or amino and Y is S. In another embodiment, X_2 is aryl, alkynyl, or amino and Y is S. In another embodiment, X_2 is halogen or amino and Y is S. In another embodiment, X_2 is halogen or alkynyl and Y is S. In another embodiment, X_2 is halogen or aryl and Y is S. In another embodiment, X_2 is halogen and Y is S. In another embodiment, X_2 is aryl and Y is S. In another embodiment, X_2 is alkynyl and Y is S. In another embodiment, X_2 is amino and Y is S. In another embodiment, X_2 is halogen, heteroaryl, alkynyl, or amino and Y is S. In another embodiment, X_2 is halogen, heteroaryl, or alkynyl and Y is S. In another embodiment, X_2 is halogen, heteroaryl, or amino and Y is S. In another embodiment, X_2 is heteroaryl, alkynyl, or amino and Y is S. In another embodiment, X_2 is halogen or heteroaryl and Y is S. In another embodiment, X_2 is heteroaryl and Y is S. In another embodiment, X_2 is alkyl-substituted heteroaryl and Y is S. In another embodiment, X_2 is C_1-C_6 alkyl-substituted heteroaryl and Y is S. In another embodiment, X_2 is methyl-, ethyl-, n-propyl-, or isopropyl-substituted heteroaryl and Y is S. In another embodiment, X_2 is methyl- or ethyl-substituted heteroaryl and Y is S. In another embodiment, X_2 is methyl-substituted heteroaryl and Y is S. In another embodiment, X_2 is ethyl-substituted heteroaryl and Y is S. In another embodiment, X_2 is Br, I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl,

propynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino and Y is S. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino and Y is S. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino and Y is S. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino and Y is S. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino and Y is S. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino and Y is S. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is S. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino and Y is S. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino and Y is S.

In another embodiment, X_2 is halogen, aryl, or alkynyl and Y is CH_2. In another embodiment, X_2 is halogen, aryl, or amino and Y is CH_2. In another embodiment, X_2 is halogen, alkynyl, or amino and Y is CH_2. In another embodiment, X_2 is aryl, alkynyl, or amino and Y is CH_2. In another embodiment, X_2 is halogen or amino and Y is CH_2. In another embodiment, X_2 is halogen or alkynyl and Y is CH_2. In another embodiment, X_2 is halogen or aryl and Y is CH_2. In another embodiment, X_2 is halogen and Y is CH_2. In another embodiment, X_2 is aryl and Y is CH_2. In another embodiment, X_2 is alkynyl and Y is CH_2. In another embodiment, X_2 is amino and Y is CH_2. In another embodiment, X_2 is halogen, heteroaryl, alkynyl, or amino and Y is CH_2. In another embodiment, X_2 is halogen, heteroaryl, or alkynyl and Y is CH_2. In another embodiment, X_2 is halogen, heteroaryl, or amino and Y is CH_2. In another embodiment, X_2 is heteroaryl, alkynyl, or amino and Y is CH_2. In another embodiment, X_2 is halogen or heteroaryl and Y is CH_2. In another embodiment, X_2 is heteroaryl and Y is CH_2. In another embodiment, X_2 is alkyl-substituted heteroaryl and Y is CH_2. In another embodiment, X_2 is C_1-C_6 alkyl-substituted heteroaryl and Y is CH_2. In another embodiment, X_2 is methyl-, ethyl-, n-propyl-, or isopropyl-

substituted heteroaryl and Y is CH_2. In another embodiment, X_2 is methyl- or ethyl-substituted heteroaryl and Y is CH_2. In another embodiment, X_2 is methyl-substituted heteroaryl and Y is CH_2. In another embodiment, X_2 is ethyl-substituted heteroaryl and Y is CH_2. In another embodiment, X_2 is Br, I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, propynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino and Y is CH_2. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino and Y is CH_2. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino and Y is CH_2. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino and Y is CH_2. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino and Y is CH_2. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino and Y is CH_2. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino and Y is CH_2. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino and Y is CH_2. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino and Y is CH_2.

In another embodiment, X_4 is H and Y is S. In another embodiment, X_4 is halogen and Y is S. In another embodiment, X_4 is F, Cl, or Br and Y is S. In another embodiment, X_4 is F, Cl, or I and Y is S. In another embodiment, X_4 is F, Br, or I and Y is S. In another embodiment, X_4 is Cl, Br, or I and Y is S. In another embodiment, X_4 is F or I and Y is S. In another embodiment, X_4 is F or Br and Y is S. In another embodiment, X_4 is F or Cl and Y is S. In another embodiment, X_4 is Cl or I and Y is S. In another embodiment, X_4 is Cl or Br and Y is S. In another embodiment, X_4 is Br or I and Y is S. In another embodiment, X_4 is F and Y is S. In another embodiment, X_4 is Cl and Y is S. In another embodiment, X_4 is Br and Y is S. In another embodiment, X_4 is I and Y is S.

In another embodiment, X_4 is H, F, Cl, or Br and Y is S. In another embodiment, X_4 is H, F, Cl, or I and Y is S. In another embodiment, X_4 is H, F, Br, or I and Y is S. In another embodiment, X_4 is H, Cl, Br, or I and Y is S. In another embodiment, X_4 is H, F, or I and Y is S. In another embodiment, X_4 is H, F, or Br and Y is S. In another embodiment, X_4 is H, F, or Cl and Y is S. In another embodiment, X_4 is H, Cl, or I and Y is S. In another embodiment, X_4 is H, Cl, or Br and Y is S. In another embodiment, X_4 is H, Br, or I and Y is S. In another embodiment, X_4 is H or F and Y is S. In another embodiment, X_4 is H or Cl and Y is S. In another embodiment, X_4 is H or Br and Y is S. In another embodiment, X_4 is H or I and Y is S.

In another embodiment, X_4 is H and Y is CH_2. In another embodiment, X_4 is halogen and Y is CH_2. In another embodiment, X_4 is F, Cl, or Br and Y is CH_2. In another embodiment, X_4 is F, Cl, or I and Y is CH_2. In another embodiment, X_4 is F, Br, or I and Y is CH_2. In another embodiment, X_4 is Cl, Br, or I and Y is CH_2. In another embodiment, X_4 is F or I and Y is CH_2. In another embodiment, X_4 is F or Br and Y is CH_2. In another embodiment, X_4 is F or Cl and Y is CH_2. In another embodiment, X_4 is Cl or I and Y is CH_2. In another embodiment, X_4 is Cl or Br and Y is CH_2. In another embodiment, X_4 is Br or I and Y is CH_2. In another embodiment, X_4 is F and Y is CH_2. In another embodiment, X_4 is Cl and Y is CH_2. In another embodiment, X_4 is Br and Y is CH_2. In another embodiment, X_4 is I and Y is CH_2.

In another embodiment, X_4 is H, F, Cl, or Br and Y is CH_2. In another embodiment, X_4 is H, F, Cl, or I and Y is CH_2. In another embodiment, X_4 is H, F, Br, or I and Y is CH_2. In another embodiment, X_4 is H, Cl, Br, or I and Y is CH_2. In another embodiment, X_4 is H, F, or I and Y is CH_2. In another embodiment, X_4 is H, F, or Br and Y is CH_2. In another embodiment, X_4 is H, F, or Cl and Y is CH_2. In another embodiment, X_4 is H, Cl, or I and Y is CH_2. In another embodiment, X_4 is H, Cl, or Br and Y is CH_2. In another embodiment, X_4 is H, Br, or I and Y is CH_2. In another embodiment, X_4 is H or F and Y is CH_2. In another embodiment, X_4 is H or Cl and Y is CH_2. In another embodiment, X_4 is H or Br and Y is CH_2. In another embodiment, X_4 is H or I and Y is CH_2.

In another embodiment, X_2 is halogen, aryl, or alkynyl, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen, aryl, or amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen, alkynyl, or amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is aryl, alkynyl, or amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen or amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen or alkynyl, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen or aryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen, X_4 is H or F, and Y is S. In another embodiment, X_2 is aryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is alkynyl, X_4 is H or F, and Y is S. In another embodiment, X_2 is amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen, heteroaryl, alkynyl, or amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen, heteroaryl, or alkynyl, X_4 is H or F, and Y is S.

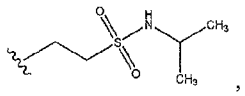
In another embodiment, X_2 is halogen, heteroaryl, or amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is heteroaryl, alkynyl, or amino, X_4 is H or F, and Y is S. In another embodiment, X_2 is halogen or heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is alkyl-substituted heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is C_1-C_6 alkyl-substituted heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is methyl-, ethyl-, n-propyl-, or isopropyl-substituted heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is methyl- or ethyl-substituted heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is methyl-substituted heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is ethyl-substituted heteroaryl, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, propynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is S.

In another embodiment, X_2 is halogen, aryl, or alkynyl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen, aryl, or amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen, alkynyl, or amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is aryl, alkynyl, or amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen or amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen or alkynyl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen or aryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is aryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is alkynyl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen, heteroaryl, alkynyl, or amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen, heteroaryl, or alkynyl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen, heteroaryl, or amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is heteroaryl, alkynyl, or amino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is halogen or heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is alkyl-substituted heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is C_1-C_6 alkyl-substituted heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is methyl-, ethyl-, n-propyl-, or isopropyl-substituted heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is methyl- or ethyl-substituted heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is methyl-substituted heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is ethyl-substituted heteroaryl, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, propynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br,

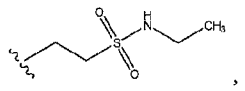
thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, thiazol-2-yl, 5-methylthiazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, dimethylamino, diethylamino, or methylethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is I, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2. In another embodiment, X_2 is Br, oxazol-2-yl, 5-methyloxazol-2-yl, ethynyl, or dimethylamino, X_4 is H or F, and Y is CH_2.

In connection with each of the R groups containing a sulfonamide structure, the corresponding structure in which the sulfonamide has the reverse orientation or in which R contains a sulfinamide or an amide (each of either orientation) is within the scope of the disclosure as if each was specifically disclosed herein. In connection with each of the R groups containing a sulfinamide structure, the corresponding structure in which the sulfinamide has the reverse orientation or in which R contains a sulfonamide or an amide (each of either orientation) is within the scope of the disclosure as if each was specifically disclosed herein. In connection with each of the R groups containing an amide structure, the corresponding structure in which the amide has the reverse orientation or in which R contains a sulfonamide or a sulfinamide (each of either orientation) is within the scope of the disclosure as if each was specifically disclosed herein. Thus, by way of example, in each instance the disclosure of a compound in which the R group contains an -$SO_2N(R_A)$- structure should also be considered as a disclosure of a compound in which the R group contains an -NR_ASO_2-, -$S(O)N(R_A)$-, -$NR_AS(O)$-, -$C(O)N(R_A)$-, or -$NR_AC(O)$- structure in place of the -$SO_2N(R_A)$- structure.

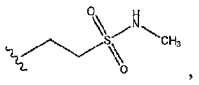
Specific R groups include without limitation: 2-ethanesulfonic acid isopropylamide, *i.e.*,



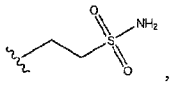
2-ethanesulfonic acid ethylamide, *i.e.*,



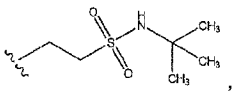
2-ethanesulfonic acid methylamide, *i.e.*,



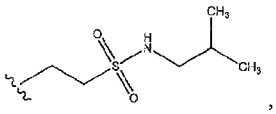
2-ethanesulfonic acid amide, *i.e.*,



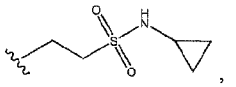
2-ethanesulfonic acid t-butylamide, *i.e.*,



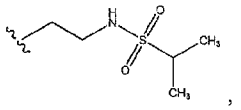
2-ethanesulfonic acid isobutylamide, *i.e.*,



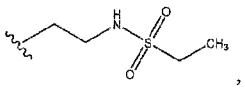
2-ethanesulfonic acid cyclopropylamide, *i.e.*,



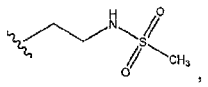
isopropanesulfonic acid 2-ethylamide, *i.e.*,



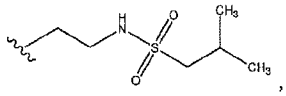
ethanesulfonic acid 2-ethylamide, *i.e.*,



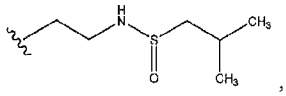
N-2 ethyl methanesulfonamide, *i.e.*,



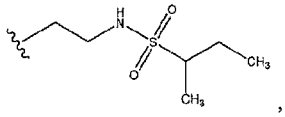
2-methyl-propane-2-sulfonic acid 2-ethylamide, *i.e.*,



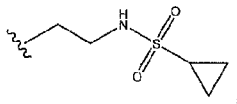
2-methyl-propane-2-sulfinic acid 2-ethylamide, *i.e.*,



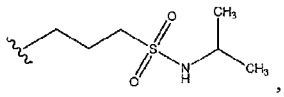
2-methyl-propane-1-sulfonic acid 2-ethylamide, *i.e.*,



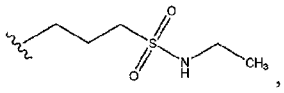
cyclopropanesufonic acid 2-ethylamide, *i.e.*,



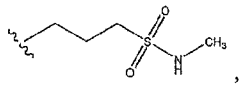
3-propane-1-sulfonic acid isopropylamide, *i.e.*,



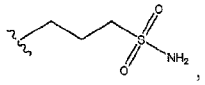
3-propane-1-sulfonic acid ethylamide, *i.e.*,



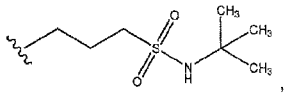
3-propane-1-sulfonic acid methylamide, *i.e.*,



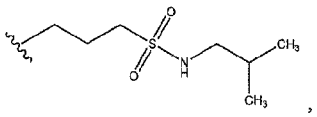
3-propane-1-sulfonic acid amide, *i.e.*,



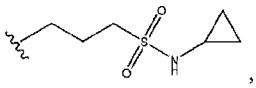
3-propane-1-sulfonic acid t-butylamide, *i.e.*,



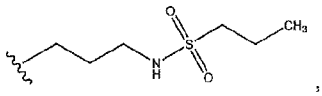
3-propane-1-sulfonic acid isobutylamide, *i.e.*,



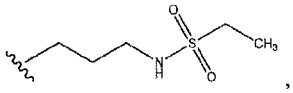
3-propane-1-sulfonic acid cyclopropylamide, *i.e.*,



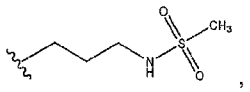
propane-2-sulfonic acid 3-propylamide, *i.e.*,



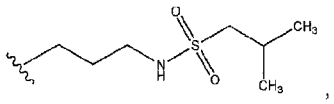
ethanesulfonic acid 3-propylamide, *i.e.*,



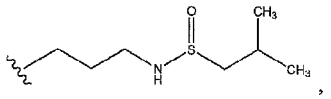
N-3-propyl methanesulfonamide, *i.e.*,



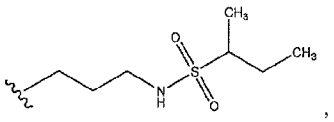
2-methyl-propane-2-sulfonic acid 3-propylamide, *i.e.*,



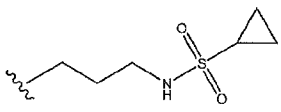
2-methyl-propane-2-sulfinic acid 3-propylamide, *i.e.*,



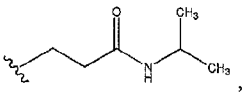
2-methyl-propane-1-sulfonic acid 3-propylamide, *i.e.*,



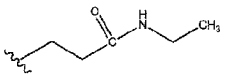
cyclopropanesulfonic acid 3-propylamide, *i.e.*,



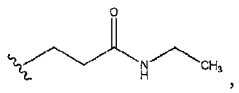
3-N-isopropyl propionamide, *i.e.*,



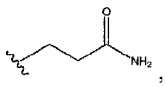
3-N-ethyl propionamide, *i.e.*,



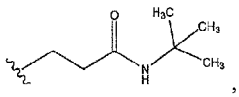
3-N-methyl propionamide, *i.e.*,



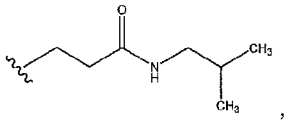
3-propionamide, *i.e.*,



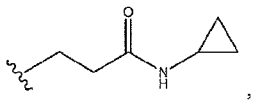
3-N-t-butyl propionamide, *i.e.*,



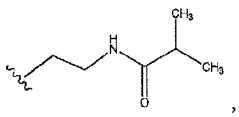
3-N-isobutyl propionamide, *i.e.*,



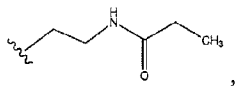
3-N-cyclopropyl propionamide, *i.e.*,



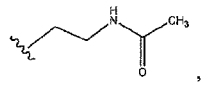
N-2-ethyl isobutyramide, *i.e.*,



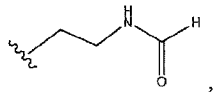
N-2-ethyl propionamide, *i.e.*,



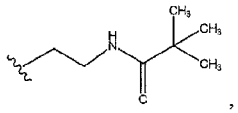
N-2-ethyl acetamide, *i.e.*,



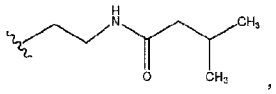
N-2-ethyl formamide, *i.e.*,



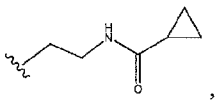
N-2-ethyl 2,2-dimethyl-propionamide, *i.e.*,



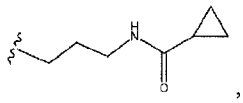
N-2-ethyl 3-methylbutyramide, *i.e.*,



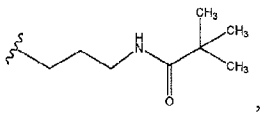
cyclopropane carboxylic acid 2-ethyl-amide, *i.e.*,



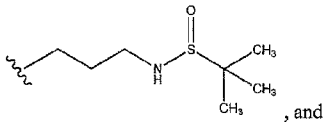
cyclopropane carboxylic acid 3-propyl-amide, *i.e.*,



N-3-propyl 2,2-dimethyl-propionamide, *i.e.*,

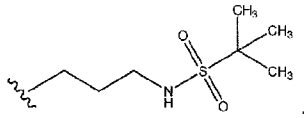


N-propyl-2-methyl-propane-2-sulfinamide, *i.e.*,



, and

t-butanesulfonic acid 3-propylamide, *i.e.*,



In connection with each of the X_4 groups of the structures disclosed herein, a corresponding structure in which X_4 is hydrogen, a fluoro group, or other halogen is within the scope of the disclosure as if each was specifically disclosed herein.

In a further aspect of the invention, each of the compounds described above can be made as a precursor compound in which X_2 is a leaving group which can be replaced by iodine for use as a radiolabel, for example ^{124}I or ^{131}I, useful as imaging tools. Exemplary leaving groups include without limitation trialkyl tin, for example trimethyl, or tributyl tin, trialkyl silicon, trialkyl geranium, or fluorus analogs of trialkyl tin such as $-Sn(CH_2CH_2(CF_2)_5CF_3)_3$, aryl boronic acids, thalium trifluroacetates, triazines, and metallated arenes. Techniques for radioiodination are well known in the art, for example from **Seevers, et al.** *Chem. Rev.*, **1982**, *82* (6), pp 575–590 and McIntee et al., *J. Org. Chem.* **2008**, *73*, 8236–8243 wghich are incorporated herein by reference.

The precursor compound in which X_2 is a leaving group are provided as reagents or in kits for addition of a radiolabeled X_2 substituent, for example ^{124}I or ^{131}I in the time immediately prior to use as an imaging marker. The precursor is readily shipped and stored prior to use since it is not itself radioactive, but it is readily converted to the labeled imaging marker.

In another embodiment, a pharmaceutical composition is formed from a Compound of Formulae (IA) or (IB) and a pharmaceutically acceptable carrier by a method known in the art. Thus, another embodiment relates to a pharmaceutical composition comprising a Compound of Formulae (IA) or (IB) and a pharmaceutically acceptable carrier. Such a composition is useful for treating or preventing cancer or a neurodegenerative disorder, *e.g.*, in a patient in need thereof.

Another embodiment relates to a method for treating or preventing cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a Compound of Formulae (IA) and/or (IB). Another embodiment relates to a

method for treating or preventing cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a Compound of Formulae (IA) and/or (IB). Another embodiment relates to a method for treating cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a Compound of Formulae (IA) and/or (IB). Another embodiment relates to a method for treating cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a Compound of Formulae (IA) and/or (IB). Another embodiment relates to a method for preventing cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a Compound of Formulae (IA) and/or (IB). Another embodiment relates to a method for preventing cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising a Compound of Formulae (IA) and/or (IB). Another embodiment relates to the use of a Compound of Formulae (IA) or (IB) in the manufacture of a medicament useful for treating cancer or a neurodegenerative disorder or for preventing cancer or a neurodegenerative disorder.

Another embodiment relates to a method for the inhibition of Hsp90, comprising contacting Hsp90 with an Hsp90 function inhibiting amount of a Compound of Formulae (IA) or (IB). An exemplary determination of an Hsp90 function inhibiting amount is provided in the example below entitled "Hsp90 Binding Assay." In one embodiment, the IC_{50} determined by the "Hsp90 Binding Assay" provided herein is less than 10 μM. In another embodiment, the IC_{50} determined by the "Hsp90 Binding Assay" provided herein is less than 1 μM. In another embodiment, the IC_{50} determined by the "Hsp90 Binding Assay" provided herein is ≤0.1 μM. Another embodiment relates to the use of a Compound of Formulae (IA) or (IB) in formulating a pharmaceutical composition for the inhibition of Hsp90.

The following examples are set forth to assist in understanding the invention and should not be construed as specifically limiting the invention as described and claimed herein. Variations of the invention, including the substitution of all equivalents now known or later developed, that would be within the purview of those in the art, and changes in formulation or changes in experimental design, are to be considered to fall within the scope of the invention incorporated herein.

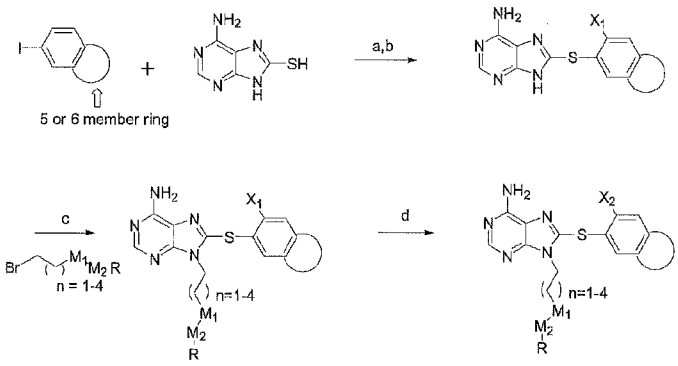
4. EXAMPLES

Certain examples below relate to the synthesis of illustrative compounds of the disclosure.

Synthetic Methods:

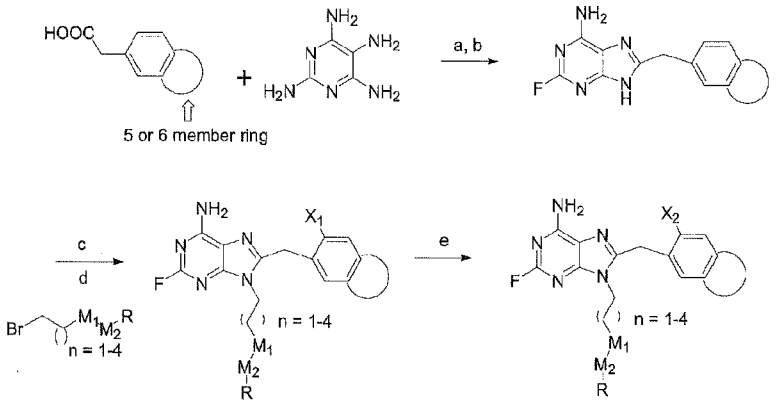
-M_1-M_2-R is -S(O)NR_AR_B, -$NR_AS(O)R_B$, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -C(O)NR_AR_B, or -$NR_AC(O)R_B$, wherein each R_A and R_B is independently selected from H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

Scheme 1. Synthesis of S-linker Adenine Derivatives



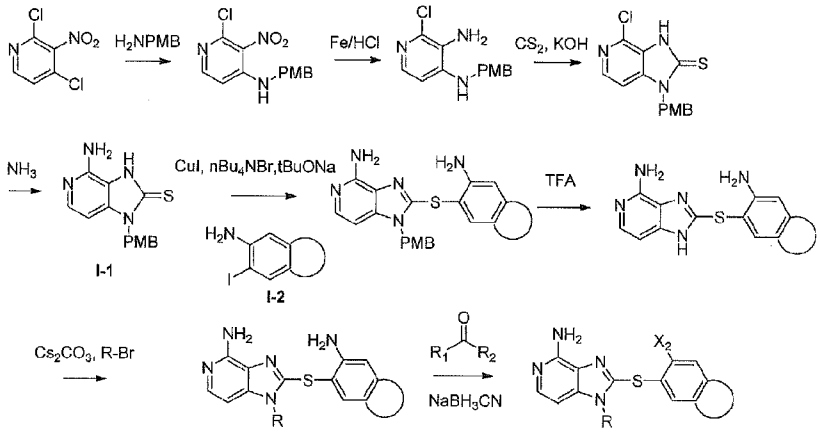
(a) CuI, neocuproine, NaO*t*-Bu, DMF, 110 °C; (b) NIS, acetonitrile, RT; (c) Cs_2CO_3; (d) X_2M, Pd (cat.), DMF, 50-100 °C.

Scheme 2. Synthesis Methylene-linker Adenine Derivatives



(a) triphenyl phosphite, pyridine, microwave; (b) HF-pyridine, $NaNO_2$; (c) NIS, acetonitrile, rt; (d) Cs_2CO_3; (e)X_2M, Pd (cat.), DMF, 50-100 °C.

Scheme 3. Synthesis of Pyridine Derivatives (The definitions of R and X_2 as an amino group in this scheme are described above.)



General Methods:

^1H and ^{13}C NMR spectra were recorded on a Bruker 500 MHz instrument. Chemical shifts are reported in δ values in ppm downfield from TMS as the internal standard. ^1H data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multuplet), coupling constant (Hz), integration. ^{13}C chemical shifts are reported in δ values in ppm downfield from TMS as the internal standard. High resolution mass spectra were recorded on a Waters LCT Premier system. Low resolution mass spectra were obtained on a Waters Acquity Ultra Performance LC with electrospray ionization and SQ detector. High-performance liquid chromatography analyses were performed on a Waters Autopurification system with PDA, MicroMass ZQ, and ELSD detector, and a reversed phase column (Waters X-Bridge C18, 4.6 x 150 mm, 5 μm).

N-(3-(6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl)-propyl)-methanesulfonamide (WS34):

To a solution of 2-bromoethaneamomium bromide (2g, 9.8 mmol) in 60 mL of CH_2Cl_2 was added triethylamine (3.4 mL, 24.4 mmol). The resulting mixture was stirred at a temperature of about 25°C for 30 min, then cooled down at 0°C, methanesulfonic chloride (0.83 mL, 10.7 mmol) was added dropwise, kept stirring for 1 hr and allowed to warm up to a temperature of about 25°C and stirred for about 16 hours. The resulting mixture was condensed and dried under reduced

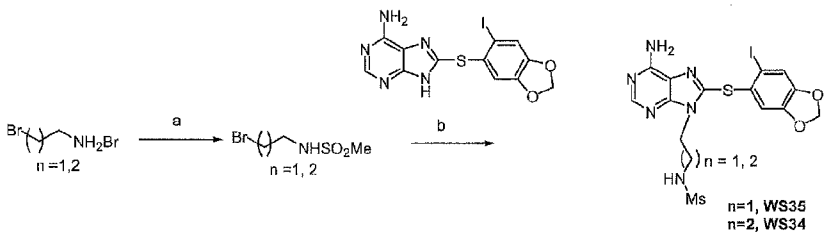
pressure to provide N-(2-bromoethyl)methanesulfonamide without further purification. N-(3-bromopropyl)methanesulfonamide was prepared in a similar manner.

To a solution of 8-((6-iodobenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine (150 mg, 0.36 mmol) in 10 mL of dry DMF was added N-(3-bromopropyl)methanesulfonamide (300 mg, 1.4 mmol) and Cs_2CO_3 (190 mg, 0.58 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS34 as white solid (49 mg, 25% yield).

^{1}H NMR (500 MHz, MeOH-d_4/$CDCl_3$, δ): 8.21 (s, 1H), 7.41 (s, 1H), 7.10 (s, 1H), 6.08 (s, 2H), 4.34 (t, J = 7.2 Hz, 2H), 3.16 (t, J = 6.5 Hz, 2H), 2.96 (s, 3H), 2.09 (m, 2H).

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{14}H_{18}IN_6O_4S_2$ = 548.9876; found 548.9858.

Scheme 4. Synthesis of WS34 and WS35



(a) triethylamine, MsCl, RT; (b) Cs_2CO_3, RT

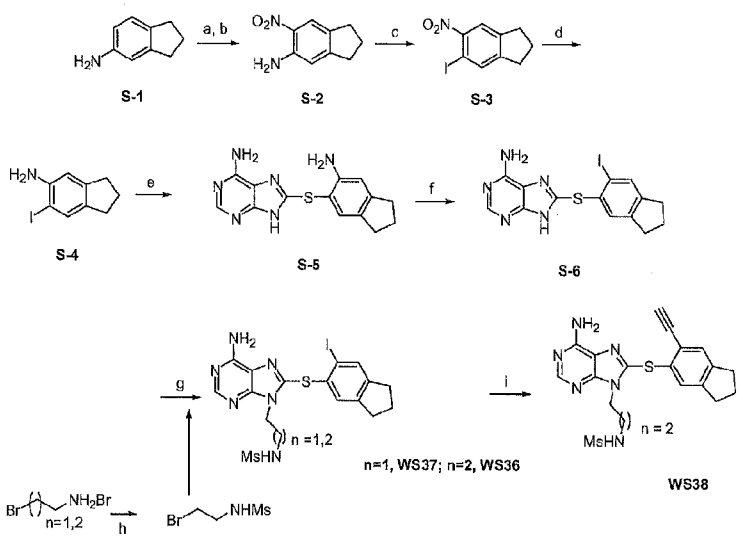
N-(2-(6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl)-ethyl)-methanesulfonamide (WS35):

To a solution of 8-((6-iodobenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine (100 mg, 0.24 mmol) in 5 mL of dry DMF was added *N*-(2-bromoethyl)methanesulfonamide (150 mg, 0.7 mmol) and Cs_2CO_3 (150 mg, 0.46 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS35 as white solid (35 mg, 27% yield).

^{1}H NMR (500 MHz, MeOH-d_4/$CDCl_3$, δ): 8.19 (s, 1H), 7.41 (s, 1H), 7.18 (s, 1H), 6.07 (s, 2H), 4.23 (m, 2H), 3.65 (m, 2H), 2.97 (s, 3H).

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{15}H_{16}IN_6O_4S_2$ = 534.9719; found 534.9709.

Scheme 5. Synthesis of WS36, WS37, and WS38



Reagents and conditions: (a)Ac_2O, dioxane, 0°C to rt; (b) KNO_3, H_2SO_4, 0°C to rt; (c) $NaNO_2$, KI, AcOH, 0°C to rt; (d) Fe, NH_4Cl, isopropanol, reflux; (e) 8-mercaptoadenine, CuI, nBu_4NBr, NaOt-Bu, mv; (f) $NaNO_2$, KI, AcOH, 0°C; (g) 1,3-dibromopropane or 1,2-dibromoethane, Cs_2CO_3, DMF, rt; (h)triethylamine, MsCl, 0°-rt; (i) CuI, $PdCl_2(PPh_3)_2$, trimethylsilanylacetylene, Et_3N, DMF, 90°C.

5-Amino-6-nitro-indane (S-2):

A solution of 5-aminoindane (S-1; 10 g, 75 mmol) in 100 mL of dioxane cooled in ice bath was added acetic anhydride (15 mL) dropwise and kept stirring at a temperature of about 25°C for 2 days. The resulting mixture was condensed and dried under reduced pressure. The residue was dissolved in 100 mL of concentrated H_2SO_4, cooled in ice bath. KNO_3 in 15 mL of concentrated H_2SO_4 was added dropwise. The resulting solution was stirred at 0°C for 2 h and then at a temperature of about 25°C for 2 h. The reaction mixture was poured into 150 g of ice and the resulting yellow precipitate was filtered and washed with cold water to provide S-2 (7.1 g, 43% yield).

^1H NMR (500 MHz, $CDCl_3$, δ): 7.94 (s, 1H), 6.65 (s, 1H), 6.02 (br, 2H), 2.83 (m, 4H), 2.06 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, δ): 154.4, 144.2, 134.1, 131.2, 120.8, 113.5, 33.1, 31.4, 25.7.

5-Iodo-6-nitro-indane (S-3):

To a solution of S-2 (0.14 g, 0.78 mmol) in acetic acid cooled in ice bath was added $NaNO_2$ (65 mg, 0.94 mmol). The reaction mixture was stirred for 2 minutes. KI (0.39g, 2.45 mmol) was added and the mixture was stirred at a temperature of about 25°C for 20 minutes. The resulting suspension was quenched with water (15 mL) and extracted with ethyl acetate (2 x 20 mL). The organic layer was washed with saturated aqueous $Na_2S_2O_3$ solution, washed with brine and dried over $MgSO_4$ and evaporated to dryness to provide a residue that was purified by flash chromatography (ethyl acetate/hexane, gradient 0% to 50%) to provide S-3 (0.12 g, 65% yield) as a yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.83 (s, 1H), 7.71 (s, 1H), 2.95 (m, 4H), 2.11 (m, 2H).

5-Amino-6-iodo-indane (S-4):

To a solution of S-3 (1.65 g, 5.7 mmol) in isopropanol (100 mL) and saturated aqueous NH_4Cl solution (20 mL) was added iron powder (1.1 g). The resulting suspension was refluxed for 1h. The reaction mixture was filtered and the filtrate was condensed and purified by flash chromatography (ethyl acetate/hexane, gradient 0% to 50%) to provide S-4 (1.36 g, 92% yield) as a pale yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.44 (s, 1H), 6.59 (s, 1H), 3.88 (s, 2H), 2.74 (m, 4H), 1.98 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, δ): 146.2, 144.9, 136.5, 134.1, 111.0, 32.8, 31.8, 26.1.

MS (ESI): $m/z = 259.99$ $[M+H]^+$.

8-((6-Amino-2,3-dihydro-1*H*-inden-5-yl)thio)-9-*H*-purin-6-amine (S-5):

The mixture of 8-mercaptoadenine (64 mg, 0.38 mmol), S-4 (100 mg, 0.38 mmol), CuI (14.7 mg, 0.07 mmol), sodium t-butoxide (111 mg, 1.15 mmol) and tetrabutylammonium bromide (24.9 mg, 0.07 mmol) in anhydrous DMF (4 mL) was vortexed and heated at 190°C under microwave for 1h. The resulting mixture was condensed and purified by flash chromatography (methylene chloride/methanol, gradient 0% to 10%) to provide S-5 (54 mg, 47% yield) as a while solid.

^{1}H NMR (500 MHz, MeOH-d_4/$CDCl_3$, δ): 8.11 (s, 1H), 7.36 (s, 1H), 6.81 (s, 1H), 2.85 (m, 4H), 2.06 (m, 2H).

MS (ESI): $m/z = 299.02$ $[M+H]^+$.

8-((6-Iodo-2,3-dihydro-1*H*-inden-5-yl)thio)-9-*H*-purin-6-amine (S-6):

To a solution of S-5 (54 mg, 0.18 mmol) in acetic acid (5 mL) cooled in ice bath was added $NaNO_2$ (15 mg, 0.22 mmol) followed by KI (90 mg, 0.54 mmol). The reaction mixture was stirred

at 0°C for 15 min and quenched with water (10 mL). The resulting mixture was extracted with methylene chloride (2 x 20 mL). The organic layer was washed with saturated aqueous $Na_2S_2O_3$, washed with brine, dried over $MgSO_4$ and evaporated to dryness. The residue was purified by flash chromatography (methylene chloride/methanol, gradient 0% to 10%) to provide S-6 (42 mg, 56% yield) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.12 (s, 1H), 7.84 (s, 1H), 7.39 (s, 1H), 2.91 (m, 4H), 2.11 (m, 2H).

MS (ESI): m/z = 410.10 $[M+H]^+$.

N-(3-(6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl)-propyl)-methanesulfonamide (WS36):

To a solution of S-6 (50 mg, 0.12 mmol) in 3 mL of dry DMF was added N-(3-bromopropyl)methanesulfonamide (200 mg, 0.9 mmol) and Cs_2CO_3 (100 mg, 0.31 mmol). The resulting mixture was stirred at a temperature of about 25°C for about 16 hours, condensed under reduced pressure and purified by flash chromatography to provide compound WS36 as a white solid (30 mg, 30% yield).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.33 (s, 1H), 7.78 (s, 1H), 7.17 (s, 1H), 5.89 (br, 2H), 4.37 (t, J = 6.2 Hz, 2H), 2.99 (q, 2H), 2.90 (t, J = 7.5 Hz, 2H), 2.81 (t, J = 7.5 Hz, 2H), 2.08 (m, 2H), 1.94 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, δ): 154.7, 153.0, 151.9, 147.6, 146.6, 136.1, 132.6, 127.9, 119.9, 98.4, 40.7, 40.2, 39.1, 32.5, 32.3, 30.3, 25.5.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{18}H_{22}IN_6O_4S_2$ = 545.0290; found 545.0284.

N-(2-(6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl)-ethyl)-methanesulfonamide (WS37):

To a solution of S-6 (50 mg, 0.12 mmol) in 3 mL of dry DMF was added N-(3-bromopropyl)methanesulfonamide (200 mg, 0.99 mmol) and Cs_2CO_3 (100 mg, 0.31 mmol). The resulting mixture was stirred at a temperature of about 25°C for about 16 hours, condensed under reduced pressure and purified by flash chromatography to provide compound WS37 as a white solid (18 mg, 28% yield).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.29 (s, 1H), 7.74 (s, 1H), 7.01 (s, 1H), 6.91 (br, 1H), 5.96 (br, 2H), 4.41 (t, J = 5.4 Hz, 2H), 3.60 (m, 2H), 2.88 (m, 2H), 2.76 (t, J = 10.2 Hz, 2H), 2.05 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, δ): 154.6,153.5, 151.8, 147.5, 146.8, 146.0, 135.9, 133.2, 127.1, 119.8, 97.3, 44.7, 42.5, 40.7, 32.5, 32.2, 25.4.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{17}H_{20}IN_6O_2S_2$ = 531.0134; found 531.0121.

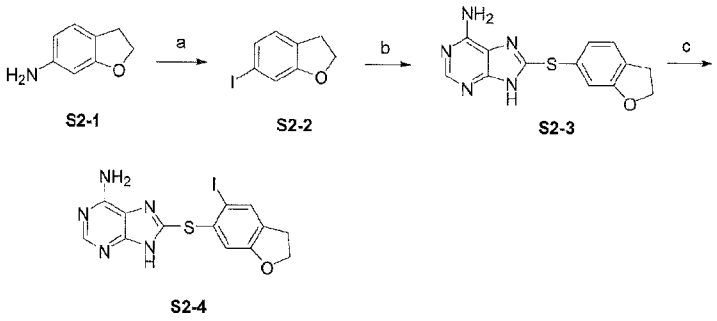
N-(3-(6-amino-8-(6-ethynyl-indan-5-ylsulfanyl)-purin-9-yl)propyl)-methanesulfonamide (WS38):

To a solution of WS36 (10 mg, 0.02 mmol) in 2 mL of DMF was added CuI (0.7 mg, 0.004 mmol), $PhCl_2(Ph_3)_2$ (2.6 mg, 0.004 mmol), ethynyltrimethylsilane (8.6 μL, 0.06 mmol) and triethylamine (25 μL). The resulting mixture was stirred at 60°C for 15 min, condensed and purified by chromatography. The intermediate was treated with KOH (5 mg) in methanol (1 mL) for 30 min at a temperature of about 25°C. The reaction mixture was condensed and purified by flash chromatography to provide compound WS38 as white solid (1.8 mg, 22% yield).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.25 (s, 1H), 7.36 (s, 1H), 7.11 (s, 1H), 6.33(br, 1H), 5.54 (br, 2H), 4.30 (t, J = 6.1 Hz, 2H), 3.25 (s, 1H), 2.89 (q, 2H), 2.80 (m, 4H), 2.00 (m, 2H), 1.88 (m, 2H).

HRMS (ESI) *m/z* $[M+H]^+$ calc'd. for $C_{20}H_{23}N_6O_2S_2$ = 443.1324; found 443.1328.

Scheme 6. Synthesis of Dihydrobenzofuran Intermediate



Reagents and conditions: (a) $NaNO_2$, KI, AcOH/TFA, 0°C; (b) 8-mercaptoadenine, Cs_2CO_3, $PdCl_2$(dppf), DMF, 80°C, 48h; (c) NIS, TFA, CH_3CN, rt, 2h

6-Iodo-2,3-dihydrobenzofuran (S2-2):

A solution of 2,3-dihydrobenzofuran-6-amine (S2-1; 0.74 g, 5.5 mmol) in acetic acid (25 mL) and TFA (2 mL) was cooled in an ice bath for 5 minutes. $NaNO_2$ (0.454g, 6.6 mmol) was added in 3 portions followed by KI (2.73 g, 16.4 mmol). The resulting mixture was stirred at 0°C for 15 minutes and quenched with H_2O (20 mL). The mixture was extracted with EtOAc (3 x 150 mL) and the organic layer was washed with $Na_2S_2O_3$, washed with brine, dried over $MgSO_4$ and filtered. The filtrate was condensed under reduced pressure and the residue was purified by flash

chromatography (hexane:EtOAc, 90:10 to 40:60) to provide S2-2 (0.82 g, 61% yield) as a pale-yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 7.14 (d, J = 7.6 Hz, 1H), 7.11 (s, 1H), 6.89 (d, J = 7.6 Hz, 1H), 4.54 (t, J = 8.7 Hz, 2H), 3.14 (t, J = 8.7 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, δ): 161.1, 129.4, 127.1, 126.4, 118.7, 91.7, 71.6, 29.4.

8-(2,3-Dihydrobenzofuran-6-ylthio)-9*H*-purin-6-amine (S2-3):

To a solution of S2-2 (50 mg, 0.2 mmol) in DMF (2 mL) was added 8-mercaptoadenine (34 mg, 0.2 mmol), Cs_2CO_3 (99.4 mg, 0.3 mmol) and $PdCl_2$(dppf) (33 mg, 0.02 mmol). The mixture was degassed for 5 minutes with argon and stirred at 80°C under argon protection for 48 h. The resulting mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (CH_2Cl_2:MeOH, 100:0 to 90:10) to provide S2-3 (25 mg, 44% yield) as a yellow solid.

^{1}H NMR (500 MHz, CD_3OD, δ): 8.14 (s, 1H), 7.24 (d, J = 7.6 Hz, 1H), 7.07 (d, J = 7.3 Hz, 1H), 6.97 (s, 1H), 4.62 (t, J = 8.7 Hz, 2H), 3.25 (t, J = 8.7 Hz, 2H).

MS (ESI): m/z = 285.8 $[M+H]^+$.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{13}H_{12}N_5OS$ = 286.0763; found 286.0768.

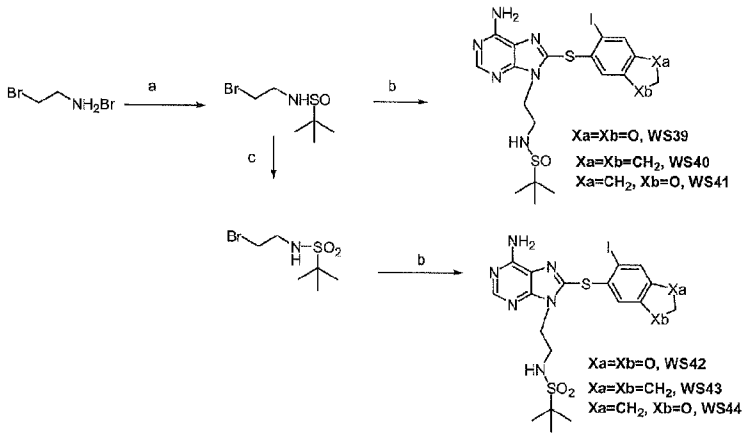
8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9*H*-purin-6-amine (S2-4):

To a solution of S2-3 (40 mg, 0.14 mmol) in 6 mL of acetonitrile was added TFA (40 μL) and NIS (63 mg, 0.28 mmol). The resulting mixture was stirred at a temperature of about 25°C for 2 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (CH_2Cl_2:MeOH, 100:0 to 90:10) to provide S2-4 (48 mg, 53% yield) as a yellow gum.

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.26 (s, 1H), 7.79 (s, 1H), 7.12 (s, 1H), 4.65 (t, J = 8.8 Hz, 2H), 3.28 (t, J = 8.7 Hz, 2H).

MS (ESI): m/z = 412.0 $[M+H]^+$.

Scheme 7. Synthesis of Compounds from WS39 through WS44



(a): triethylamine, tbutylsulfinic chloride; (b) adenine intermediates, Cs_2CO_3; (c) MCPBA

2-Methyl-propane-2-sulfinic acid (2-bromo-ethyl)-amide:

To a solution of 2-bromoethaneamomium bromide (410 mg, 2 mmol) in 20 mL of CH_2Cl_2 was added triethylamine (3697 μL, 5 mmol). The resulting mixture was stirred at a temperature of about 25°C for 30 min, then cooled down at 0°C. 2-methylpropane-2-sulfinic chloride (0.73 mL, 2.2 mmol) was added dropwise, kept stirring for 1 hr and allowed to warm up to a temperature of about 25°C and stirred for about 16 hours. The resulting mixture was condensed and purified by flash chromatography to provide 2-methyl-propane-2-sulfinic acid (2-bromo-ethyl)-amide as a white solid (0.42g, 86% yield).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 3.80 (br, 1H), 3.45-3.56 (m, 4H), 1.20 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$, δ): 56.1, 47.3, 33.4, 22.6.

2-Methyl-propane-2-sulfonic acid (2-bromo-ethyl)-amide:

To a solution of 2-methyl-propane-2-sulfinic acid (2-bromo-ethyl)-amide (0.8g, 3.5 mmol) was added mCPBA (77%, 0.95g, 4.2 mmol) and stirred at a temperature of about 25°C for 2 hrs. The reaction mixture was condensed and purified to provide 2-methyl-propane-2-sulfonic acid (2-bromo-ethyl)-amide as a white solid (0.4g, 46% yield).

^{1}H NMR (500 MHz, MeOH-d_4/$CDCl_3$, δ): 3.87-3.97 (m, 2H), 3.36-3.47 (m, 2H), 1.32 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$, δ): 42.8, 29.6, 25.6, 23.2.

2-Methyl-propane-2-sulfinic acid (2-(6-amino-8-(6-iodo-benzo[1,3]dioxol-5-ylsulfanyl)-purin-9-yl)-ethyl)-amide (WS39):

To a solution of 8-((6-iodobenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine (100 mg, 0.24 mmol) in 3 mL of dry DMF was added 2-methyl-propane-2-sulfinic acid (2-bromo-ethyl)-amide (90 mg, 0.37 mmol) and Cs_2CO_3 (159 mg, 0.49 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS39 as pale yellow solid (70 mg, 51% yield).

^{1}H NMR (500 MHz, MeOH-d_4/$CDCl_3$, δ): 8.21 (s, 1H), 7.39 (s, 1H), 7.04 (s, 1H), 6.06 (s, 2H), 4.81 (m, 1H), 4.35-4.44 (m, 2H), 3.63 (m, 1H), 3.46 (m, 1H), 1.11 (s, 9H).

^{13}C NMR (125 MHz, MeOH-d_4/$CDCl_3$, δ): 154.8, 153.2, 151.9, 149.4, 149.1, 146.1, 128.0, 120.1, 119.2, 112.0, 102.4, 90.6, 56.0, 45.1, 44.4, 22.6.

MS (ESI): m/z = 561.0 $[M+H]^+$.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{18}H_{22}IN_5O_3S_2$ = 561.0239; found 561.0233.

2-Methyl-propane-2-sulfinic acid {2-[6-amino-8-(6-iodo-indan-5-ylsulfanyl)-purin-9-yl]-ethyl}-amide (WS40):

To a solution of S-6 (50 mg, 0.12 mmol) in 3 mL of dry DMF was added 2-methyl-propane-2-sulfinic acid (2-bromo-ethyl)-amide (40 mg, 0.18 mmol) and Cs_2CO_3 (80 mg, 0.25 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS40 as pale yellow solid (35 mg, 51% yield).

^{1}H NMR (500 MHz, MeOH-d_4/$CDCl_3$, δ): 8.22 (s, 1H), 7.82 (s, 1H), 7.34 (s, 1H), 4.36-4.44 (m, 2H), 3.60 (m, 1H), 3.44 (m, 1H), 2.92 (t, J = 7.4 Hz, 2H), 2.86 (t, J = 7.5 Hz, 2H), 2.10 (m, 2H), 1.10 (s, 9H).

MS (ESI): m/z = 557.0 $[M+H]^+$.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{20}H_{26}IN_5OS_2$ = 557.0654; found 557.0676.

N-(2-(6-amino-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfinamide (WS41):

To a solution of S2-4 (10 mg, 0.02 mmol) in 1 mL of dry DMF was added 2-methyl-propane-2-sulfinic acid (2-bromo-ethyl)-amide (27 mg, 0.12 mmol) and Cs_2CO_3 (16 mg, 0.05 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS41 as pale yellow solid (2.7 mg, 20% yield).

MS (ESI): $m/z = 559.0$ $[M+H]^+$.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{19}H_{21}IN_6O_2S_2 = 559.0447$; found 559.0439.

N-(2-(6-amino-8-((6-iodobenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide (WS42):

To a solution of 8-((6-iodobenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine (30.4 mg, 0.07 mmol) in 3 mL of dry DMF was added 2-methyl-propane-2-sulfonic acid (2-bromo-ethyl)-amide (90 mg, 0.37 mmol) and Cs_2CO_3 (80 mg, 0.25 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS42 as pale yellow solid (17 mg, 41% yield).

^1H NMR (500 MHz, $CDCl_3$, δ): 8.16 (s, 1H), 7.19 n(s, 2H), 6.83 (br, 1H), 5.90 (br, 2H), 5.88 (s, 2H), 4.32 (t, J = 5.6 Hz, 2H), 3.68 (m, 2H), 1.23 (s, 9H).

MS (ESI): $m/z = 577.1$ $[M+H]^+$.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{18}H_{22}IN_6O_4S_2 = 577.0189$; found 577.0172.

N-(2-(6-amino-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide (WS43):

To a solution of S2-4 (25 mg, 0.06 mmol) in 2 mL of dry DMF was added 2-methyl-propane-2-sulfonic acid (2-bromo-ethyl)-amide (90 mg, 0.37 mmol) and Cs_2CO_3 (60 mg, 0.18 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS43 as a white powder (3.6 mg, 10% yield).

^1H NMR (500 MHz, $CDCl_3$, δ): 8.25 (s, 1H), 7.56 (s, 1H), 6.42 (s, 1H), 5.88 (brs, 1H), 5.58 (brs, 2H), 4.49 (m, 2H), 4.31 (m, 2H), 3.51 (m, 2H), 3.11 (m, 2H), 1.12 (s, 9H).

MS (ESI): $m/z = 575.0$ $[M+H]^+$.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{19}H_{24}IN_6O_3S_2 = 575.0396$; found 575.0399.

N-(2-(6-amino-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)-2-methylpropane-2-sulfonamide (WS44):

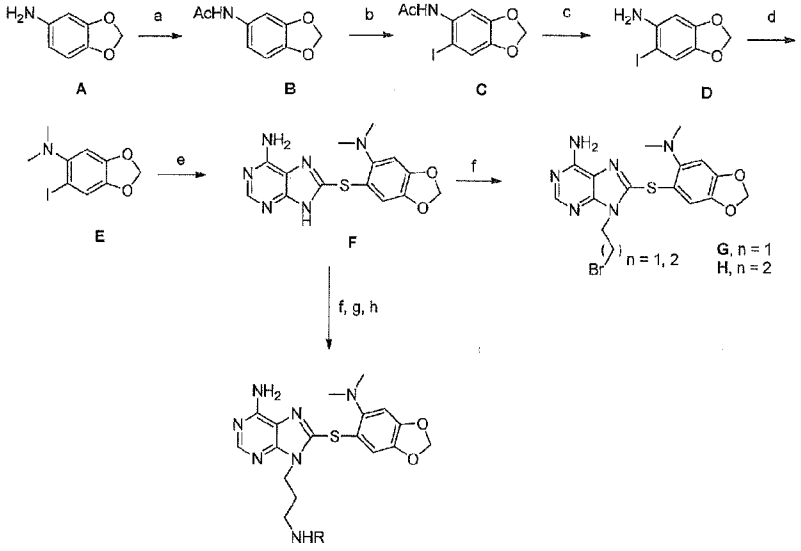
To a solution of S-6(20 mg, 0.05 mmol) in 2 mL of dry DMF was added 2-methyl-propane-2-sulfonic acid (2-bromo-ethyl)-amide (90 mg, 0.37 mmol) and Cs_2CO_3 (60 mg, 0.18 mmol). The resulting mixture was stirred at a temperature of about 25°C for 3 hrs, condensed under reduced pressure and purified by flash chromatography to provide compound WS44 as a white powder (11 mg, 31% yield).

^{1}H NMR (500 MHz, $CDCl_3$, δ): 8.34 (s, 1H), 7.74 (s, 1H), 6.89 (s, 1H), 6.58 (brs, 1H), 5.78 (brs, 2H), 4.42 (m, 2H), 3.71 (m, 2H), 2.89 (m, 2H), 2.75 (m, 2H), 2.06 (m, 2H), 1.32 (s, 9H).

MS (ESI): m/z = 573.1 $[M+H]^+$.

HRMS (ESI) m/z $[M+H]^+$ calc'd. for $C_{20}H_{26}IN_6O_2S_2$ = 573.0603; found 573.0597.

Scheme 8. Synthesis of S-linked dimethylamino derivatives.



Reagents and conditions: (a) Ac_2O, AcOH, rt; (b) ICl, CH_2Cl_2, AcOH, rt; (c) NaOH, EtOH, H_2O, reflux; (d) paraformaldehyde, $NaBH_3CN$, MeOH, 50°C; (e) 8-mercaptoadenine, neocuproine, CuI, NaOtBu, DMF, 115°C; (f) 2-(3-bromopropyl)isoindoline-1,3-dione, Cs_2CO_3, DMF, rt; (g) hydrazine hydrate, CH_2Cl_2/MeOH, rt; (h) TEA, corresponding acid chlorides or sulfonamide, DMF;

2-(3-(6-Amino-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)isoindoline-1,3-dione. F (0.720 g, 2.18 mmol), Cs_2CO_3 (0.851 g, 2.62 mmol), 2-(3-bromopropyl)isoindoline-1,3-dione (2.05 g, 7.64 mmol) in DMF (15 mL) was stirred for

2 h at rt. The mixture was dried under reduced pressure and the residue purified by column chromatography (CH_2Cl_2:MeOH:AcOH, 15:1:0.5) to give 0.72 g (63%) of the titled compound. ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 8.16 (s, 1H), 7.85-7.87 (m, 2H), 7.74-7.75 (m, 2H), 6.87 (s, 1H), 6.71 (s, 1H), 5.88 (s, 2H), 4.37 (t, J = 6.4 Hz, 2H), 3.73 (t, J = 6.1 Hz, 2H), 2.69 (s, 6H), 2.37-2.42 (m, 2H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{25}H_{24}N_7O_4S$, 518.1610; found 518.1601.

9-(3-Aminopropyl)-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine. 2-(3-(6-Amino-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)isoindoline-1,3-dione (0.72 g, 1.38 mmol), hydrazine hydrate (2.86 g, 2.78 mL, 20.75 mmol), in CH_2Cl_2:MeOH (4 mL:28 mL) was stirred for 2 h at rt. The mixture was dried under reduced pressure and the residue purified by column chromatography (CH_2Cl_2:MeOH-NH_3(7N), 20:1) to give 430 mg (80%) of the titled compound. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33 (s, 1H), 6.77 (s, 1H), 6.49 (s, 1H), 5.91 (s, 2H), 5.85 (br s, 2H), 4.30 (t, J = 6.9 Hz, 2H), 2.69 (s, 6H), 2.65 (t, J = 6.5 Hz, 2H), 1.89-1.95 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.5, 153.1, 151.7, 148.1, 147.2, 146.4, 144.8, 120.2, 120.1, 109.3, 109.2, 101.7, 45.3, 45.2, 40.9, 38.6, 33.3; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{17}H_{22}N_7O_2S$, 388.1556; found 388.1544.

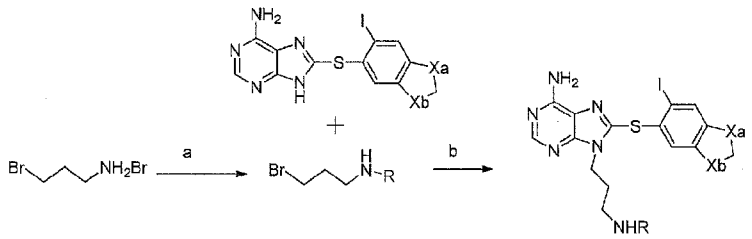
N-(3-(6-Amino-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)cyclopropanecarboxamide (MRP-I-28). 9-(3-Aminopropyl)-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine (60 mg, 0.155 mmol), triethylamine (17 mg, 24 μL, 0.170 mmol), cyclopropane carbonyl chloride (16 mg, 14 μL , 0.155 mmol) in CH_2Cl_2 (3 mL) was stirred for 2 h at rt. The mixture was dried under reduced pressure and the residue purified by preparatory TLC (CH_2Cl_2:MeOH-NH_3(7N) , 20:1) to give **MRP-I-28** (66 mg, 93%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.40 (t, J = 6.1 Hz, 1H), 6.77 (s, 1H), 6.52 (s, 1H), 6.40 (br s, 2H), 5.90 (s, 2H), 4.29 (t, J = 6.2 Hz, 2H), 3.11 (q, J = 6.0 Hz, 2H), 2.68 (s, 6H), 1.87-1.91 (m, 2H), 1.45-1.49 (m, 1H), 0.98-0.96 (m, 2H), 0.77-0.74 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 173.7, 154.9, 153.0,151.8, 148.3, 147.5, 146.6, 144.7, 119.9, 119.5, 109.6, 102.5, 101.7, 45.3, 40.6, 35.3, 29.1, 14.9, 7.1 HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{21}H_{26}N_7O_3S$, 456.1818; found 456.1812.

N-(3-(6-Amino-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)pivalamide (MRP-I-29). 9-(3-Aminopropyl)-8-(6-

(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine (60 mg, 0.155 mmol), triethylamine (17 mg, 24 μL, 0.170 mmol), pivaloyl chloride (19 mg, 19 μL , 0.155 mmol) in CH_2Cl_2 (3 mL) was stirred for 2 h at rt. The mixture was dried under reduced pressure and the residue purified by preparatory TLC (CH_2Cl_2:MeOH-NH_3(7N) , 20:1) to give **MRP-I-29** (65 mg, 89%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.65 (t, J = 6.2 Hz, 1H), 6.77 (s, 1H), 6.50 (s, 1H), 6.39 (br s, 2H), 5.90 (s, 2H), 4.26 (t, J = 6.0 Hz, 2H), 3.04 (q, J = 6.0 Hz, 2H), 2.68 (s, 6H), 1.83-1.87 (m, 2H), 1.27 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 178.8, 154.9, 152.9, 151.9, 148.3, 147.5, 146.6, 144.7, 119.8, 119.7, 109.5, 102.5, 101.7, 45.3, 40.3, 38.8, 34.8, 28.9, 27.7; (ESI) *m/z* $[M+H]^+$ calcd. for $C_{22}H_{30}N_7O_3S$, 472.2131; found 472.2128.

N-(3-(6-Amino-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)cyclopropanesulfonamide (MRP-I-31). 9-(3-Aminopropyl)-8-(6-(dimethylamino)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine (61 mg, 0.158 mmol), triethylamine (18 mg, 24 μL, 0.174 mmol), cyclopropane sulfonyl chloride (22 mg, 17 μL , 0.158 mmol) in CH_2Cl_2 (3 mL) was stirred for 2 h at rt. The mixture was dried under reduced pressure and the residue purified by preparatory TLC (CH_2Cl_2:MeOH-NH_3(7N) , 20:1) to give **MRP-I-31** (55 mg, 71%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.30 (s, 1H), 6.78 (s, 1H), 6.66 (t, J = 6.8 Hz, 1H), 6.51 (s, 1H), 6.29 (br s, 2H), 5.91 (s, 2H), 4.31 (t, J = 6.0 Hz, 2H), 3.02 (q, J = 6.1 Hz, 2H), 2.70 (s, 6H), 2.34-2.38 (m, 1H), 1.95-1.99 (m, 2H), 1.15-1.17 (m, 2H), 0.93-0.96 (m,2H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 154.9, 153.1, 151.7, 148.4, 147.6, 146.3, 144.8, 119.8, 119.4, 109.6, 102.4, 101.8, 45.4, 40.0, 39.0, 30.4, 30.2, 5.26; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{20}H_{26}N_7O_4S_2$, 492.1488; found 492.1468.

Scheme 9. Synthesis of S-linked amide, sulfonamide or sulfinamide derivatives



Xa=Xb=O, R = t-butylcarbonyl **WS45**
Xa=Xb=O, R = i-propylcarbonyl **WS46**
Xa=Xb=O, R = i-propylsulfonyl **WS48**
Xa=Xb=O, R = t-butylsulfinyl **WS49**
Xa=Xb=O, R = isobutylsulfonyl **WS50**
Xa=Xb=O, R = cyclopropanecarbonyl **WS51**
Xa=Xb=O, R = t-butylsulfonyl **WS52**
Xa=Xb=O, R = lactyl **WS55**
Xa=Xb=O, R = cyclopropanesulfonyl **WS56**
Xa=Xb=O, R =2-hydroxy-2-methylpropanyl **WS58**

Xa=CH_2, Xb=O, R= cyclopropanecarbonyl **WS61**
X=CH2, Xb=O, R= t-butylsulfinyl **WS62**
Xa=Xb=CH_2, R= t-butylsulfinyl **WS63**
Xa=H, Xb=O, R= t-butylcarbonyl **WS64**

Reagents and conditions: (a) triethylamine, acid chloride or sulfonyl chloride or sulfinyl chloride; (b) Cs_2CO_3, DMF.

***N*-(3-Bromopropyl)pivalamide.** To a suspension of 3-bromopropylamine hydrobromide (290 mg, 1.3 mmol) in CH_2Cl_2 (10 mL) cooled in ice bath was added triethylamine (470 uL). The resulting mixture was stirred for 5 min and trimethylacetyl chloride (163 uL, 1.3 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for 2 hrs, condensed under vacuum, purified by flash chromatography to yield *N*-(3-bromopropyl)pivalamide as colorless oil (160 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$): δ (5.97 (br s, 1H), 3.40 (m, 4H), 2.07 (m, 2H), 1.17 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.7, 37.2, 32.1, 31.1, 27.6.

The preparation of other amides, sulfonamides and sulfinamides followed the same procedure as described above using 3-bromopropylamine hydrobromide and corresponding acid chloride, sulfonyl chloride or sulfinyl chloride.

***N*-(3-(6-amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)pivalamide (WS45).** To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (74 mg, 0.18 mmol) in DMF (2 mL) was added N-(3-bromopropyl)pivalamide (80 mg, 0.36 mmol) and Cs_2CO_3 (117 mg, 0.36 mmol). The

resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS45** as a white solid (18 mg, 18%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.23 (s,1H), 7.45 (br s, 1H), 7.19 (s, 1H), 6.88 (s, 1H), 5.93 (s, 2H), 5.69 (br s, 2H), 4.20 (t, J = 6.1 Hz, 2H), 3.00 (m, 2H), 1.80 (m, 2H), 1.21 (s, 9H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{29}H_{24}IN_6O_3S$, 555.0675; found 555.0681.

***N*-(3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)isobutyramide (WS46).** To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (50 mg, 0.12 mmol) in DMF (2 mL) was added *N*-(3-bromopropyl)isobutyramide (50 mg, 0.24 mmol) and Cs_2CO_3 (78 mg, 0.24 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS46** as a white solid (22 mg, 34%). ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 8.22 (s,1H), 7.61 (br s, 1H), 7.41 (s, 1H), 7.08 (s, 1H), 6.07 (s, 2H), 4.27 (m, 2H), 3.21 (m, 2H), 2.45 (s, 1H), 2.02 (m, 2H), 1.19 (d, J = 6.9 Hz, 6H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{19}H_{22}IN_6O_3S$, 541.0519; found 541.0508.

***N*- (3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)propane-2-sulfonamide (WS48).** To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (118 mg, 0.28 mmol) in DMF (2 mL) was added *N*-(3-bromopropyl)propane-2-sulfonamide (350 mg, 1.4 mmol) and Cs_2CO_3 (188 mg, 0.56 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS48** as a white solid (33 mg, 20%). ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 8.20 (s, 1H), 7.41 (s, 1H), 7.09 (s, 1H), 6.08 (s, 2H), 4.35 (t, J = 7.0 Hz, 2H), 3.10-3.22 (m, 3H), 2.07 (m, 2H), 1.37 (d, J = 6.9 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$/MeOH-d_4): δ 158.4, 156.1, 155.1, 153.9, 153.5, 151.8, 129.2, 123.5, 123.3, 117.9, 106.6, 98.3, 57.0, 44.8, 43.9, 34.3, 20.2; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{22}IN_6O_4S_2$, 577.0189; found 577.0193.

***N*-3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide (WS49).** To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (118 mg, 0.07 mmol) in DMF (2 mL) was added *N*-(3-bromopropyl)-2-methlpropane-2-sulfinamide (50 mg, 0.21 mmol) and Cs_2CO_3 (23 mg,

0.14 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS49** as a white solid (14 mg, 35%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.33 (s, 1H), 6.94 (s, 1H), 6.02 (s, 2H), 5.87 (br s, 2H), 4.91 (t, J = 6.7 Hz, 1H), 4.40-4.45 (m, 1H), 4.31-4.36 (m, 1H), 3.10-3.17 (m, 1H), 2.97-3.04 (m, 1H), 2.11-2.17 (m, 1H), 1.96-2.08 (m, 1H), 1.26 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 154.5, 152.9, 151.9, 149.3, 149.2, 146.5, 127.3, 119.9, 119.3, 112.6, 102.4, 91.8, 55.9, 42.1, 40.5, 31.1, 22.8; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{19}H_{24}IN_6O_3S_2$, 575.0396; found 575.0379.

***N*-3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)-2-methylpropane-1-sulfonamide (WS50)**. To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (24 mg, 0.06 mmol) in DMF (1.5 mL) was added *N*-(3-bromopropyl)-2-methlpropane-1-sulfonamide (60 mg, 0.24 mmol) and Cs_2CO_3 (38 mg, 0.12 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS50** as a white solid (16 mg, 46%). ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 8.07 (s, 1H), 7.25 (s, 1H), 6.94 (s, 1H), 5.93 (s, 2H), 4.20 (t, J = 6.2 Hz, 2H), 2.97 (t, J = 5.6 Hz, 2H), 2.78 (d, J = 6.5 Hz, 2H), 2.05-2.16 (m, 1H), 1.87-1.97 (m, 2H), 0.98 (d, J = 6.7 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$/MeOH-d_4): δ 158.3, 156.2, 155.1, 153.9, 153.4, 151.6, 129.3, 123.5, 123.2, 117.9, 106.6, 98.3, 64.2, 44.7, 43.4, 34.0, 28.8, 26.3; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{19}H_{24}IN_6O_4S_2$, 591.0345; found 591.0333.

***N*-3-(6-amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)cyclopropane carboxamide (WS51)**. To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (30 mg, 0.07 mmol) in DMF (1.5 mL) was added *N*-(3-bromopropyl) cyclopropanecarboxamide (60 mg, 0.28 mmol) and Cs_2CO_3 (48 mg, 0.14 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS51** as a white solid (14 mg, 35%). ^{1}H NMR (500 MHz, $CDCl_3$/ MeOH-d_4): δ 8.16 (s,1H), 7.31 (s, 1H), 6.99 (s, 1H), 5.98 (s, 2H), 4.21 (t, J = 7.0 Hz, 2H), 3.16 (t, J = 6.6 Hz, 2H), 1.88-1.98 (m, 2H), 1.40-1.44 (m, 1H), 0.83-0.91 (m, 2H), 0.66-0.74 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$/MeOH-d_4): δ

179.1, 174.7, 154.3, 152.2, 151.2, 149.9, 149.4, 147.7, 125.4, 119.5, 113.9, 102.6, 94.3, 41.1, 35.9, 28.9, 14.5, 7.0; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{19}H_{20}IN_6O_3S$, 539.0362; found 539.0362.

***N*-3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)-2-methylpropane-2-sulfonamide (WS52).** To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (37 mg, 0.09 mmol) in DMF (1.5 mL) was added *N*-(3-bromopropyl)-2-methylpropane-2-sulfonamide (70 mg, 0.27 mmol) and Cs_2CO_3 (59 mg, 0.18 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS52** as a white solid (9 mg, 16%). ^1H NMR (600 MHz, $CDCl_3$): δ 8.20 (s, 1H), 7.25 (s, 1H), 6.89 (s, 1H), 6.35 (t, J = 6.7 Hz, 1H), 5.94 (s, 2H), 5.69 (br s, 2H), 4.32 (t, J = 6.0 Hz, 2H), 2.93-2.99 (m, 2H), 1.87-1.99 (m, 2H), 1.28 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 154.5, 152.8, 152.0, 149.34, 149.32, 146.9, 126.9, 119.8, 119.4, 112.9, 102.4, 92.3, 59.7, 40.3, 40.1, 31.3, 24.4; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{19}H_{24}IN_6O_4S_2$, 591.0345; found 591.0353.

***(S)*-*N*-3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)-2-hydroxypropanamide (WS55).** To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (71 mg, 0.17 mmol) in DMF (2 mL) was added (S)-1-(3-bromopropyl)amino)-1-oxopropa-2-yl acetate (130 mg, 0.51 mmol) and Cs_2CO_3 (112 mg, 0.34 mmol). The resulting mixture was stirred at room temperature over night. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS55** as a white solid (13 mg, 14%). ^1H NMR (600 MHz, $CDCl_3$): δ 8.23 (s,1H), 7.64 (t, J = 6.0 Hz, 1H), 7.26 (s, 1H), 6.90 (s, 1H), 5.94 (s, 2H), 5.73 (br s, 2H), 4.10-4.23 (m, 3H), 3.05-3.25 (m, 2H), 1.85-1.95 (m, 2H), 1.39 (dd, J = 15.1, 6.8 Hz, 3H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{20}IN_6O_4S$, 543.0312; found 543.0310.

***N*-3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)cyclopropanesulfonamide (WS56).** To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (45 mg, 0.11 mmol) in DMF (2 mL) was added *N*-(3-bromopropyl)cyclopropanesulfonamide (120 mg, 0.44 mmol) and Cs_2CO_3 (71 mg, 0.22 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC

(CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS56** as a white solid (12 mg, 19%). ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4): δ 8.13 (s, 1H), 7.32 (s, 1H), 7.00 (s, 1H), 5.99 (s, 2H), 4.26 (t, J = 7.0 Hz, 2H), 3.08 (t, J = 6.3 Hz, 2H), 2.32-2.38 (m, 1H), 1.95-2.02 (m, 2H), 1.03-1.09 (m, 2H), 0.89-0.95 (m, 2H); HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{18}H_{20}IN_6O_4S_2$, 575.0032; found 575.0042.

1-((3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)amino)-2-methyl-1-oxopropan-2-yl acetate (WS57). To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (59 mg, 0.14 mmol) in DMF (1.5 mL) was added 1-((3-bromopropyl)amino)-2-methyl-1-oxopropan-2-yl acetate (120 mg, 0.48 mmol) and Cs_2CO_3 (93 mg, 0.28 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS57** as a white solid (19 mg, 22%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.23 (s,1H), 7.90 (t, J = 6.0 Hz, 1H), 7.26 (s, 1H), 6.85 (s, 1H), 5.95 (s, 2H), 5.54 (br s, 2H), 4.21 (t, J = 5.9 Hz, 2H), 2.93-2.99 (m, 2H), 2.08 (s, 3H), 1.83-1.90 (m, 2H), 1.59 (s, 6H); HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{21}H_{24}IN_6O_5S$, 599.0574; found 599.0579.

***N*-(3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)-2-hydroxy-2-methylpropanamide (WS58).** To a solution of **WS57** in MeOH/THF/H_2O (0.3 mL/0.3 mL/0.3 mL) was added LiOH (5 mg). The reaction mixture was stirred at room temperature for 2 hrs. The resulting mixture was condensed, purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS58** as a white solid (10 mg, 83%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.79 (br s, 1H), 7.25 (s, 1H), 6.88 (s, 1H), 5.94 (s, 2H), 5.67 (br s, 2H), 4.20 (t, J = 6.4 Hz, 2H), 3.02-3.20 (m, 2H), 1.83-1.96 (m, 2H), 1.43 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$): δ 176.9, 154.5, 152.9, 151.9, 149.32, 149.31, 146.9, 127.0, 120.0, 119.4, 112.9, 102.4, 92.3, 72.9, 40.6, 35.4, 29.2, 28.0; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{19}H_{22}IN_6O_4S$, 557.0468; found 557.0447.

***N*-(3-(6-Amino-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9*H*-purin-9-yl)propyl)cyclopropanecarboxamide (WS61).** To a solution of 8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9*H*-purin-6-amine (26 mg, 0.06 mmol) in DMF (1.5 mL) was added *N*-(3-bromopropyl) cyclopropanecarboxamide (39 mg, 0.18 mmol) and Cs_2CO_3 (41 mg, 0.12 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC

(CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS61** as a white solid (12 mg, 35%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.57 (s, 1H), 7.16 (m, 1H), 6.55 (s, 1H), 5.67 (br s, 2H), 4.50 (t, J = 8.8 Hz, 2H), 4.22 (t, J = 6.3 Hz, 2H), 3.13 (t, J = 8.6 Hz, 2H), 3.01-3.07 (m, 2H), 1.80-1.86 (m, 2H), 1.38-1.44 (m, 1H), 0.87-0.93 (m, 2H), 0.67-0.72 (m, 2H); HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{22}IN_6O_2S$, 537.0570; found 537.0567.

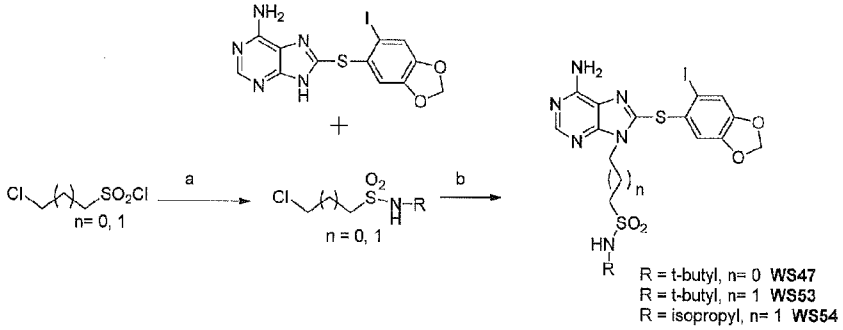
***N*-(3-(6-Amino-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9*H*-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide (WS62).** To a solution of 8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9*H*-purin-6-amine (26 mg, 0.06 mmol) in DMF (1.5 mL) was added *N*-(3-bromopropyl)-2-methlpropane-2-sulfinamide (49 mg, 0.18 mmol) and Cs_2CO_3 (41 mg, 0.12 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS62** as a white solid (11 mg, 30%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.33 (s, 1H), 7.66 (s, 1H), 6.61 (s, 1H), 5.85 (br s, 2H), 4.84 (t, J = 6.7 Hz, 1H), 4.59 (t, J = 8.7 Hz, 2H), 4.37-4.44 (m, 1H), 4.29-4.35 (m, 1H), 3.22 (t, J = 8.5 Hz, 2H), 3.09-3.16 (m, 1H), 2.95-3.02 (m, 1H), 2.06-2.15 (m, 1H), 1.93-2.05 (m, 1H), 1.29 (s, 9H); HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{26}IN_6O_2S_2$, 573.0603; found 573.0620.

***N*-(3-(6-Amino-8-((6-iodo-2,3-dihydro-1*H*-inden-5-yl)thio)-9*H*-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide (WS63).** To a solution of 8-((6-iodo-2,3-dihydro-1*H*-inden-5-yl)thio)-9*H*-purin-6-amine (13 mg, 0.03 mmol) in DMF (1.5 mL) was added *N*-(3-bromopropyl)-2-methlpropane-2-sulfinamide (23 mg, 0.1 mmol) and Cs_2CO_3 (21 mg, 0.06 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS63** as a white solid (5 mg, 27%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.22 (s, 1H), 7.68 (s, 1H), 7.05 (s, 1H), 5.70 (br s, 2H), 4.83 (t, J = 6.7 Hz, 1H), 4.28-4.36 (m, 1H), 4.17-4.27 (m, 1H), 2.99-3.07 (m, 1H), 2.85-2.93 (m, 1H), 2.81 (t, J = 7.4 Hz, 2H), 2.72 (t, J = 7.5 Hz, 2H), 1.83-2.08 (m, 4H), 1.20 (m, 9H); HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{21}H_{28}IN_6OS_2$, 571.0811; found 571.0809.

***N*-(3-(6-Amino-8-((2-iodo-5-methoxyphenyl)thio)-9H-purin-9-yl)propyl)pivalamide (WS64).** To a solution of 8-((2-iodo-5-methoxyphenyl)thio)-9*H*-purin-6-amine (200 mg, 0.5 mmol) in DMF (3 mL) was added *N*-(3-bromopropyl)pivalamide (445 mg, 2 mmol)

and Cs_2CO_3 (326 mg, 1 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS64** as a white solid (53 mg, 20%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (s,1H), 7.66 (d, J = 8.7 Hz, 1H), 7.43 (br s, 1H), 6.66 (s, 1H), 6.50 (d, J = 8.7 Hz, 1H), 5.86 (br s, 2H), 4.20 (t, J = 6.1 Hz, 2H), 3.61 (s, 3H), 2.78 (m, 2H), 1.82 (m, 2H), 1.21 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 178.8, 160.5, 155.0, 153.2, 152.0, 145.0, 140.6, 137.7, 120.1, 117.2, 115.4, 88.4, 55.5, 40.7, 38.8, 34.8, 29.1, 27.7; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{20}H_{26}IN_6O_2S$, 541.0883; found 541.0898.

Scheme 10. Synthesis of S-linked reversed sulfonamide derivatives

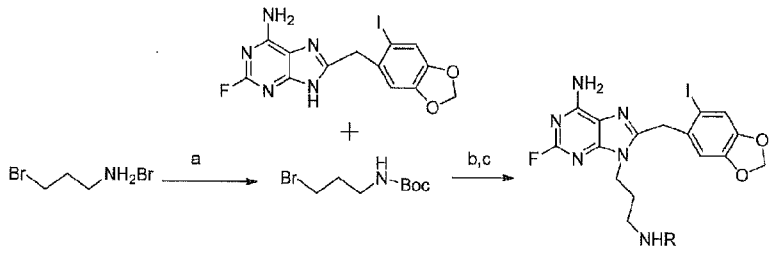


2-(6-Amino-8-((6-iodobenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-N-(*tert*-butyl)ethanesulfonamide (WS47). To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (56 mg, 0.13 mmol) in DMF (2 mL) was added *N*-t-butyl-2-chloroethanesulfonamide (50 mg, 0.25 mmol) and Cs_2CO_3 (88 mg, 0.27 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS47** as a white solid (10 mg, 13%). ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 8.22 (s,1H), 7.39 (s, 1H), 7.08 (s, 1H), 6.06 (s, 2H), 4.69 (t, J = 7.0 Hz, 2H), 3.57 (t, J = 7.1 Hz, 2H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$/MeOH-d_4): δ 158.3, 156.4, 155.1, 153.9, 153.4, 151.5, 129.2, 123.5, 123.3, 117.8, 106.6, 98.1, 58.5, 57.3, 42.7, 33.8; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{22}IN_6O_4S_2$, 577.0189; found 577.0217.

3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)-*N*-(tert-butyl)propane-1-sulfonamide (WS53). To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (56 mg, 0.13 mmol) in DMF (2 mL) was added *N*-t-butyl-3-chloro-*N*-propane-1-sulfonamide (144 mg, 0.65 mmol) and Cs_2CO_3 (88 mg, 0.27 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS53** as a white solid (18 mg, 22%). ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4): δ 8.21 (s, 1H), 7.40 (s, 1H), 7.06 (s, 1H), 6.06 (s, 2H), 4.38 (t, J = 7.3 Hz, 2H), 3.12 (t, J = 7.4 Hz, 2H), 2.13-2.44 (m, 2H), 1.33 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$/MeOH-d_4): δ 155.8, 153.8, 152.4, 151.5, 151.0, 149.0, 126.7, 121.0, 120.8, 115.3, 104.1, 95.7, 55.7, 51.1, 43.6, 31.5, 25.9; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{19}H_{24}IN_6O_4S_2$, 591.0345; found 591.0361.

3-(6-Amino-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)-*N*-isopropylpropane-1-sulfonamide (WS54). To a solution of 8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)thio-9*H*-purin-6-amine (39 mg, 0.09 mmol) in DMF (2 mL) was added 3-chloro-*N*-isopropylpropane-1-sulfonamide (100 mg, 0.45 mmol) and Cs_2CO_3 (62 mg, 0.19 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed under vacuum and the residue was purified by Prep TLC (CH_2Cl_2:NH_3-MeOH (7N), 20:1) to yield **WS54** as a white solid (14 mg, 26%). ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 8.00 (s,1H), 7.19 (s, 1H), 6.86 (s, 1H), 5.86 (s, 2H), 4.17 (t, J = 7.3 Hz, 2H), 3.34 (septet, J = 6.6 Hz, 1H), 2.89 (t, J = 7.6 Hz, 2H), 2.05-2.13 (m, 2H), 0.99 (d, J = 6.6 Hz, 6H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{22}IN_6O_4S_2$, 577.0189; found 577.0194.

Scheme 11. Synthesis of methylene-linked amide, sulfonamide and sulfinamide derivatives



R = t-butylsulfinyl **WS60**

R = H **WS65**

R = t-butylcarbonyl **WS66**

R = cyclopropanecarbonyl **WS71**

R = cyclopropanesulfonyl **WS72**

Reagents and conditions: (a) triethylamine, $(Boc)_2O$; (b) TFA; (c) acid chloride, or sulfonyl chloride or sufinyl chloride.

***t*-Butyl (3-bromopropyl)carbamate.** To a suspension of 3-bromopropylamine hydrobromide (10 g, 45.7 mmol) in CH_2Cl_2 (100 mL) cooled in an ice bath was added triethylamine (15.9 mL, 113 mmol). Di-t-butyl-dicarbonate (10 g, 45.7 mmol) was added slowly in portions and the resulting mixture was stirred at 0 °C for 2 hrs and allowed to warm up to room temperature and stirred over-night. The reaction mixture was filtered, condensed and purified by flash chromatography to yield t-butyl (3-bromopropyl)carbamate (9.8 g, 90%). ^{1}H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 4.75 (br s, 1H), 3.44 (t, J = 6.6 Hz, 2H), 3.27 (m, 2H), 2.05 (m, 2H), 1.45 (s, 9H).

9-(3-Aminopropyl)-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-6-amine (WS65). To a solution of 2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-6-amine (3.3 g, 8 mmol) in DMF (50 mL) was added t-butyl (3-bromopropyl)carbamate (9.6 g, 40 mmol) and Cs_2CO_3 (5.26 g, 16 mmol). The resulting mixture was stirred at room temperature for 1 day. The reaction mixture was condensed and purified by flash chromatography to yield t-butyl (3-(6-amino-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-9-yl)propyl)carbamate as white solid (3.1 g, 66%). The solution of t-butyl (3-(6-amino-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-9-yl)propyl)carbamate (1.9 g, 3.3 mmol) in the mixture of TFA/CH_2Cl_2 (10 mL/2 mL) was stirred at room temperature for 2 hrs. The reaction mixture

was condensed, purified by flash chromatography to yield 9-(3-aminopropyl)-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-6-amine as yellow solid (1.4 g, 89%). ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4): δ 7.28 (s, 1H), 6.70 (s, 1H), 5.98 (s, 2H), 4.21 (s, 2H), 4.13 (t, J = 7.1 Hz, 2H), 2.67 (t, J = 6.8 Hz, 2H), 1.89 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$/MeOH-d_4): δ 160.8, 159.4, 157.8, 153.7, 152.1, 150.4, 149.4, 132.4, 120.1, 117.2, 111.3, 103.4, 89.8, 41.7, 40.4, 39.3, 33.6; HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{16}H_{17}IFN_6O_2$, 471.0436; found 471.0442.

***N*-(3-(6-Amino-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-9-yl)propyl)-2-methylpropane-2-sulfinamide (WS60).** To a solution of 9-(3-aminopropyl)-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-6-amine (80 mg, 0.17 mmol) in DCM (3mL) was added t-butylsulfinyl chloride (28 uL, 0.25 mmol) and triethylamine (30 uL, 0.25 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed and purified by flash chromatography to yield **WS60** as a white solid (45 mg, 46%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28 (s, 1H), 6.62 (s, 1H), 6.04 (brs, 2H), 5.97 (s, 2H), 4.60 (t, J = 6.5 Hz, 1H), 4.24 (s, 2H), 4.20 (m, 1H), 4.09 (m, 1H), 3.13 (m, 1H), 2.97 (m, 1H), 2.00 (m, 1H), 1.85 (m, 1H), 1.27 (s, 9H). HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{20}H_{25}FIN_6O_3S$, 575.0725; found 575.0738.

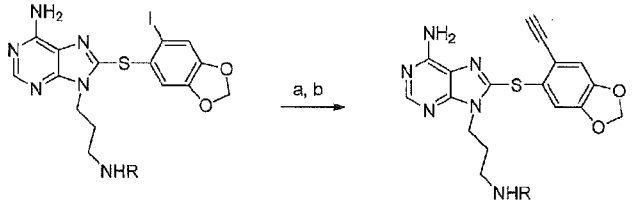
***N*-(3-(6-Amino-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-9-yl)propyl)pivalamide (WS66).** To a solution of **WS65** (100 mg, 0.21 mmol) in DMF (3mL) was added trimethylacetyl chloride (40 μL, 0.32 mmol) and triethylamine (90 μL, 0.96 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed and purified by flash chromatography to yield **WS66** as white solid (80 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (s, 1H), 6.58 (s, 1H), 6.37 (br s, 2H), 5.90 (s, 2H), 4.17 (s, 2H), 4.00 (t, J = 6.1 Hz, 2H), 3.10 (m, 2H), 1.66-1.73 (m, 2H), 1.16 (s, 9H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{21}H_{25}IFN_6O_3$, 555.1017; found 555.1015.

***N*-(3-(6-Amino-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-9-yl)propyl)cyclopropanecarboxamide (WS71).** To a solution of 9-(3-aminopropyl)-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-6-amine (100 mg, 0.21 mmol) in DMF (3 mL) was added cyclopropanecarbonyl chloride (29 μL, 0.32 mmol) and triethylamine (90 μL, 0.96 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed and purified by flash chromatography to yield **WS71** as a white solid (75 mg, 65%). ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4): δ 7.32

(s, 1H), 6.77 (s, 1H), 6.02 (s, 2H), 4.24 (s, 2H), 4.16 (t, J = 7.3 Hz, 2H), 3.26 (t, J = 6.2 Hz, 2H), 1.91-2.01 (m, 2H), 1.50-1.57 (m, 1H), 0.90-0.95 (m, 2H), 0.76-0.82 (m, 2H); HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{21}FIN_6O_3$, 539.0704; found 539.0705.

N-(3-(6-Amino-2-fluoro-8-((6-iodobenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)cyclopropanesulfonamide (WS72). To a solution of 9-(3-aminopropyl)-2-fluoro-8-((6-iodobenzo[*d*][1,3]dioxol-5-yl)methyl)-9*H*-purin-6-amine (100 mg, 0.21 mmol) in DMF (3mL) was added cyclopropanesulfonyl chloride (89 mg, 0.32 mmol) and triethylamine (90 uL, 0.96 mmol). The resulting mixture was stirred at room temperature overnight. The reaction mixture was condensed and purified by flash chromatography to yield **WS72** as a white solid (82 mg, 67%). ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4): δ 7.32 (s, 1H), 6.79 (s, 1H), 6.02 (s, 2H), 4.27 (s, 2H), 4.22 (t, J = 7.3 Hz, 2H), 3.18 (t, J = 6.4 Hz, 2H), 2.45-2.50 (m, 1H), 2.00-2.06 (m, 2H), 1.12-1.17 (m, 2H), 0.99-1.04 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$/MeOH-d_4): δ 159.0 (d, J = 209.8 Hz), 156.9 (d, J = 19.7 Hz), 152.4 (d, J = 18.5 Hz), 151.2 (d, J = 2.3 Hz), 149.3, 148.4, 131.4, 119.0, 116.3 (d, J = 3.6 Hz), 110.4, 102.4, 88.7, 40.7, 40.1, 39.3, 30.2, 29.9, 5.3; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{19}H_{21}FIN_6O_4S$, 575.0374; found 575.0390.

Scheme 12. Synthesis of S-linked acetylene derivatives.



R = cyclopropanecarbonyl **WS68**

R = t-butylcarbonyl **WS69**

R = cyclopropanesulfonyl **WS70**

Reagents and conditions: (a) CuI, $PdCl_2(PPh_3)_2$, trimethylsilanylacetylene, Et_3N, DMF, 60°C; (b) KOH.

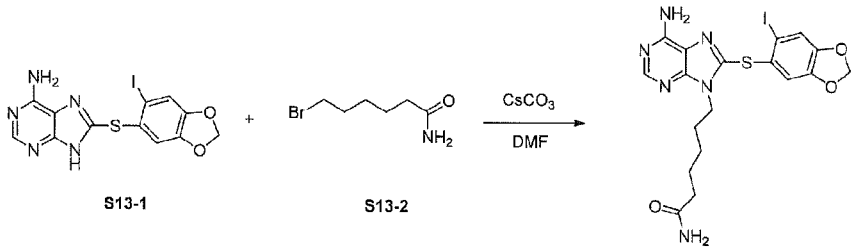
***N*-(3-(6-Amino-8-((6-ethynylbenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)cyclopropanecarboxamide (WS68).** To a solution of **WS51** (150 mg, 0.28 mmol) in DMF (3 mL) was added trimethylsilanylacetylene (116 µL, 0.84 mmol),

$PdCl_2(PPh_3)_2$ (20 mg, 0.03 mmol), CuI (5 mg, 0.03 mmol) and triethylamine (389 uL, 2.8 mmol). The resulting mixture was stirred at 60 °C for 30 min, condensed and filtered through silica gel. The filtrate was condensed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2/MeOH (1 mL/ 1 mL). To the resulting mixture was added KOH (20 mg) and stirred for 3 hrs. The reaction mixture was condensed and purified by flash chromatography to yield **WS68** as a white solid (42 mg, 35%). ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4): δ 8.11 (s,1H), 6.96 (s, 1H), 6.89 (s, 1H), 5.98 (s, 2H), 4.21 (t, J = 7.3 Hz, 2H), 3.45 (s, 1H), 3.18 (m, 2H), 1.88-1.96 (m, 2H), 1.43-1.49 (m, 1H), 0.78-0.84 (m, 2H), 0.65-0.71 (m, 2H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{21}H_{21}N_6O_3S$, 437.1396; found 437.1393.

***N*-(3-(6-Amino-8-((6-ethynylbenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)pivalamide (WS69).** To a solution of **WS45** (150 mg, 0.27 mmol) in DMF (3 mL) was added trimethylsilanylacetylene (113 µL, 0.81 mmol), $PdCl_2(PPh_3)_2$ (19 mg, 0.03 mmol), CuI (5 mg, 0.03 mmol) and triethylamine (377 uL, 2.7 mmol). The resulting mixture was stirred at 60 °C for 30 min, condensed and filtered through silica gel. The filtrate was condensed under reduced pressure and the resulting residue was dissolved in CH_2Cl_2/MeOH (1 mL/ 1 mL). To the resulting mixture was added KOH (20 mg) and stirred for 3 hrs. The reaction mixture was condensed and purified by flash chromatography to yield **WS69** as a white solid (53 mg, 43%). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.31 (s, 1H), 7.56 (t, J = 6.1 Hz, 1H), 7.00 (s, 1H), 6.88 (s, 1H), 6.01 (s, 2H), 5.77 (br s, 2H), 4.29 (t, J = 5.9 Hz, 2H), 3.30 (s, 1H), 3.02-3.09 (m, 2H), 1.86-1.94 (m, 2H), 1.28 (s, 9H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{22}H_{25}N_6O_2S$, 453.1709; found 453.1721.

***N*-(3-(6-Amino-8-((6-ethynylbenzo[*d*][1,3]dioxol-5-yl)thio)-9*H*-purin-9-yl)propyl)cyclopropanesulfonamide (WS70).** To a solution of **WS56** (100 mg, 0.17 mmol) in DMF (3 mL) was added trimethylsilanylacetylene (72 µL, 0.61 mmol), $PdCl_2(PPh_3)_2$ (12 mg, 0.02 mmol), CuI (3 mg. 0.02 mmol) and triethylamine (243 µL, 1.7 mmol). The resulting mixture was stirred at 60 °C for 30 min, condensed and filtered through silica gel. The filtrate was concentrated under reduced pressure and the resulting residue was dissolved in CH_2Cl_2/MeOH (1 mL/ 1 mL). To the resulting mixture was added KOH (20 mg) and stirred for 3 hrs. The reaction mixture was condensed and purified by flash chromatography to yield **WS70** as a white solid (43 mg, 52%). ^{1}H NMR (600 MHz, $CDCl_3$/MeOH-d_4): δ 8.20 (s, 1H), 7.06 (s, 1H), 7.00 (s, 1H), 6.08 (s, 2H), 4.37 (t, J = 7.1

Hz, 2H), 3.54 (s, 1H), 3.18 (t, J = 6.6 Hz, 2H), 2.43-2.51 (m, 1H), 2.04-2.12 (m, 2H), 1.10-1.14 (m, 2H), 0.99-1.04 (m, 2H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{20}H_{21}N_6O_4S_2$, 473.1066; found 473.1053.



S13-1 S13-2 DZ5-49-N9

Scheme 13. Synthesis of DZ5-49-N9.

6-(6-Amino-8-(6-iodobenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)hexanamide [DZ5-49-N9]. 50 mg (0.121 mmol) of 8-(6-iodobenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine (**S13-1**) was dissolved in DMF (2 mL). 47 mg (0.145 mmol) of Cs_2CO_3 and 117.4 mg (0.605 mmol) of 6-bromohexanamide (**S13-2**) were added and the mixture was stirred at rt for 2 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2:MeOH-NH_3 (7N), 10:1) to give 12.7 mg (20%) of **DZ5-49-N9**. ^1H NMR (500 MHz, $CDCl_3$/MeOH-d_4): δ 8.13 (s, 1H), 7.31 (s, 1H), 6.97 (s, 1H), 5.98 (s, 2H), 4.13 (t, J = 7.6 Hz, 2H), 2.14 (t, J = 7.6 Hz, 2H), 1.71-1.80 (m, 2H), 1.55-1.65 (m, 2H), 1.28-1.39 (m, 2H); HRMS (ESI) *m/z* $[M+H]^+$ calcd. for $C_{18}H_{20}IN_6O_3S$, 527.0362; found 527.0364.

Hsp90 Binding Assay:

For the binding studies, fluorescence polarization (FP) assays were performed similarly as was previously reported [Du *et al.* (2007) "High-throughput screening fluorescence polarization assay for tumor-specific Hsp90" *J. Biomol. Screen* 12:915-924]. Briefly, FP measurements were performed on an Analyst GT instrument (Molecular Devices, Sunnyvale, CA). Measurements were taken in black 96-well microtiter plates (Corning # 3650) where both the excitation and the emission occurred from the top of the well. A stock of 10 μM cy3B-GM was prepared in DMSO

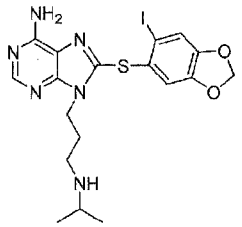
and diluted with HFB buffer (20 mM Hepes (K), pH 7.3, 50 mM KCl, 2 mM DTT, 5 mM $MgCl_2$, 20 mM Na_2MoO_4, and 0.01% NP40 with 0.1 mg/mL BGG). The test compounds were dissolved in DMSO and added at several concentrations to the HFB assay buffer containing both 6 nM cy3B-GM and transgenic mouse brain lysate (6 μg JNPL3 lysate) or human cancer cell lysate (3 μg SKBr3 lysate) in a final volume of 100 μL. Drugs were added to triplicate wells. Free cy3B-GM (6 nM cy3B-GM), bound cy3B-GM (6 nM cy3B-GM + lysate, as indicated above) and buffer only containing wells (background) were included as controls in each plate. Plates were incubated on a shaker at 4°C, and polarization values measured at 24 h. Percentage inhibition was calculated as follows: (% Control) = 100 - ((mP_c - mP_f)/(mP_b - mP_f)) x 100, where mP_c is the recorded mP from compound wells, mP_f is the average recorded mP from cy3B-GM-only wells, and mP_b is the average recorded mP from wells containing both cy3B-GM and lysate, and plotted against values of competitor concentrations. The inhibitor concentration at which 50% of bound cy3B-GM was displaced was obtained by fitting the data using a nonlinear regression analysis as implemented in Prism 4.0 (GraphPad Software).

hERG Fluorescence Polarization Assay:

Following the manufacturer's protocol, the hERG assay was performed using Predictor hERG Fluorescence Polarization Assay kit (catalog no. PV5365) from Invitrogen. Briefly, FP measurements were performed on an Analyst GT instrument (Molecular Devices, Sunnyvale, CA). Measurements were taken in black 384-well plates (Corning # 3677), where both the excitation and the emission occurred from the top of the well. The test compounds were dissolved in DMSO and added at several concentrations to the Predictor hERG FP assay buffer containing 4 nM Predictor hERG tracer red and 10 uL of Predictor hERG membrane in a final volume of 20 uL. Drugs were added to triplicate wells. E-4031 as positive control was included in each plate. Plates were then kept on a shaker at room temperature and polarization values were measured after 4 hrs. The inhibition concentration at which 50% of tracer red gets displaced was obtained by fitting the data using a nonlinear regression analysis as implemented in Prism 5.0 (GraphPad Software).

Table 12 shows results of testing for various representative compounds for their activity in Hsp90 binding assays and hERG fluorescence polarization assay. In interpreting these test results, it will be appreciated that binding to Hsp90 is desirable for activity in the treatment of cancer or neurodegenerative disorders. In contrast, it is generally undersirable to have binding to hERG since binding to hERG can result in undesirable cardiac side effects. Therefore, having a low value for binding to Hsp90 and a high value for binding to hERG is desirable, bearing in mind that the units for the two measurement are different.

For comparison, it is noted that values for PU-H71, a compound with the structure



has a Hsp90 binding value of 20 nM and an hERG assay result of 1 μM . Many of the compounds of the invention tested, have hERG values more than 100 times greater than PU-H71 and are therefore expected to have lower toxicity/side effect issues.

Table 12

Compound Designation No.	Synthetic Designation	Hsp90 Binding Assay (nM)	hERG assay (μM)
1A-10	WS35	6.3	NA
1A-11	WS42	71.5	NA
1A-12	WS39	33	NA
1A-15	WS54	20.5	>100
1A-19	WS53	44	NA
1A-22	WS48	47	>100
1A-24	WS34	11.5	NA
1A-25	WS52	24	NA
1A-26	WS49	12	>100
1A-27	WS50	64	NA
1A-28	WS56	19.7	NA
1A-43	WS45	11	>100
1A-44	WS46	68	NA
1A-45	WS51	9.8	>100

Compound Designation No.	Synthetic Designation	Hsp90 Binding Assay (nM)	hERG assay (μM)
1A-46	WS55	24.2	NA
1A-47	WS57	16.5	NA
1A-48	WS58	22.1	12
1A-49	WS64	28.3	NA
1A-5	WS47	78	NA
1A-50	DZ5-49-N9	76.5	NA
1B-28	WS70	53	>100
1B-43	WS69	28	>100
1B-45	WS68	37	>100
1G-28	MRP-I-31	22	NA
1G-43	MRP-I-29	11	>100
1G-45	MRP-I-28	15	76
2A-11	WS43	51	NA
2A-12	WS41	68	NA
2A-26	WS62	17	NA
2A-45	WS61	11.8	NA
3A-10	WS36	3.5	NA
3A-11	WS44	68	NA
3A-12	WS40	29.6	NA
3A-24	WS37	8.1	NA
3A-26	WS63	20.1	NA
3A-43	WS38	37.4	NA
4A-26	WS60	26.2	>100

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Compound Designation No.	Synthetic Designation	Hsp90 Binding Assay (nM)	hERG assay (μM)
4A-28	WS72	24	>100
4A-43	WS66	33.1	>100
4A-45	WS71	20	>100

The invention is not to be limited in scope by the specific embodiments disclosed in the examples that are intended as illustrations of a few aspects of the invention and any embodiments that are functionally equivalent are within the scope of this invention. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those in the art and are intended to fall within the scope of the appended claims. A number of references have been cited, the entire disclosures of which are incorporated herein by reference for all purposes.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

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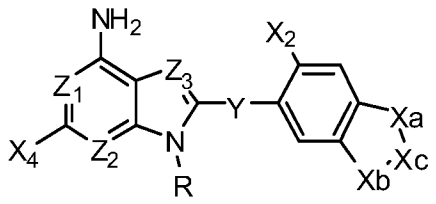
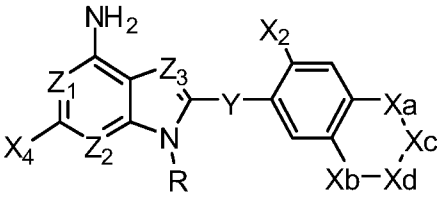
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A Compound of Formula (IA) or (IB):



(IA)



(IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is N;

(b) Y is S;

(c) Xa, Xb, Xc and Xd are O, O, CH_2, and CH_2, respectively;

(d) X_4 is hydrogen or halogen; and

(e) X_2 and R are a combination selected from the following:

(i) in formula (IA):

(a) X_2 is NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

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(b) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, or -C(O)N($R_A$)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(c) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -NR_AC(O)- groups, and/or terminated by an -NR_AC(O)R_B group, wherein each R_A is independently selected from C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(d) X_2 is aryl or alkynyl, R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, or -NR_AC(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -N$R_A$$SO_2$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl,

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C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(e) X_2 is aryl or alkynyl, R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -NR_ASO_2- or -$C(O)N(R_A)$- groups, and/or terminated by an -$SO_2NR_AR_B$ or -$C(O)NR_AR_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl;

(f) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl; and R is straight-chain- substituted or unsubstituted alkyl, straight-chain- substituted or unsubstituted alkenyl, straight-chain- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an -$S(O)NR_AR_B$, -$NR_AS(O)R_B$, -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -$C(O)NR_AR_B$, or -$NR_AC(O)R_B$ group, wherein R_A is independently selected from hydrogen, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

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(ii) in formula (IB):

(g) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched-substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, or -SO_2N(R_A)- groups, and/or terminated by an -S(O)NR_AR_B or -NR_AS(O)R_B group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(h) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched-substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -$NR_A$$SO_2$, -C(O)N($R_A$)-, or -$NR_A$C(O)- groups, and/or terminated by an -$SO_2NR_AR_B$, -$NR_ASO_2R_B$, -C(O)NR_AR_B, or -NR_AC(O)R_B group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

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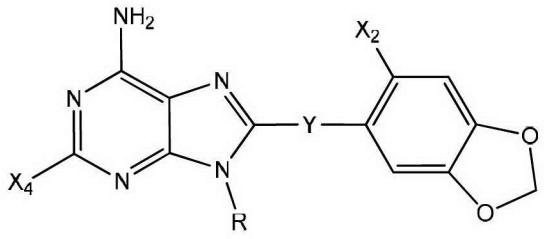
(i) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl; and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight- chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched-substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is independently selected from C_2-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

2. The compound of claim 1, which is a Compound of Formula (1):



(1)

or a pharmaceutically acceptable salt thereof, or a Compound of Formula (6):

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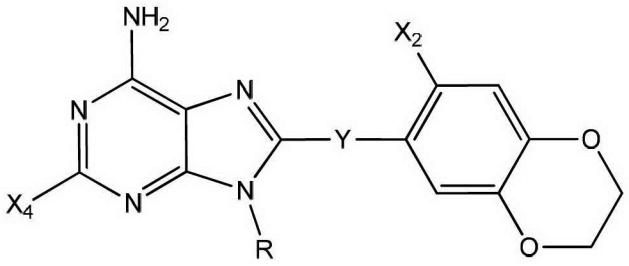

(6)

or a pharmaceutically acceptable salt thereof.

3. The compound of claim 1, wherein in formula (IA):

(i)(b) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, or -C(O)N($R_A$)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(i)(c) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -NR_AC(O)- groups, and/or terminated by an -NR_AC(O)R_B group, wherein each R_A is independently selected from C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6

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alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

4. The compound of claim 3, wherein R is straight-chain- unsubstituted C_1-C_6 alkyl, which is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, or -C(O)N($R_A$)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, and cycloalkyl.

5. The compound of claim 4, wherein X_2 is Iodo, R is straight-chain- unsubstituted C_1-C_6 alkyl, which is terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$ group, wherein R_A is hydrogen, and R_B is tert-butyl or cyclopropyl.

6. The compound of claim 1, wherein in formula (IA):

(i)(d) X_2 is aryl or alkynyl, R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, or -NR_AC(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -N$R_A$$SO_2$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(i)(e) X_2 is aryl or alkynyl, R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -N$R_A$$SO_2$- or -C(O)N($R_A$)- groups, and/or terminated by an -SO_2N$R_A$$R_B$ or -C(O)N$R_A$$R_B$ group, wherein each R_A is independently selected

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from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

7. The compound of claim 1, wherein in formula (IA),

(i)(f) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl; and R is straight-chain- substituted or unsubstituted alkyl, straight-chain- substituted or unsubstituted alkenyl, straight-chain- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein R_A is independently selected from hydrogen, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

8. The compound of claim 7, wherein X_2 is halogen, optionally Iodo; and R is straight-chain- unsubstituted C_1-C_6 alkyl, which is terminated by a $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein R_A is hydrogen, and each R_B is independently selected from C_1-C_6 alkyl and cycloalkyl, optionally tert-butyl or cyclopropyl.

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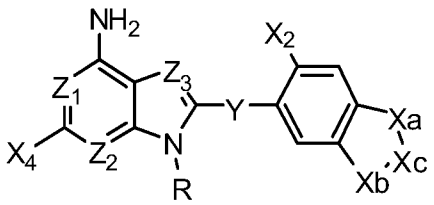
9. The compound of claim 7, wherein X_2 is alkynyl, optionally ethynyl; R is straight-chain- unsubstituted C_1-C_6 alkyl, which is terminated by a $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein R_A is hydrogen, and each R_B is independently selected from C_1-C_6 alkyl and cycloalkyl, optionally tert-butyl or cyclopropyl.

10. The compound of claim 1, wherein R is cyclopropane carboxylic acid 3-propyl-amide, N-3-propyl 2,2-dimethyl-propionamide, N-propyl-2-methyl-propane-2-sulfinamide, t-butanesulfonic acid 3-propylamide, or cyclopropanesulfonic acid 3-propylamide.

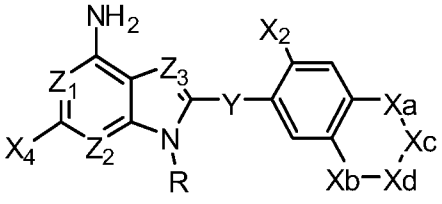
11. The compound of any one of claims 1-10, wherein X_4 is H or F.

12. The compound of claim 1, wherein
X_2 is optionally substituted heteroaryl, which is optionally furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, or 5-methyloxazol-2-yl; or
X_2 is alkynyl or NR_1R_2, optionally ethynyl or dimethylamino; or
X_2 is halo, optionally Iodo.

13. A Compound of Formula (IA) or (IB):



(IA)



(IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is N;

(b) Y is CH_2;

(c) Xa, Xb, Xc and Xd are O, O, CH_2, and CH_2, respectively;

(d) X_4 is hydrogen or halogen; and

(e) X_2 and R are a combination selected from the following:

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(i) in formula (IA):

(a) X_2 is NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$ groups, and/or terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-SO_2NR_AR_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(b) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$ groups, and/or terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(c) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or

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unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by a $-SO_2NR_AR_B$ group, wherein R_A is selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(d) X_2 is aryl or alkynyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$ groups, and/or terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(e) X_2 is aryl or alkynyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-SO_2NR_AR_B$ or $-C(O)NR_AR_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl,

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arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; and

(ii) in formula (IB),

(a) X_2 is NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(b) X_2 is halogen, aryl, or alkynyl, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -N$R_A$$SO_2$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl,

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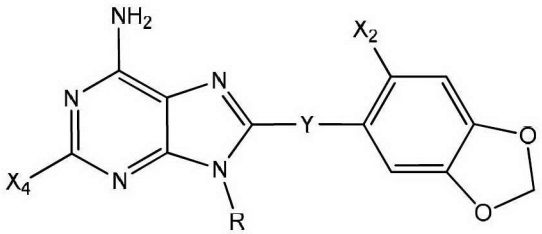
heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(c) X_2 is halogen, aryl, or alkynyl, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-SO_2NR_AR_B$ or $-C(O)NR_AR_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

14. The compound of claim 13, which is a Compound of the following Formula:



or a pharmaceutically acceptable salt thereof.

15. The compound of claim 13 or claim 14, wherein

X_2 is optionally substituted heteroaryl, and wherein the optionally substituted heteroaryl comprises furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-

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pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, or 5-methyloxazol-2-yl; or

X_2 is ethynyl, I, or dimethylamino.

16. The compound of claim 13, wherein in formula (IA), X_2 is NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

17. The compound of claim 13, wherein in formula (IA):

(i)(d) X_2 is aryl or alkynyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -N$R_A$$SO_2$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(i)(e) X_2 is aryl or alkynyl, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted

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alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by an $-SO_2NR_AR_B$ or $-C(O)NR_AR_B$ group, wherein each R_A is independently selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and each R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

18. The compound of claim 13, wherein in formula (IA):

(b) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more $-S(O)N(R_A)-$, $-NR_AS(O)-$, $-SO_2N(R_A)-$, $-NR_ASO_2-$, $-C(O)N(R_A)-$, or $-NR_AC(O)-$ groups, and/or terminated by an $-S(O)NR_AR_B$, $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, $-C(O)NR_AR_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl; or

(c) X_2 is halogen, and R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is terminated by a $-SO_2NR_AR_B$ group, wherein R_A is selected from C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl, and R_B is selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

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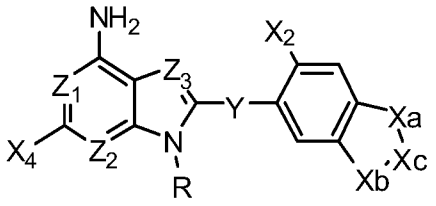
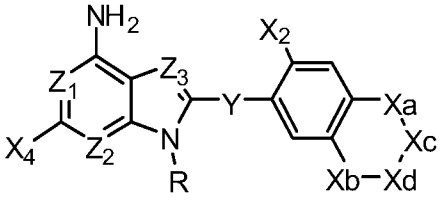
19. The compound of claim 18, wherein X_2 is halogen, optionally Iodo; R is straight-chain- unsubstituted C_1-C_6 alkyl, which is terminated by a $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen and C_1-C_6 alkyl, optionally wherein R_A is hydrogen and R_B is tert-butyl or cyclopropyl.

20. The compound of claim 17, wherein X_2 is alkynyl, optionally ethynyl; and R is straight-chain- unsubstituted C_1-C_6 alkyl, which is terminated by a $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen and C_1-C_6 alkyl, optionally wherein R_A is hydrogen, and R_B is tert-butyl or cyclopropyl.

21. A Compound of Formula (IA) or (IB):



(IA)



(IB)

or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is N;

(b) Y is O;

(c) Xa, Xb, Xc and Xd are independently selected from CH, CH_2, O, N, NH, S, carbonyl, fluoromethylene, and difluoromethylene selected so as to satisfy valence, wherein each bond to an X group is either a single bond or a double bond;

(d) X_2 is halogen, aryl, alkynyl, or NR_1R_2, wherein R_1 and R_2 are each independently H, C_1-C_6 alkyl, C_1-C_6 alkenyl, C_1-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, or alkylheteroarylalkyl;

(e) X_4 is hydrogen or halogen; and

(f) R is straight-chain- or branched- substituted or unsubstituted alkyl, straight-chain- or branched- substituted or unsubstituted alkenyl, straight-chain- or

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branched- substituted or unsubstituted alkynyl, or substituted or unsubstituted cycloalkyl wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups, and/or terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, and alkylheteroarylalkyl.

22. The compound of claim 21, wherein

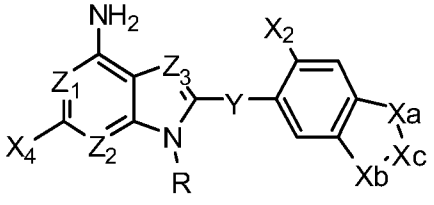
X_2 is optionally substituted heteroaryl, and wherein the optionally substituted heteroaryl comprises furan-2-yl, furan-3-yl, 5-methylfuran-2-yl, 1H-pyrazol-2-yl, 1H-pyrazol-3-yl, thiazol-2-yl, 5-methylthiazol-2-yl, oxazol-2-yl, or 5-methyloxazol-2-yl; or

X_2 is ethynyl, I, or dimethylamino.

23. The compound of claim 21 or claim 22, wherein the R group is interrupted by one or more -S(O)N(R_A)-, -NR_AS(O)-, -SO_2N(R_A)-, -N$R_A$$SO_2$-, -C(O)N($R_A$)-, or -N$R_A$C(O)- groups.

24. The compound of claim 21 or claim 22, wherein the R group is terminated by an -S(O)N$R_A$$R_B$, -N$R_A$S(O)$R_B$, -$SO_2NR_A$$R_B$, -N$R_A$$SO_2$$R_B$, -C(O)N$R_A$$R_B$, or -N$R_A$C(O)$R_B$ group.

25. A Compound of Formula (IA)



or a pharmaceutically acceptable salt thereof, wherein:

(a) each of Z_1, Z_2 and Z_3 is N;

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(b) Y is S or CH_2;

(c) Xa-Xc-Xb are $-CH_2-CH_2-CH_2-$, $-O-CH_2-CH_2-$, or $-CH_2-CH_2-O-$;

(d) X_4 is hydrogen or halogen;

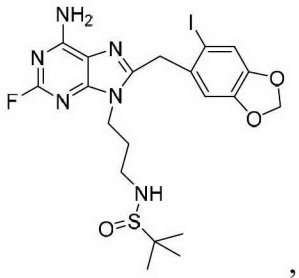
(e) X_2 is halogen or alkynyl; and

(f) R is straight-chain- C1-C6 alkyl, which is terminated by a $-NR_AS(O)R_B$, $-NR_ASO_2R_B$, or $-NR_AC(O)R_B$ group, wherein each R_A and R_B is independently selected from hydrogen, C_1-C_6 alkyl, or cycloalkyl.

26. The compound of claim 25, wherein X_2 is iodo or ethynyl.

27. The compound of claim 25 or claim 26, wherein R_A is hydrogen, and R_B is C_1-C_6 alkyl or cycloalkyl, optionally tert-butyl or cyclopropyl.

28. A compound of the formula: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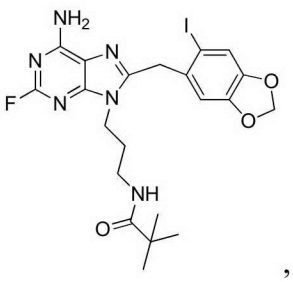
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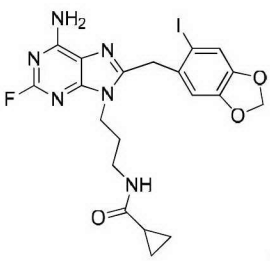
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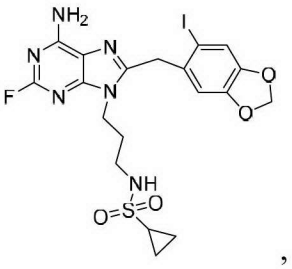
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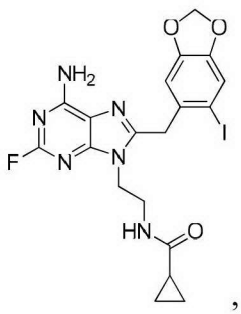
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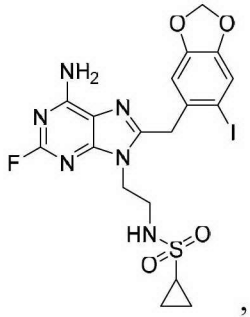
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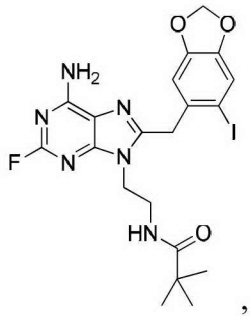
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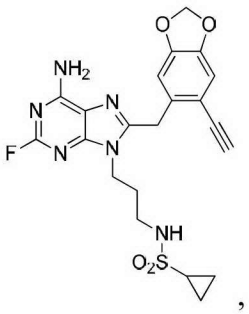
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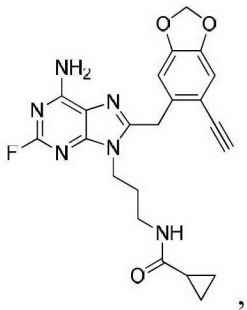
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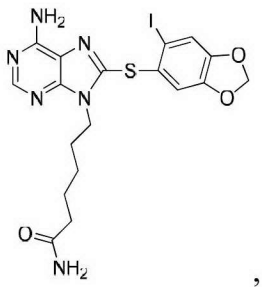
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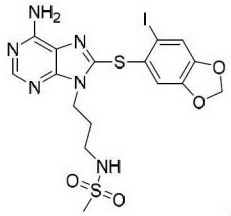
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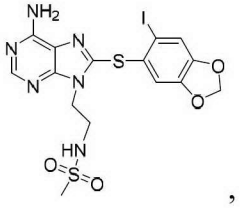
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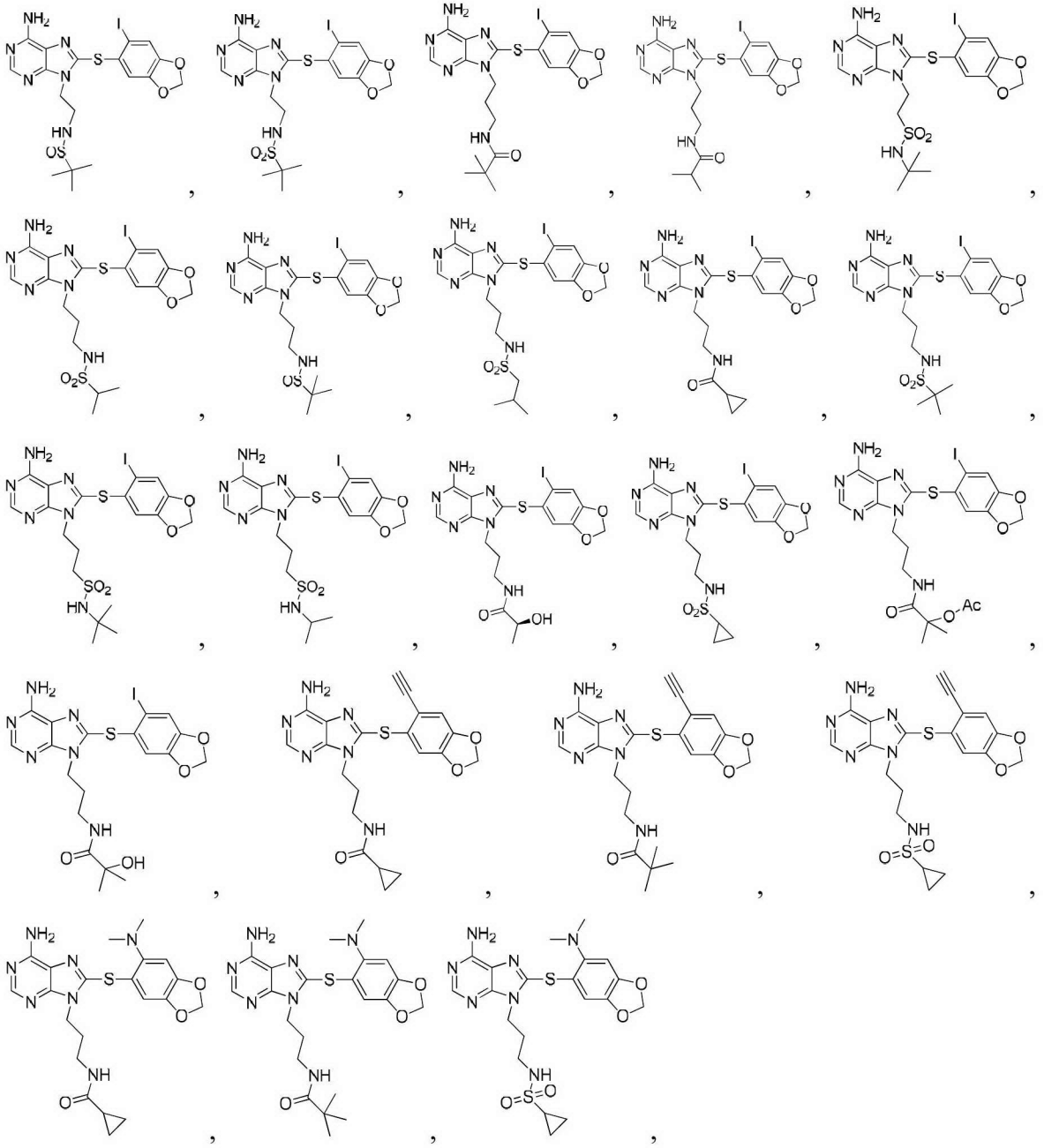

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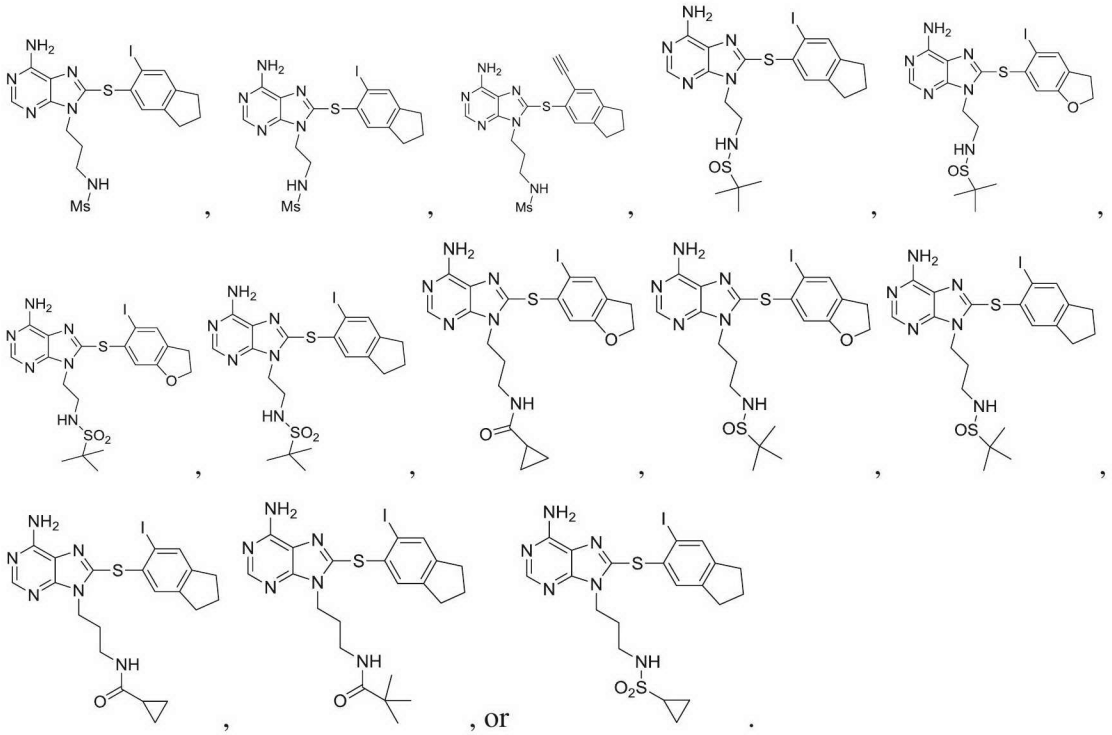

29. A pharmaceutical composition comprising the compound of any one of claims 1-28 and a pharmaceutically acceptable carrier.

30. A method for treating or preventing cancer or a neurodegenerative disorder, comprising administering to a patient in need thereof a therapeutically effective amount of a compound of any one of claims 1-28, optionally wherein the neurodegenerative disorder is tauopathies.

31. Use of a compound of any one of claims 1-28 in the manufacture of a medicament for treating or preventing cancer or a neurodegenerative disorder, optionally wherein the neurodegenerative disorder is tauopathies.

32. The method of claim 30 or use of claim 31, wherein the neurodegenerative disorder is selected from chronic traumatic encephalopathy, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, age-related memory loss, senility, and age-related dementia, and wherein the cancer is hematopoietic disorders, optionally

selected from myeloproliferative disorders, myelofibrosis, polycythemia vera, and essential thrombocytosis.

33. A method for the inhibition of Hsp90, comprising contacting Hsp90 with an Hsp90 function inhibiting amount of a compound of any one of claims 1-28.