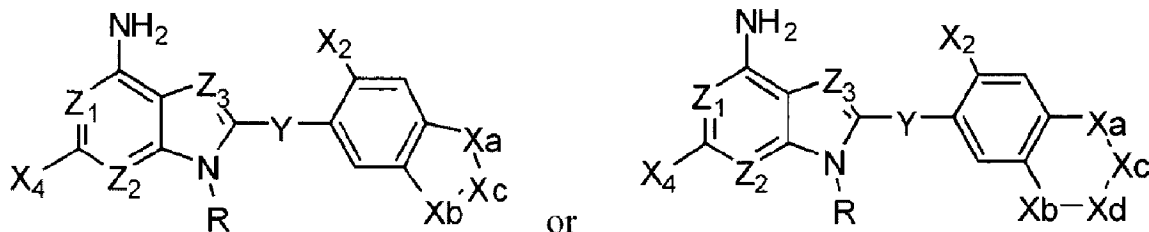




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(54) Title: HSP90 INHIBITORS

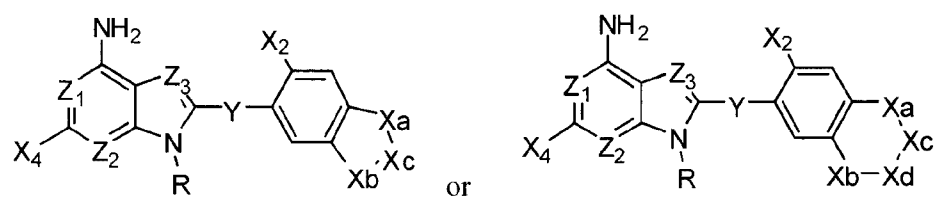


(57) Abrégé/Abstract:

The present application provides substituted purine derivatives and related compounds of the formulas: (see above formula). The compounds are useful as inhibitors of HSP90, and hence in the treatment of related diseases such as cancer or neurodegenerative disease.

ABSTRACT

The present application provides substituted purine derivatives and related compounds of the formulas:



The compounds are useful as inhibitors of HSP90, and hence in the treatment of related diseases such as cancer or neurodegenerative disease.

HSP90 INHIBITORS

Background of the Invention

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 (Hsp 60, 90 and 70 and p23), forming a "refoldosome" and ultimately the ATP-dependent release of the chaperones from the refolded protein.

Hsp90 may 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 transmembrane 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.

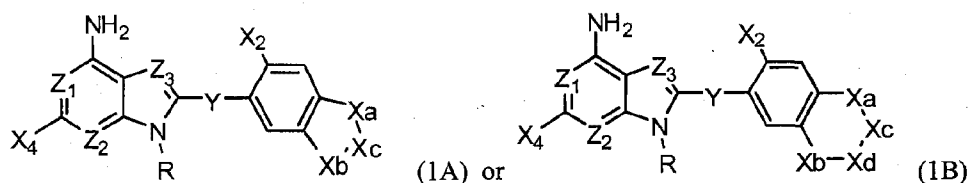
Hsp90 has been shown to be overexpressed in multiple tumor types and as a function of oncogenic transformation. Whether it plays a necessary role in maintaining transformation is unknown, but it could have at least three functions in this regard. Cancer cells grow in an environment of hypoxia, low pH 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.

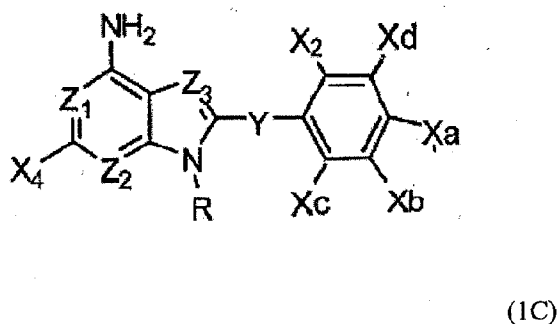
Exemplary small molecule therapeutics that bind to the same binding pocket of Hsp90 as ATP and the ansamycin antibiotics are disclosed in PCT Publication Nos. WO02/36075, WO2006/084030, WO09/042646 and WO09/065035, and US Patent

Publications 2005/0113339, 2005/0004026, 2005/0049263, 2005/0256183, 2005/0119292, 2005/0113340, 2005/0107343, 2008/0096903, 2008/0234297, 2008/0234314 and 2008/0253965.

Many of these compounds are based on a scaffold of the type disclosed by Chiosis et al in PCT Publication No. WO02/36075, with variations in substituents. In some cases, the compositions can be described by one of the following two general formulas:



wherein Z1, Z2, Z3 are selected from C and N in which numerous options are disclosed for each variable substituent, resulting in an astronomical number of combinations and permutations. In other cases, the compositions can be described by a structural formula in which Xa, Xb, Xc and Xd are not connected to one another but are simply substituents on the benzene ring. These structures have the general formula:



wherein Z1, Z2, Z3 are selected from C and N. While these compounds are generally active as inhibitors of Hsp90, the level of activity is extremely variable with measured values for EC₅₀ and IC₅₀ being reported in both micromolar and nanomolar ranges.

Summary of the Invention

The present application provides compounds useful in the inhibition of Hsp90, and hence in the treatment of disease.

Brief Description of the Figures

Fig. 1 shows examples of unsubstituted aryl groups, including some heterocyclic aryl groups.

Fig. 2 shows examples of unsubstituted heterocyclic groups.

Fig. 3 shows average tumor volume in mice treated with compound 1B-1-HCl or with vehicle.

Detailed Description of the Invention

The present invention provides compounds within the scope of Formula 1A, 1B or 1C with particular combinations of substituents that are effective to inhibit Hsp90. Inhibitors of Hsp90 are recognized as effective in treatments of cancer, and also can be used in the treatment of neurodegenerative diseases as described in PCT Patent Publication WO2008/005397. WO 2007/14360 discloses the use of Hsp90 inhibitors in treatment of neurofibromatosis. Thus, the compounds of the invention can be used in therapeutic methods in the same manner as used other known Hsp90 inhibitors, by administering a therapeutically effective amount of a compound of the invention to an individual, including a human, in need of treatment for cancer, neurodegenerative disease or other condition for which Hsp90 inhibition is relevant.

As used in this application, the term "treatment" refers to delaying the onset of symptoms, reducing the severity or delaying the symptomatic progression of cancer, neurodegenerative disease or other condition in the individual. A cure of the disease is not required to fall within the scope of treatment. Further, it will be appreciated that the specific results of these treatment goals will vary from individual to individual, and that some individuals may obtain greater or lesser benefits than the statistical average for a representative population. Thus, treatment refers to administration of composition to an individual in need, with the expectation that they will obtain a therapeutic benefit.

The term "administering" refers to the act of introducing into the individual the therapeutic compound. In general, any route of administration can be used. Thus, administration by oral, intrathecal, intravenous, intramuscular or parenteral injection is appropriate depending on the nature of the condition to be treated. Administration may also be done to the brain by inhalation because there is a compartment at the upper side of the nose that connects with the brain without having the BBB capillaries. Compounds that cross the blood brain barrier are preferred for this mode of administration, although this characteristic is not strictly required.

The term "therapeutically effective amount" encompasses both the amount of the compound administered and the schedule of administration that on a statistical basis obtains the result of preventing, reducing the severity or delaying the progression of the disease in the individual. As will be appreciated, preferred amounts will vary from compound to compound in order to balance toxicity/tolerance with therapeutic efficacy and the mode of administration. Determination of maximum tolerated dose and of the treatment regime in terms of number and frequency of dosing is a routine part of early clinical evaluation of a compound.

In all of the compounds of the present invention, the compound may be as depicted, or as a pharmaceutically acceptable salt or ester thereof.

In naming options for X_2 , X_4 and R, the name refers to the type of group that is directly attached to the central structure, which group may include additional functionality. Thus, "*alkyl*" group refers to a linear, cyclic or branched saturated hydrocarbon, for example a hydrocarbon having from 1 to 10 carbon atoms, in which the atom directly attached to the central structure is a carbon atom. Such an alkyl group may include substituents other than hydrogen, for example an oxygen-containing group including without limitation hydroxyl and alkoxy; a halogen group; a nitrogen-containing group including without limitation amino, amido and alkylamino; an aryl group; a sulfur-containing group including without limitation thioalkyl; and/or a non-aromatic cyclic group including heterocycles and carbocycles. Carbon atoms in these substituents may increase the total number of carbon atoms in the alkyl group to above 10 without departing from the invention. All references to alkyl groups in the specification and claims hereof encompass both substituted and unsubstituted alkyl groups unless the context is clearly to the contrary.

“Alkenyl” group refers to a linear, cyclic or branched hydrocarbon, for example a hydrocarbon having from 1 to 10 carbon atoms, and at least one double bond, in which the atom directly attached to the central structure is a carbon atom. The alkenyl group may include any of the substituents mentioned above for an alkyl group. All references to alkenyl groups in the specification and claims hereof encompass both substituted and unsubstituted alkenyl groups unless the context is clearly to the contrary.

“Alkynyl” group refers to a linear, cyclic or branched hydrocarbon, for example a hydrocarbon having from 1 to 10 carbon atoms, and at least one triple bond, in which the atom directly attached to the central structure is a carbon atom. The alkynyl group may include any of the substituents mentioned above for an alkyl group. All references to alkynyl groups in the specification and claims hereof encompass both substituted and unsubstituted alkynyl groups unless the context is clearly to the contrary.

“Aryl” group refers to any group derived from a simple aromatic ring. Aryl group includes heteroaryl. (See Fig. 1) Aryl groups may be substituted or unsubstituted. When X_2 , X_4 and R is identified as an aryl group, an atom of the aryl ring is bound directly to an atom of the central structure. An aryloxy substituent is an aryl group connected to the central structure through an oxygen atom. The aryl group may include any of the substituents mentioned above for an alkyl group, and in addition an aryl group may include an alkyl, alkenyl or alkynyl group. All references to aryl groups in the specification and claims hereof encompass both substituted and unsubstituted aryl groups unless the context is clearly to the contrary.

“Amino” group refers to any group which consists of a nitrogen attached by single bonds to carbon or hydrogen atoms. In certain instances, the nitrogen of the amino group is directly bound to the central structure. In other instances, an amino group may be a substituent on or within a group, with the nitrogen of the amino group being attached to the central structure through one or more intervening atoms. Examples of amino groups include NH_2 , alkylamino, alkenylamino groups and N-containing non-aromatic heterocyclic moiety (i.e., cyclic amines). Amino groups may be substituted or unsubstituted. All references to amino groups in the specification and claims hereof encompass substituted and unsubstituted amino groups unless the context is clearly to the contrary.

“Halogen” group refers to fluorine, chlorine, bromine or iodine.

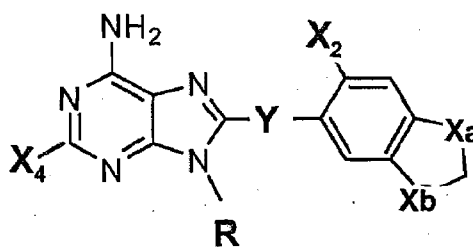
"Heterocyclic" group refers to a moiety containing at least one atom of carbon, and at least one atom of an element other than carbon, such as sulfur, oxygen or nitrogen within a ring structure. These heterocyclic groups may be either aromatic rings or saturated and unsaturated non-aromatic rings. Some examples are given in Fig. 2. Heterocyclic groups may be substituted or unsubstituted. All references to heterocyclic groups in the specification and claims encompass substituted and unsubstituted heterocyclic groups unless the context is clearly to the contrary.

In the compounds of the invention, all of the atoms have sufficient hydrogen or non-hydrogen substituents to satisfy valence, or the compound includes a pharmaceutically acceptable counterion, for example in the case of a quaternary amine.

In the structures set forth below examples are provided in which all of Z1, Z2 and Z3 are nitrogen. These examples are intended as exemplary, and are not intended to exclude options in which one or more of Z1, Z2 and Z3 is carbon. In particular, corresponding compositions in which Z2 or Z3 is carbon are considered to be within the scope of this disclosure.

A. Structures of formula 1A in which Xa or Xb is O

In accordance with a first embodiment of the invention, the compounds have general formula 1A, in which one of Xa or Xb is O, and Xc and the other of Xa and Xb is CH₂. Thus, the compounds of this embodiment may be represented by the general formula



(2)

wherein:

one of Xa and Xb is O and the other is -CH₂-;

Y is -CH₂- or -S-;

X₄ is hydrogen or halogen; and

X₂ and R are in combinations as discussed below.

A-I. In some embodiments of the invention, X₂ is halogen. In these embodiments, R is suitably a primary aminoalkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, with the proviso that R is not a piperidino moiety. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1A and 1B (Compounds 1A-1 to 1A-4, 1A-6, 1A-11, 1A-18 to 1A-28, 1A-30, 1A-31, 1A-49, 1B-1 to 1B-5, 1B-18, 1B-23 to 1B-25, 1B-29 to 1B-32, 1B-34, 1B-35, 1B-37, 1B-49, 1B-52 1B-56 and 1B-57).

As shown, in preferred embodiments of formula (2), X₄ is H, chlorine or fluorine.

In a particular preferred embodiment of formula (2), Y is S, X₄ is H, X₂ is I.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is Cl, X₂ is I.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is F, X₂ is I.

In a particular preferred embodiment of formula (2), Y is S, X₄ is F, X₂ is I.

Tests were run on compounds in accordance with the first embodiment of the invention, and the EC₅₀ for Hsp90 binding in JNPL3 brain cell lysate and SKBr3 cell lysate was assessed. The results are summarized in Table 2A. While all of the compounds had desirable low EC₅₀ values, both compounds tested in which X_b is O were superior to the related compound in which X_a is O. In addition, compound 1B-1 was superior to an otherwise identical compound in which both X_a and X_b are O (PU-HZ150 disclosed in US

12/307,063) which has an EC_{50} of 12-14.4 nM and compound 1B-2 was superior to an otherwise identical molecule in which both Xa and Xb are O (PU-H71 disclosed in US 11/814,506) which has an EC_{50} of 30.8-54 nM in the same experimental system.

Animal Studies. Four- to 6-week-old nu/nu athymic female mice were obtained from Taconic Farms. Experiments were carried out under an Institutional Animal Care and Use Committee approved protocol, and institutional guidelines for the proper and humane use of animals in research were followed. Before administration, a solution of 1B-1-HCl was formulated in PBS (pH 7.4). All mice received Augmentin (amoxicillin/clavulanate potassium; SmithKline Beecham) in their drinking water while on therapy. Mice were killed by CO₂ euthanasia.

Mice bearing MDA-MB-468 tumors (n=5) reaching a volume of 100-150 mm³ were treated i.p. (i.p.) using 1B-1-HCl at 50 mg/kg 3 x week or vehicle. Tumor volume was determined by measurement with Vernier calipers, and tumor volume was calculated as the product of its length x width² x 0.4. Tumor volume was expressed on indicated days as the median tumor volume $\pm$ SD indicated for groups of mice. The average tumor volumes are summarized in Fig. 3. As shown, in the 35 days of the experiment the average tumor volume in the control mice increased by about a factor of 3X, while the tumor size in the mice treated with 1B-1-HCl decreased.

Table 2B shows measured values for EC_{50} in JNPL3 brain cell lysates for compounds 1B-3, 1B-4 and 1B-25 in accordance with this embodiment of the invention which incorporates a fluorine as X₄ and in which Y is -CH₂-. Desirably low values of EC_{50} were observed.

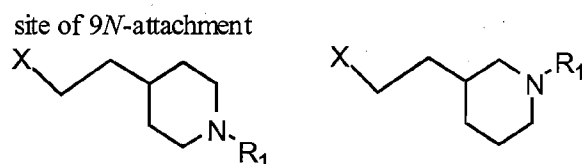
In addition, Table 2B shows measured values for EC_{50} in JNPL3 brain cell lysates for compound 1B-24 in accordance with this embodiment of the invention which incorporates a hydrogen as X₄ and in which Y is S. Desirably low values of EC_{50} were observed.

A-II. In some embodiments of the invention, X₂ is an aryl group. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. Table 8 provides a summary of the R groups from these patents and applications.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

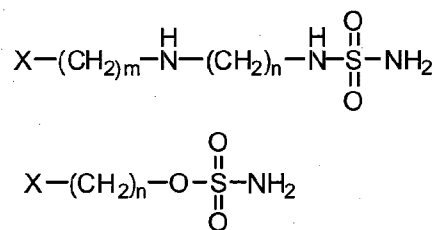
In embodiments of formula (2) within this group, R has the formula:



where R_1 is selected from COH, COMe, COEt, CONPr, CO i Pr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

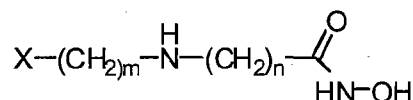
site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In embodiments within this group, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is an aromatic heterocycle.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, pyrrole, oxazole or thiazole.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, oxazole or thiazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-, 3- furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1A and 1B (Compounds 1A-5, 1A-7, 1A-12, 1A-13, 1A-15 to 1A-17, 1A-36, 1A-37, 1A-42, 1A-45 to 1A-48, 1A-50 to 1A-52, 1B-6, 1B-8, 1B-12, 1B-14, 1B-15, 1B-17, 1B-26, 1B-27, 1B-33, 1B-42 to 1B-44, 1B-46, 1B-50, 1B-51, 1B-53 to 1B-55). As shown, in preferred embodiments of formula (2) in which X₂ is an aryl group, X₄ is H, chlorine or fluorine.

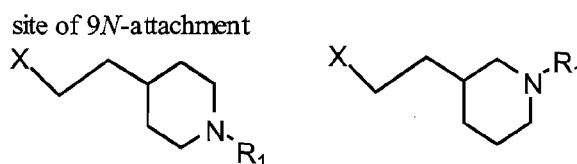
Table 2C shows measured values for EC₅₀ in JNPL3 brain cell lysates for compounds 1B-26 and 1B-27 in accordance with this embodiment of the invention which incorporates a hydrogen as X₄ and in which Y is S. Desirably low values of EC₅₀ were observed.

A-III. In some embodiments of the invention, X₂ is an alkynyl group. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. See Table 8.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl-amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl-amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

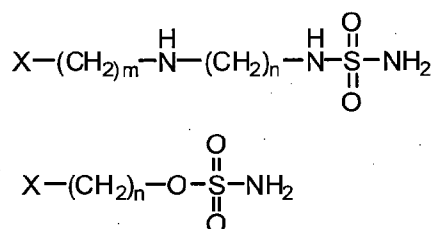
In embodiments of formula (2) within this group, R has the formula:



where R_1 is selected from COH, COMe, COEt, CO_nPr , COiPr, SO_2Me , CH_2OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

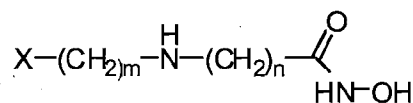
site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In embodiments within this group, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is acetylene.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is acetylene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is acetylene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is acetylene.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is acetylene.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1A and 1B (Compounds 1A-8, 1A-14, 1A-29, 1A-32 to 1A-35, 1B-10, 1B-13, 1B-16, 1B-19, 1B-28, 1B-36, 1B-38 to 1B-41, 1B-45 1B-47 and 1B-58). As shown, in preferred embodiments of formula (2) in which X_2 is an alkynyl group, X_4 is H, chlorine or fluorine.

Table 2D shows a measured value for EC_{50} in JNPL3 brain cell lysates for compound 1B-28 in accordance with this embodiment of the invention which incorporates a hydrogen as X_4 and in which Y is S. A desirably low value of EC_{50} was observed.

A-IV. In some embodiments of the invention, X_2 is a cyano group. In these embodiments, R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, and with the proviso that R is not a piperidino moiety. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl,

3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

In a particular preferred embodiment of formula (2), Y is S, X₄ is H, X₂ is CN.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is Cl, X₂ is CN.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is F, X₂ is CN.

In a particular preferred embodiment of formula (2), Y is S, X₄ is F, X₂ is CN.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Table 1A and 1B (Compounds 1A-9, 1B-11 and 1B-20).

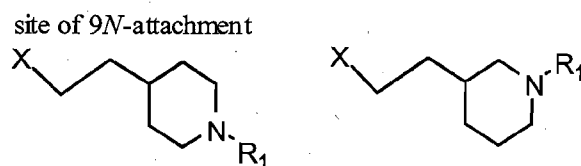
A-V. In some embodiments of the invention, X₂ is an amino group. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. See Table 8.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

In embodiments of formula (2) within this group, R has the formula:

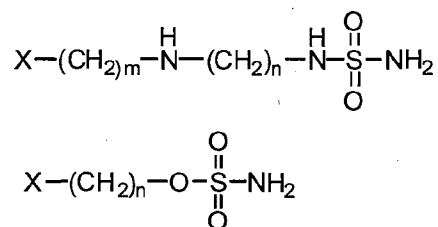
16



where R₁ is selected from COH, COMe, COEt, CONPr, COiPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

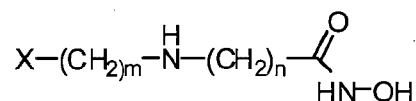
site of 9*N*-attachment



where m= 2-3 and n= 1-6.

In embodiments within this group, R has the formula

site of 9*N*-attachment



where m= 2-3 and n= 1-6.

In a particular preferred embodiment of formula (2), Y is S, X₄ is H, X₂ is dimethylamino

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is Cl, X₂ is dimethylamino

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is F, X₂ is dimethylamino.

In a particular preferred embodiment of formula (2), Y is S, X₄ is F, X₂ is dimethylamino.

In a particular preferred embodiment of formula (2), Y is S, X₄ is H, X₂ is aziridino.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is Cl, X₂ is aziridino.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is F, X₂ is aziridino.

In a particular preferred embodiment of formula (2), Y is S, X₄ is F, X₂ is aziridino.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1A and 1B (Compounds 1A-10, 1A-38 to 1A-41, 1A-43, 1A-44, 1B-7, 1B-21 and 1B-48).

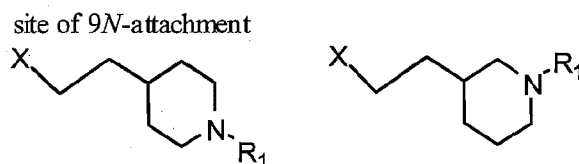
A-VI. In some embodiments of the invention, X₂ is a cycloalkyl or a cycloalkenyl. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. See Table 8.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

In embodiments of formula (2) within this group, R has the formula:

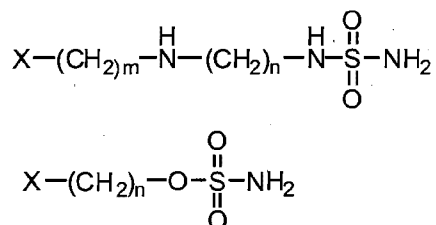
18



where R_1 is selected from COH, COMe, COEt, CONPr, COiPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

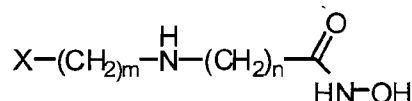
site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In embodiments within this group, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is a cycloalkyl with one ring.

In specific embodiments, X_2 is a cyclopropane, a cyclobutane or a cyclopentane.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is cyclopentyl.

In particular embodiments of formula (2), Y is CH₂, X_4 is F, X_2 is cyclopentyl.

In particular embodiments of formula (2), Y is CH₂, X_4 is Cl, X_2 is cyclopentyl.

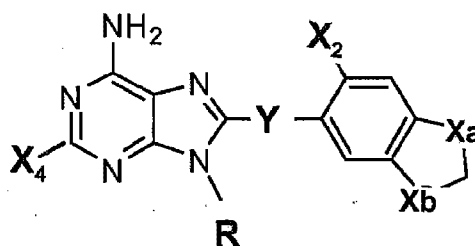
In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is cyclopentyl.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Table 1B (Compounds 1B-9, and 1B-22) although the embodiment is not limited to the option in which Xb is O, and includes compounds in which Xa is O.

B. Structures of formula 1A in which Xa or Xb is S

In accordance with a second embodiment of the invention, the compounds have general formula 1A, in which one of Xa or Xb is S, and Xc and the other of Xa and Xb is CH₂. Thus, the compounds of this embodiment may be represented by the general formula



(2)

wherein:

one of Xa and Xb is S and the other is -CH₂-;

Y is -CH₂- or -S-,

X₄ is hydrogen or halogen; and

X₂ and R are as discussed below.

In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein.

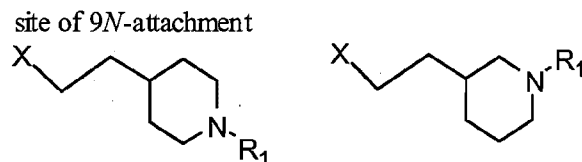
See Table 8.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a

nonaromatic heterocycle-alkyl. In some of these embodiments, R is a primary, secondary or tertiary alkyl-amino-alkyl, alkyl-aryl, or an alkyl-nonaromatic heterocycle. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

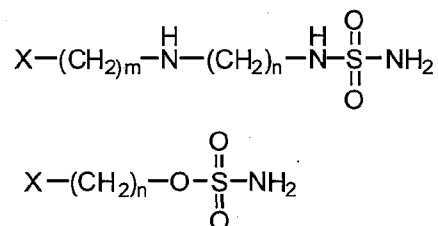
In embodiments of formula (2) within this group, R has the formula:



where R₁ is selected from COH, COMe, COEt, CO_nPr, CO_iPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

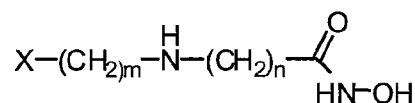
site of 9N-attachment



where m= 2-3 and n= 1-6.

In embodiments within this group, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In embodiments of formula (2) in which X_a or X_b is S, X_2 may be any group shown to be attached to the same position as X_2 in any of the compounds disclosed herein or in the various patents and patent applications cited above. Specifically, X_2 may be alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, saturated or unsaturated heterocycle, aryl, halogen, aryloxy, alkoxy, halogenated alkoxy, alkenyloxy, hydroxyalkyl, amino, alkylamino, dialkylamino, acylamino, carbamyl, amido, dialkylamido, alkylamido, alkylsulfonamido, sulfonamido, trihalocarbon, -thioalkyl, SO_2 -alkyl, -COO-alkyl, -COalkyl, OH, NO_2 , CN or alkyl-CN, or part of a ring formed by R;

In particular embodiments of the invention, X_2 is halogen, and R is an (alkylamino) alkyl or (dialkylamino) alkyl.

In particular embodiments, X_2 is halogen and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is an aryl group.

In particular embodiments, X_2 is aryl and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is a heteroaryl group.

In some embodiments, X_2 is a heteroaryl group and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments, X_2 is 2- or 3-furan and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments, X_2 is 2- or 3-thiophene and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments, X_2 is 3-pyrazolyl and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl,

3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is an alkynyl group.

In some embodiments of the invention, X_2 is an alkynyl group, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments of the invention, X_2 is acetylene, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is CN.

In particular embodiments of the invention, X_2 is CN, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is an amine.

In some embodiments of the invention, X_2 is an amine, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-

amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl-amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments of the invention, X₂ is dimethyl amine, azetidino or aziridino, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1C and 1D.

C. Structures of formula 1A in which X_a, X_b and X_c are all carbon

In accordance with a third embodiment of the invention, the compounds have general formula 1A, in which X_a, X_b and X_c are all carbon, connected by two single or one single bond and one double bond, and wherein

Y is -CH₂- or -S-;

X₄ is hydrogen or halogen; and

X₂ and R are in combinations as discussed below.

C-I. In some embodiments of the invention in which X_a, X_b and X_c are all carbon, X₂ is halogen.

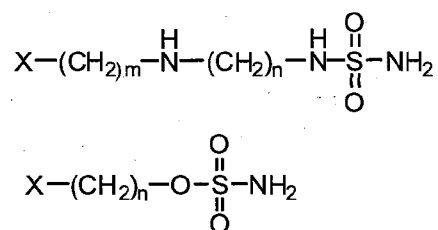
In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur with the proviso that R does not include a piperidino moiety.

In some embodiments, R is suitably an optionally substituted primary alkyl-amino, an optionally substituted secondary or tertiary alkyl-amino-alkyl, alkyl-aryl, or an alkyl-nonaromatic heterocycle, with the proviso that R is not a piperidino moiety.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is a primary, secondary or tertiary alkyl-amino-alkyl, alkyl-aryl, or an alkyl-nonaromatic heterocycle, with the proviso that R does not include a piperidino moiety. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

In embodiments of the invention within this group, R has the formula

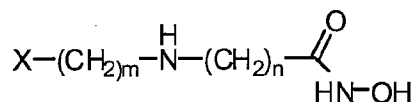
site of 9N-attachment



where m= 2-3 and n= 1-6.

In embodiments within this group, R has the formula

site of 9N-attachment



where $m=2-3$ and $n=1-6$.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1E (Compounds 1E-1 to 1E-4, 1E-6, 1E-18, 1E-21, 1E-23 to 1E-26, 1E-35, 1E-38, 1E-39, 1E-42 to 1E-48, 1E-68 to 1E-76). As shown, in preferred embodiments of formula (2), X_4 is H, chlorine or fluorine.

In a particular preferred embodiment of formula (2), Y is S, X_4 is H, X_2 is I.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is Cl, X_2 is I.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is F, X_2 is I.

In a particular preferred embodiment of formula (2), Y is S, X_4 is F, X_2 is I.

Table 2E shows measured values for EC_{50} in JNPL3 brain and SKBr3 cell lysates for compounds 1E-2, 1E21 and 1E-23 in accordance with this embodiment of the invention which incorporates a hydrogen as X_4 and in which Y is S. Desirably low values of EC_{50} were observed.

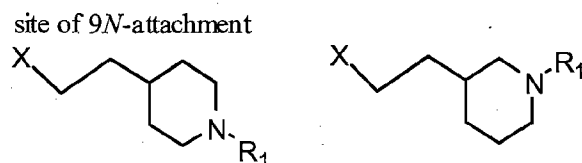
C-II. In some embodiments of the invention, X_2 is an aryl group. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. See Table 8.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-

(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

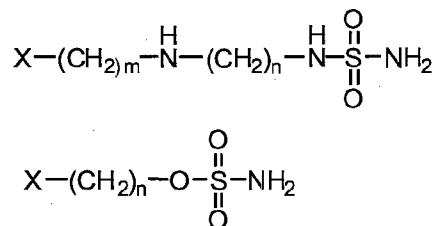
In embodiments of formula (2) within this group, R has the formula:



where R_1 is selected from COH, COMe, COEt, CONPr, COiPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

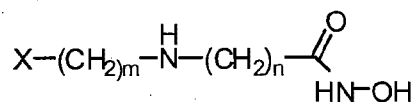
site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In embodiments within this group, R has the formula

site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is an aromatic heterocycle.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, pyrrole, oxazole and thiazole.

In specific embodiments of the X_2 is a furan, thiophene, pyrazole, oxazole and thiazole or imidazole.

In specific embodiments, X_2 is an aromatic heterocycle.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, pyrrole, oxazole or thiazole.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, oxazole or thiazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-, 3- furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1E (Compounds 1E-5, 1E-7, 1E-11 to 1E-13, 1E-15 to 1E-17, 1E-27, 1E-29 to 1E-33, 1E-36, 1E-37, 1E-41, 1E-59 to 1E-76, 1E-84 and 1E-85). As shown, in preferred embodiments of formula (2) in which X₂ is an aryl group, X₄ is H, chlorine or fluorine.

C-III. In some embodiments of the invention, X₂ is an alkynyl group. In these embodiments, R may be as described above in Section CII.

In specific embodiments, X₂ is acetylene.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is acetylene.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is acetylene.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is acetylene.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is acetylene.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1E (Compounds 1E-8, 1E-14, 1E-19, 1E-20, 1E-22, 1E-40, 1E-49 to 1E-58 and 1E-77 to 1E-82). As shown, in preferred embodiments of formula (2) in which X₂ is an alkynyl group, X₄ is H, chlorine or fluorine.

Table 2F shows a measured value for EC₅₀ in JNPL3 brain cell lysates for compound 1E-22 in accordance with this embodiment of the invention which incorporates a hydrogen as X₄ and in which Y is S. A desirably low value of EC₅₀ was observed.

C-IV. In some embodiments of the invention, X_2 is a cyano group. In these embodiments, R may be as described above in Section C-II, with the proviso that R does not include a piperidino moiety.

In a particular preferred embodiment of formula (2), Y is S, X_4 is H, X_2 is CN.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is Cl, X_2 is CN.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is F, X_2 is CN.

In a particular preferred embodiment of formula (2), Y is S, X_4 is F, X_2 is CN.

In these particular embodiments, R may be any one of the types of groups described above.

A specific example of a compound in accordance with this embodiment of the invention is listed in Table 1E (Compound 1E-9).

C-V. In some embodiments of the invention, X_2 is an amino group. In these particular embodiments, R may be any one of the types of groups described in Section C-II.

In a particular preferred embodiment of formula (2), Y is S, X_4 is H, X_2 is azetidino.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is Cl, X_2 is azetidino.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is F, X_2 is azetidino.

In a particular preferred embodiment of formula (2), Y is S, X_4 is F, X_2 is azetidino.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Table 1E (Compound 1E-10, 1E-28 and 1E-34).

C-VI. In some embodiments of the invention, X_2 is a cycloalkyl or a cycloalkenyl. In these particular embodiments, R may be any one of the types of groups described in Section C-II.

In specific embodiments, X_2 is a cycloalkyl with one ring.

In specific embodiments, X_2 is a cyclopropane, cyclobutane or cyclopentane.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is cyclopentyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is cyclopentyl.

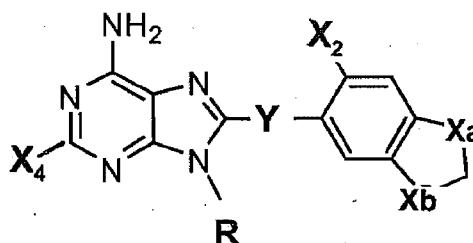
In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is cyclopentyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is cyclopentyl.

In these particular embodiments, R may be any one of the types of groups described above.

D. Structures of formula 1A in which Xa or Xb is N

In accordance with a fourth embodiment of the invention, the compounds have general formula 1A, in which one of Xa or Xb is N, and Xc and the other of Xa and Xb are CH₂. The N may be unsubstituted (i.e. NH) or substituted, for example with methyl, ethyl, acetyl. Thus, the compounds of this embodiment may be represented by the general formula



(2)

wherein:

one of Xa and Xb is N bonded to H or a substituent, and the other is -CH₂-;

Y is -CH₂- or -S-;

X₄ is hydrogen or halogen; and

X₂ and R are as discussed below.

In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen herein or in the various patents and applications cited above. See Table 8. In some embodiments, R includes a nitrogen heteroatom. In further embodiments, R is any of the options discussed above in Section B.

X₂ may be any group shown to be attached to the same position in any of the compounds disclosed in the various patents and patent applications cited above, or as described above in Section B.

In particular embodiments of the invention, X₂ is halogen, and R is an amino alkyl, an alkylaminoalkyl, dialkylaminoalkyl, or trialkylammonioalkyl group, in which each alkyl portion may be linear, cyclic or branched, or an alkyl heterocycle, where the alkyl may be

bound to a nitrogen in the heterocyclic group. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is an aryl group.

In particular embodiments, X_2 is aryl and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is a heteroaryl group.

In some embodiments, X_2 is a heteroaryl group and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments, X_2 is 2- or 3-furan and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino)

propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments, X_2 is 2- or 3-thiophene and R is 2-(methyl, t-butyl-amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl-amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments, X_2 is 3-pyrazolyl and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl, or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is an alkynyl group.

In some embodiments of the invention, X_2 is an alkynyl group, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

In particular embodiments of the invention, X_2 is acetylene, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is CN.

In particular embodiments of the invention, X_2 is CN, and R is 2-(methyl, t-butyl-amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl-amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

In some embodiments of the invention, X_2 is an amine.

In some embodiments of the invention, X_2 is an amine, and R is 2-(methyl, t-butyl-amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl-amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

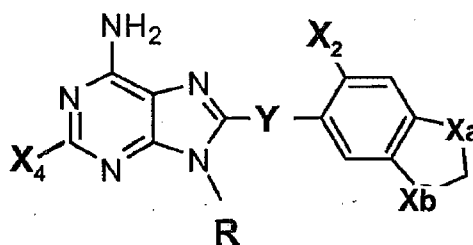
In particular embodiments of the invention, X_2 is dimethyl amine or aziridino, and R is 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-

(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(N-morpholino) propyl or 3-(hydroxyethyl, isopropyl amino) propyl.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1F and 1G.

E. Structures of formula 1A in which Xa or Xb is carbonyl or thiocarbonyl

In accordance with a fifth embodiment of the invention, the compounds have general formula 1A, in which one of Xa or Xb is carbonyl (C=O) or thiocarbonyl (C=S), and Xc and the other of Xa and Xb is CH₂. Thus, the compounds of this embodiment may be represented by the general formula



(2)

wherein:

one of Xa and Xb is C=O or C=S, and the other is -CH₂-;

Y is -CH₂- or -S-;

X₄ is hydrogen or halogen; and

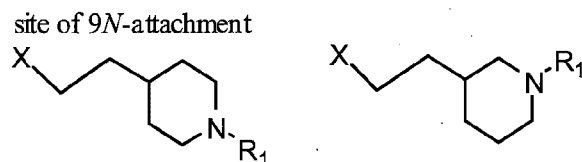
X₂ and R are as discussed below.

In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein (See Table 8), with the proviso that when X₂ is halogen or CN, R does not include a piperidino moiety.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur. In some embodiments, the heteroatom is nitrogen. In these embodiments, R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-aryl, or a

nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl, and 3-(1H-imidazolyl) propyl.

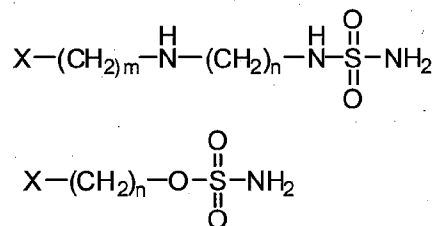
In embodiments of formula (2) within this group when X_2 is thiocarbonyl, R may have the formula:



where R_1 is selected from COH, COMe, COEt, CONPr, COiPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

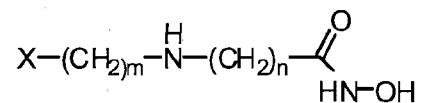
site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In embodiments within this group, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

X_2 may be any substituent shown to be attached at the same position in any of the compounds disclosed in the various patents and patent applications cited above, or as described above in Section B.

In particular embodiments of the invention, X_2 is halogen, and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is an aryl group.

In particular embodiments, X_2 is aryl and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-

(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is a heteroaryl group.

In some embodiments, X_2 is a heteroaryl group and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In particular embodiments, X_2 is 2- or 3-furan and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In particular embodiments, X_2 is 2- or 3-thiophene and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In particular embodiments, X_2 is 3-pyrazolyl and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is an alkynyl group.

In some embodiments of the invention, X_2 is an alkynyl group, and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-

(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, and 3-(1H-imidazolyl) propyl.

In particular embodiments of the invention, X_2 is acetylene, and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is CN.

In particular embodiments of the invention, X_2 is CN, and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, with the proviso that R does not include a piperidino moiety. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl

amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is an amine.

In some embodiments of the invention, X_2 is an amine, and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, and 3-(1H-imidazolyl) propyl.

In particular embodiments of the invention, X_2 is dimethyl amine or aziridino, and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-

(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, and 3-(1H-imidazolyl) propyl.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 1H and 1I.

F. Structures of formula 1A in which Xa, Xb and Xc include at least one non-carbon atom and -Xa-Xc-Xb- includes a double bond

In accordance with a sixth embodiment of the invention, the compounds have general formula 1A, with Xa, Xc, Xb and the bonds between them selected from a combination in the following table:

Xa	Bond	Xc	bond	Xb
C	double	C	single	O
C	double	C	single	N
C	double	C	single	S
O	single	C	double	C
N	single	C	double	C
S	single	C	double	C
N	double	C	single	O
N	double	C	single	S
N	single	C	double	N
O	single	C	double	N
S	single	C	double	N
N	double	N	single	O

N	double	N	single	S
N	double	N	single	C
O	single	N	double	N
N	single	N	double	N
S	single	N	double	N
C	single	N	double	N

Y is -CH₂- or -S-,

X₄ is hydrogen or halogen; and

X₂ and R are as discussed below.

In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen herein or in the various patents and applications cited above. In some embodiments, R includes a nitrogen heteroatom. In further embodiments, R is any of the options discussed above in Section B.

X₂ may be any group shown to be attached at the same position in any of the compounds disclosed in the various patents and patent applications cited above, or as described above in B.

In particular embodiments of the invention, X₂ is halogen, and R is an aminoalkyl (alkylamino) alkyl or (dialkylamino) alkyl.

In particular embodiments, X₂ is halogen and R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-

(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is an aryl group.

In particular embodiments, X_2 is aryl and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is a heteroaryl group.

In some embodiments, X_2 is a heteroaryl group and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-

(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In particular embodiments, X_2 is 2- or 3-furan and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In particular embodiments, X_2 is 2- or 3-thiophene and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is an alkynyl group, and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation

2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In particular embodiments of the invention, X_2 is acetylene, and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is CN.

In particular embodiments of the invention, X_2 is CN, and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-

(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In some embodiments of the invention, X_2 is an amine.

In some embodiments of the invention, X_2 is an amine, and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

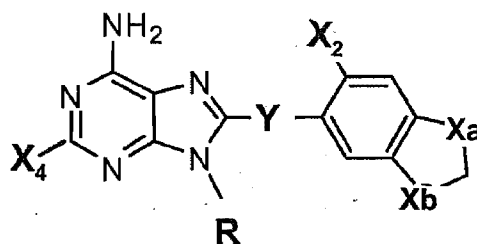
In particular embodiments of the invention, X_2 is dimethyl amine or aziridino, and R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl,

cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 3A-3F.

G. Structures of formula 1A in which Xa and Xb are both O

In accordance with a seventh embodiment of the invention, the compounds have general formula 1A, in which Xa and Xb are O and Xc is CH₂. Thus, the compounds of this embodiment may be represented by the general formula



(2)

wherein:

in which Xa and Xb are O,

Y is -CH₂- or -S-,

X₄ is hydrogen or halogen; and

X₂ and R are in combinations as discussed below.

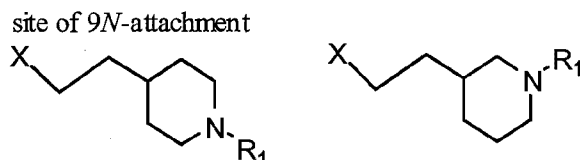
G-I. In some embodiments of the invention, X₂ is an aryl group. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. See Table 8.

In some embodiments within this group, R includes a heteroatom, such as nitrogen, oxygen or sulfur.

In some embodiments, the heteroatom is nitrogen. In some of these embodiments, R is suitably a primary amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-

butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(*t*-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(*N*-morpholino) propyl, and 3-(1*H*-imidazolyl) propyl.

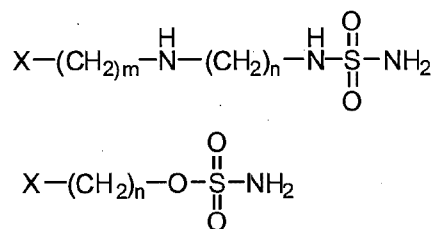
In embodiments of formula (2) within this group, R has the formula:



where R₁ is selected from COH, COMe, COEt, CO*n*Pr, CO*i*Pr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

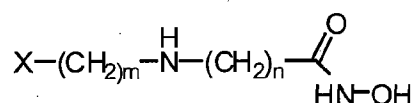
site of 9*N*-attachment



where *m* = 2-3 and *n* = 1-6.

In embodiments within this group, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is a heterocycle.

In specific embodiments, X_2 is phenyl, furan, thiophene, pyrazole, imidazole, thiazole, oxazole or pyrrole.

In specific embodiments of the X_2 is phenyl, furan, methylfuran, thiophene, pyrazole, thiazole, oxazole or imidazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-, 3- furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is optionally substituted phenyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is optionally substituted phenyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is optionally substituted phenyl.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is optionally substituted phenyl.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is optionally substituted pyridine.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is optionally substituted pyridine.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is optionally substituted pyridine.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is optionally substituted pyridine.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is optionally substituted isooxazole.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is optionally substituted isooxazole.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is optionally substituted isooxazole.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is optionally substituted isooxazole.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is optionally substituted imidazole.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is optionally substituted imidazole.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is optionally substituted imidazole.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is optionally substituted imidazole.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 4A, 4C, 4D, 4F, 4G and 4H. As shown, in preferred embodiments of formula (2) in which X₂ is an aryl group, X₄ is H, chlorine or fluorine.

Table 2G shows measured values for EC₅₀ in JNPL3 brain cell lysates and in SKBr3 cell lysate for compounds 4A-1 to 4A-8, 4C1 to 4C-11, 4C14, 4C-16, 4C-38 to 4C-41, 4D-1 to 4D-3, 4D-16, 4D-17, 4F-1, 4G-1 to 4G-7, 4G-9, 4H-1 to 4H-7 in accordance with this embodiment of the invention which incorporates a hydrogen as X₄ and in which Y is S or a fluorine as X₄ and in which Y is -CH₂-. Desirably low values of EC₅₀ were observed for several examples.

G-II. In some embodiments of the invention, X₂ is an alkynyl group. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. See Table 8.

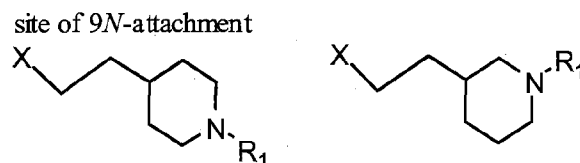
In some embodiments, when X₂ is alkynyl, R includes a nitrogen heteroatom.

In a further embodiment, when X₂ is alkenyl, R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl.

Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-

(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

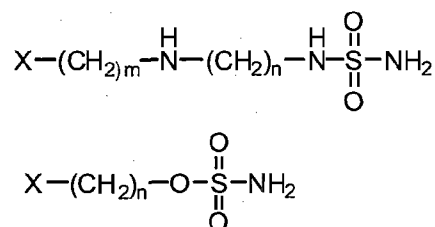
In embodiments of formula (2) when X_2 is alkynyl, R has the formula:



where R_1 is selected from COH, COMe, COEt, CONPr, COiPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention when X_2 is alkynyl, R has the formula

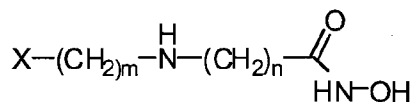
site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In embodiments when X_2 is alkynyl, R has the formula

site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is acetylene.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is acetylene.

In particular embodiments of formula (2), Y is CH₂, X_4 is Cl, X_2 is acetylene.

In particular embodiments of formula (2), Y is CH₂, X_4 is F, X_2 is acetylene.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is acetylene.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 4B. As shown, in preferred embodiments of formula (2) in which X_2 is an alkynyl group, X_4 is H, chlorine or fluorine.

Table 2H shows measured values for EC_{50} in JNPL3 brain cell lysates and in SKBr3 cell lysate for compounds 4B-1 to 4B-4, 4B13 and 4B-14 in accordance with this embodiment of the invention which incorporates a hydrogen as X_4 and in which Y is S, or a fluorine as X_4 and in which Y is $-CH_2-$. Desirably low values of EC_{50} were observed.

G-III. In some embodiments of the invention, X_2 is a cyano or cyanoalkyl group. In these embodiments, R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

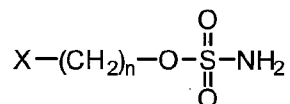
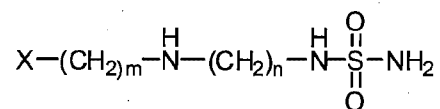
In a particular preferred embodiment of formula (2), Y is S, X_4 is H, X_2 is CN.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is Cl, X_2 is CN.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is F, X_2 is CN.

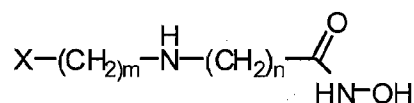
In a particular preferred embodiment of formula (2), Y is S, X_4 is F, X_2 is CN.

In other embodiments in which X_2 is cyano or cyanoalkyl group, R is site of 9*N*-attachment



where $m=2-3$ and $n=1-6$, or

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

A specific example of a compound in accordance with this embodiment of the invention is listed in Table 4E.

Table 2I shows measured values for EC_{50} in JNPL3 brain cell lysates and in SKBr3 cell lysate for compounds (4E-1 to 4E-4) in accordance with this embodiment of the invention which incorporates a hydrogen as X_4 and in which Y is S or a fluorine as X_4 and in which Y is $-CH_2-$. Desirably low values of EC_{50} were observed for several examples.

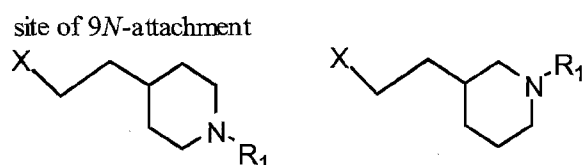
G-IV. In some embodiments of the invention, X_2 is a cycloalkyl (saturated carbocyclic) or cycloalkenyl. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. (See Table 8)

In some embodiments within this group, R includes a nitrogen heteroatom.

In a further embodiment within this group, R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-

(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

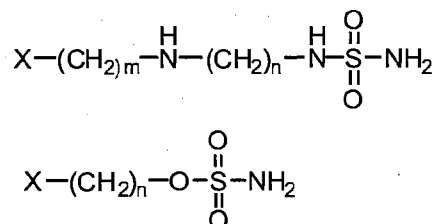
In embodiments of formula (2) within this group, R has the formula:



where R_1 is selected from COH, COMe, COEt, CONPr, COiPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention within this group, R has the formula

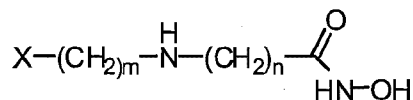
site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In embodiments when X_2 is aryl, R has the formula

site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is a cycloalkyl with one ring.

In specific embodiments, X_2 is a cyclopropane, cyclobutane or cyclopentane.
In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is cyclopentyl.
In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is cyclopentyl.
In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is cyclopentyl.
In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is cyclopentyl.
In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds of this type are shown in Table 4I.

Table 2J shows measured values for EC_{50} in JNPL3 brain cell lysates and in SKBr3 cell lysate for compound 4I-12 in accordance with this embodiment of the invention which incorporates a hydrogen as X_4 and in which Y is S. Desirably low values of EC_{50} were observed for several examples.

Table 2G shows results for EC_{50} measured in SKBr3 breast cancer cells and JNPL3 brain cell lysates for compounds listed in Table 4A. As shown, compounds of this type are generally more active with respect to brain cancer cells. As shown, the greatest activity was observed for compound 4A-1, in which there is no substituent on the X_2 phenyl group, and the least activity is seen for compounds 4A-3 and 4A-4 in which electron withdrawing CF_3 substituents are at the meta positions.

An embodiment of the invention therefore has the structure (2) shown above, in which Y is S, X_4 is hydrogen, X_2 is phenyl, optionally substituted at the para position, and R includes a nitrogen heteroatom, and therefore is an alkylamino, an (alkylamino) alkyl or (dialkylamino) alkyl. Preferred R groups of this type are as listed above.

Examples of compounds within this seventh embodiment of the invention, in which X_2 is alkynyl are shown in Table 4B. Table 2H shows results for EC_{50} for Hsp90 binding in JNPL3 brain cell lysates. As shown, all of the compounds tested were active, however, those with an acetylene substituent, such as 4B-1, 4B-4, 4B-13 and 4B-14, were most active.

Examples of compounds within this seventh embodiment of the invention, in which X_2 is an aryl group containing an oxygen atom are shown in Table 4C. Specific suitable substituent groups are 2-furanyl, 3-furanyl and 5-methyl-2-furanyl.

Table 2G shows results for EC_{50} for Hsp90 binding in SKBr3 breast cancer cells and JNPL3 brain cell lysates for some of the compounds shown in Table 4C. All of the

compounds show good activity in both experimental systems. In Table 4C, compound 4C-11 has X_2 = isoxazole, whereas 4C-11, 4C-38 and 4C-39 have X_2 = oxazolyl, including both a nitrogen and an oxygen. Compounds with X_2 = 2-oxazolyl (4C-38 and 4C-39) were more active than those with X_2 = iso-oxazolyl (4C-11).

Examples of compounds within this seventh embodiment of the invention, in which X_2 is an aryl group containing a sulfur atom in the aryl ring are shown in Table 4D. Table 2G shows results for EC_{50} for Hsp90 binding in SKBr3 breast cancer cells and JNPL3 brain cell lysates for some of the compounds shown in Table 4D. All of the compounds show good activity in both experimental systems. In Table 4D, compounds 4D-16 and 4D-17 have X_2 = 2-thiazolyl, including both a nitrogen and an oxygen.

Examples of compounds within this seventh embodiment of the invention, in which X_2 is -CN or cyanoalkyl are shown in Table 4E. Table 2I shows results for EC_{50} for Hsp90 binding in JNPL3 brain cell lysates for the two -CN compounds shown in Table 4E. Both of the compounds show good activity in both experimental systems.

An example of a compound within this seventh embodiment of the invention, in which X_2 is a 6-membered aryl ring containing a nitrogen atom in the aryl ring, with the proviso that there is not also an oxygen in the ring, is shown in Table 2 (labeled as 4F-1). In Compound 4F-1, X_2 is 4-pyridinyl. X_2 could also be 2-pyridinyl, 3-pyridinyl, or pyrazinyl, 4-pyrimidinyl, 5-pyrimidinyl, 3-pyridazinyl or 4-pyridazinyl.

EC_{50} for Hsp90 binding in SKBr3 breast cancer cells and JNPL3 brain cells were determined for compound 4F-1 to be 9,620 nM and 4,120 nM, respectively.

Examples of compounds within this seventh embodiment of the invention, in which X_2 is a 5-membered aryl rings containing 2 nitrogens in the ring are shown in Table 4G. The specific X_2 groups shown are 3-, 4- and 5-pyrazolyl. Other examples of X_2 groups in this category are 4- or 5-imidazolyl.

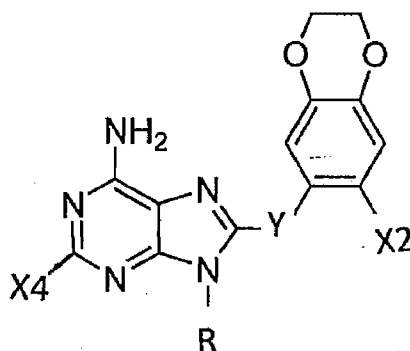
EC_{50} for Hsp90 binding in SKBr3 breast cancer cells and JNPL3 brain cell lysates were determined for some of the compounds listed in Table 4G. The results are summarized in Table 2K. Particularly good results were observed for compounds 4G-3, 4G-6 and 4G-9 in which the substituent is a 3-pyrazolyl.

Examples of compounds within this seventh embodiment of the invention, in which X_2 is a pyrrolyl group are shown in Table 4H. The specific X_2 groups shown are 2 or 3-pyrrolyl.

EC_{50} for Hsp90 binding in SKBr3 breast cancer cells and JNPL3 brain cell lysates were determined for some of the compounds listed in Table 4H. The results are summarized in Table 2L.

H. Structures of formula 1B in which X_a and X_b are O

In accordance with an eighth embodiment of the invention, the compounds have general formula 1B, in which both X_a and X_b are O, and X_c and X_d are CH_2 . Thus, compounds of this embodiment are represented by the formula:



(3)

wherein

Y is $-CH_2-$, $-O-$ or $-S-$;

X_4 is hydrogen or halogen; and

X_2 and R are as discussed below.

H-I. In some embodiments of compounds in accordance with formula (3), X_2 is halogen. In these embodiments, R is suitably an amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, with the proviso that R does not include a piperidino moiety.

Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In specific embodiments of the invention, X₂ is I.

In particular embodiments of the invention X₂ is I, Y is S and X₄ is H.

Specific examples of compounds within this group are shown in Table 5A.

Examples of compounds within this group, in which X₂ is a halogen, are shown in Table 5A (5A-1 to 5A-19). Table 2M shows EC₅₀ values for binding of Hsp90 in JNPL3 brain cells for some of the compounds of Table 5A. All show values of less than 100 nM.

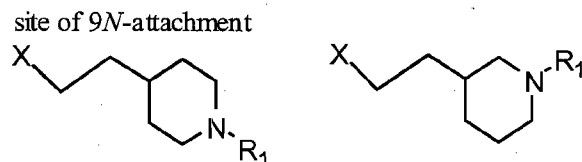
H-II. In some embodiments of compounds in accordance with formula (3), X₂ is aryl. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen in this application, or in the various patents and patent applications cited herein. See Table 8.

In some embodiments, when X₂ is aryl, R includes a nitrogen heteroatom.

In these embodiments, R is suitably an amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino)

propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

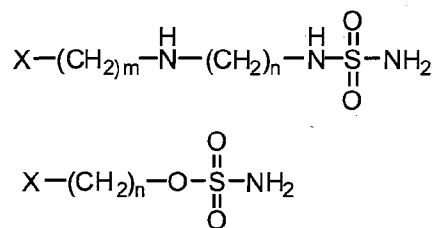
In embodiments of formula (2) when X_2 is aryl, R has the formula:



where R_1 is selected from COH, COMe, COEt, CONPr, COiPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention when X_2 is aryl, R has the formula

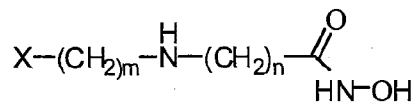
site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In embodiments when X_2 is aryl, R has the formula

site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is an aromatic heterocycle.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, pyrrole, oxazole or thiazole.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, oxazole or thiazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-, 3- furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In these particular embodiments, R may be any one of the types of groups described above.

Examples of compounds in which X₂ is an aryl group containing an oxygen atom in the aryl ring, are shown in Table 5B.

Table 2N shows measured values for EC₅₀ in JNPL3 brain cell lysates for compounds 5B-1, 5B-7, 5B-33 and 5B-34 in accordance with this embodiment of the invention which incorporates a fluorine as X₄ and in which Y is -CH₂- or a hydrogen as X₄ and in which Y is S. Desirably low values of EC₅₀ were observed.

Examples of compounds in which X₂ is an aryl group containing a sulfur atom in the aryl ring are shown in Table 5C.

Examples of compounds in which X₂ is a 5-membered aryl rings containing 2 nitrogens in the ring are shown in Table 5D.

Table 2O shows measured values for EC₅₀ in JNPL3 brain cell lysates for compounds 5D-2 and 5D-4 in accordance with this embodiment of the invention which incorporates a fluorine as X₄ and in which Y is -CH₂- or a hydrogen as X₄ and in which Y is S. Desirably low values of EC₅₀ were observed.

An embodiment of the invention has the structure shown in formula (3), in which Y is -CH₂- or S, X₄ is hydrogen or fluorine, X₂ is a pyrazolyl, particularly a 3-pyrazolyl, or an imidazolyl. Preferred R groups of this type are as listed above.

H-III. In some embodiments of the invention, X₂ is an alkynyl group. In these embodiments, R may be as described above in Section H-II.

In specific embodiments, X₂ is acetylene.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is acetylene.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is acetylene.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is acetylene.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is acetylene.

In these particular embodiments, R may be any one of the types of groups described above.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Tables 5E. As shown, in preferred embodiments of formula (2) in which X₂ is an alkynyl group, X₄ is H, chlorine or fluorine.

H-IV. In some embodiments of the invention, X₂ is a cyano group. In these embodiments, R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, with the proviso that R does not contain a piperidino moiety. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In a particular preferred embodiment of formula (2), Y is S, X₄ is H, X₂ is CN.

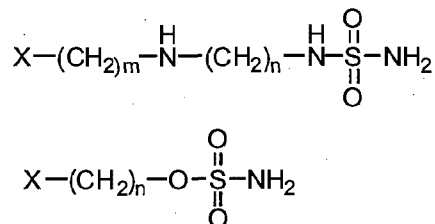
In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is Cl, X₂ is CN.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is F, X₂ is CN.

In a particular preferred embodiment of formula (2), Y is S, X₄ is F, X₂ is CN.

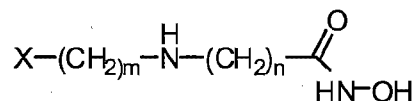
In other embodiments in which X₂ is cyano or cyanoalkyl group, R is

site of 9N-attachment



where $m=2-3$ and $n=1-6$, or

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

Specific examples of compounds in accordance with this embodiment of the invention are listed in Table 5F.

H-V. In some embodiments of the invention, X_2 is an amino group. In these particular embodiments, R may be any of the R groups described in Section H-II.

In a particular preferred embodiment of formula (2), Y is S, X_4 is H, X_2 is azetidino.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is Cl, X_2 is azetidino.

In a particular preferred embodiment of formula (2), Y is CH_2 , X_4 is F, X_2 is azetidino.

In a particular preferred embodiments of formula (2), Y is S, X_4 is F, X_2 is azetidino.

A specific examples of a compounds in accordance with this embodiment of the invention is listed in Table 5G

H-VI. In some embodiments of the invention, X_2 is a cycloalkyl or cycloalkenyl. In these particular embodiments, R may be any of the R groups described in Section H-II.

In specific embodiments, X_2 is a cycloalkyl with one ring.

In specific embodiments, X_2 is a cyclopropane, cyclobutane or cyclopentane.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is cyclopentyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is cyclopentyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is cyclopentyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is cyclopentyl.

A specific examples of a compounds in accordance with this embodiment of the invention is listed in Table 5H

I. Structures of formula 1B in which Xa and/or Xb is a heteroatom, but not both O

In accordance with a ninth embodiment of the invention, the compounds have general formula 1B, in which one or both of Xa or Xb is a heteroatom such as O, N or S, with the proviso that both of Xa and Xb are not O (see Section H). Specific examples of compounds within this group are shown in Table 6A.

I-I. In some embodiments of compounds in accordance with formula (3), X₂ is halogen. In these embodiments, R is suitably an amino-alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, with the proviso that R is not a piperidino moiety.

Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino)-propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In specific embodiments of the invention, X₂ is I.

In particular embodiments of the invention X₂ is I, Y is S and X₄ is H.

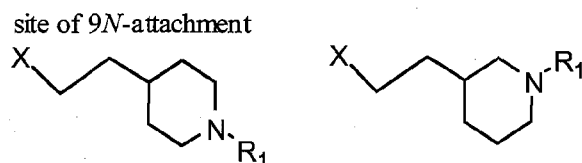
I-II. In some embodiments of compounds in accordance with formula (3), X₂ is aryl.

In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen herein or in the various patents and applications cited above. See Table 8.

In some embodiments, when X₂ is aryl, R includes a nitrogen heteroatom.

In these embodiments, R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, aryl-alkyl, or a nonaromatic heterocycle-alkyl. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

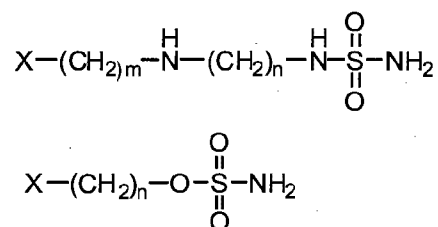
In embodiments of formula (2) when X_2 is aryl, R has the formula:



where R_1 is selected from COH, COMe, COEt, CONPr , COiPr , SO_2Me , CH_2OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention when X_2 is aryl, R has the formula

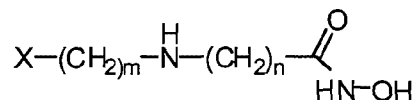
site of 9N-attachment



where $m=2-3$ and $n=1-6$.

In embodiments when X_2 is aryl, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In specific embodiments, X_2 is an aromatic heterocycle.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, pyrrole, oxazole or thiazole.

In specific embodiments, X_2 is a furan, thiophene, pyrazole, imidazole, oxazole or thiazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-, 3- furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2-, 3-furan or 5-methyl-2-furanyl.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- thiophene.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-thiophene.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2- or 3- pyrazole.

In particular embodiments of formula (2), Y is CH_2 , X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is F, X_2 is 2- or 3-pyrazole.

In particular embodiments of formula (2), Y is S, X_4 is H, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH_2 , X_4 is Cl, X_2 is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl or 5-methyl-2-oxazolyl.

In these particular embodiments, R may be any one of the types of groups described above.

I-III. In some embodiments of the invention, X₂ is an alkynyl group. In these embodiments, R may be as described above in Section I-II.

In specific embodiments, X₂ is acetylene.

In particular embodiments of formula (2), Y is S, X₄ is H, X₂ is acetylene.

In particular embodiments of formula (2), Y is CH₂, X₄ is Cl, X₂ is acetylene.

In particular embodiments of formula (2), Y is CH₂, X₄ is F, X₂ is acetylene.

In particular embodiments of formula (2), Y is S, X₄ is F, X₂ is acetylene.

In these particular embodiments, R may be any one of the types of groups described above.

I-IV. In some embodiments of the invention, X₂ is a cyano group. In these embodiments, R is suitably an amino alkyl, a secondary or tertiary alkyl-amino-alkyl, a trialkylammonioalkyl group, an aryl-alkyl, or a nonaromatic heterocycle-alkyl, with the proviso that R does not include a piperidino moiety. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl

amino) propyl, 3-(*t*-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(*N*-morpholino) propyl and 3-(1*H*-imidazolyl) propyl.

In a particular preferred embodiment of formula (2), Y is S, X₄ is H, X₂ is CN.

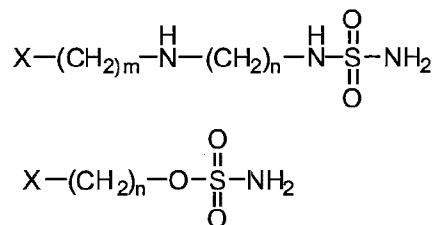
In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is Cl, X₂ is CN.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is F, X₂ is CN.

In a particular preferred embodiment of formula (2), Y is S, X₄ is F, X₂ is CN.

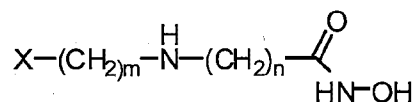
In other embodiments in which X₂ is cyano or cyanoalkyl group, R is

site of 9*N*-attachment



where m= 2-3 and n= 1-6, or

site of 9*N*-attachment



where m= 2-3 and n= 1-6.

I-V. In some embodiments of the invention, X₂ is an amino group. In these particular embodiments, R may be any of the R groups described in Section I-II.

In a particular preferred embodiment of formula (2), Y is S, X₄ is H, X₂ is aziridino.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is Cl, X₂ is aziridino.

In a particular preferred embodiment of formula (2), Y is CH₂, X₄ is F, X₂ is aziridino.

In a particular preferred embodiment of formula (2), Y is S, X₄ is F, X₂ is aziridino.

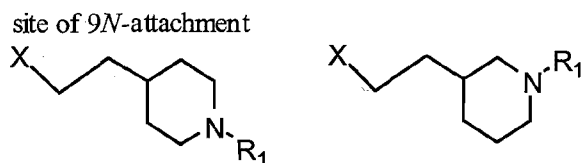
J. Structures of formula 1B in which Xa, Xc, Xd and Xb are all carbon

In accordance with a tenth embodiment of the invention, the compounds have general formula 1B, in which Xa, Xc, Xd and Xb are all carbon connected by single or double bonds. In these embodiments, R may be any of the groups disclosed as a substituent at the 9-position nitrogen herein or in the various patents and applications cited above. (See Table 8)

In some embodiments, when X₂ is aryl, R includes a nitrogen heteroatom.

In these embodiments, R is suitably an aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, or trialkylammonioalkyl group, in which each alkyl portion may be linear, cyclic or branched, or an alkyl heterocycle, where the alkyl may be bonded to a nitrogen in the heterocyclic group. Specific R groups include without limitation 2-(methyl, t-butyl-amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl-amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

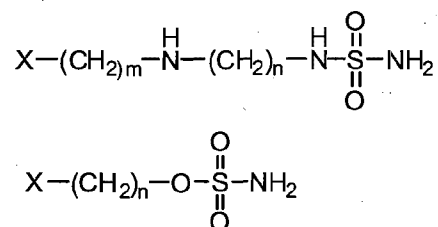
In embodiments of formula (2) when X₂ is aryl, R has the formula:



where R₁ is selected from COH, COMe, COEt, CO_nPr, CO_iPr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of the invention when X_2 is aryl, R has the formula

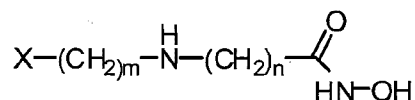
site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In embodiments when X_2 is aryl, R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

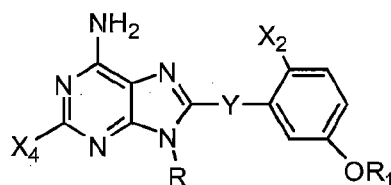
Specific examples of compounds within this embodiment of the invention are shown in Table 6B.

Table 2P shows measured values for EC_{50} in JNPL3 brain cell lysates for compounds 6B-25 in accordance with this embodiment of the invention which incorporates a hydrogen as X_4 and in which Y is S. Desirably low values of EC_{50} were observed.

K. Structures of formula 1C

In some embodiments of the present invention having the general formula 1C, the compounds of the invention can be represented by the general formula:

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(4)

in which

R1 is alkyl, for example methyl or ethyl,

Y is S or CH₂,

X₄ is H or halogen,

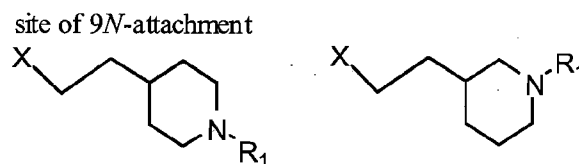
X₂ is saturated or unsaturated non-aromatic carbocycle or heterocycle, aryl, alkylamino, dialkylamino, alkynyl or part of a ring formed by R; and

R is hydrogen, alkyl, alkenyl, or alkynyl, linear, branched or cyclic, optionally including heteroatoms such as N, S or O, optionally connected to the 2'-position to form an 8 to 10 member ring.

In some embodiments, R is suitably an alkylaminoalkyl, dialkylaminoalkyl, or trialkylammonioalkyl group, in which each alkyl portion may be linear, cyclic or branched, or an alkyl heterocycle, where the alkyl may be bonded to a nitrogen in the heterocyclic group. Specific R groups include without limitation 2-(methyl, t-butyl- amino) ethyl, 2-(methyl, isopropyl amino) ethyl, 3-(neopentyl amino) propyl, 2-(isobutyl-amino) ethyl, 2-(ethyl, isopropyl amino) ethyl, 3-(isopropyl amino) propyl, 3-(t-butyl- amino) propyl, 2-(isopropyl amino) ethyl, 2-(hydroxyethyl, isopropyl amino) ethyl, 3-(cyclopentylamino) propyl, 3-(cyclopentyl, methyl amino) propyl, 3-(ethylamino) propyl, 3-(ethyl, methyl amino) propyl, 2-(neopentyl amino) ethyl, 3-(methyl, isopropyl amino) propyl, 3-(ethyl, isopropyl amino) propyl, 3-(hydroxyethyl, isopropyl amino) propyl, 3-(methyl, propargyl amine) propyl, 2-(methyl, propargyl amine) ethyl, 3-(allyl, methyl amino) propyl, 3-(propyl, cyclopropylmethyl amino) propane, 3-(hydroxyethyl, cyclohexyl amino) propyl, 2-(cyclopropylmethyl amino) ethyl, 2-(methyl, isobutyl amino) ethyl, 3-(N-morpholino) propyl and 3-(1H-imidazolyl) propyl.

In embodiments of formula (3), R has the formula:

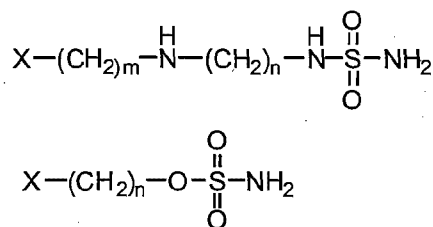
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where R_1 is selected from COH, COMe, COEt, CO n Pr, CO i Pr, SO₂Me, CH₂OX where X can be H or oxygen, nitrogen, sulphur or halogen containing alkyl of linear, branched or cyclic nature.

In embodiments of formula (3), R has the formula

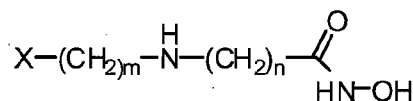
site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In embodiments of formula (3) R has the formula

site of 9*N*-attachment



where $m=2-3$ and $n=1-6$.

In some embodiments, X_2 is alkynyl, such as acetylene. Examples of such structures are shown in Table 7A

In some embodiments, X_2 is cyano or cyanomethyl. Examples of such structures are shown in Table 7B.

In some embodiments, X_2 is a heterocycle, including without limitation aziridine, azetidine, oxetane, thietane, tetrahydrofuran, tetrahydropyrrole, tetrahydrothiophane, imidazolidine, oxazolidine, thiazolidine, azirine, oxirine, pyrroline, pyrrole, dihydrofuran, furan, dihydrothiophene, thiophene, pyrazole, imidazole, oxazole, isoxazole, thiazole, isothiazole, 1,2,3-triazole, 1,2,4-triazole, dithiazole, tetrazole, pyridine, pyran, thiine, diazine, thiazine, dioxin, triazine, tetrazine. Examples of such structures are shown in Tables 7C-7F.

Table 2Q shows measured values for EC₅₀ in JNPL3 brain and SKBr3 cell lysates for compounds (7A-20, 7C-13, 7D-3 and 7E-6) in accordance with this embodiment of the invention which incorporates a hydrogen as X₄ and in which Y is S. Desirably low values of EC₅₀ were observed, although X₂ = -OCH₃ was observed to be less active than X₂ = -O-CH₂-O- in every shown instance: 4C-5 vs 7C-13 (6.5 nM vs 84nM), 4D-3 vs 7D-3 (18.5nM vs 240nM) and 4G-9 vs 7E-6 (5.5nM vs 32nM).

L. Structures in which X₂ is alkynyl

In accordance with a further aspect of the present invention, compounds are provided in accordance with any of formulas (1A), (1B) or (1C) in which X₂ is alkynyl. In these compounds,

Y is CH₂, S, O, C=O, C=S, N or any other linking group disclosed in a compound with the same scaffold structure herein or in the patents and patent applications cited above;

X₄ is H or halogen or any other group disclosed at this position in a compound with the same scaffold structure herein or in the patents and patent applications cited above;

X_a, X_b, X_c and X_d are any group(s) disclosed at this position herein or in the patents and patent applications cited above; and

R is any R group disclosed at this position of the same scaffold structure herein or in the patents and patent applications cited above. (See Table 8)

In some embodiments, Z₁, Z₂, and Z₃ are all nitrogen.

In some embodiments, Z₁ and Z₃ are nitrogen and Z₂ is carbon.

In some embodiments, Z₃ is carbon.

M. Structures in which X₂ is Furan, Thiophene, Pyrazole, Oxazole or Thiazole

In accordance with a further aspect of the present invention, compounds are provided in accordance with any of formulas (1A), (1B) or (1C) in which X₂ is a furan, thiophene, 3-pyrazole, oxazole or thiazole. In these compounds,

Y is CH₂, S, O, C=O, C=S, N or any other linking group disclosed in a compound with the same scaffold structure herein or in the patents and patent applications cited above;

X₄ is H or halogen or any other group disclosed at this position in a compound with the same scaffold structure herein or in the patents and patent applications cited above;

X_a, X_b, X_c and X_d are any group(s) disclosed at this position herein or in the patents and patent applications cited above; and

R is any R group disclosed at this position of the same scaffold structure herein or in the patents and patent applications cited above.

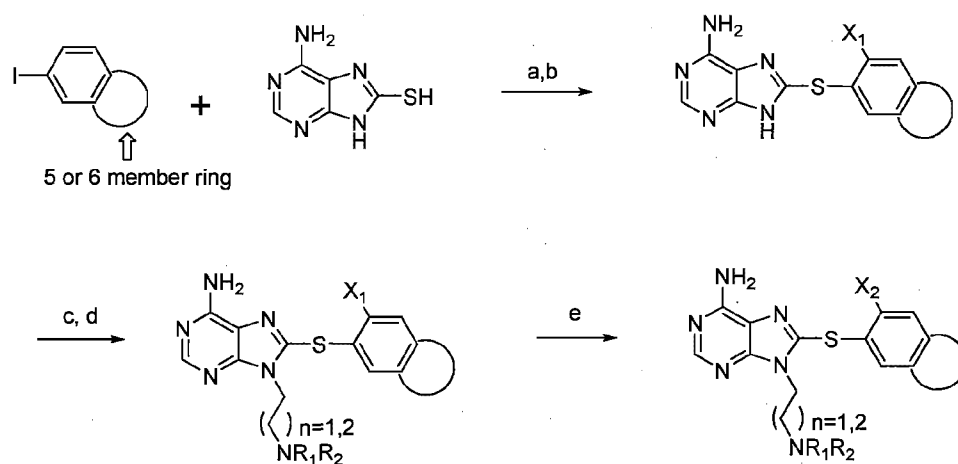
In some embodiments, Z1, Z2, and Z3 are all nitrogen.

In some embodiments, Z1 and Z3 are nitrogen and Z2 is carbon.

In some embodiments, Z3 is carbon.

Synthetic Methods

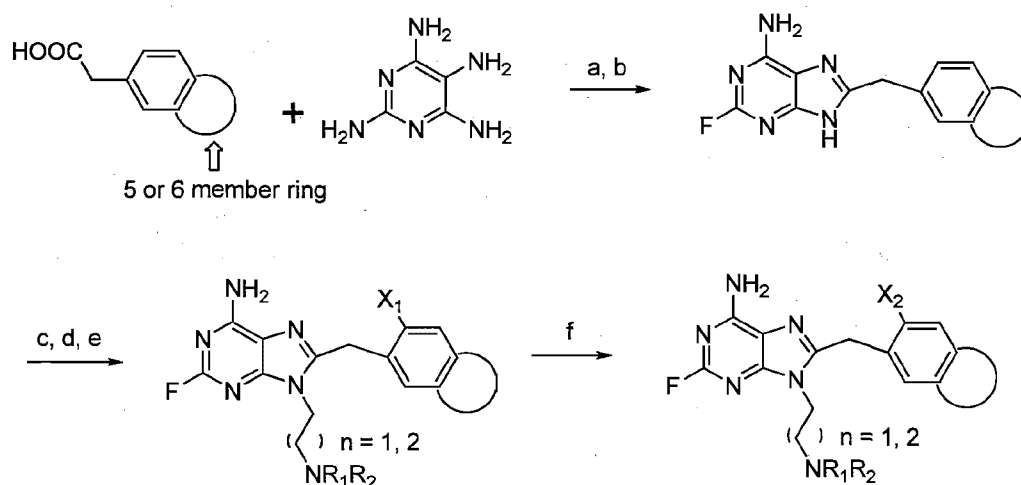
Compounds in accordance with formulas (1A) and (1B) can be made through the application of the following methodologies.



(a) CuI, neocuproine, NaOt-Bu, DMF, 110 °C; (b) NIS, acetonitrile, RT; (c) Cs₂CO₃, 1,2-dibromoethane or 1,3-dibromopropane; (d) HNR₁R₂, DMF, rt; (e) X₂M, Pd (cat.), DMF, 50-100 °C.

Scheme 1.

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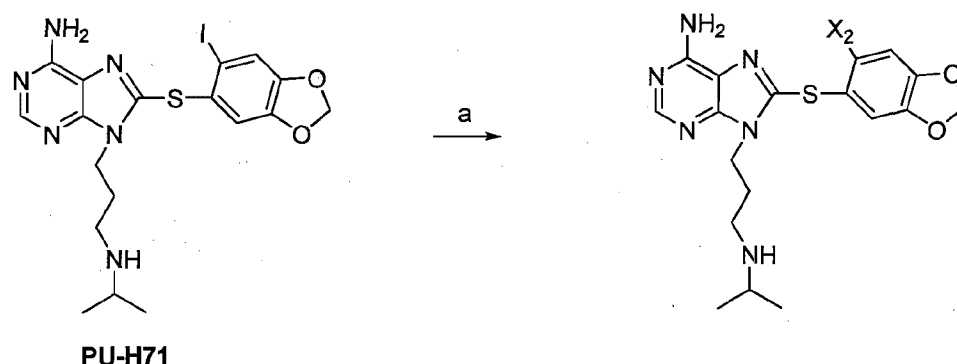
(a) triphenyl phosphite, pyridine, microwave; (b) HF-pyridine, NaNO₂; (c) NIS, acetonitrile, rt; (d) Cs₂CO₃, 1,2-dibromoethane or 1,3-dibromopropane; (e) HNR₁R₂, DMF, rt; (f) X₂M, Pd (cat.), DMF, 50-100 °C.

Scheme 2.

General Methods: ¹H and ¹³C 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 = multiplet), coupling constant (Hz), integration. ¹³C 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) using a gradient of; method A (a) H₂O + 0.1% TFA and (b) CH₃CN + 0.1% TFA, 5 to 95% b over 10 minutes at 1.2 mL/min; method B (a) H₂O + 0.1% TFA and (b) CH₃CN + 0.1% TFA, 20 to 90% b over 16 minutes at 1.0 mL/min. Column chromatography was performed using 230-400 mesh silica gel (EMD).

Specific compounds were synthesized as follows;

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Reagents and conditions: (a) RB(OH)_2 , $\text{PdCl}_2(\text{PPh}_3)_2$, NaHCO_3 , H_2O , DMF, 90°C .

Scheme 3. Suzuki coupling of PU-H71.

9-(3-(isopropylamino)propyl)-8-(6-phenylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ2-388]. Phenylboronic acid (10.7 mg, 0.0876 mmol) was added to PU-H71 (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (0.5 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 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 19.8 mg (73%) of **DZ2-388**. ^1H NMR (500 MHz, MeOH- d_4) δ 8.14 (s, 1H), 7.28-7.34 (m, 3H), 7.17-7.21 (m, 2H), 7.12 (s, 1H), 6.90 (s, 1H), 6.09 (s, 2H), 4.03 (t, $J = 6.4$ Hz, 2H), 3.27 (septet, $J = 6.6$ Hz, 1H), 2.72 (t, $J = 6.6$ Hz, 2H), 2.13 (m, 2H), 1.40 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (125 MHz, MeOH- d_4) δ 156.0, 153.4, 152.1, 151.1, 150.3, 149.4, 142.3, 141.8, 130.4, 129.1, 128.7, 120.3, 119.8, 115.7, 112.2, 103.8, 52.2, 43.2, 41.1, 27.6, 19.3; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{24}\text{H}_{27}\text{N}_6\text{O}_2\text{S}$, 463.1916; found 463.1905; HPLC: method A $R_t = 6.50$, method B $R_t = 7.40$.

8-(6-(4-*tert*-butylphenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ2-390]. 4-*tert*-Butylphenylboronic acid (15.6 mg, 0.0876 mmol) was added to PU-H71 (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (0.5 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This

was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 3 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 4:5:2:1) to give 25.0 mg (83%) of **DZ2-390**. ¹H NMR (500 MHz, MeOH-*d*₄) δ 8.11 (s, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.14 (s, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.86 (s, 1H), 6.06 (s, 2H), 3.93 (t, *J* = 6.9 Hz, 2H), 2.92 (septet, *J* = 6.5 Hz, 1H), 2.61 (t, *J* = 7.3 Hz, 2H), 1.86 (m, 2H), 1.28 (s, 9H), 1.12 (d, *J* = 6.5 Hz, 6H); ¹³C NMR (125 MHz, MeOH-*d*₄) δ 155.9, 153.3, 151.9, 151.8, 150.9, 150.2, 149.2, 141.9, 138.8, 130.0, 125.9, 120.4, 120.3, 115.4, 112.3, 103.6, 50.6, 44.0, 41.8, 35.4, 31.8, 29.3, 21.1; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₈H₃₅N₆O₂S, 519.2542; found 519.2545; HPLC: method A R_t = 7.43, method B R_t = 9.45.

8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ2-391]. 3,5-

Bis(trifluoromethyl)phenylboronic acid (22.6 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (0.5 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 3 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 4:5:2:1) to give 24.4 mg (70%) of **DZ2-391**. ¹H NMR (500 MHz, CDCl₃) δ 8.22 (s, 1H), 7.79 (s, 3H), 7.12 (s, 1H), 6.86 (s, 1H), 6.09 (s, 2H), 5.71 (br s, 2H), 4.07 (t, *J* = 6.6 Hz, 2H), 2.82 (septet, *J* = 6.2 Hz, 1H), 2.49 (t, *J* = 6.5 Hz, 2H), 1.95 (m, 2H), 1.12 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 154.1, 152.3, 151.5, 149.6, 148.6, 147.5, 142.1, 137.2, 131.2 (q, *J* = 33 Hz), 129.6, 123.1 (q, *J* = 270 Hz), 121.3, 119.6, 119.4, 114.9, 110.8, 102.4, 49.5, 42.8, 40.6, 28.8, 21.7; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₆H₂₅F₆N₆O₂S, 599.1664; found 599.1653; HPLC: method A R_t = 7.45, method B R_t = 9.38.

8-(6-(4-(dimethylamino)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ2-392]. 4-(Dimethylamino)phenylboronic acid (14.5 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 3 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 4:5:2:1) to give 25.3 mg (85%) of **DZ2-392**. ¹H NMR (500 MHz, CDCl₃) δ 8.24 (s, 1H), 7.13 (d, *J* = 8.7 Hz, 2H), 6.93 (s, 1H), 6.83 (s, 1H), 6.67 (d, *J* = 8.7 Hz, 2H), 6.01 (br s, 2H), 5.98 (s, 2H), 4.02 (t, *J* = 6.7 Hz, 2H), 2.97 (s, 6H), 2.78 (septet, *J* = 6.3 Hz, 1H), 2.44 (t, *J* = 6.7 Hz, 2H), 1.87 (m, 2H), 1.10 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 154.4, 152.4, 151.5, 149.9, 148.5, 148.0, 147.1, 139.6, 130.0, 127.8, 120.5, 119.7, 112.8, 111.7, 111.0, 101.7, 49.3, 43.1, 40.9, 40.4, 28.9, 21.9; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₆H₃₂N₇O₂S, 506.2338; found 506.2330; HPLC: method A R_t = 5.72, method B R_t = 5.12.

9-(3-(isopropylamino)propyl)-8-(6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ2-395]. 2-Thienylboronic acid (11.2 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 12.5:1) to give 12.4 mg (45%) of **DZ2-395**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.17 (s, 1H), 7.33 (dd, *J* = 1.4, 4.9 Hz, 1H), 7.07 (s, 1H), 7.04 (s, 1H), 7.00-7.02 (m, 2H), 6.09 (s, 2H), 4.12 (t, *J* = 6.6 Hz, 2H), 2.95 (septet, *J* = 6.6 Hz, 1H), 2.62 (t, *J* = 6.8 Hz, 2H), 2.00 (m, 2H), 1.19 (d, *J* = 6.6 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.2, 152.0, 151.1, 149.4, 148.8, 148.4, 140.5, 132.9, 127.8, 126.9, 126.3, 119.2, 119.0, 114.6,

111.8, 102.3, 49.6, 42.5, 40.6, 27.8, 20.7; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{22}H_{25}N_6O_2S_2$, 469.1480; found 469.1461; HPLC: method A R_t = 6.38, method B R_t = 7.18.

8-(6-(furan-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-4]. 2-Furanylboric acid (9.8 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and $NaHCO_3$ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $Pd(PPh_3)_2Cl_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 3.5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 12.5:1) to give 19.1 mg (72%) of **DZ3-4**. ^1H NMR (500 MHz, $CDCl_3$ /MeOH- d_4) δ 8.18 (s, 1H), 7.49 (d, J = 1.8 Hz, 1H), 7.25 (s, 1H), 6.96 (s, 1H), 6.71 (d, J = 3.3 Hz, 1H), 6.47 (dd, J = 1.8, 3.2 Hz, 1H), 6.06 (s, 2H), 4.20 (t, J = 7.0 Hz, 2H), 2.87 (m, 1H), 2.61 (t, J = 6.9 Hz, 2H), 2.00 (m, 2H), 1.14 (d, J = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$ /MeOH- d_4) δ 154.3, 152.2, 151.2, 150.9, 149.5, 148.14, 148.08, 142.4, 129.0, 119.2, 117.5, 114.5, 111.5, 110.0, 109.0, 102.3, 42.8, 41.0, 28.5, 21.2; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{22}H_{25}N_6O_3S$, 453.1709; found 453.1705; HPLC: method A R_t = 6.23, method B R_t = 6.82.

9-(3-(isopropylamino)propyl)-8-(6-(4-methoxyphenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ3-3]. 4-Methoxyphenylboronic acid (13.3 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and $NaHCO_3$ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $Pd(PPh_3)_2Cl_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 12.5:1) to give 20.5 mg (71%) of **DZ3-3**. ^1H NMR (500 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.19 (d, J = 8.7 Hz, 2H), 6.95 (s, 1H), 6.86 (d, J = 8.7 Hz, 2H), 6.82 (s, 1H), 6.00 (s, 2H), 5.92 (br s, 2H), 4.01 (t, J = 6.7 Hz, 2H), 3.82 (s, 3H), 2.75 (septet, J = 6.3 Hz, 1H), 2.43 (t, J = 6.7 Hz, 2H), 1.85 (m, 2H), 1.07 (d, J = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2,

154.3, 152.5, 151.5, 148.6, 147.8, 147.5, 139.0, 132.5, 130.4, 120.6, 119.8, 113.5, 113.0, 111.0, 101.8, 55.3, 49.1, 43.2, 40.9, 29.2, 22.2; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{25}H_{29}N_6O_3S$, 493.2022; found 493.2010; HPLC: method A R_t = 6.57, method B R_t = 7.55.

9-(3-(isopropylamino)propyl)-8-(6-(pyridin-4-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ3-5]. 4-Pyridinylboronic acid (10.8 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and $NaHCO_3$ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $Pd(PPh_3)_2Cl_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 3.5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 12.5:1) to give 14.8 mg (55%) of **DZ3-5**. ^1H NMR (500 MHz, $CDCl_3$ /MeOH- d_4) δ 8.53 (dd, J = 1.6, 4.8 Hz, 2H), 8.19 (s, 1H), 7.25 (dd, J = 1.6, 4.5 Hz, 2H), 7.11 (s, 1H), 6.89 (s, 1H), 6.11 (s, 2H), 4.07 (t, J = 6.8 Hz, 2H), 2.82 (m, 1H), 2.51 (t, J = 6.8 Hz, 2H), 1.91 (m, 2H), 1.13 (d, J = 6.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$ /MeOH- d_4) δ 154.1, 152.0, 151.2, 150.0, 148.90, 148.85, 148.69, 137.9, 124.5, 119.1, 117.7, 115.3, 110.6, 102.5, 49.2, 42.8, 40.7, 28.4, 21.2; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{23}H_{26}N_7O_2S$, 464.1869; found 464.1848; HPLC: method A R_t = 5.13, method B R_t = 2.57.

8-(6-(4-bromophenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-6]. 4-Bromophenylboronic acid (17.6 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and $NaHCO_3$ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $Pd(PPh_3)_2Cl_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 4:5:2:1) to give 13.9 mg (44%) of **DZ3-6**. ^1H NMR (500 MHz, $CDCl_3$) δ 8.23 (s, 1H), 7.44 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 7.01 (s, 1H), 6.81 (s, 1H), 6.05 (s, 2H), 5.69 (br s, 2H), 4.08 (t, J = 6.0 Hz, 2H), 2.91 (m, 1H),

2.50 (t, $J = 5.9$ Hz, 2H), 1.98 (m, 2H), 1.20 (d, $J = 6.4$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 154.2, 152.0, 151.2, 149.8, 149.1, 148.2, 139.8, 139.1, 131.2, 131.0, 122.0, 119.0, 117.9, 115.0, 111.1, 102.4, 50.1, 42.1, 40.2, 27.3, 20.2; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{24}\text{H}_{26}\text{BrN}_6\text{O}_2\text{S}$, 541.1021/ 543.1001; found 541.1016/543.1004; HPLC: method A $R_t = 6.93$, method B $R_t = 8.30$.

8-(6-(furan-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-27]. 3-Furanylboronic acid (9.8 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC ($\text{CH}_2\text{Cl}_2:\text{MeOH}-\text{NH}_3$ (7N), 20:1) to give 23.9 mg (90%) of **DZ3-27**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 8.17 (s, 1H), 7.51 (s, 1H), 7.44 (s, 1H), 7.07 (s, 1H), 6.97 (s, 1H), 6.49 (s, 1H), 6.08 (s, 2H), 4.17 (t, $J = 6.9$ Hz, 2H), 2.93 (septet, $J = 6.4$ Hz, 1H), 2.64 (t, $J = 7.1$ Hz, 2H), 2.02 (m, 2H), 1.17 (d, $J = 6.4$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 154.1, 151.8, 151.0, 149.7, 149.0, 147.8, 142.6, 140.4, 131.7, 124.2, 118.9, 117.8, 114.8, 111.5, 110.7, 102.1, 49.2, 42.6, 40.6, 28.0, 20.7; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{22}\text{H}_{25}\text{N}_6\text{O}_3\text{S}$, 453.1709; found 453.1711; HPLC: method A $R_t = 6.18$, method B $R_t = 6.67$.

5-(6-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)benzo[d][1,3]dioxol-5-yl)furan-2-carbaldehyde [DZ3-33]. 2-Formyl-5-furanylboronic acid (12.3 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: $\text{CH}_2\text{Cl}_2:\text{EtOAc}:\text{MeOH}-\text{NH}_3$ (7N), 2:2:1:0.5) to give 9.5 mg (34%) of **DZ3-33**. ^1H

NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 9.57 (s, 1H), 8.18 (s, 1H), 7.36 (d, *J* = 3.8 Hz, 1H), 7.32 (s, 1H), 7.07 (s, 1H), 6.98 (d, *J* = 3.8 Hz, 1H), 6.12 (s, 2H), 4.32 (t, *J* = 6.7 Hz, 2H), 3.31 (septet, *J* = 6.6 Hz, 1H), 2.93 (t, *J* = 6.8 Hz, 2H), 2.30 (m, 2H), 1.42 (d, *J* = 6.6 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 177.5, 156.8, 154.5, 152.2, 151.9, 151.4, 150.1, 149.7, 148.1, 127.5, 124.3, 119.2, 118.7, 115.7, 112.7, 109.9, 102.9, 51.3, 41.8, 40.4, 26.4, 19.2; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₅N₆O₄S, 481.1658; found 481.1657; HPLC: method A R_t = 5.87, method B R_t = 5.93.

8-(6-(1H-pyrrol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-29]. 1-N-Boc-pyrrole-2-boronic acid (18.5 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. DMF was removed under reduced pressure and to the resulting residue was added CH₂Cl₂ (1.5 mL) and TFA (0.3 mL). The mixture was stirred for 5 h at rt, then solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 4:9:2:1) to give 5.8 mg (22%) of **DZ3-29**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.17 (s, 1H), 7.04 (s, 1H), 7.01 (s, 1H), 6.88 (m, 1H), 6.27 (m, 1H), 6.21 (m, 1H), 6.03 (s, 2H), 4.17 (t, *J* = 6.8 Hz, 2H), 3.29 (septet, *J* = 6.6 Hz, 1H), 2.80 (t, *J* = 6.7 Hz, 2H), 2.15 (m, 2H), 1.41 (d, *J* = 6.6 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₆N₇O₂S, 452.1869; found 452.1872; HPLC: method A R_t = 6.13, method B R_t = 6.43.

8-(6-(1H-pyrazol-4-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-30]. 1-Boc-pyrazole-4-boronic acid pinacol ester (25.8 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was

removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 13.7 mg (53%) of **DZ3-30**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.17 (s, 1H), 7.58 (s, 2H), 7.10 (s, 1H), 6.95 (s, 1H), 6.06 (s, 2H), 4.08 (t, *J* = 6.9 Hz, 2H), 2.89 (septet, *J* = 6.4 Hz, 1H), 2.57 (t, *J* = 7.2 Hz, 2H), 1.91 (m, 2H), 1.14 (d, *J* = 6.4 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.0, 152.1, 151.2, 149.7, 148.9, 147.5, 133.6, 132.0, 119.8, 119.1, 117.9, 115.3, 110.9, 102.1, 49.2, 42.9, 40.8, 28.3, 21.3; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₁H₂₅N₈O₂S, 453.1821; found 453.1819; HPLC: method A R_t = 5.60, method B R_t = 4.87.

9-(3-(isopropylamino)propyl)-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ3-35]. 4,4,5,5-Tetramethyl-2-(5-methyl-furan-2-yl)-(1,3,2)dioxaborolane (21.9 mg, 0.1053 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 4:9:2:1) to give 11.5 mg (42%) of **DZ3-35**. ¹H NMR (500 MHz, CDCl₃) δ 8.25 (s, 1H), 7.19 (s, 1H), 6.84 (s, 1H), 6.63 (d, *J* = 3.1 Hz, 1H), 6.07 (d, *J* = 2.5 Hz, 1H), 5.98 (s, 2H), 5.93 (br s, 2H), 4.22 (t, *J* = 6.6 Hz, 2H), 2.94 (m, 1H), 2.59 (t, *J* = 6.6 Hz, 2H), 2.34 (s, 3H), 2.05 (m, 2H), 1.20 (d, *J* = 6.3 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₇N₆O₃S, 467.1865; found 467.1869; HPLC: method A R_t = 6.49, method B R_t = 7.53.

2-(6-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)benzo[d][1,3]dioxol-5-yl)acetonitrile [DZ3-39]. 4-Isoxazoleboronic acid pinacol ester (20.5 mg, 0.1053 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under

reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 10.3 mg (%) of **DZ3-39**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.17 (s, 1H), 7.14 (s, 1H), 7.12 (s, 1H), 6.10 (s, 2H), 4.35 (t, *J* = 6.9 Hz, 2H), 3.99 (s, 2H), 3.08 (septet, *J* = 6.5 Hz, 1H), 2.82 (t, *J* = 7.0 Hz, 2H), 2.25 (m, 2H), 1.27 (d, *J* = 6.5 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.2, 152.1, 152.0, 151.5, 150.8, 148.6, 147.7, 129.5, 119.2, 117.6, 116.2, 110.3, 102.7, 49.8, 42.5, 40.7, 27.7, 22.9, 20.4; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₀H₂₄N₇O₂S, 426.1712; found 426.1712; HPLC: method A R_t = 5.69, method B R_t = 4.57.

8-(6-(1H-pyrrol-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-41]. 1-Boc-pyrrole-3-boronic acid pinacol ester (30.9 mg, 0.1053 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 7.9 mg (30%) of **DZ3-41**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.16 (s, 1H), 7.02 (s, 1H), 6.99 (s, 1H), 6.86 (m, 1H), 6.76 (m, 1H), 6.21 (m, 1H), 6.02 (s, 2H), 4.07 (t, *J* = 6.9 Hz, 2H), 2.95 (septet, *J* = 6.4 Hz, 1H), 2.59 (t, *J* = 7.1 Hz, 2H), 1.96 (m, 2H), 1.19 (d, *J* = 6.4 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.4, 152.1, 152.0, 151.0, 149.4, 146.7, 135.9, 131.6, 122.1, 119.1, 117.8, 117.5, 114.6, 111.0, 109.2, 101.9, 53.6, 42.6, 40.6, 27.8, 20.6; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₆N₇O₂S, 452.1869; found 452.1862; HPLC: method A R_t = 6.02, method B R_t = 6.27.

9-(3-(isopropylamino)propyl)-8-(6-(1-methyl-1H-pyrazol-5-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ3-44]. 1-Methyl-1-H-pyrazole-5-boronic acid pinacol ester (18.2 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the

reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 2 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 20.1 mg (74%) of **DZ3-44**. ¹H NMR (500 MHz, CDCl₃) δ 8.25 (s, 1H), 7.40 (d, *J* = 1.8 Hz, 1H), 7.05 (s, 1H), 6.80 (s, 1H), 6.08 (s, 2H), 6.06 (d, *J* = 1.8 Hz, 1H), 5.91 (br s, 2H), 4.10 (t, *J* = 6.7 Hz, 2H), 3.67 (s, 3H), 2.85 (septet, *J* = 6.3 Hz, 1H), 2.53 (t, *J* = 6.7 Hz, 2H), 1.97 (m, 2H), 1.13 (d, *J* = 6.3 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 154.4, 152.7, 151.7, 149.3, 149.0, 147.0, 140.6, 138.5, 127.7, 123.3, 120.0, 113.8, 111.7, 107.4, 102.5, 49.6, 43.2, 41.1, 37.1, 29.1, 22.0; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₇N₈O₂S, 467.1978; found 467.1985; HPLC: method A R_t = 5.74, method B R_t = 5.20.

8-(6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-46]. 1H-pyrazole-3-boronic acid (33 mg, 0.293 mmol) was added to **PU-H71** (50 mg, 0.0975 mmol) and NaHCO₃ (24.6 mg, 0.293 mmol). DMF (2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.2 mL) and Pd(PPh₃)₂Cl₂ (7 mg, 0.0098 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 3.7 mg (8%) of **DZ3-46**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.17 (s, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.10 (s, 1H), 7.07 (s, 1H), 6.38 (d, *J* = 2.0 Hz, 1H), 6.08 (s, 2H), 4.19 (t, *J* = 6.8 Hz, 2H), 3.31 (septet, *J* = 6.6 Hz, 1H), 2.89 (t, *J* = 7.2 Hz, 2H), 2.10 (m, 2H), 1.39 (d, *J* = 6.6 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.5, 152.2, 152.1, 150.7, 149.5, 148.5, 148.3, 119.3, 119.1, 114.6, 114.5, 111.0, 110.9, 106.1, 102.3, 51.1, 41.7, 40.3, 26.0, 18.7; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₁H₂₅N₈O₂S, 453.1821; found 453.1826; HPLC: method A R_t = 5.65, method B R_t = 4.83.

9-(3-(isopropylamino)propyl)-8-(6-(isoxazol-4-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ3-49]. 4-Isioxazoleboronic acid pinacol ester (20.5 mg, 0.1053 mmol) was

added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 60°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was attempted to be purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 4:7:2:1) to give 7.4 mg (28%) of an inseparable mixture of **DZ3-49** and **DZ3-39** in a ratio of approximately 71:29, respectively, as determined by HPLC. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 8.66 (s, 1H), 8.45 (s, 1H), 8.17 (s, 1H), 7.18 (s, 1H), 7.01 (s, 1H), 6.13 (s, 2H), 4.37 (t, $J = 7.0$ Hz, 2H), 3.27 (septet, $J = 7.1$ Hz, 1H), 2.89 (t, $J = 7.1$ Hz, 2H), 2.22 (m, 2H), 1.38 (d, $J = 6.5$ Hz, 6H); MS (ESI) m/z $[\text{M}+\text{H}]^+$ 454.1; HPLC: method A $R_t = 5.67$ (**DZ3-39**, 29%) and 5.87 (**DZ3-49**, 71%); method B $R_t = 4.58$ (**DZ3-39**, 34%) and 5.57 (**DZ3-49**, 66%).

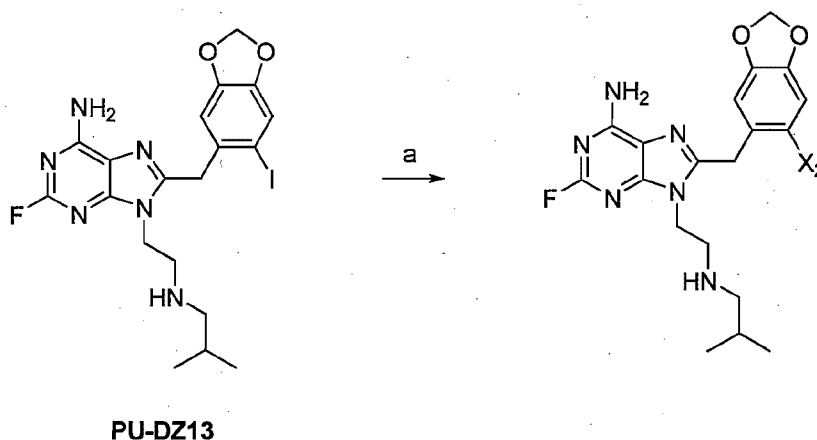
4-(6-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)benzo[d][1,3]dioxol-5-yl)benzaldehyde [DZ3-50]. 4-Formylphenylboronic acid (13 mg, 0.0877 mmol) was added to **PU-H71** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 2:2:1:0.5) to give 18.8 mg (66%) of **DZ3-50**. ^1H NMR (500 MHz, MeOH- d_4) δ 10.01 (s, 1H), 8.15 (s, 1H), 7.85 (d, $J = 8.1$ Hz, 2H), 7.47 (d, $J = 8.1$ Hz, 2H), 7.14 (s, 1H), 6.93 (s, 1H), 6.13 (s, 2H), 4.05 (t, $J = 6.8$ Hz, 2H), 2.99 (septet, $J = 6.4$ Hz, 1H), 2.62 (t, $J = 6.9$ Hz, 2H), 1.99 (m, 2H), 1.24 (d, $J = 6.4$ Hz, 6H); ^{13}C NMR (125 MHz, MeOH- d_4) δ 192.3, 154.1, 151.9, 151.0, 149.8, 148.8, 148.5, 146.4, 139.5, 135.3, 130.0, 129.4, 119.0, 117.7, 115.0, 110.8, 102.4, 49.9, 42.2, 40.3, 27.4, 20.2; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{25}\text{H}_{27}\text{N}_6\text{O}_3\text{S}$, 491.1865; found 491.1877; HPLC: method A $R_t = 6.23$, method B $R_t = 6.83$.

***tert*-Butyl 6-(3-(6-amino-8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propylamino)hexylcarbamate [TT-V-43A].**

Bis(trifluoromethyl)phenylboronic acid (22.7 mg, 0.0878 mmol) was added to PU-H71-C6-linker (39.2 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 3 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:MeOH-NH₃ (7N), 10:1) to give 27.7 mg (63%) of **TT-V-43A**. ¹H NMR (500 MHz, CDCl₃) δ 8.17 (s, 1H), 7.78 (s, 3H), 7.14 (s, 1H), 6.89 (s, 1H), 6.12 (s, 2H), 5.80 (br s, 2H), 4.68 (br s, 1H), 4.16 (t, *J* = 6.3 Hz, 2H), 3.10 (m, 2H), 2.81 (t, *J* = 7.7 Hz, 2H), 2.67 (t, *J* = 6.2 Hz, 2H), 2.21 (m, 2H), 1.81 (m, 2H), 1.30-1.53 (m, 15H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₃₄H₄₀F₆N₇O₄S, 756.2767; found 756.2753; HPLC: method A R_t = 8.17, method B R_t = 11.00.

N¹-(3-(6-amino-8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)hexane-1,6-diamine [TT-V-47B]. **TT-V-43A** (26 mg, 0.0344 mmol) was dissolved in CH₂Cl₂ (1.2 mL) and TFA (0.3 mL) was added and stirred at rt for 45 min. Then solvent was removed under reduced pressure and residue dried under high vacuum for 2 h to give **TT-V-47B**. Purified by preparatory TLC (hexane:CH₂Cl₂:MeOH-NH₃ (7N), 7:1) to give mg (%) of **TT-V-47B**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.04 (s, 1H), 7.67 (s, 1H), 7.64 (s, 2H), 7.12 (s, 1H), 6.84 (s, 1H), 6.04 (s, 2H), 3.97 (t, *J* = 6.7 Hz, 2H), 2.85 (t, *J* = 7.0 Hz, 2H), 2.84 (t, *J* = 6.9 Hz, 2H), 2.77 (t, *J* = 7.0 Hz, 2H), 2.06 (m, 2H), 1.71 (m, 2H), 1.63 (m, 2H), 1.28 (m, 4H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₉H₃₂F₆N₇O₂S, 656.2242; found 656.2242; HPLC: method A R_t = 6.98, method B R_t = 8.38.

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Reagents and conditions: (a) RB(OH)_2 , $\text{PdCl}_2(\text{PPh}_3)_2$, NaHCO_3 , H_2O , DMF, 90°C .

Scheme 4. Suzuki coupling of PU-DZ13.

2-fluoro-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [DZ3-25]. 2-Furanylboronic acid (9.8 mg, 0.0877 mmol) was added to PU-DZ13 (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd(PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 20:1) to give 19.1 mg (72%) of **DZ3-25**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 7.46 (d, $J = 1.4$ Hz, 1H), 7.08 (s, 1H), 6.64 (s, 1H), 6.46 (dd, $J = 1.4, 3.2$ Hz, 1H), 6.34 (d, $J = 3.2$ Hz, 1H), 6.00 (s, 2H), 4.34 (s, 2H), 4.08 (t, $J = 6.3$ Hz, 2H), 2.85 (t, $J = 6.3$ Hz, 2H), 2.38 (d, $J = 6.8$ Hz, 2H), 1.70 (m, 1H), 0.88 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 158.9 (d, $J = 208.5$ Hz), 156.2 (d, $J = 20.2$ Hz), 152.6, 152.3 (d, $J = 18.3$ Hz), 151.9, 147.9, 147.1, 142.1, 126.1, 124.3, 115.8, 111.3, 110.0, 108.7, 108.2, 101.6, 57.0, 48.1, 42.3, 32.0, 27.7, 20.2; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{26}\text{FN}_6\text{O}_3$, 453.2050; found 453.2041; HPLC: method A $R_t = 7.10$, method B $R_t = 8.52$.

2-fluoro-8-((6-(furan-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [DZ3-26]. 3-Furanylboronic acid (9.8 mg, 0.0877 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 20:1) to give 23.4 mg (88%) of **DZ3-26**. ^1H NMR (500 MHz, CDCl_3) δ 7.49 (m, 1H), 7.46 (m, 1H), 6.82 (s, 1H), 6.63 (s, 1H), 6.46 (m, 1H), 5.96 (s, 2H), 5.70 (br s, 2H), 4.22 (s, 2H), 3.91 (t, $J = 6.1$ Hz, 2H), 2.75 (t, $J = 6.1$ Hz, 2H), 2.29 (d, $J = 6.5$ Hz, 2H), 1.70 (m, 1H), 0.83 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.9 (d, $J = 208.5$ Hz), 156.2 (d, $J = 20.3$ Hz), 152.7 (d, $J = 18.2$ Hz), 152.2, 147.5, 146.9, 143.1, 140.1, 127.0, 125.7, 124.7, 116.6, 111.8, 110.2, 109.4, 101.4, 57.5, 48.5, 43.0, 31.9, 28.1, 20.4; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{26}\text{FN}_6\text{O}_3$, 453.2050; found 453.2044; HPLC: method A $R_t = 7.10$, method B $R_t = 8.50$.

8-((6-(1H-pyrrol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [DZ3-31]. 1-N-Boc-pyrrole-2-boronic acid (18.5 mg, 0.0877 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. DMF was removed under reduced pressure and to the resulting residue was added CH_2Cl_2 (1.5 mL) and TFA (0.3 mL). The mixture was stirred for 5 h at rt, then solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 4:15:2:1) to give 5.2 mg (20%) of **DZ3-31**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 6.91 (s, 1H), 6.84 (dd, $J = 1.4, 2.5$ Hz, 1H), 6.65 (s, 1H), 6.22 (m, 1H), 6.08 (dd, $J = 1.4, 3.3$ Hz, 1H), 5.97 (s, 2H), 4.26 (s, 2H), 4.06 (t, $J = 6.7$ Hz, 2H), 2.80 (t, $J = 6.7$ Hz, 2H), 2.55 (d, $J = 7.0$ Hz, 2H), 1.88 (m, 1H), 0.96 (d, $J = 6.7$ Hz,

6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 158.8 (d, $J = 208.1$ Hz), 156.4 (d, $J = 20.0$ Hz), 152.9, 152.3 (d, $J = 21.2$ Hz), 147.4, 129.8, 127.9, 126.7, 118.5, 110.5, 109.3, 108.7, 108.6, 101.5, 56.6, 47.4, 41.1, 31.6, 27.1, 20.2; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{27}\text{FN}_7\text{O}_2$, 452.2210; found 452.2212; HPLC: method A $R_t = 7.02$, method B $R_t = 8.30$.

5-((6-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)benzo[d][1,3]dioxol-5-yl)furan-2-carbaldehyde [DZ3-34]. 2-Formyl-5-furanylboronic acid (12.3 mg, 0.0877 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 2:2:1:0.5) to give 2.0 mg (7%) of **DZ3-34**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 9.47 (s, 1H), 7.27 (d, $J = 3.7$ Hz, 1H), 7.20 (s, 1H), 6.77 (s, 1H), 6.63 (d, $J = 3.7$ Hz, 1H), 6.06 (s, 2H), 4.45 (s, 2H), 4.32 (t, $J = 6.3$ Hz, 2H), 2.83 (t, $J = 6.3$ Hz, 2H), 2.54 (d, $J = 6.8$ Hz, 2H), 1.83 (m, 1H), 0.93 (d, $J = 6.7$ Hz, 6H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{24}\text{H}_{26}\text{FN}_6\text{O}_4$, 481.2000; found 481.1984; HPLC: method A $R_t = 6.61$, method B $R_t = 7.62$.

8-((6-((1H-pyrazol-4-yl)benzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [DZ3-32]. 1-Boc-pyrazole-4-boronic acid pinacol ester (25.8 mg, 0.0877 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.5 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.15 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4 mg, 0.00584 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 2:2:1:0.5) to give 10.6 mg (40%) of **DZ3-32**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 7.50 (s, 2H), 6.83 (s, 1H), 6.69 (s, 1H),

5.98 (s, 2H), 4.18 (s, 2H), 4.01 (t, $J = 6.6$ Hz, 2H), 2.78 (t, $J = 6.6$ Hz, 2H), 2.40 (d, $J = 7.0$ Hz, 2H), 1.71 (m, 1H), 0.88 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 158.6 (d, $J = 208.3$ Hz), 156.3 (d, $J = 19.6$ Hz), 152.3, 152.1 (d, $J = 21.2$ Hz), 147.3, 147.1, 126.4, 126.2, 120.1, 115.8, 110.7, 109.9, 101.4, 56.3, 47.3, 40.8, 31.9, 27.0, 20.0; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{22}\text{H}_{26}\text{FN}_8\text{O}_2$, 453.2163; found 453.2162; HPLC: method A $R_t = 6.23$, method B $R_t = 6.55$.

2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine [DZ3-36]. 4,4,5,5-Tetramethyl-2-(5-methyl-furan-2-yl)-(1,3,2)dioxaborolane (21.9 mg, 0.1053 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 4:15:2:1) to give 15.6 mg (57%) of **DZ3-36**. ^1H NMR (500 MHz, CDCl_3) δ 7.04 (s, 1H), 6.53 (s, 1H), 6.26 (d, $J = 3.1$ Hz, 1H), 6.21 (br s, 2H), 6.05 (d, $J = 3.1$ Hz, 1H), 5.94 (s, 2H), 4.37 (s, 2H), 3.98 (t, $J = 6.3$ Hz, 2H), 2.80 (t, $J = 6.2$ Hz, 2H), 2.34 (s, 3H), 2.31 (d, $J = 6.8$ Hz, 2H), 1.64 (m, 1H), 0.83 (d, $J = 6.7$ Hz, 6H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{24}\text{H}_{28}\text{FN}_6\text{O}_3$, 467.2207; found 467.2200; HPLC: method A $R_t = 7.29$, method B $R_t = 9.13$.

8-((6-(1H-pyrrol-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [DZ3-38]. 1-Boc-pyrrole-3-boronic acid pinacol ester (30.9 mg, 0.1053 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.2 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h, then at 120°C for 6.5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 4:7:2:1)

to give 20.9 mg (79%) of **DZ3-38**. ^1H NMR (500 MHz, CDCl_3) δ 8.72 (br s, 1H), 6.85 (s, 1H), 6.83 (m, 1H), 6.76 (m, 1H), 6.62 (s, 1H), 6.34 (br s, 2H), 6.23 (m, 1H), 5.91 (s, 2H), 4.29 (s, 2H), 3.84 (t, $J = 6.3$ Hz, 2H), 2.67 (t, $J = 6.3$ Hz, 2H), 2.28 (d, $J = 6.8$ Hz, 2H), 1.60 (m, 1H), 0.82 (d, $J = 6.6$ Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.8 (d, $J = 208.0$ Hz), 156.4 (d, $J = 19.8$ Hz), 153.0, 152.9 (d, $J = 21.3$ Hz), 146.82, 146.76, 130.0, 126.5, 123.3, 118.4, 116.9, 116.6, 110.6, 109.8, 109.3, 101.3, 57.6, 48.7, 43.0, 32.0, 28.3, 20.7; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{27}\text{FN}_7\text{O}_2$, 452.2210; found 452.2204; HPLC: method A $R_t = 6.77$, method B $R_t = 7.93$.

2-((6-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)benzo[d][1,3]dioxol-5-yl)acetonitrile [DZ3-40]. 4-Isloxazoleboronic acid pinacol ester (20.5 mg, 0.1053 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 4:7:2:1) to give 8.3 mg (%) of **DZ3-40**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 6.94 (s, 1H), 6.70 (s, 1H), 6.00 (s, 2H), 4.39 (t, $J = 6.7$ Hz, 2H), 4.31 (s, 2H), 3.84 (s, 2H), 3.18 (t, $J = 6.6$ Hz, 2H), 2.65 (d, $J = 7.1$ Hz, 2H), 1.94 (m, 1H), 0.99 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 158.7 (d, $J = 210.4$ Hz), 156.6 (d, $J = 20.1$ Hz), 152.1 (d, $J = 18.2$ Hz), 150.5, 148.1, 147.7, 126.7, 122.4, 117.9, 116.1, 110.6, 109.9, 101.8, 56.5, 47.4, 41.2, 31.3, 27.1, 21.5, 20.0; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{21}\text{H}_{25}\text{FN}_7\text{O}_2$, 426.2054; found 426.2048; HPLC: method A $R_t = 6.48$, method B $R_t = 7.10$.

8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [DZ3-43]. 1H-pyrazole-3-boronic acid (11.8 mg, 0.1053 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction

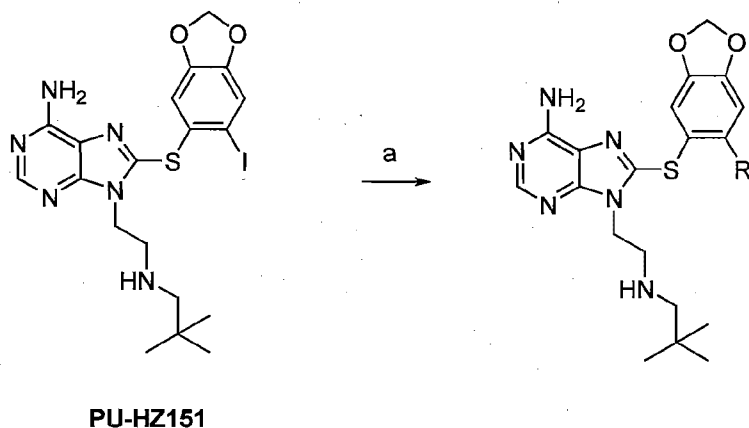
mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4.5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 3.5 mg (13%) of **DZ3-43**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 7.63 (d, *J* = 2.15 Hz, 1H), 6.95 (s, 1H), 6.82 (s, 1H), 6.34 (d, *J* = 2.15 Hz, 1H), 6.01 (s, 2H), 4.35 (t, *J* = 6.8 Hz, 2H), 4.29 (s, 2H), 2.98 (t, *J* = 6.9 Hz, 2H), 2.64 (d, *J* = 7.0 Hz, 2H), 1.96 (m, 1H), 0.99 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 158.8 (d, *J* = 208.7 Hz), 156.6 (d, *J* = 19.3 Hz), 152.4, 152.2 (d, *J* = 18.7 Hz), 148.3, 147.3, 127.1, 115.94, 115.93, 110.3, 110.1, 105.6, 101.8, 56.3, 47.4, 40.5, 31.5, 27.0, 20.2; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₆FN₈O₂, 453.2163; found 453.2149; HPLC: method A R_t = 6.37, method B R_t = 6.93.

2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(1-methyl-1H-pyrazol-5-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine [DZ3-45]. 1-Methyl-1-H-pyrazole-5-boronic acid pinacol ester (18.2 mg, 0.0877 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO₃ (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 2 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 4:7:2:1) to give 26.5 mg (97%) of **DZ3-45**. ¹H NMR (500 MHz, CDCl₃) δ 7.49 (d, *J* = 1.5 Hz, 1H), 6.76 (s, 1H), 6.74 (s, 1H), 6.28 (br s, 2H), 6.17 (d, *J* = 1.5 Hz, 1H), 6.01 (s, 2H), 3.99 (s, 2H), 3.90 (t, *J* = 6.3 Hz, 2H), 3.66 (s, 3H), 2.76 (t, *J* = 6.3 Hz, 2H), 2.31 (d, *J* = 6.8 Hz, 2H), 1.72 (m, 1H), 0.84 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 159.0 (d, *J* = 208.7 Hz), 156.4 (d, *J* = 20.0 Hz), 152.8 (d, *J* = 18.5 Hz), 151.5, 149.0, 147.1, 141.3, 138.8, 129.4, 123.4, 116.6, 110.7, 109.9, 106.9, 101.9, 57.8, 48.7, 43.1, 36.9, 31.8, 28.3, 20.6; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₈FN₈O₂, 467.2319; found 467.2323; HPLC: method A R_t = 6.37, method B R_t = 6.90.

2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine [DZ3-48]. 2-Thienylboronic acid (11.2 mg, 0.0877 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 2 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 2:2:1:0.5) to give 18.3 mg (67%) of **DZ3-48**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 7.31 (d, $J = 5.0$ Hz, 1H), 7.03 (dd, $J = 3.1, 5.0$ Hz, 1H), 6.92 (s, 1H), 6.87 (d, $J = 3.0$ Hz, 1H), 6.74 (s, 1H), 6.01 (s, 2H), 4.19 (s, 2H), 3.99 (t, $J = 6.5$ Hz, 2H), 2.78 (t, $J = 6.5$ Hz, 2H), 2.37 (d, $J = 6.9$ Hz, 2H), 1.70 (m, 1H), 0.88 (d, $J = 6.7$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 158.7 (d, $J = 209.4$ Hz), 156.4 (d, $J = 19.6$ Hz), 152.21 (d, $J = 18.4$ Hz), 152.20, 148.1, 147.0, 141.5, 127.7, 127.3, 127.0, 126.0, 125.8, 115.9, 111.3, 110.0, 101.6, 57.1, 48.1, 42.2, 32.0, 27.8, 20.3; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{26}\text{FN}_6\text{O}_2\text{S}$, 469.1822; found 469.1830; HPLC: method A $R_t = 7.21$, method B $R_t = 8.93$.

2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(isoxazol-4-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine [DZ3-51]. 4-Isoxazoleboronic acid pinacol ester (20.5 mg, 0.1053 mmol) was added to **PU-DZ13** (30 mg, 0.0585 mmol) and NaHCO_3 (14.7 mg, 0.1755 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 60°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane: CH_2Cl_2 :EtOAc:MeOH- NH_3 (7N), 2:2:1:0.5) to give 7.8 mg (29%) of an inseparable mixture of **DZ3-51** and **DZ3-40** in a ratio of approximately 44:56, respectively, as determined by HPLC. MS (ESI) m/z $[\text{M}+\text{H}]^+$ 454.4; HPLC: method A $R_t = 6.46$ (**DZ3-40**, 56%) and 6.65 (**DZ3-51**, 44%); method B $R_t = 7.08$ (**DZ3-40**, 65%) and 7.52 (**DZ3-51**, 35%).

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Reagents and conditions: (a) RB(OH)_2 , $\text{PdCl}_2(\text{PPh}_3)_2$, NaHCO_3 , H_2O , DMF, 90°C .

Scheme 5. Suzuki coupling of PU-HZ151.

8-(6-(furan-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [TT5-53A]. 2-Furanylboronic acid (42.4 mg, 0.379 mmol) was added to **PU-HZ151** (66.4 mg, 0.126 mmol) and NaHCO_3 (63.6 mg, 0.756 mmol). DMF (2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.4 mL) and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (17.6 mg, 0.025 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 3.5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 20:1) to give 25.2 mg (43%) of **TT5-53A**. ^1H NMR (500 MHz, CDCl_3) δ 8.30 (s, 1H), 7.49 (d, $J = 1.3$ Hz, 1H), 7.17 (s, 1H), 6.84 (s, 1H), 6.75 (d, $J = 3.3$ Hz, 1H), 6.48 (dd, $J = 1.8, 3.3$ Hz, 1H), 5.97 (s, 2H), 5.89 (br s, 2H), 4.18 (t, $J = 6.5$ Hz, 2H), 2.86 (t, $J = 6.5$ Hz, 2H), 2.25 (s, 2H), 0.83 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 154.6, 153.0, 151.7, 151.1, 148.4, 147.9, 146.8, 142.2, 127.2, 120.8, 120.0, 112.8, 111.5, 110.0, 108.7, 101.9, 61.9, 49.6, 43.9, 31.5, 27.6; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{23}\text{H}_{27}\text{N}_6\text{O}_3\text{S}$, 467.1865; found 467.1870; HPLC: method A $R_t = 6.78$, method B $R_t = 7.83$.

8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [DZ3-56]. 4,4,5,5-Tetramethyl-2-(5-methyl-furan-2-yl)-(1,3,2)dioxaborolane (17.7 mg, 0.0853 mmol) was added to **PU-HZ151** (30 mg, 0.0569 mmol) and NaHCO₃ (14.3 mg, 0.1707 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0113 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4.5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 15:1) to give 9.3 mg (34%) of **DZ3-56**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.19 (s, 1H), 7.24 (s, 1H), 6.89 (s, 1H), 6.62 (d, *J* = 3.2 Hz, 1H), 6.05 (d, *J* = 3.2 Hz, 1H), 6.03 (s, 2H), 4.36 (t, *J* = 6.0 Hz, 2H), 3.04 (t, *J* = 6.0 Hz, 2H), 2.47 (s, 2H), 2.33 (s, 3H), 0.95 (s, 9H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.5, 152.4, 152.3, 151.2, 149.4, 149.2, 148.5, 147.7, 129.1, 119.4, 117.4, 114.3, 111.2, 108.6, 107.8, 102.2, 61.4, 49.3, 43.2, 31.4, 27.7, 13.7; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₄H₂₉N₆O₃S, 481.2022; found 481.2002; HPLC: method A R_t = 6.89, method B R_t = 7.58.

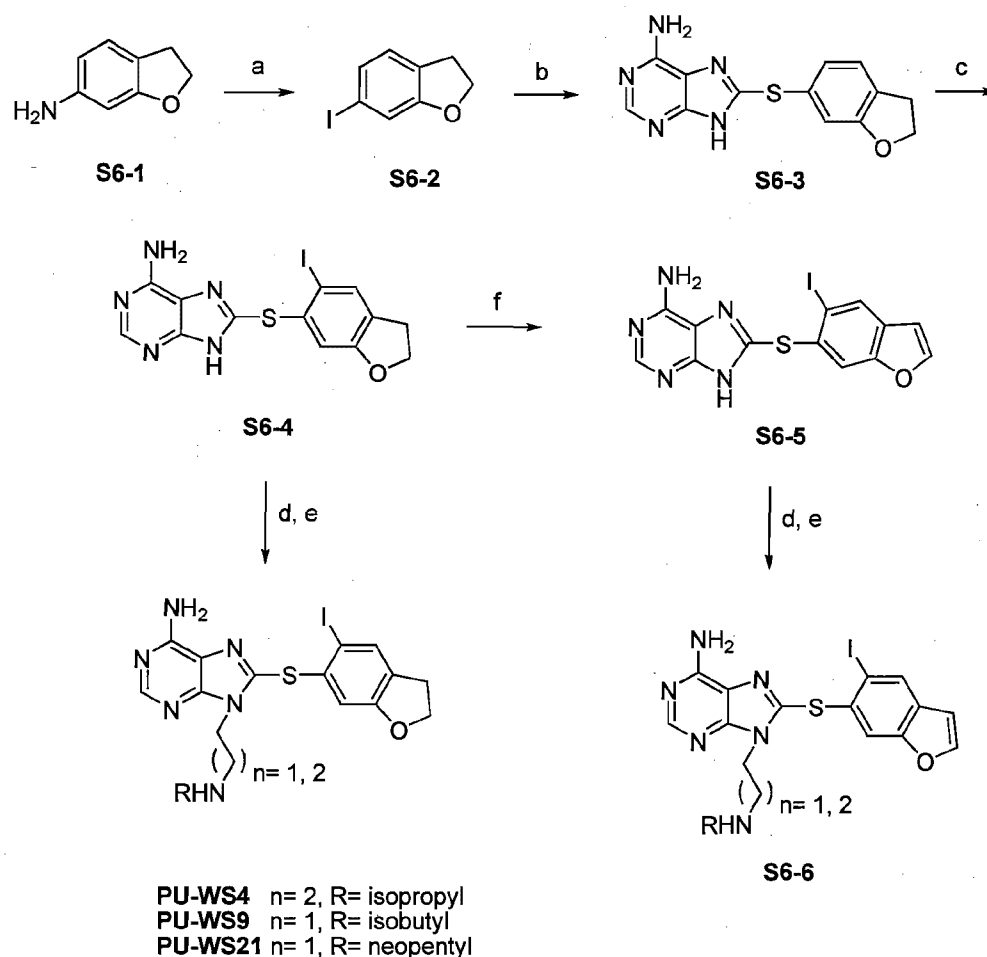
9-(2-(neopentylamino)ethyl)-8-(6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ3-58]. 2-Thiopheneboronic acid (10.9 mg, 0.0853 mmol) was added to **PU-HZ151** (30 mg, 0.0569 mmol) and NaHCO₃ (14.3 mg, 0.1707 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0113 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 16.0 mg (58%) of **DZ3-58**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.18 (s, 1H), 7.32 (dd, *J* = 1.6, 4.7 Hz, 1H), 6.98-7.03 (m, 4H), 6.07 (s, 2H), 4.29 (t, *J* = 5.4 Hz, 2H), 3.03 (t, *J* = 5.4 Hz, 2H), 2.48 (s, 2H), 0.97 (s, 9H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.3, 152.0, 150.8, 149.2, 148.9, 148.3, 140.5, 132.5, 127.8, 127.0, 126.3, 120.1, 119.2, 114.4, 111.8, 102.2, 61.1, 49.0, 42.9, 31.2, 27.6; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₇N₆O₂S₂, 483.1637; found 483.1621; HPLC: method A R_t = 7.14, method B R_t = 7.73.

8-(6-(1H-pyrrol-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [DZ3-59]. 1-Boc-pyrrole-3-boronic acid pinacol ester (25 mg, 0.0853 mmol) was added to **PU-HZ151** (30 mg, 0.0569 mmol) and NaHCO₃ (14.3 mg, 0.1707 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0113 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 10.1 mg (38%) of **DZ3-59**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.15 (s, 1H), 7.03 (s, 1H), 6.95 (s, 1H), 6.85 (m, 1H), 6.76 (m, 1H), 6.20 (dd, *J* = 1.7, 2.4 Hz, 1H), 6.01 (s, 2H), 4.24 (t, *J* = 5.7 Hz, 2H), 2.98 (t, *J* = 5.7 Hz, 2H), 2.50 (s, 2H), 0.98 (s, 9H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.3, 152.1, 149.6, 149.3, 146.8, 135.7, 122.3, 119.3, 118.6, 117.9, 117.4, 114.5, 111.1, 109.4, 101.9, 61.0, 49.3, 42.7, 31.2, 27.7; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₈N₇O₂S, 466.2025; found 466.2016; HPLC: method A R_t = 6.86, method B R_t = 7.20.

8-(6-(furan-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [DZ3-60]. 3-Furanylboronic acid (9.5 mg, 0.0853 mmol) was added to **PU-HZ151** (30 mg, 0.0569 mmol) and NaHCO₃ (14.3 mg, 0.1707 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0113 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 13.8 mg (52%) of **DZ3-60**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.17 (s, 1H), 7.50 (s, 1H), 7.43 (d, *J* = 1.5 Hz, 1H), 7.02 (s, 1H), 6.94 (s, 1H), 6.49 (d, *J* = 1.5 Hz, 1H), 6.06 (s, 2H), 4.29 (t, *J* = 5.9 Hz, 2H), 3.02 (t, *J* = 5.8 Hz, 2H), 2.46 (s, 2H), 0.94 (s, 9H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.3, 152.0, 151.1, 149.6, 149.3, 147.9, 142.8, 140.6, 131.5, 124.3, 119.3, 118.8, 114.7, 111.7, 110.9, 102.2, 61.4, 49.1, 43.0, 31.3, 27.6; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₇N₆O₃S, 467.1865; found 467.1845; HPLC: method A R_t = 6.65, method B R_t = 7.09.

8-(6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [DZ3-61]. 1H-Pyrazole-3-boronic acid (19 mg, 0.1707 mmol) was added to **PU-HZ151** (30 mg, 0.0569 mmol) and NaHCO₃ (14.3 mg, 0.1707 mmol). DMF (1.2 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0113 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 4 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 15:1) to give 6.5 mg (25%) of **DZ3-61**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.18 (s, 1H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.05 (s, 2H), 6.40 (d, *J* = 2.0 Hz, 1H), 6.06 (s, 2H), 4.36 (t, *J* = 6.0 Hz, 2H), 3.01 (t, *J* = 6.0 Hz, 2H), 2.51 (s, 2H), 0.97 (s, 9H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.6, 152.3, 150.8, 149.4, 148.6, 148.5, 120.1, 119.2, 114.5, 110.9, 106.0, 102.3, 61.2, 49.1, 42.5, 31.1, 27.5; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₇N₈O₂S, 467.1978; found 467.1972; HPLC: method A R_t = 6.50, method B R_t = 6.61.

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Reagents and conditions: (a) NaNO_2 , KI, AcOH/TFA , 0°C ; (b) 8-mercaptoadenine, Cs_2CO_3 , $\text{PdCl}_2(\text{dppf})$, DMF, 80°C , 48h; (c) NIS, TFA, CH_3CN , rt, 2h; (d) 1,3-dibromopropane or 1,2-dibromoethane, Cs_2CO_3 , DMF, rt; (e) isopropylamine or isobutylamine or neopentylamine, DMF, rt; (f) DDQ, dioxane, 100°C .

Scheme 6. Synthesis of PU-WS4, PU-WS9 and PU-WS21.

6-iodo-2,3-dihydrobenzofuran (S6-2). A solution of 2,3-dihydrobenzofuran-6-amine (**S6-1**; 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 NaS₂O₃, brine, dried over MgSO₄ 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 yield **S6-2** (0.82 g, 61%) as a pale-yellow solid. ¹H NMR (500 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃) δ 161.1, 129.4, 127.1, 126.4, 118.7, 91.7, 71.6, 29.4.

8-(2,3-dihydrobenzofuran-6-ylthio)-9H-purin-6-amine (S6-3). To a solution of **S6-2** (50 mg, 0.2 mmol) in DMF (2 mL) was added 8-mercaptoadenine (34 mg, 0.2 mmol), Cs₂CO₃ (99.4 mg, 0.3 mmol) and PdCl₂(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 (CH₂Cl₂:MeOH, 100:0 to 90:10) to yield **S6-3** (25 mg, 44%) as a yellow solid. ¹H NMR (500 MHz, CD₃OD) 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]⁺ calcd. for C₁₃H₁₂N₅OS, 286.0763; found 286.0768.

8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-6-amine (S6-4) To a solution of **S6-3** (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 rt for 2 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (CH₂Cl₂:MeOH, 100:0 to 90:10) to afford **S6-4** (48 mg, 53%) as a yellow gum. ¹H NMR (500 MHz, CDCl₃) 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)⁺.

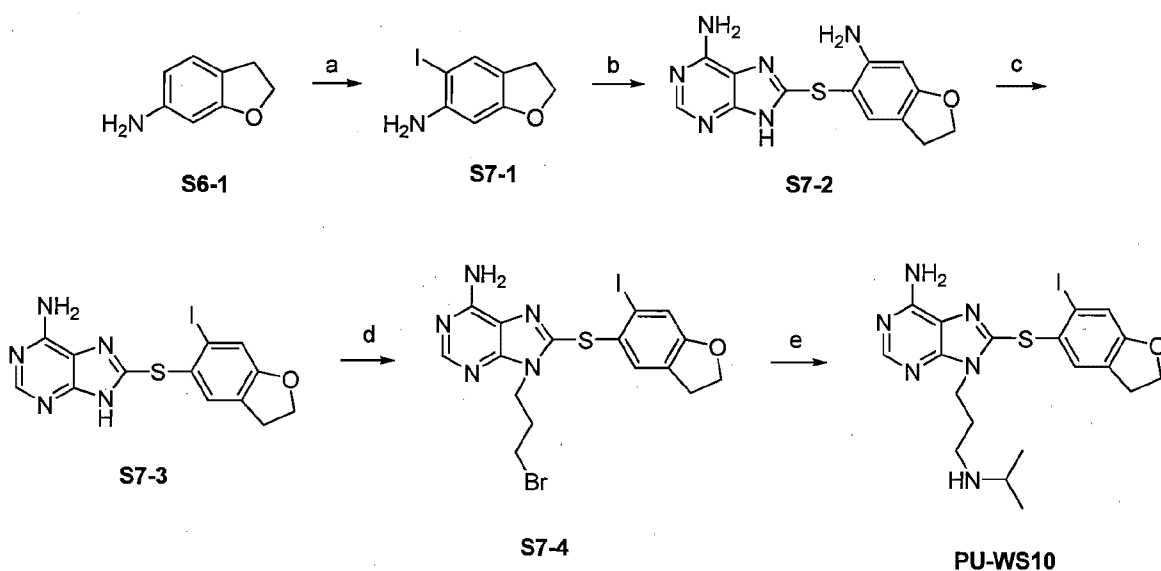
8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-9-(3-isopropylamino-propyl)-9H-purin-6-ylamine (PU-WS4). A mixture of **S6-4** (54 mg, 0.13 mmol), Cs₂CO₃ (127 mg, 0.39 mmol) and 1,3-dibromopropane (202 mg, 0.65 mmol) in anhydrous DMF (2 mL) was stirred at rt for 2 h. Solvent was removed under reduced pressure and the residue purified by chromatography (CH₂Cl₂:MeOH:AcOH). The resulting solid was dissolved in DMF (2 mL) and isopropylamine (0.347 g, 0.5 mL, 5.9 mmol) was added and the solution stirred overnight

at rt. The reaction afforded **PU-WS4** (13 mg, 20%; over two-steps) as a yellow solid after purification. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ 8.26 (s, 1H), 7.77 (s, 1H), 7.07 (s, 1H), 4.65 (t, $J = 8.7$ Hz, 2H), 4.47 (t, $J = 6.9$ Hz, 2H), 3.20-3.33 (m, 3H), 3.01 (t, $J = 7.5$ Hz, 2H), 2.33 (m, 2H), 1.34 (d, $J = 6.5$ Hz, 6H); MS (ESI) m/z 511.2 $[\text{M}+\text{H}]^+$; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{19}\text{H}_{24}\text{IN}_6\text{OS}$, 511.0777; found 511.0779.

8-(5-iodo-2,3-dihydro-benzofuran-6-ylsulfanyl)-9-(2-isobutylamino-ethyl)-9H-purin-6-amine (PU-WS9). A mixture of **S6-4** (30 mg, 0.073 mmol), Cs_2CO_3 (71 mg, 0.22 mmol) and 1,2-dibromoethane (69 mg, 0.365 mmol) in anhydrous DMF (1 mL) was stirred at rt for 2 h. Solvent was removed under reduced pressure and the residue purified by chromatography ($\text{CH}_2\text{Cl}_2:\text{MeOH}:\text{AcOH}$). The resulting solid was dissolved in DMF (2 mL) and isobutylamine (0.241 g, 0.33 mL, 3.3 mmol) was added and the solution stirred overnight at rt. The reaction afforded **PU-WS9** (15 mg, 40%; over two-steps) as a pale yellow solid. ^1H NMR (500 MHz, CDCl_3) δ 8.26 (s, 1H), 7.63 (s, 1H), 6.56 (s, 1H), 6.27 (br s, 2H), 4.57 (t, $J = 8.5$ Hz, 2H), 4.50 (t, $J = 5.5$ Hz, 2H), 3.20 (t, $J = 8.5$ Hz, 2H), 3.12 (t, $J = 5.5$ Hz, 2H), 2.59 (d, $J = 7$ Hz, 2H), 1.99 (m, 1H), 0.97 (d, $J = 7$ Hz, 6H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{19}\text{H}_{24}\text{IN}_6\text{OS}$, 511.0777; found 511.0790.

8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine (PU-WS21). Following the procedure to make **PU-WS9**, compound **PU-WS21** was obtained as a white solid. ^1H NMR (500 MHz, CDCl_3 , δ): 7.56 (s, 1H), 6.60 (s, 1H), 4.47 (t, $J = 8.7$ Hz, 2H), 4.37 (m, 2H), 3.06-3.11 (m, 4H), 2.45 (s, 2H), 0.83 (s, 9H); HRMS (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{26}\text{IN}_6\text{OS}$ 525.0933; found 525.0927.

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Reagents and conditions: (a) NIS, CH₃CN, 0°C, 20 min.; (b) 8-mercaptoadenine, neocuproine, CuI, NaO*t*-Bu, DMF, 110°C; (c) NaNO₂, KI, AcOH/TFA, 0°C; (d) 1,3-dibromopropane, Cs₂CO₃, DMF, rt; (e) isopropylamine, DMF, rt.

Scheme 7. Synthesis of PU-WS10.

5-iodo-2,3-dihydrobenzofuran-6-amine (S7-1). To a solution of 2,3-dihydrobenzofuran-6-amine (**S6-1**; 95 mg, 0.7 mmol) in acetonitrile (3 mL) cooled in an ice-bath was added NIS (158 mg, 0.7 mmol). After stirring at 0 °C for 20 min, the mixture was condensed and purified by flash chromatography (hexane:EtOAc, 90:10 to 20:80) to yield **S7-1** (180 mg, 98%) as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 7.38 (s, 1H), 6.26 (s, 1H), 4.53 (t, *J* = 8.5 Hz, 2H), 3.09 (t, *J* = 8.4 Hz, 2H); MS (ESI) *m/z* 261.9 [M+H]⁺.

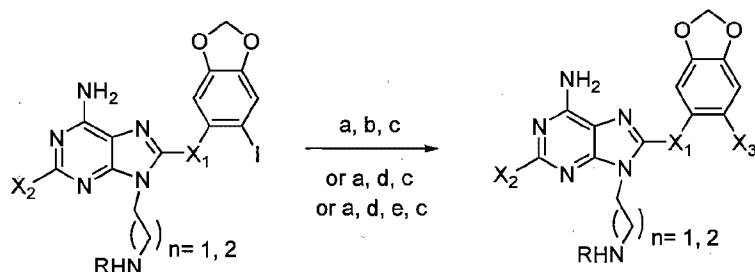
8-(6-amino-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-6-amine (S7-2). The mixture of **S7-1** (80 mg, 0.31 mmol), 8-mercaptoadenine (52 mg, 0.3 mmol), neocuproine (7 mg, 0.03 mmol), CuI (7 mg, 0.03 mmol) and sodium *t*-butoxide (100 mg, 1.04 mmol) was suspended in 10 mL of DMF and stirred at 110 °C overnight. The mixture was concentrated under reduced pressure and the residue purified by flash chromatography (hexane:EtOAc, 90:10 to 20:80) to yield **S7-2** (50 mg, 56%) as a pale yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 8.15

(s, 1H), 7.33 (s, 1H), 6.35 (s, 1H), 4.57 (t, $J = 8.5$ Hz, 2H), 3.14 (t, $J = 8.4$ Hz, 2H); MS (ESI) m/z 301.0 $[M+H]^+$.

8-(6-iodo-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-6-amine (S7-3). To a solution of S7-2 (25 mg, 0.08 mmol) in acetic acid/TFA (5 mL/1 mL) cooled in ice-bath was added NaNO₂ (7 mg, 0.1 mmol) and KI (27 mg, 0.16 mmol). The mixture was stirred at 0°C for 10 minutes and condensed under reduced pressure. The residue was purified by flash chromatography (CH₂Cl₂:MeOH, 100:0 to 90:10) to yield S7-3 (13 mg, 41%) as a yellow solid. ¹H NMR (500 MHz, CD₃OD) δ 8.13 (s, 1H), 7.57 (s, 1H), 7.44 (s, 1H), 4.66 (t, $J = 8.5$ Hz, 2H), 3.22 (t, $J = 8.6$ Hz, 2H); MS (ESI) m/z 411.9 $[M+H]^+$.

9-(3-bromopropyl)-8-(6-iodo-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-6-amine (S7-4). To a solution of S7-3 (13 mg, 0.03 mmol) in DMF (2 mL) was added 1,3-dibromopropane (16 μ L, 0.16 mmol) and Cs₂CO₃ (20 mg, 0.06 mmol) and the resulting mixture was stirred at rt for 40 minutes. The mixture was condensed under reduced pressure and the residue was purified by flash chromatography to yield S7-4 (6.2 mg, 34%). ¹H NMR (500 MHz, CDCl₃) δ 8.31 (s, 1H), 7.37 (s, 2H), 6.00 (br s, 2H), 4.62 (t, $J = 8.7$ Hz, 2H), 4.36 (t, $J = 6.7$ Hz, 2H), 3.42 (t, $J = 6.2$ Hz, 2H), 3.18 (t, $J = 8.9$ Hz, 2H), 2.39 (m, 2H); MS (ESI) m/z 531.9/533.9 $[M+H]^+$.

8-(6-iodo-2,3-dihydro-benzofuran-5-ylsulfanyl)-9-(3-isobutylamino-ethyl)-9H-purin-6-ylamine (PU-WS10). A solution of S7-4 (6.2 mg, 0.012 mmol) and isopropylamine (0.2 mL) in DMF (1 mL) was stirred for 12 h. Solvent was removed under reduced pressure and the residue purified by preparative thin layer chromatography (CHCl₃:MeOH-NH₃ (7N), 20:1) to afford PU-WS10 (4.0 mg, 60%) as a pale yellow solid. ¹H NMR (400 MHz, CDCl₃) δ 8.27 (s, 1H), 7.69 (s, 1H), 7.27 (s, 1H), 5.93 (br s, 2H), 4.66 (t, $J = 8.8$ Hz, 2H), 4.29 (t, $J = 7$ Hz, 2H), 3.33 (t, $J = 8.7$ Hz, 2H), 2.74 (septet, $J = 6.2$ Hz, 1H), 2.58 (t, $J = 6.8$ Hz, 2H), 1.98 (m, 2H), 1.05 (d, $J = 6.5$ Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 162.0, 154.4, 152.7, 151.9, 147.8, 141.7, 130.2, 128.6, 121.1, 120.0, 74.1, 71.7, 48.9, 44.0, 41.6, 30.9, 30.2; MS (ESI) m/z 511.1 $[M+H]^+$.



PU-DZ8 $X_1=CH_2$, $X_2=F$, $n=2$, R = isopropyl

PU-H71 $X_1=S$, $X_2=H$, $n=2$, R = isopropyl

PU-HZ150 $X_1=S$, $X_2=H$, $n=1$, R = isobutyl

PU-HZ151 $X_1=S$, $X_2=H$, $n=1$, R = neopentyl

PU-DZ13 $X_1=CH_2$, $X_2=F$, $n=1$, R = isobutyl

PU-WS3 $X_1=CH_2$, $X_2=F$, $X_3=CN$, $n=2$, R = isopropyl

PU-WS5 $X_1=S$, $X_2=H$, $X_3=CN$, $n=2$, R = isopropyl

PU-WS6 $X_1=S$, $X_2=H$, $X_3=CCt-Bu$, $n=2$, R = isopropyl

PU-WS7 $X_1=S$, $X_2=H$, $X_3=CCPh$, $n=2$, R = isopropyl

PU-WS8 $X_1=S$, $X_2=H$, $X_3=CCH$, $n=2$, R = isopropyl

PU-WS16 $X_1=S$, $X_2=H$, $X_3=CCH$, $n=1$, R = isobutyl

PU-WS19 $X_1=S$, $X_2=H$, $X_3=CCH$, $n=1$, R = neopentyl

PU-WS20 $X_1=CH_2$, $X_2=F$, $X_3=CCH$, $n=1$, R = isobutyl

Reagents and conditions: (a) Boc_2O , Et_3N , THF, rt, 12h; (b) $PdCl_2(dppf)$, $Zn(CN)_2$, Zn , DMF, $130^\circ C$; (c) 10% TFA- CH_2Cl_2 , rt, 2-5h; (d) CuI , $PdCl_2(PPh_3)_2$, *t*-butylacetylene or phenylacetylene or trimethylsilylacetylene, Et_3N , DMF, $90^\circ C$, 24h; (e) KOH , MeOH, rt, 2h.

Scheme 8. Synthesis of PU-WS3, PU-WS5, PU-WS6, PU-WS7 and PU-WS8, PU-WS16, PU-WS19 and PU-WS20.

6-[6-amino-2-fluoro-9-(3-isopropylamino-propyl)-9H-purin-8-ylmethyl]-benzo[1,3]dioxole-5-carbonitrile (PU-WS3). A solution of **PU-DZ8** (118 mg, 0.231 mmol), $(Boc)_2O$ (55 mg, 0.254 mmol) and triethylamine (16 mg, 0.231 mmol) in THF (2 mL) was stirred at room temperature for 12 h. Following solvent removal, the residue was purified by preparative thin layer chromatography ($CHCl_3$:MeOH- NH_3 (7N), 20:1) to afford Boc-protected **PU-DZ8** (120 mg, 85%; MS (ESI) m/z 613.05 $[M+H]^+$). To a solution of Boc-protected **PU-DZ8** (26 mg, 0.04 mmol) in DMF (3 mL) was added $PdCl_2(dppf)$ (17 mg, 0.02 mmol), $Zn(CN)_2$ (10 mg, 0.08 mmol) and Zn (3 mg, 0.04 mL) and the resulting mixture was stirred at $130^\circ C$ overnight. The reaction mixture was condensed under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:MeOH- NH_3 (7N), 20:1) to yield Boc-protected **PU-WS3** as a white solid. To a solution of this in 2 mL of CH_2Cl_2 was added

0.2 mL of TFA and the mixture was stirred at room temperature for 5 h. The reaction mixture was condensed under reduced pressure and the residue purified by flash chromatography (CHCl_3 :MeOH- NH_3 (7N), 20:1) to yield **PU-WS3** as a white solid in quantitative yield (12 mg, 59% for three steps). ^1H NMR (500 MHz, CD_3OD) δ 7.13 (s, 1H), 6.96 (s, 1H), 6.03 (s, 2H), 4.31 (s, 2H), 4.25 (t, $J = 7$ Hz, 2H), 3.26 (m, 1H), 3.01 (t, $J = 7.5$ Hz, 2H), 2.14 (m, 2H), 1.23 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 160.4 (d, $J = 208$ Hz), 158.5 (d, $J = 19$ Hz), 153.8, 153.5 (d, $J = 19$ Hz), 151.7, 149.1, 137.2, 119.1, 117.4, 112.6, 112.4, 106.3, 104.4, 52.3, 43.4, 40.8, 33.2, 27.7, 19.3; MS (ESI) m/z 412.3 $[\text{M}+\text{H}]^+$.

6-[6-amino-9-(3-isopropylamino-propyl)-9H-purin-8-ylsulfanyl]benzo[1,3]dioxole-5-carbonitrile (PU-WS5). The procedure for the preparation of **PU-WS3** was followed starting from **PU-H71**. The reaction afforded **PU-WS5** (6.5 mg, 32% for three steps) as a white solid. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ 8.21 (s, 1H), 7.22 (s, 1H), 7.19 (s, 1H), 6.19 (s, 2H), 4.40 (t, $J = 7$ Hz, 2H), 3.09 (septet, $J = 6.5$ Hz, 1H), 2.83 (t, $J = 7.5$ Hz, 2H), 2.26 (m, 2H), 1.25 (d, $J = 6.5$ Hz, 6H); MS (ESI) m/z 412.2 $[\text{M}+\text{H}]^+$; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{19}\text{H}_{22}\text{N}_7\text{O}_2\text{S}$, 412.1556; found 412.1560.

8-[6-(3,3-dimethyl-but-1-ynyl)-benzo[1,3]dioxol-5-ylsulfanyl]9-(3-isopropylamino-propyl)-9H-purin-6-ylamine (PU-WS6). A solution of **PU-H71** (70 mg, 0.137 mmol), $(\text{Boc})_2\text{O}$ (35 mg, 0.161 mmol) and triethylamine (13 mg, 0.137 mmol) in THF (2 mL) was stirred at room temperature for 12 h. Following solvent removal, the residue was purified by preparative thin layer chromatography (CHCl_3 :MeOH- NH_3 (7N), 20:1) to afford Boc-protected **PU-H71** (74 mg, 88%; MS (ESI) m/z 612.89 $[\text{M}+\text{H}]^+$). To a solution of Boc-protected **PU-H71** (0.24 g, 0.39 mmol) in DMF (2 mL) was added CuI (4 mg, 0.1 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (14 mg, 0.02 mmol), *t*-butylacetylene (72 μL , 0.59 mmol) and triethylamine (137 μL) and the mixture was stirred at 90 °C for 24 h. The reaction mixture was condensed under reduced pressure and purified by chromatography to afford a solid. To a solution of the solid in 15 mL of CH_2Cl_2 was added TFA (1.5 mL) and stirred at RT for 2 hrs. The mixture was condensed and purified by flash chromatography to afford **PU-WS6** (97 mg, 52 % for three steps) as a white solid. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ 8.25 (s, 1H), 6.99 (s, 1H), 6.97 (s, 1H), 6.05 (s, 2H), 4.41 (t, $J = 7$ Hz, 2H), 3.29 (m, 1H), 2.98 (t, $J = 7.5$ Hz, 2H),

2.24 (m, 2H), 1.34 (d, $J = 6.5$ Hz, 6H), 1.18 (s, 9H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ 50.5, 41.3, 40.2, 30.3, 27.8, 25.9, 18.5; MS (ESI) m/z 467.3 $[\text{M}+\text{H}]^+$; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{24}\text{H}_{31}\text{N}_6\text{O}_2\text{S}$, 467.2229; found 467.2233.

9-(3-isopropylamino-propyl)-8-(6-phenylethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-9H-purin-6-ylamine (PU-WS7). The procedure for the preparation of **PU-WS6** was followed with phenylacetylene (65 μL , 0.59 mmol) to afford **PU-WS7** (46 mg, 34% in three steps) as a white solid. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ 8.2 (s, 1H), 7.30-7.40 (m, 5H), 7.08 (s, 1H), 6.96 (s, 1H), 6.06 (s, 2H), 4.27 (m, 2H), 2.69 (m, 1H), 2.51 (m, 2H), 1.97 (m, 2H), 1.01 (d, $J = 6.5$ Hz, 6H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD}$) δ 154.3, 152.3, 151.1, 148.8, 147.3, 131.3, 128.7, 128.3, 124.4, 122.4, 120.4, 119.3, 112.9, 112.4, 102.3, 94.2, 86.6, 50.5, 43.1, 41.3, 29.2, 21.7; MS (ESI) m/z 487.2 $[\text{M}+\text{H}]^+$; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{26}\text{H}_{27}\text{N}_6\text{O}_2\text{S}$, 487.1903; found 487.1913.

8-(6-ethynyl-benzo[1,3]dioxol-5-ylsulfanyl)-9-(3-isopropylamino-propyl)-9H-purin-6-ylamine (PU-WS8). The procedure for the preparation of **PU-WS6** was followed with trimethylsilanylacetylene (82 μL , 0.59 mmol), and following coupling a white solid was obtained and used without further purification. To this was added MeOH (10 mL) and KOH (90 mg) and was stirred at rt for 2 hrs. The reaction mixture was concentrated under reduced pressure and to the resulting residue was added 2 mL of 10% TFA- CH_2Cl_2 and was stirred at rt for 2 hrs. The mixture was concentrated under reduced pressure and the residue chromatographed to afford **PU-WS8** (5.2 mg, 26% for four steps) as a pale yellow solid. ^1H NMR (500 MHz, CDCl_3) δ 8.32 (s, 1H), 6.99 (s, 1H), 6.84 (s, 1H), 6.00 (s, 2H), 5.61 (br s, 2H), 4.31 (t, $J = 7$ Hz, 2H), 3.31 (s, 1H), 2.71 (m, 1H), 2.56 (t, $J = 7$ Hz, 2H), 1.97 (m, 2H), 1.02 (d, $J = 6.5$ Hz, 6H); MS (ESI) m/z 411.2 $[\text{M}+\text{H}]^+$; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{20}\text{H}_{23}\text{N}_6\text{O}_2\text{S}$, 411.1603; found 411.1605.

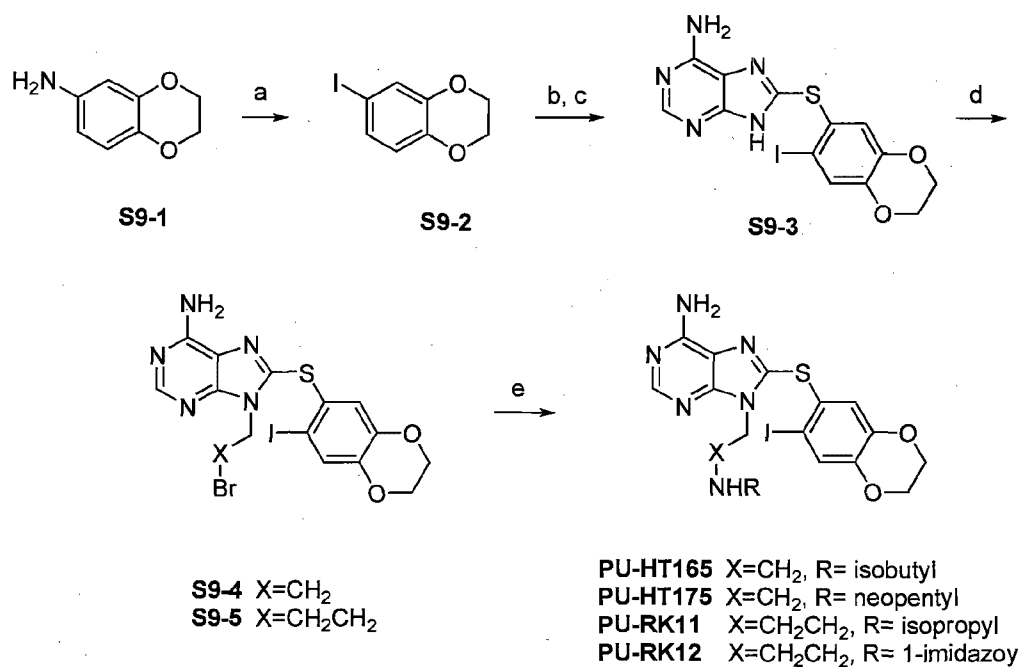
8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine (PU-WS16). Following the procedure to make **PU-WS8**, **PU-WS16** was obtained as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 8.24 (s, 1H), 6.91 (s, 1H), 6.77 (s, 1H), 6.01 (s, 2H), 5.78 (br s, 2H), 4.33 (t, $J = 6.1$ Hz, 2H), 3.24 (s, 1H), 2.92 (t, $J = 6.1$ Hz, 2H), 2.38 (d, J

= 6.8 Hz, 2H), 1.63 (m, 1H), 0.77 (d, J = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 155.1, 153.5, 151.9, 149.6, 148.5, 147.0, 128.0, 124.1, 117.0, 114.8, 111.3, 102.6, 82.9, 81.4, 57.9, 49.3, 44.2, 28.8, 28.4, 20.9; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{20}\text{H}_{22}\text{N}_6\text{O}_2\text{S}$, 411.1603; found 411.1606.

8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine (PU-WS19). Following the procedure to make PU-WS8, PU-WS19 was obtained as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 8.32 (s, 1H), 6.97 (s, 1H), 6.83 (s, 1H), 5.98 (s, 2H), 5.76 (br s, 2H), 4.35 (m, 2H), 3.06 (s, 1H), 2.97 (m, 2H), 2.33 (s, 2H), 0.82 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 154.5, 152.9, 151.5, 149.1, 147.9, 146.5, 120.1, 117.7, 112.9, 111.9, 102.2, 82.3, 81.0, 61.9, 49.8, 43.9, 31.5, 27.7; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{21}\text{H}_{25}\text{N}_6\text{O}_2\text{S}$, 425.1760; found 425.1753.

8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine (PU-WS20). Following the procedure to make PU-WS8, PU-WS20 was obtained from PU-DZ13 as a white solid. ^1H NMR ($\text{MeOH}-d_4$, 500 MHz) δ : 6.98 (s, 1H), 6.70 (s, 1H), 6.02 (s, 2H), 4.36 (s, 2H), 4.20 (t, J = 6.4 Hz, 2H), 2.92 (t, J = 6.4 Hz, 2H), 2.42 (d, J = 6.9 Hz, 2H), 2.03 (s, 1H), 1.69 (m, 1H), 0.87 (d, J = 6.8 Hz, 6H); ^{13}C NMR ($\text{MeOH}-d_4$, 125 MHz) δ : 159.8, 158.1, 152.6, 151.4, 149.8, 147.2, 134.3, 116.2, 114.2, 112.5, 109.8, 102.3, 80.9, 57.5, 43.0, 32.6, 29.8, 28.2, 20.5.

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Reagents and conditions: (a) NaNO₂, 10% HCl, 0°C; KI, 0°C to rt; (b) 8-mercaptoadenine, neocuproine, CuI, NaOt-Bu, DMF, 110°C, 24 h; (c) NIS, TFA, CH₃CN, rt; (d) 1,2-dibromoethane or 1,3-dibromopropane, Cs₂CO₃, DMF, rt; (e) isobutylamine or neopentylamine or isopropylamine or imidazole, DMF, rt.

Scheme 9. Synthesis of PU-HT165, PU-HT175, PU-RK11, PU-RK12.

6-Iodo-2,3-dihydrobenzo[b][1,4]dioxine (S9-2). 2,3-dihydrobenzo[b][1,4]dioxin-6-amine (**S9-1**; 5 g, 33 mmol) was dissolved in 10% HCl solution and cooled to 0°C. Then, 30 mL of a cold aqueous solution of NaNO₂ (4.6 g, 66 mmol) was added over a period of 15 min and the reaction mixture was stirred at 0°C for an additional 10 min, followed by the addition of urea (1.6 g, 27 mmol). After 15 min, 40 mL of a suspension of KI (16.5 g, 100 mmol) in water/CH₂Cl₂ (1:1) was added. The reaction mixture was stirred overnight at room temperature then extracted with CH₂Cl₂, dried over MgSO₄. And condensed under reduced pressure and the residue was purified by flash chromatography (hexane:EtOAc, 100:0 to 90:10) to afford **S9-2** (7.4 g, 86%) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 7.28 (s, 1H), 7.13 (d, *J* = 8.5 Hz, 1H), 6.63 (d, *J* = 8.5 Hz, 1H), 4.27-4.24 (m, 4H).

8-(7-Iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine (S9-3). To a solution of **S9-2** (1.26 g, 4.8 mmol) in DMF (15 mL) was added 8-mercaptopurine (0.400 g, 2.4 mmol), neocuproine (0.056 g, 0.24 mmol), CuI (0.044 g, 0.24 mmol) and NaOtBu (0.460 g, 4.8 mmol). The reaction mixture was stirred at 110 °C for 24h. Solids were filtered and the filtrate was condensed under reduced pressure. The residue was flash chromatographed (CHCl₃:MeOH:AcOH, 60:0.5:0.5 to 30:0.5:0.5) to yield 0.578 g (80%) of intermediate coupling product (MS (ESI) m/z 301.9 [M+H]⁺). To 0.400 g (1.4 mmol) of this and NIS (0.945 g, 4.2 mmol) in acetonitrile (15 mL) was added TFA (540 μ L, 0.800 g, 7 mmol) and the mixture was stirred at room temperature overnight. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (CHCl₃:MeOH:AcOH, 60:0.5:0.5 to 30:0.5:0.5) to give **S9-3** (0.436 g, 73%). ¹H NMR (DMSO-d₆, 500 MHz) δ 8.37 (s, 1H), 8.03 (br s, 2H), 7.47 (s, 1H), 7.10 (s, 1H), 4.25-4.27 (m, 4H); MS (ESI) m/z 427.9 [M+H]⁺.

9-(2-Bromoethyl)-8-(7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine (S9-4). A mixture of **S9-3** (0.213 g, 0.5 mmol), 1,2-dibromoethane (0.500 g, 2.5 mmol) and Cs₂CO₃ (0.184 g, 0.75 mmol) in anhydrous DMF (6 mL) was stirred at room temperature for 3h. Solids were filtered and the filtrate was condensed under reduced pressure to give a residue that was purified by preparative thin layer chromatography (CHCl₃:MeOH-NH₃ (7N), 20:1) to give **S9-4** (0.107 g, 40%). ¹H NMR (CDCl₃, 500 MHz) δ 8.29 (s, 1H), 7.36 (s, 1H), 7.00 (s, 1H), 6.23 (br s, 2H), 4.62 (t, J = 7.0 Hz, 2H), 4.16-4.24 (m, 4H), 3.69 (t, J = 7.0 Hz, 2H); MS (ESI) m/z 533.9/535.9 [M+H]⁺.

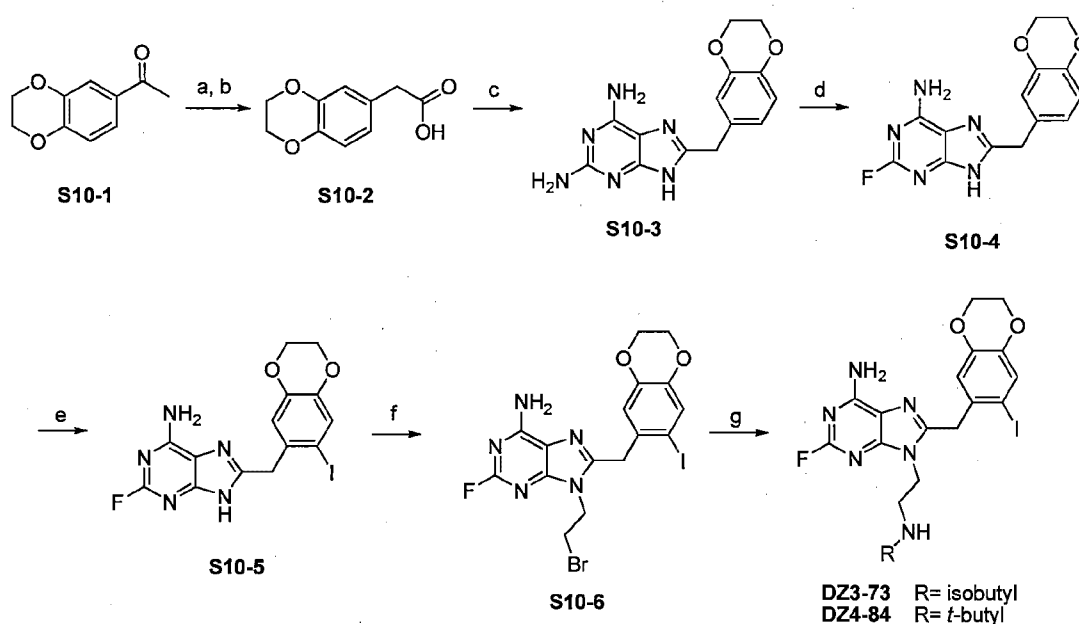
9-(3-Bromopropyl)-8-(7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine (S9-5). A mixture of **S9-3** (0.213 g, 0.5 mmol), 1,3-dibromopropane (0.512 g, 2.5 mmol) and Cs₂CO₃ (0.184 g, 0.75 mmol) in anhydrous DMF (6 mL) was stirred at room temperature for 3h. Solids were filtered and the filtrate was condensed under reduced pressure to give a residue that was purified by preparative thin layer chromatography (CHCl₃:MeOH-NH₃ (7N), 20:1) to give **S9-5** (0.104 g, 38 %). ¹H NMR (CDCl₃, 500 MHz) δ 8.26 (s, 1H), 7.32 (s, 1H), 6.94 (s, 1H), 5.6 (br s, 2H), 4.27 (t, J = 7.0 Hz, 2H), 4.10-4.17 (m, 4H), 3.32 (t, J = 7.0 Hz, 2H), 2.26 (m, 2H); MS (ESI) m/z 547.9/549.8 [M+H]⁺.

8-(7-Iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(isobutylamino)ethyl)-5,9-dihydro-4H-purin-6-amine (PU-HT165). S9-4 (0.052 g, 0.097 mmol) and isobutylamine (0.354 g, 4.9 mmol) in DMF (1 ml) was stirred overnight at rt. Solvent was removed under reduced pressure and the resulting residue was purified by chromatography (CH₂Cl₂:MeOH) to give 0.040 g, 78%) of **PU-HT165** as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 8.24 (s, 1H), 7.37 (s, 1H), 6.94 (s, 1H), 6.24 (br s, 2H), 4.44 (br s, 2H), 4.22-4.24 (m, 4H), 3.08 (m, 2H), 2.52 (d, *J* = 5.7 Hz, 2H), 1.92 (m, 1H), 0.92 (d, *J* = 6.0 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 155.4, 152.8, 151.4, 147.7, 145.5, 145.2, 128.9, 127.5, 122.0, 120.5, 91.6, 64.9, 64.7, 57.3, 49.0, 43.9, 28.0, 21.0; MS (ESI) *m/z* 527.1 [M+H]⁺.

8-(7-Iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(neopentylamino)ethyl)-5,9-dihydro-4H-purin-6-amine (PU-HT175). S9-4 (0.052, 0.097 mmol) and neopentylamine (0.426 g, 4.9 mmol) in DMF (1 mL) was stirred overnight at rt. Solvent was removed under reduced pressure and the resulting residue was purified by chromatography (CH₂Cl₂:MeOH) to give 0.038 g (73%) of **PU-HT175** as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 8.31 (s, 1H), 7.37 (s, 1H), 6.94 (s, 1H), 5.79 (br s, 2H), 4.33 (t, *J* = 6.5 Hz, 2H), 4.20-4.24 (m, 4H), 2.99 (t, *J* = 6.5 Hz, 2H), 2.34 (s, 2H), 0.84 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 154.5, 152.9, 151.7, 147.0, 144.7, 144.6, 128.2, 127.8, 121.2, 120.2, 90.7, 64.3, 64.2, 62.0, 49.8, 44.0, 31.6, 27.7; MS *m/z* 541.1 [M+H]⁺.

8-(7-Iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine (PU-RK11). S9-5 (0.045 g, 0.082 mmol) and isopropylamine (0.242 g, 4.1 mmol) in DMF (1 mL) was stirred overnight at rt. Solvent was removed under reduced pressure and the resulting residue was purified by chromatography (CH₂Cl₂:MeOH) to give 0.038 g (88%) of **PU-RK11**. ¹H NMR (500 MHz, CDCl₃) δ 8.30 (s, 1H), 7.38 (s, 1H), 6.95 (s, 1H), 5.65 (br s, 2H), 4.32 (t, *J* = 6.9 Hz, 2H), 4.22-4.24 (m, 4H), 2.80 (septet, *J* = 6.7 Hz, 1H), 2.61 (t, *J* = 6.7 Hz, 2H), 2.07 (m, 2H), 1.11 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 154.4, 152.8, 151.7, 146.7, 144.8, 144.6, 128.3, 127.8, 121.3, 120.1, 91.0, 64.3, 64.2, 49.0, 43.6, 41.6, 29.8, 22.5; MS (ESI) *m/z* 527.1 [M+H]⁺.

9-(3-(1H-imidazol-1-yl)propyl)-8-(7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine (PU-RK12). **S9-5** (0.045 g, 0.082 mmol) and imidazole (0.056 g, 0.82 mmol) in DMF (1 mL) was stirred overnight at rt. Solvent was removed under reduced pressure and the resulting residue was purified by chromatography (CH₂Cl₂:MeOH) to give 0.029 g (67%) of **PU-RK12**. ¹H NMR (500 MHz, CDCl₃) δ 8.34 (s, 1H), 7.62 (s, 1H), 7.39 (s, 1H), 7.09 (s, 1H), 6.98 (s, 1H), 6.94 (s, 1H), 5.70 (br s, 2H), 4.19-4.28 (m, 6H), 4.00 (t, *J* = 7.5 Hz, 2H), 2.25 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 154.5, 153.2, 151.8, 146.3, 145.0, 144.7, 137.1, 129.6, 128.3, 126.9, 121.3, 120.1, 118.7, 90.9, 64.3, 64.2, 44.3, 41.0, 31.8; MS (ESI) *m/z* 536.1 [M+H]⁺.



Reagents and conditions: (a) sulfur, morpholine, 140°C, 14 h; (b) 10% KOH (aq.), reflux, 12 h; (c) 2,4,5,6-tetraaminopyrimidine, triphenyl phosphite, pyridine, microwave irradiation at 220°C, 75 min.; (d) HF/pyridine, NaNO₂, 0 °C to rt, 1 h; (e) NIS, TFA, CH₃CN, rt overnight; (f) Cs₂CO₃, 1,2-dibromoethane, DMF, rt, 3.5 h; (g) isobutylamine or *t*-butylamine, DMF, overnight, rt.

Scheme 10. Synthesis of DZ3-73 and DZ4-84.

2-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)acetic acid (S10-2). A mixture of 1,4-benzodioxan-6-yl methyl ketone (**S10-1**; 5.5 g, 30.9 mmol), sulfur (1.98 g, 61.8 mmol) and morpholine (6.73 g, 6.76 mL, 77.3 mmol) was refluxed at 140°C for 14 h. After cooling to rt,

the reaction mixture was diluted with 150 mL of CH_2Cl_2 , transferred to a separatory funnel and washed with 25 mL of ice-cold brine. The aqueous layer was further extracted with CH_2Cl_2 (2 x 75 mL). The organic layers were combined, dried with Na_2SO_4 , and filtered. Activated charcoal was added to the filtrate and after several minutes was filtered and concentrated to give 12.7 g of a brown oil. A mixture of this in 75 mL of 10% KOH (aq.) was refluxed for 12h. After cooling the reaction mixture was transferred to a separatory funnel and washed with ether (30 mL). The aqueous layer was acidified with 6N HCl (~25 mL) to pH 2 and extracted with CH_2Cl_2 (4 x 100 mL). The organic layers were combined, washed with distilled water (100 mL), dried with Na_2SO_4 and filtered. This was treated with charcoal, filtered, and solvent removed under reduced pressure and the resulting residue was purified by chromatography (hexane:EtOAc, 90:10 to 70:30) to give 3.90 g (65%) of **S10-2**. ^1H NMR (500 MHz, CDCl_3) δ 6.80-6.82 (m, 2H), 6.74 (dd, $J = 2.0, 8.2$ Hz, 1H), 4.24 (s, 4H), 3.53 (s, 2H); MS (ESI) m/z 195.1 $[\text{M}+\text{H}]^+$.

8-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purine-2,6-diamine (S10-3). A mixture of **S10-2** (1.00 g, 5.15 mmol), 2,4,5,6-tetraaminopyrimidine (0.868 g, 6.19 mmol), triphenyl phosphite (1.92 g, 1.63 mL, 6.19 mmol) in 15 mL of pyridine was sonicated for several minutes. It was then subjected to microwave irradiation at 220°C for 75 minutes. The mixture was concentrated and the resulting residue was purified by chromatography (CH_2Cl_2 :MeOH:MeOH- NH_3 (7N), 60:0.5:0.5 to 20:0.5:0.5) to give 1.12 g (73%) of **S10-3**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 6.75-6.84 (m, 3H), 4.24 (s, 4H), 3.98 (s, 2H); MS (ESI) m/z 299.3 $[\text{M}+\text{H}]^+$.

8-((2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-6-amine (S10-4). To a solution of **S10-3** (1.00 g, 3.35 mmol) in HF/pyridine (2.4 mL) at 0 °C, NaNO_2 (0.3 g, 4.36 mmol) was slowly added. The reaction was brought to room temperature and further stirred for 1 h. Following dilution with CH_2Cl_2 (20 mL), the excess HF was quenched by stirring for 1 h with CaCO_3 (1.19 g). The mixture was dried under reduced pressure and subsequently purified by chromatography (CH_2Cl_2 :MeOH:AcOH, 90:1:0.5) to give 1.15 g (96%) of **S10-4**. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 6.75-6.84 (m, 3H), 4.24 (s, 4H), 4.04 (s, 2H); MS (ESI) m/z 302.3 $[\text{M}+\text{H}]^+$.

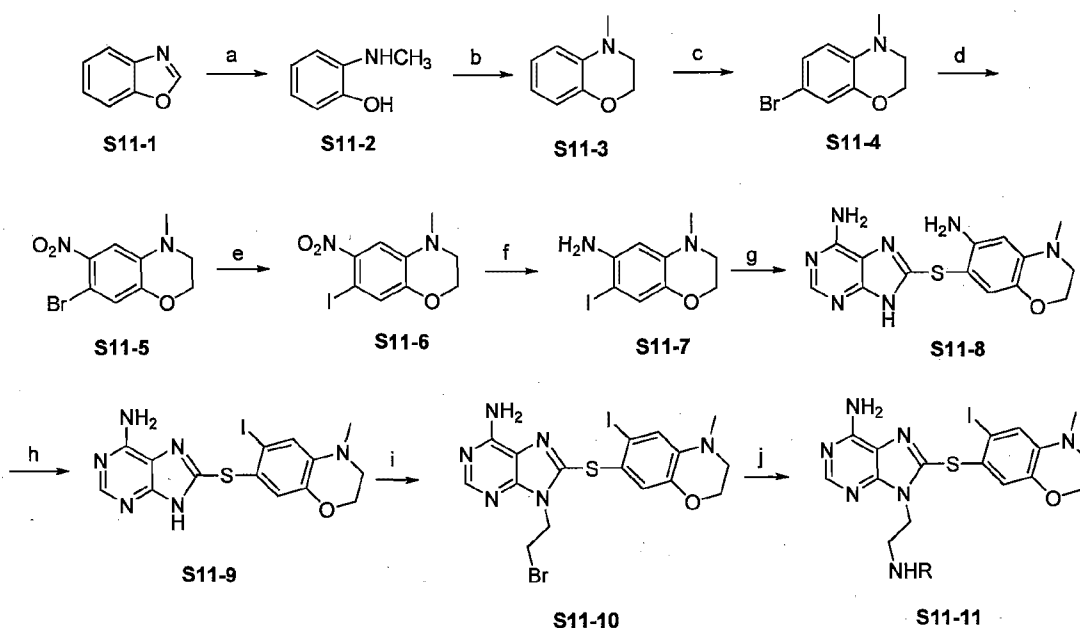
2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine (S10-5). S10-4 (0.310 g, 1.03 mmol), NIS (0.301 g, 1.34 mmol), CH₃CN (20 mL), TFA (2.34 g, 1.56 mL, 20.5 mmol) was stirred at rt overnight. The mixture was dried under reduced pressure and the residue chromatographed (CH₂Cl₂:MeOH:AcOH, 120:1:0.5 to 90:1:0.5) to give 0.340 g (77%) of a mixture of S10-5 (m/z 428.2 [M+H]⁺) along with diiodinated compound (m/z 554.1 [M+H]⁺). LC-MS shows ratio of S10-5 to diiodinated compound to be 83:17. This mixture was not separated but used further in the following step. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*4) δ 7.37 (s, 1H), 6.82 (s, 1H), 4.25 (s, 4H), 4.18 (s, 2H); MS (ESI) m/z 428.2 [M+H]⁺.

9-(2-bromoethyl)-2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine (S10-6). S10-5 (0.340 g, 0.796 mmol), Cs₂CO₃ (0.337 g, 1.035 mmol), 1,2-dibromoethane (0.747 g, 0.343 mL, 3.99 mmol) in DMF (10 mL) was stirred at rt for 3.5 h. The mixture was dried under reduced pressure and the residue chromatographed (CH₂Cl₂:MeOH:AcOH, 200:1:0.5 to 120:1:0.5) to give 0.360 g (85%) of a mixture of S10-6 (m/z 534.0/536.2 [M+H]⁺) along with diiodinated compound (m/z 659.5/661.9 [M+H]⁺). LC-MS shows ratio of titled compound to diiodinated compound to be 80:20. This mixture was not separated but used further in the following step.

2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [DZ3-73]. S10-6 (0.360 g, 0.674 mmol) and isobutylamine (2.46 g, 3.38 ml) in DMF (8 mL) was stirred overnight at rt. Solvent was removed under reduced pressure and the resulting residue was chromatographed (CH₂Cl₂:MeOH:MeOH-NH₃ (7N), 120:0.5:0.5 to 60:0.5:0.5) to give 0.220 g of a mixture of DZ3-73 along with the diiodinated compound. This mixture was separated by reverse phase HPLC ((a) H₂O + 0.1% TFA and (b) CH₃CN + 0.1% TFA, 10 to 75% b over 22 minutes at 16 mL/min) to give 0.196 g (58%) of DZ3-73. ¹H NMR (500 MHz, CDCl₃) δ 7.35 (s, 1H), 6.57 (s, 1H), 6.37 (br s, 2H), 4.24 (s, 2H), 4.20 (s, 4H), 4.08 (t, J = 6.4 Hz, 2H), 2.91 (t, J = 6.4 Hz, 2H), 2.37 (d, J = 6.3 Hz, 2H), 1.64 (m, 1H), 0.85 (d, J = 6.2 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃) δ 158.8 (d, J = 208.1 Hz), 156.4 (d, J = 19.5 Hz), 152.8 (d, J = 18.8 Hz), 151.2,

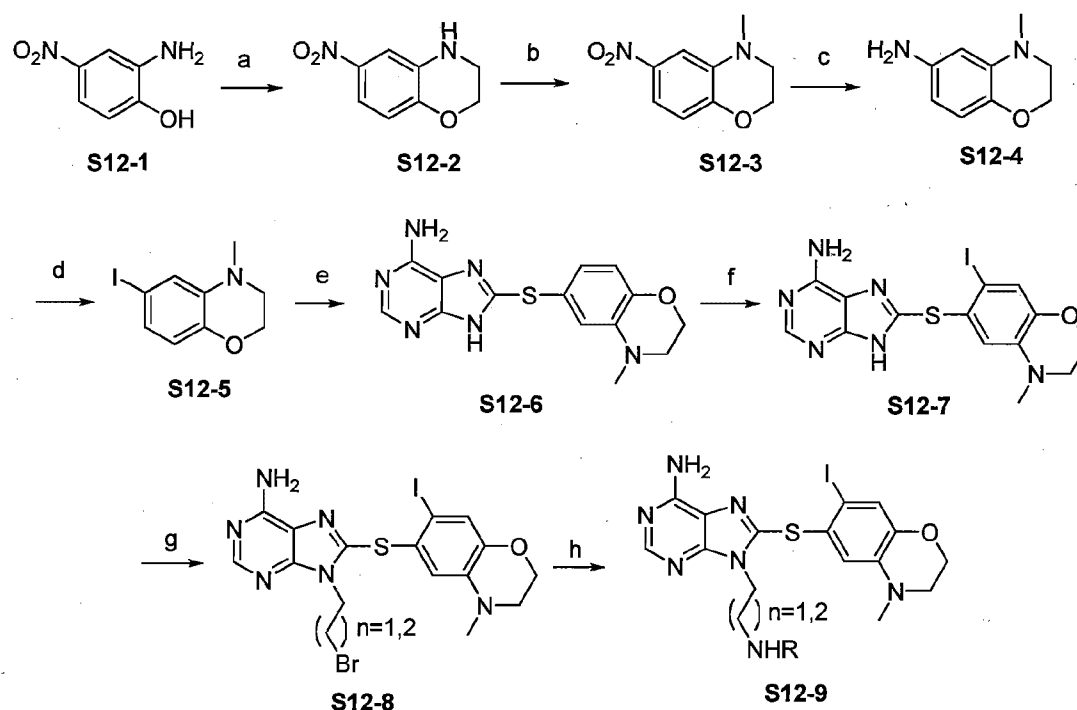
144.2, 143.6, 131.5, 127.6, 117.9, 116.7, 88.3, 64.5, 57.8, 48.8, 43.5, 38.6, 28.4, 20.5; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{20}H_{25}FIN_6O_2$, 527.1068; found 527.1066; HPLC: method A R_t = 6.91, method B R_t = 8.48.

9-(2-(tert-butylamino)ethyl)-2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine [DZ4-84]. **S10-6** (8 mg, 0.0149 mmol) and *tert*-butylamine (109 mg, 157 μ l) in DMF (0.5 mL) was stirred overnight at rt. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 7:2:1:0.5) to give 6 mg (77%) of **DZ4-84**. ¹H NMR (500 MHz, CDCl₃) δ 7.36 (s, 1H), 6.55 (s, 1H), 5.86 (br s, 2H), 4.29 (s, 2H), 4.17-4.23 (m, 4H), 4.04 (t, J = 6.4 Hz, 2H), 2.85 (t, J = 6.4 Hz, 2H), 0.99 (s, 9H); MS (ESI) m/z 527.1 $[M+H]^+$.



Reagents and conditions: (a) NaBH₄, AcOH, THF, rt; (b) dibromoethane, acetone, H₂O, K₂CO₃, reflux; (c) NBS, DMF, 80°C; (d) KNO₃, H₂SO₄; (e) NaI, CuI, N,N'-dimethylethylenediamine, dioxane, 110°C; (f) Fe, NH₄Cl, isopropanol, reflux; (g) 8-mercaptoadenine, neocuproine, CuI, NaOtBu, DMF, 115°C; (h) NaNO₂, KI, AcOH, 0°C; (i) Cs₂CO₃, 1,2-dibromoethane or 1,3-dibromopropane, DMF, rt; (j) NH₂R, DMF, rt.

Scheme 11. Synthesis of Morpholine-type compounds S11-11.



Reagents and conditions: (a) 1,2-dibromoethane, K_2CO_3 , DMF, $125^\circ C$; (b) MeI, DMF, $0^\circ C$ then rt; (c) Pd/C, H_2 , MeOH, rt; (d) $NaNO_2$, AcOH, KI, $0^\circ C$; (e) 8-mercaptoadenine, neocuproine, CuI, NaOtBu, DMF, $115^\circ C$; (f) NIS, CH_3CN , rt; (g) Cs_2CO_3 , 1,3-dibromopropane or 1,2-dibromoethane, DMF, rt; (h) NH_2R , DMF, rt.

Scheme 12. Synthesis of Morpholine-type compounds S12-9.

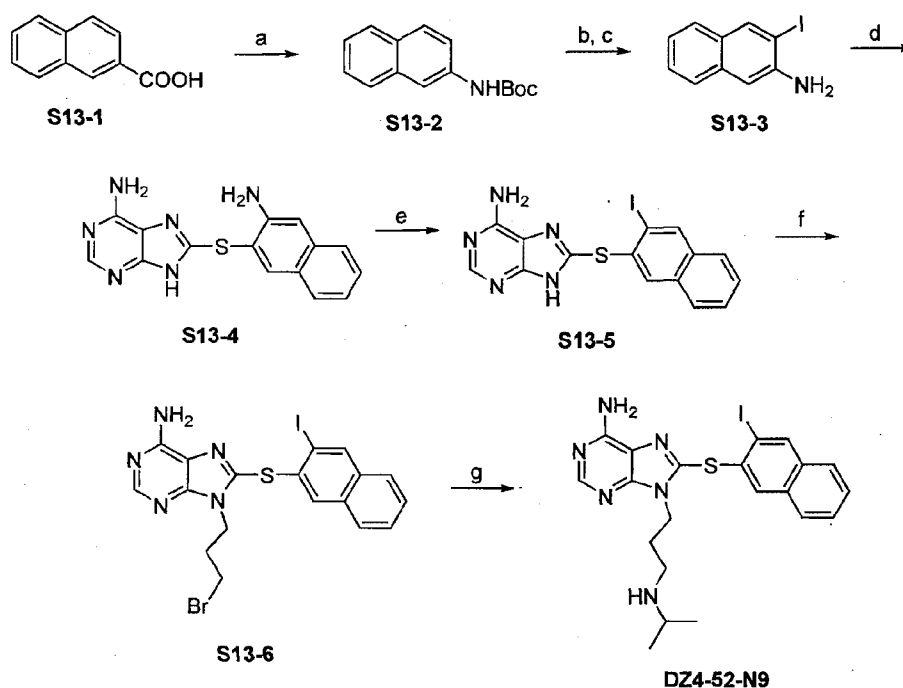
6-Nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine [S12-2]. To a solution of 2-amino-4-nitrophenol (S12-1; 1.5 g, 9.7 mmol) in 50 mL of DMF was added K_2CO_3 (4.04 g, 29.2 mmol) and 1,2-dibromoethane (1 mL, 11.7 mmol). The resulting mixture was stirred at $125^\circ C$ under argon overnight. The resulting mixture was concentrated under vacuum and purified by flash chromatography to give S12-2 (1.2 g, 68%) as a yellow solid. ^1H NMR ($CDCl_3$, 500 MHz) δ 7.55-7.58 (dd, $J = 2.7, 8.9$ Hz, 1H), 7.48 (d, $J = 2.6$ Hz, 1H), 6.81 (d, $J = 8.9$ Hz,

1H), 4.34 (m, 2H), 4.12 (br s, 1H), 3.47 (m, 2H); ¹³C NMR (CDCl₃, 125 MHz) δ 149.4, 141.8, 133.8, 115.0, 114.8, 110.2, 65.6, 40.0.

4-Methyl-6-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine [S12-3]. To a solution of **S12-2** (0.66 g, 3.7 mmol) in 30 mL of DMF was added NaH (106 mg, 4.4 mmol) and stirred at 0 °C for 30 min. To the resulting mixture was added MeI (229 μL, 3.7 mmol) and kept stirring at rt for 2 h. The reaction mixture was concentrated in vacuum and purified by flash chromatography to give compound **S12-3** (564 mg, 79%) as yellow solid. ¹H NMR (CDCl₃, 500 MHz) δ 7.56 (d, *J* = 8.8 Hz, 1H), 7.45 (s, 1H), 6.76 (d, *J* = 8.8 Hz, 1H), 4.36 (m, 2H), 3.32 (m, 2H), 2.95 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ: 149.7, 142.2, 136.5, 115.4, 114.5, 106.9, 65.3, 47.9, 38.6; MS (ESI) *m/z* 194.8 (M+H)⁺.

4- Methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-amine [S12-4]. To a solution of **S12-3** (560 mg, 2.9 mmol) in 20 mL of methanol was added Pd/C powder (10%, 96 mg). The resulting suspension was stirred at rt under hydrogen overnight. The reaction mixture was filtered, concentrated in vacuum and purified by flash chromatography to give **S12-4** (420 mg, 89%) as a yellow solid. ¹H NMR (CDCl₃, 500 MHz) δ 6.56 (d, *J* = 8.3 Hz, 1H), 6.04 (d, *J* = 2.5 Hz, 1H), 5.98 (dd, *J* = 2.5, 8.3 Hz, 1H), 4.19 (t, *J* = 4.4 Hz, 2H), 3.21 (t, *J* = 4.5 Hz, 2H), 2.82 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 140.8, 137.4, 137.0, 116.2, 104.8, 100.4, 64.6, 49.5, 38.7.

6-Iodo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazine [S12-5]. To solution of **S12-4** (2.1 g, 12.8 mmol) in 50 mL of acetic acid cooled in ice bath was added NaNO₂ (1.77g, 26.9 mmol) slowly in portions. The resulting mixture was stirred at 0 °C for 10 min and was added KI (4.24 g, 38.4 mmol) in portions. The reaction mixture was stirred at 0 °C for 30 min, allowed to warm up to rt and stirred for 2 h. The resulting mixture was quenched with 100 mL of water, extracted with ethyl acetate (3 x 150 mL). The organic layer was combined, treated with Na₂S₂O₃, washed with brine, dried over MgSO₄ and purified by flash chromatography to give **S12-5** (1.86 g, 53%) as a yellow solid. ¹H NMR (CDCl₃, 500 MHz) δ 6.64 (d, *J* = 8.3 Hz, 1H), 6.56 (s, 1H), 6.48 (d, *J* = 8.4 Hz, 1H), 4.25 (m, 2H), 3.24 (m, 2H), 2.85 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 138.1, 126.6, 120.5, 117.6, 111.9, 83.7, 64.8, 48.7, 36.5.



Reagents or conditions: (a) $(\text{C}_6\text{H}_5\text{O})_2\text{P}(\text{O})\text{N}_3$, *t*-BuOH, Et_3N , toluene, reflux; (b) *t*-BuLi, THF, -20°C , then $\text{ICH}_2\text{CH}_2\text{I}$, -78°C to rt; (c) TFA, CH_2Cl_2 , rt; (d) 8-mercaptoadenine, neocuproine, CuI , NaOtBu , DMF, 115°C ; (e) KI , NaNO_2 , HCl , H_2O , $< 5^\circ\text{C}$; (f) 1,3-dibromopropane, Cs_2CO_3 , DMF, rt; (g) isopropylamine, DMF, rt.

Scheme 13. Synthesis of DZ4-52-N9.

***tert*-Butyl naphthalen-2-ylcarbamate (S13-2).** 2-Naphthoic acid (**S13-1**; 2.5 g, 14.3 mmol) in *tert*-BuOH (85 mL) and toluene (85 mL) was treated with Et_3N (2.3 mL, 16.4 mmol), 3 Å molecular sieves (16.7 g) and diphenyl phosphorylazide (3.5 mL, 16.4 mmol). The reaction mixture was refluxed for 24 h. After cooling to rt, solid was filtered off through Celite and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc (75 mL) and washed with 1N aqueous HCl (2 x 50 mL), saturated aqueous NaHCO_3 (2 x 50 mL), dried over sodium sulfate and concentrated under reduced pressure. Chromatography (10% EtOAc in hexanes) afforded 2.5 g (71%) of **S13-2**. ^1H NMR (500 MHz, CDCl_3) δ 7.99 (s,

1H), 7.72-7.78 (m, 3H), 7.44 (t, $J = 7.8$ Hz, 1H), 7.31-7.38 (m, 2H), 6.61 (br s, 1H), 1.55 (s, 9H); MS (ESI) m/z 244.02 $[M+H]^+$.

2-Amino-3-iodonaphthalene (S13-3). To a solution of **S13-2** (1.0 g, 4.11 mmol) in 20 mL dry THF under argon at -20°C was added *tert*-butyl lithium (1.5 M solution in pentane, 6.9 mL, 10.27 mmol) dropwise and was stirred for 2 h at -20°C . After cooling to -78°C , a solution of diiodoethane (2.9 g, 10.27 mmol) in 10 mL dry THF was added dropwise and then allowed to warm to rt for 3 h. A saturated aqueous NH_4Cl solution was added, and the solution was extracted with diethyl ether. The organic layer was washed with 10% sodium thiosulfate solution and dried over MgSO_4 . The solvents were evaporated under reduced pressure and the residue was purified by chromatography (3% EtOAc in hexanes) to afford 1.1 g of a 79/21 mixture (NMR) of regioisomeric 3-iodo and 1-iodo Boc-protected 2-aminonaphthalene, respectively. This mixture (1.1 g) was dissolved in dichloromethane (12.5 mL), and trifluoroacetic acid (12.5 mL) was added dropwise at rt. After stirring for 1 h at rt, the solution was neutralized with a concentrated NaOH solution. The organic layer was separated and the aqueous layer was extracted with dichloromethane. The organic layers were combined, dried over MgSO_4 , concentrated under reduced pressure and the resulting residue was purified by chromatography (0.5% EtOAc in hexanes) to afford 0.50 g (45%) of **S13-3**. ^1H NMR (500 MHz, CDCl_3) δ 8.25 (s, 1H), 7.59 (d, $J = 8.3$ Hz, 1H), 7.56 (d, $J = 8.3$ Hz, 1H), 7.37 (dt, $J = 1.0, 7.5$ Hz, 1H), 7.22 (dt, $J = 0.8, 7.5$ Hz, 1H), 7.09 (s, 1H), 4.23 (br s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.3, 139.5, 135.3, 129.9, 127.5, 127.2, 126.3, 123.7, 109.0, 88.7; MS (ESI) m/z 269.96.

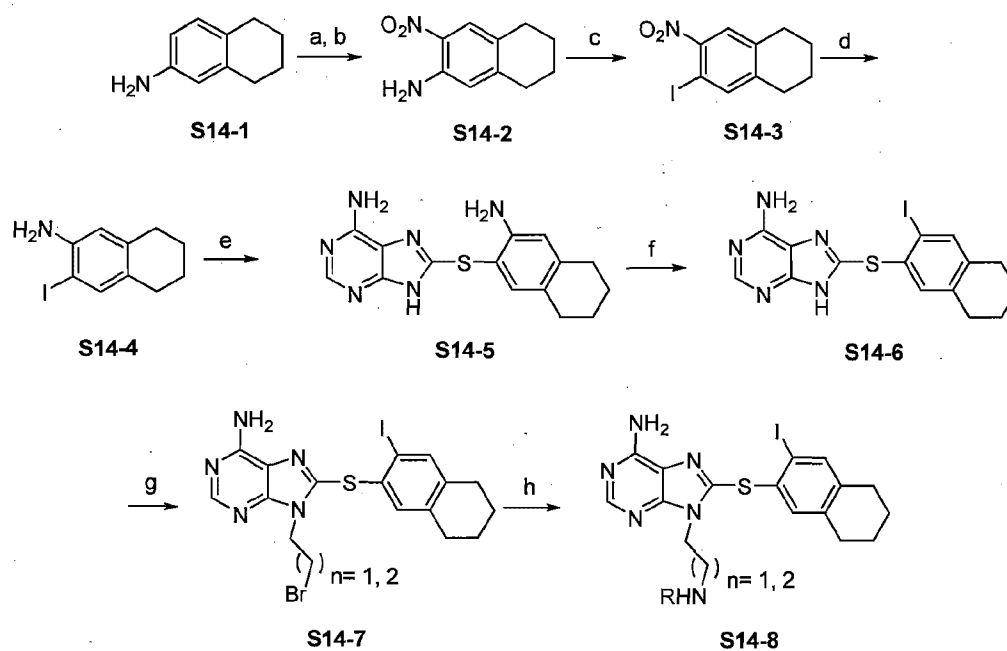
8-(3-aminonaphthalen-2-ylthio)-9H-purin-6-amine (S13-4). A mixture of 8-mercaptoadenine (20.7 mg, 0.124 mmol), neocuproine hydrate (3.9 mg, 0.0185 mmol), CuI (3.5 mg, 0.0185 mmol), sodium *tert*-butoxide (23.7 mg, 0.24 mmol), **S13-3** (100 mg, 0.37 mmol) and DMF (2 mL) were heated at 115°C for 20 h. The solvent was removed under reduced pressure and the residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 10:1) to give 14 mg (37%) of **S13-4** as a solid. ^1H NMR (500 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 8.18 (s, 1H), 8.12 (s, 1H), 7.71 (d, $J = 8.3$ Hz, 1H), 7.62 (d, $J = 8.1$ Hz, 1H), 7.40-7.46 (m, 1H), 7.24-7.30 (m, 1H), 7.20 (s, 1H); MS (ESI) m/z 308.95 $[M+H]^+$.

8-(3-iodonaphthalen-2-ylthio)-9H-purin-6-amine (S13-5). To a suspension of S13-4 (14 mg, 0.0454 mmol) in water (150 μ L) at 5°C was added 6 M HCl (140 μ L) over 5 min. Then a solution of NaNO₂ (6.3 mg, 0.0908 mmol) in water (70 μ L) was added dropwise over 30 min. at below 5°C. The mixture was stirred for an additional 10 min., then urea (1.9 mg, 0.0317 mmol) was added slowly. After 10 minutes, a solution of KI (22.6 mg, 0.136 mmol) in water (70 μ L) was added dropwise over 5 min. and the mixture was stirred overnight. The solvent was removed under reduced pressure and the residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 8:1) to give 8 mg (42%) of S13-5 as a solid. ¹H NMR (500 MHz, CDCl₃/MeOH-d₄) δ 8.51 (s, 1H), 8.17 (s, 2H), 7.75-7.80 (m, 2H), 7.52-7.60 (m, 2H); MS (ESI) m/z 420.01 [M+H]⁺.

9-(3-bromopropyl)-8-(3-iodonaphthalen-2-ylthio)-9H-purin-6-amine (S13-6). S13-5 (8 mg, 0.019 mmol), Cs₂CO₃ (7.4 mg, 0.0228 mmol), 1,3-dibromopropane (19.2 mg, 9.7 μ L, 0.095 mmol) in DMF (0.2 mL) was stirred for 30 min. Then additional Cs₂CO₃ (7.4 mg, 0.0228 mmol) and 1,3-dibromopropane (19.2 mg, 9.7 μ L, 0.095 mmol) was added and the mixture stirred for 30 min. The mixture was dried under reduced pressure and the residue purified by preparatory TLC (CH₂Cl₂:MeOH:AcOH, 15:1:0.5) to give 4.6 mg (45%) of S13-6. ¹H NMR (500 MHz, CDCl₃/MeOH-d₄) δ 8.51 (s, 1H), 8.27 (s, 1H), 8.05 (s, 1H), 7.74-7.80 (m, 2H), 7.53-7.60 (m, 2H), 4.42 (t, J = 7.1 Hz, 2H), 3.45 (t, J = 6.6 Hz, 2H), 2.45 (m, 2H); MS (ESI) m/z 539.84/541.89 [M+H]⁺.

8-(3-iodonaphthalen-2-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ4-52-N9]. S13-6 (4.6 mg, 0.0085 mmol) and isopropylamine (100 μ L) in DMF (100 μ L) was stirred overnight at rt. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 10:1) to give 4.0 mg (91%) of DZ4-52-N9. ¹H NMR (500 MHz, CDCl₃) δ 8.44 (s, 1H), 8.34 (s, 1H), 7.77 (s, 1H), 7.70-7.74 (m, 1H), 7.64-7.68 (m, 1H), 7.45-7.54 (m, 2H), 4.36 (t, J = 6.9 Hz, 2H), 2.74 (septet, J = 6.1 Hz, 1H), 2.58 (t, J = 6.8 Hz, 2H), 2.06 (m, 2H), 1.05 (d, J = 6.3 Hz, 6H); MS (ESI) m/z 518.82 [M+H]⁺.

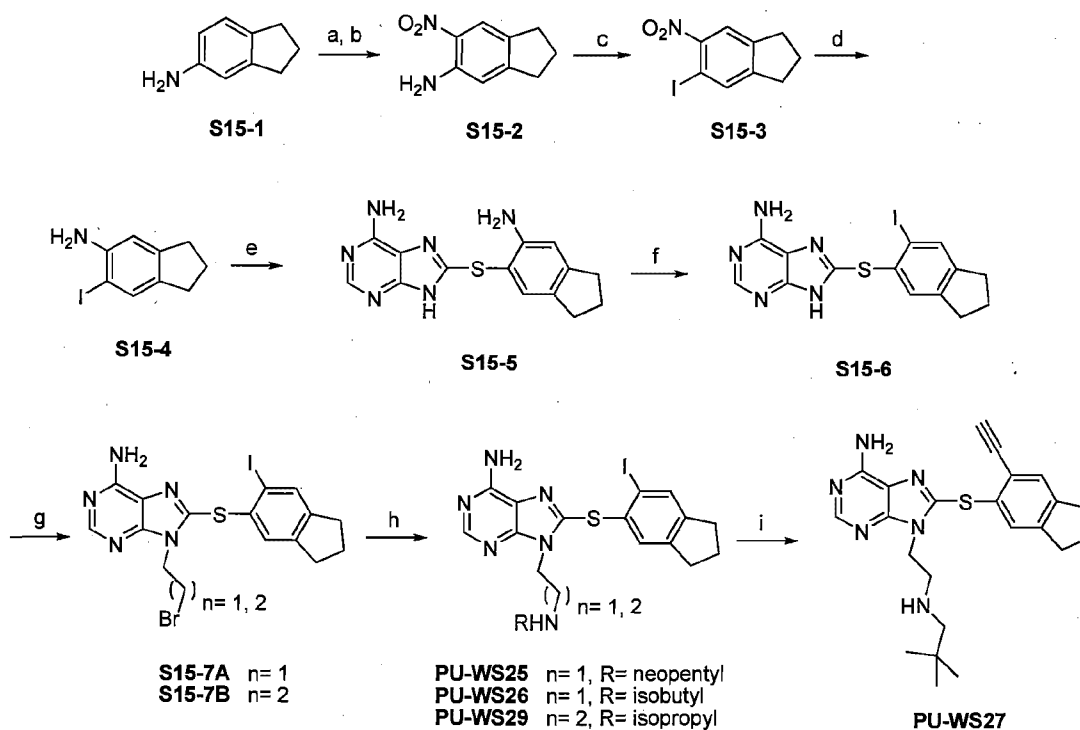
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Reagents and conditions: (a) Ac_2O , dioxane, 0°C to rt; (b) KNO_3 , H_2SO_4 , 0°C to rt; (c) NaNO_2 , KI, AcOH , 0°C to rt; (d) Fe, NH_4Cl , isopropanol, reflux; (e) 8-mercaptoadenine, CuI, $n\text{Bu}_4\text{NBr}$, NaOt-Bu, mv; (f) NaNO_2 , KI, AcOH , 0°C ; (g) 1,3-dibromopropane or 1,2-dibromoethane, Cs_2CO_3 , DMF, rt; (h) amine, DMF, rt.

Scheme 14.

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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 , $n\text{Bu}_4\text{NBr}$, NaOt-Bu , mv; (f) NaNO_2 , KI , AcOH , 0°C ; (g) 1,3-dibromopropane or 1,2-dibromoethane, Cs_2CO_3 , DMF, rt; (h) isopropylamine or isobutylamine or neopentylamine, DMF, rt; (i) CuI , $\text{PdCl}_2(\text{PPh}_3)_2$, trimethylsilylacetylene, Et_3N , DMF, 90°C .

Scheme 15. Synthesis of PU-WS25, PU-WS26, PU-WS29 and PU-WS27.

5-amino-6-nitro-indane (S15-2). A solution of 5-aminoindane (**S15-1**; 10 g, 75 mmol) in 100 mL of dioxane cooled in ice bath was added acetic anhydride (15 mL) dropwise and kept stirring at room temperature for 2 days. The resulting mixture was condensed and dried under vacuum. 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 rt 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 give **S15-2** (7.1 g, 43%). ^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 (S15-3). To a solution of **S15-2** (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 (0.39 g, 2.45 mmol) was added and the mixture was stirred at rt 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 $\text{Na}_2\text{S}_2\text{O}_3$ solution, brine and dried over MgSO_4 and evaporated to dryness to give a residue that was purified by flash chromatography (ethyl acetate/hexane, gradient 0 to 50%) to give **S15-3** (0.12 g, 65%) as a yellow solid. ^1H 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 (S15-4). To a solution of **S15-3** (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 give **S15-4** (1.36 g, 92%) as a pale yellow solid. ^1H 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 $[\text{M}+\text{H}]^+$.

8-((6-amino-2,3-dihydro-1H-inden-5-yl)thio)-9-H-purin-6-amine (S15-5). The mixture of 8-mercaptopadenine (64 mg, 0.38 mmol), **S15-4** (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 give **S15-5** (54 mg, 47%) as a white solid. ^1H NMR (500 MHz, $\text{MeOH}-d_4/\text{CDCl}_3$) 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 $[\text{M}+\text{H}]^+$.

8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-H-purin-6-amine (S15-6). To a solution of **S15-5** (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 $\text{Na}_2\text{S}_2\text{O}_3$, brine, dried over MgSO_4 and evaporated to dryness. The residue was purified by flash chromatography (methylene chloride/methanol, gradient 0 to 10%) to give **S15-6** (42 mg, 56%) as a white solid. ^1H 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 $[\text{M}+\text{H}]^+$.

9-(2-bromoethyl)-8-((6-iodo-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine (S15-7A).

To a solution of **S15-6** (70 mg, 0.17 mmol) in DMF (3 mL) was added 1,2-dibromoethane (74 μL , 0.86 mmol) and Cs_2CO_3 (111 mg, 0.34 mmol). The resulting mixture was stirred at rt for 2 h. **S15-7A** (36 mg, 41%) was obtained following preparatory TLC (methylene chloride/methanol, 20/1) as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 8.36 (s, 1H), 7.75 (s, 1H), 7.18 (s, 1H), 4.62 (t, 2H), 3.68 (t, 2H), 2.88 (t, 2H), 2.81 (t, 2H), 2.06 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3 , δ): 155.9, 153.9, 152.4, 149.8, 148.9, 148.1, 137.6, 132.8, 131.1, 101.7, 46.3, 33.9, 29.7, 26.8; MS (ESI): m/z 516.15, 518.16 $[\text{M}, \text{M}+2]^+$.

8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine (PU-WS25). To a solution of **S15-7A** (31 mg, 0.06 mmol) in DMF (1.5 mL) was added neopentylamine (250 μL). The reaction mixture was stirred at rt overnight and condensed under vacuum. **PU-WS25** (28 mg, 89%) was obtained following preparatory TLC (methylene chloride/methanol, 10/1) as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 8.32 (s, 1H), 7.73 (s, 1H), 7.1 (s, 1H), 5.63 (br, 2H), 4.38 (m, 2H), 3.03 (m, 2H), 2.87 (t, $J = 7.4$ Hz, 2H), 2.78 (t, $J = 7.4$ Hz, 2H), 2.37 (s, 2H), 2.04 (m, 2H), 0.93 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3 , δ): 154.7, 152.9, 151.6, 147.1, 146.7, 146.4, 135.9, 133.5, 127.5, 120.2, 97.7, 61.8, 50.7, 49.7, 43.9, 32.5, 32.2, 31.5, 27.7, 25.5; HRMS (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{21}\text{H}_{28}\text{IN}_6\text{S}$, 523.1141; found 523.1140.

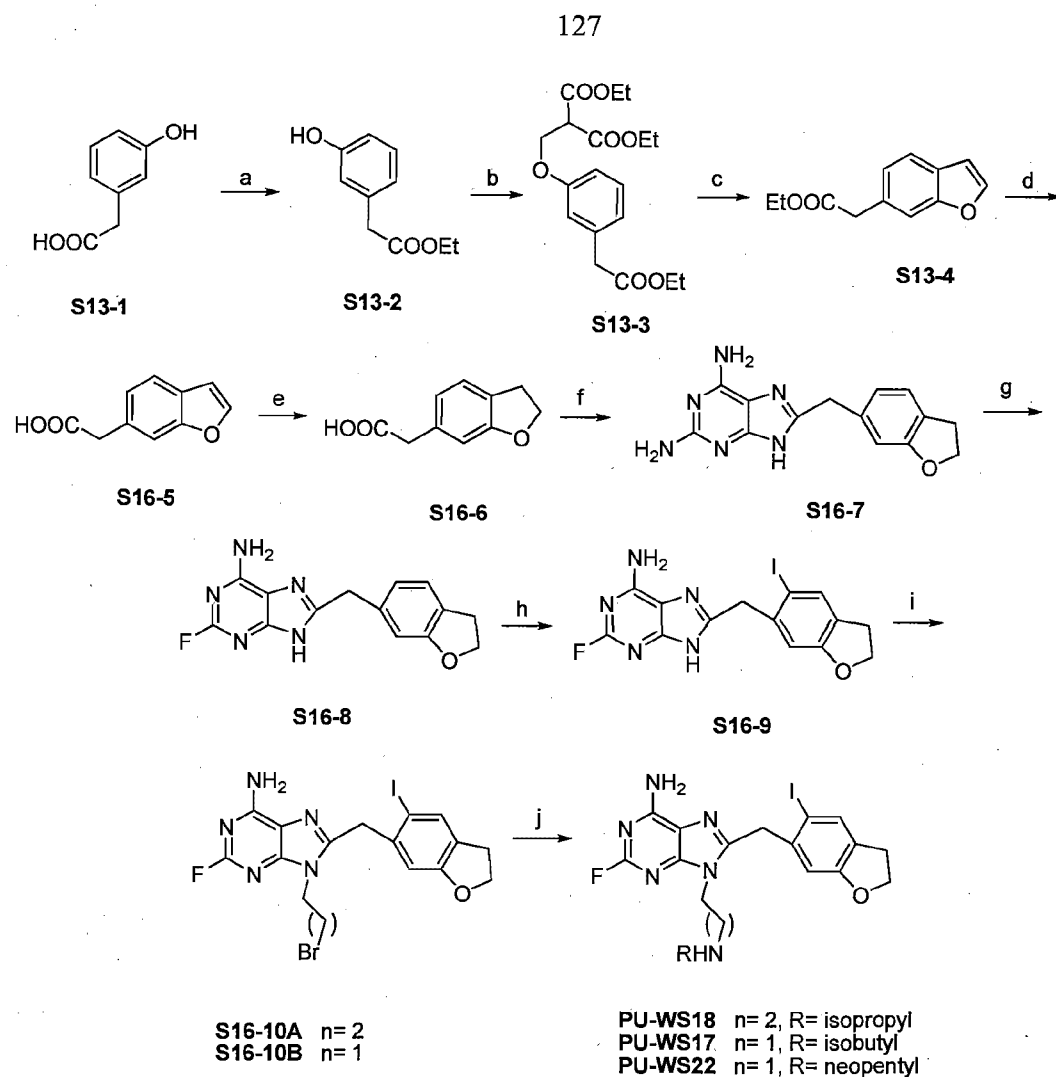
8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine (PU-WS26). To a solution of **S15-7A** (6 mg, 0.01 mmol) in DMF (1 mL) was added isobutylamine (150 μL). The reaction mixture was stirred at rt overnight and condensed under vacuum. **PU-WS26** (5.9 mg, 99%) was obtained following preparatory TLC (methylene chloride/methanol, 10/1) as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 8.31 (s, 1H), 7.74 (s,

1H), 7.11 (s, 1H), 5.73 (br, 2H), 4.43 (m, 2H), 3.04 (m, 2H), 2.87 (t, $J = 7.4$ Hz, 2H), 2.78 (t, $J = 7.4$ Hz, 2H), 2.49 (d, $J = 6.6$ Hz, 2H), 2.05 (m, 2H), 1.81 (m, 1H), 0.92 (m, 6H); HRMS (m/z): $[M+H]^+$ calcd for $C_{20}H_{26}IN_6S$ 509.0984; found 509.0990.

9-(3-bromopropyl)-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine (S15-7B). To a solution of **S15-6** (30 mg, 0.07 mmol) in DMF (3 mL) was added 1,3-dibromopropane (37 μ L, 0.86 mmol) and Cs_2CO_3 (46 mg, 0.14 mmol). The resulting mixture was stirred at rt for 2 h. **S15-7B** (8 mg, 21%) was obtained following preparatory TLC (methylene chloride/methanol, 20/1) as a white solid. ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.75 (s, 1H), 7.12 (s, 1H), 6.55 (br s, 2H), 4.33 (m, 2H), 2.88 (m, 2H), 2.79 (t, $J = 7.4$ Hz, 2H), 2.29 (m, 2H), 1.97 (m, 2H); MS (ESI): m/z 530.3, 532.3 $[M, M+2]^+$.

8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine (PU-WS29). To a solution of **S15-7B** (8 mg, 0.015 mmol) in DMF (3 mL) was added isopropylamine (100 μ L), stirred at rt overnight and condensed under vacuum. **PU-WS29** (5.9 mg, 99%) was obtained following preparatory TLC (methylene chloride/methanol, 10/1) as a white solid. ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.75 (s, 1H), 7.12 (s, 1H), 5.73 (br s, 2H), 4.29 (t, 2H), 2.87 (t, $J = 7.4$ Hz, 2H), 2.7-2.79 (m, 3H), 2.55 (t, 2H), 2.03-2.09 (m, 4H), 1.05 (d, $J = 11.2$ Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.5, 152.9, 151.7, 147.2, 146.5, 135.9, 133.1, 127.6, 120.2, 97.9, 48.8, 43.7, 41.7, 32.5, 32.2, 30.0, 25.5, 22.7; HRMS (m/z): $[M+H]^+$ calcd for $C_{20}H_{26}IN_6S$ 509.0984; found 509.1003.

8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine (PU-WS27). Following the procedure to make **PU-WS8**, **PU-WS27** was obtained from **PU-WS25** as a white solid. ^1H NMR ($CDCl_3$, 500 MHz) δ 8.32 (s, 1H), 7.41 (s, 1H), 7.13 (s, 1H), 5.67 (br s, 2H), 4.42 (m, 2H), 3.48 (s, 1H), 3.02 (m, 2H), 2.77-2.91 (m, 4H), 2.39 (s, 2H), 2.06 (m, 2H), 0.89 (s, 9H); HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{23}H_{28}N_6S$, 421.2174; found 421.2164.



Reagents and conditions: (a) EtOH, H₂SO₄, reflux; (b) 2-bromomethylmalonate, NaH, DMF, 110°C; (c) PPA, toluene, reflux; (d) NaOH, MeOH, rt, then HCl; (e) Pd/C, H₂ (2 atm.), MeOH; (f) 2,4,5,6-tetraaminopyrimidine, triphenyl phosphite, pyridine, microwave, 210°C; (g) HF/pyridine, NaNO₂, 0°C to rt; (h) NIS, TFA, ACN; (i) 1,3-dibromopropane or 1,2-dibromoethane, Cs₂CO₃, DMF, rt; (j) isopropylamine or isobutylamine or neopentylamine, DMF, rt.

Scheme 16. Synthesis of PU-WS17, PU-WS18, PU-WS22.

Ethyl 2-(3-hydroxyphenyl)acetate (S16-2). To a solution of 2-(3-hydroxyphenyl)acetic acid (S16-1; 10 g, 65.8 mmol) in 200 mL of ethanol was added 8 mL of concentrated sulfuric acid. The resulting mixture was refluxed overnight and condensed under vacuum. The residue was dissolved in ethyl acetate and washed with water. The organic layer was combined, washed

with brine, dried over MgSO_4 , evaporated to dryness and purified by flash chromatography to give **S16-2** as a colorless oil in quantitative yield. ^1H NMR (500 MHz, CDCl_3) δ 7.35 (br, 1H), 7.12 (m, 1H), 6.69-6.78 (m, 3H), 4.12 (m, 2H), 3.53 (s, 2H), 1.21 (m, 3H).

Diethyl 2-((3-ethoxy-2-oxoethyl)phenoxy)methylmalonate (S16-3). To a solution of **S16-2** (11.8 g, 65.5 mmol) in 150 mL of DMF cooled in ice bath was added NaH (2.36 g, 98 mmol) and stirred at 0 °C under argon for 20 min. To the resulting mixture was added diethyl 2-bromomethylmalonate (11.8 mL, 78 mmol) dropwise. The reaction mixture was stirred at 110 °C overnight, evaporated to dryness and purified by flash chromatography to give compound **S16-3** (15.2 g, 66%) as a colorless oil. ^1H NMR (500 MHz, CDCl_3) δ 7.19 (t, 1H), 6.80-6.86 (m, 3H), 4.81 (m, 1H), 4.12 (m, 2H), 3.97 (m, 2H), 3.74 (m, 2H), 3.63 (m, 2H), 3.55 (s, 2H), 1.19 (m, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.3, 158.8, 135.6, 129.5, 121.8, 115.6, 113.3, 100.5, 68.5, 62.5, 60.7, 41.3, 15.4, 14.1.

Ethyl 2-(benzofuran-6-yl) acetate (S16-4). To a solution of **S16-3** (6 g, 17 mmol) in 100 mL of toluene was added 3 g of polyphosphoric acid. The resulting mixture was refluxed overnight, condensed and purified by flash chromatography to give **S16-4** (1.42 g, 41%) as colorless oil. ^1H NMR (500 MHz, CDCl_3) δ 7.31-7.42 (m, 3H), 6.95 (m, 1H), 6.51 (s, 1H), 3.94 (m, 2H), 3.51 (s, 2H), 1.02 (m, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.6, 155.2, 145.1, 130.6, 126.4, 124.3, 121.1, 112.2, 106.4, 60.9, 41.5, 14.2.

2-(benzofuran-6-yl) acetic acid (S16-5). To a solution of **S16-4** (3 g, 14.7 mmol) in 100 mL methanol was add 25 mL of 1 N NaOH. The resulting mixture was stirred at rt for 2 h, neutralized with concentrated HCl, and adjusted pH to 2. The reaction mixture was condensed, purified by flash chromatography to yield **S16-5** as a white solid in quantitative yield. ^1H NMR (500 MHz, $\text{MeOH}-d_4$) δ 7.73 (s, 1H), 7.53 (d, $J = 7.9$ Hz, 1H), 7.43 (s, 1H), 7.15 (d, $J = 8.0$ Hz, 1H), 6.79 (s, 1H), 3.70 (s, 2H); ^{13}C NMR (125 MHz, $\text{MeOH}-d_4$) δ 175.7, 156.6, 146.6, 132.5, 127.7, 125.4, 121.9, 113.0, 107.4, 41.9.

2-(2,3-dihydrobenzofuran-6-yl)acetic acid (S16-6). To a solution of **S16-5** (1.8 g, 10 mmol) in 20 mL of methanol was added Pd/C (10%, 120 mg) and stirred at rt under H_2 (2 atm)

overnight. The reaction mixture was filtered, washed with cold methanol, evaporated to dryness and purified by flash chromatography to give **S16-6** (1.6 g, 88%) as a white solid. ^1H NMR (500 MHz, $\text{MeOH-}d_4$) δ 7.12 (d, $J = 7.6$ Hz, 1H), 6.73 (d, $J = 7.9$ Hz, 1H), 6.71 (s, 1H), 4.55 (m, 2H), 3.56 (s, 2H), 3.16 (m, 2H); ^{13}C NMR (125 MHz, $\text{MeOH-}d_4$) δ 177.9, 160.4, 133.3, 126.2, 124.8, 121.5, 110.5, 71.5, 41.1, 29.4.

8-((2,3-dihydrobenzofuran-6-yl)methyl)-9H-purine-2,6-diamine (S16-7). The mixture of 2,4,5,6-tetraaminopyrimidine (200 mg, 1.4 mmol), **S16-6** (254 mg, 1.4 mmol) and triphenyl phosphite (451 μL , 1.7 mmol) in 2 mL of pyridine was irradiated in the microwave for 15 min at 210 $^\circ\text{C}$. After cooling, the reaction mixture was concentrated under vacuum and the residue purified by flash chromatography to give **S16-7** (350 mg, 89%) as a yellow solid. ^1H NMR (500 MHz, $\text{MeOH-}d_4$) δ 7.16 (m, 1H), 6.79 (m, 1H), 6.73 (s, 1H), 4.57 (m, 2H), 4.12 (s, 2H), 3.18 (m, 2H); MS: m/z 283.2 ($\text{M}+\text{H}$) $^+$.

8-((2,3-dihydrobenzofuran-6-yl)methyl)-2-fluoro-9H-purin-6-amine (S16-8). A plastic tube charged with **S16-7** (0.72 g, 2.5 mmol) was cooled in ice bath, added HF/pyridine (73%, 1.76 mL) and stirred to dissolve. To the resulting mixture was added NaNO_2 (0.23 g, 3.3 mmol) in portions and kept stirring for 5 min. The reaction mixture was allowed to warm up to rt and stirred for 3 h. CaCO_3 (0.68 g) was added to quench excess HF. The resulting suspension was stirred for 1 h, filtered, concentrated in vacuo and purified by flash chromatography to give **S16-8** (0.45 g, 62%) as a yellow solid. ^1H NMR (500 MHz, $\text{MeOH-}d_4$) δ : 7.16 (m, 1H), 6.77 (m, 1H), 6.71 (s, 1H), 4.57 (m, 2H), 4.12 (s, 2H), 3.19 (m, 2H); MS: m/z 286.0 ($\text{M}+\text{H}$) $^+$.

2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-6-amine (S16-9). To a suspension of **S16-8** (0.45 g, 1.6 mmol) in 50 mL acetonitrile was added 1 mL of TFA. To the resulting solution was added NIS (1.06 g, 4.7 mmol) and the reaction mixture was stirred at rt for 3 h. It was then evaporated to dryness and purified by flash chromatography to give **S16-9** (0.408 g, 63%) as a yellow solid. ^1H NMR (500 MHz, $\text{MeOH-}d_4$) δ 7.67 (s, 1H), 6.76 (s, 1H), 4.59 (m, 2H), 4.28 (s, 2H), 3.21 (m, 2H); MS: m/z 412 ($\text{M}+\text{H}$) $^+$.

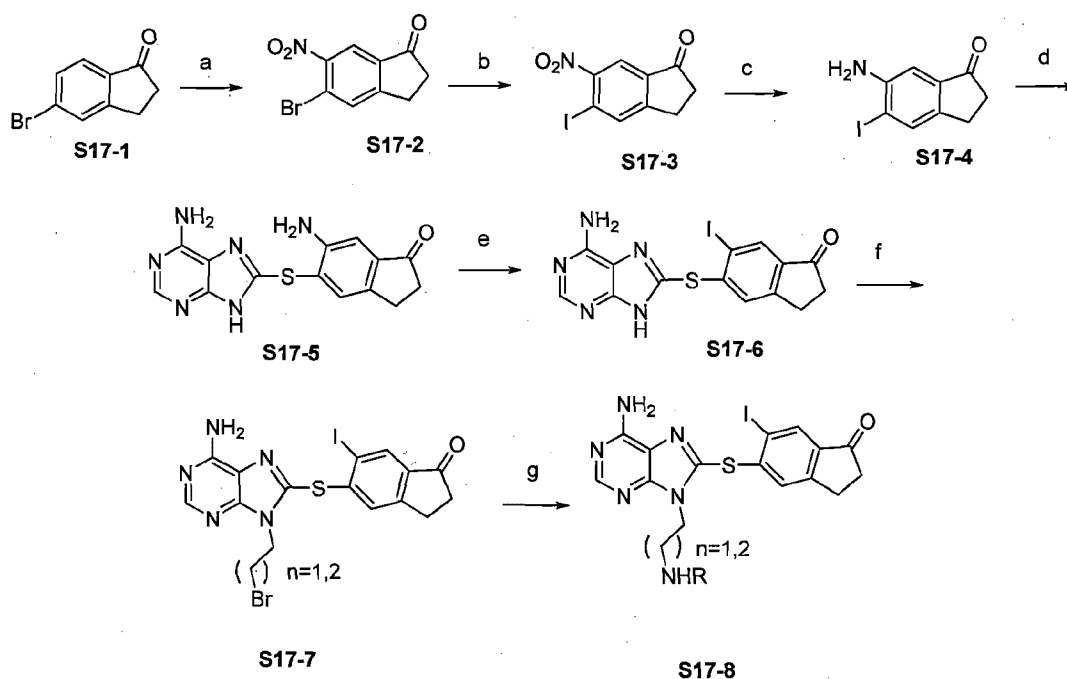
9-(3-bromopropyl)-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-6-amine (S16-10A). To a solution of **S16-9** (50 mg, 0.12 mmol) in 2 mL of DMF was added 1,3-dibromopropane (150 μ L) and Cs_2CO_3 (80 mg, 0.24 mmol). The resulting mixture was stirred at rt for 2 h, evaporated to dryness and purified by preparatory TLC to give **S16-10A** (23 mg, 36%) as a white solid. ^1H NMR (500 MHz, $\text{MeOH-}d_4$) δ 7.48 (s, 1H), 6.31 (s, 1H), 4.35 (m, 2H), 4.12 (s, 2H), 3.92 (m, 2H), 3.14 (m, 2H), 3.01 (m, 2H), 2.03 (m, 2H); MS: m/z 530, 532 (M, M+2) $^+$.

2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine (PU-WS18). To a solution of **S16-10A** (15 mg, 0.03 mmol) in 1 mL of DMF was added isopropylamine (0.5 mL), stirred at rt overnight, evaporated to dryness and purified by flash chromatography to give **PU-WS18** (13 mg, 90%) as a white solid. ^1H NMR (500 MHz, $\text{MeOH-}d_4$) δ 7.67 (s, 1H), 6.72 (s, 1H), 4.63 (m, 2H), 4.26 (m, 4H), 3.22-3.29 (m, 3H), 2.93 (t, $J = 7.1$ Hz, 2H), 2.27 (t, $J = 7.0$ Hz, 2H), 1.38 (d, $J = 6.5$ Hz, 6H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{20}\text{H}_{25}\text{N}_6\text{OFI}$, 511.1119; found 511.1103.

2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [PU-WS17]. To a solution of **S16-9** (70 mg, 0.17 mmol) in 2 mL of DMF was added 1,2-dibromoethane (150 μ L) and Cs_2CO_3 (110 mg, 0.34 mmol). The resulting mixture was stirred at rt for 2 h, evaporated to dryness and purified by preparatory TLC to give bromide intermediate **S16-10B**. To a solution of **S16-10B** (10 mg, 0.19 mmol) in 1 mL of DMF was added isobutylamine (100 μ L), stirred at rt overnight, evaporated to dryness and purified by flash chromatography to give **PU-WS17** as a white solid. ^1H NMR ($\text{MeOH-}d_4/\text{CDCl}_3$, 500 MHz) δ : 7.67 (s, 1H), 6.62 (s, 1H), 4.59 (t, $J = 8.7$ Hz, 2H), 4.29 (s, 2H), 4.15 (t, $J = 6.5$ Hz, 2H), 3.22 (t, $J = 8.7$ Hz, 2H), 2.93 (t, $J = 6.5$ Hz, 2H), 2.45 (d, $J = 6.9$ Hz, 2H), 1.69 (m, 1H), 0.88 (d, $J = 6.8$ Hz, 6H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{20}\text{H}_{25}\text{FIN}_6\text{O}$, 511.1119; found 511.1113.

2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [PU-WS22]. To a solution of **S16-9** (70 mg, 0.17 mmol) in 2 mL of DMF was added 1,2-dibromoethane (150 μ L) and Cs_2CO_3 (110 mg, 0.34 mmol). The resulting

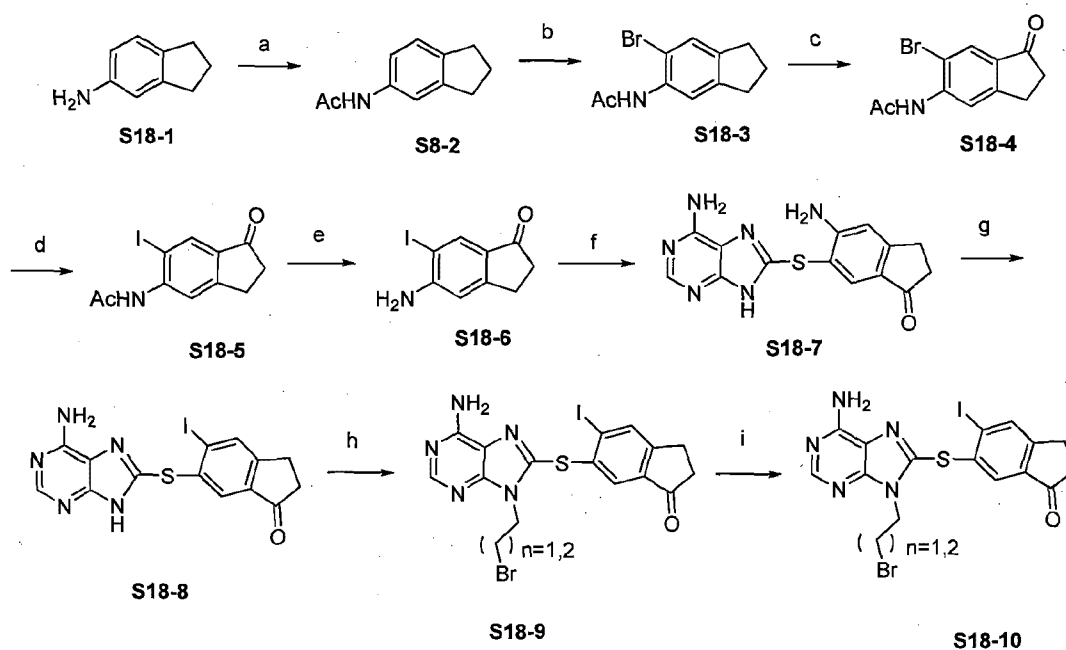
mixture was stirred at rt for 2 h, evaporated to dryness and purified by preparatory TLC to give bromide intermediate **S16-10B**. To a solution of **S16-10B** (65 mg, 0.13 mmol) in 1 mL of DMF was added neopentylamine (50 μ L), stirred at rt overnight, evaporated to dryness and purified by flash chromatography to give compound **PU-WS22** as a white solid. ^1H NMR (CDCl_3 , 500 MHz) δ 7.46 (s, 1H), 6.53 (s, 1H), 5.79 (s, 2H), 5.52 (br, 2H), 4.52 (m, 2H), 4.09 (m, 2H), 3.19 (m, 2H), 2.94-3.02 (m, 2H), 2.34 (s, 2H), 0.91 (s, 9H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{21}\text{H}_{27}\text{FIN}_6\text{O}$, 525.1275; found 525.1249.



Reagents and conditions: (a) HNO_3 , H_2SO_4 ; (b) NaI , CuI , $\text{N,N'$ -dimethylethylenediamine, dioxane, 110°C ; (c) Fe , HCl ; (d) 8-mercaptoadenine, neocuproine, CuI , NaOtBu , DMF, 115°C ; (e) KI , NaNO_2 , HCl , $<5^\circ\text{C}$; (f) Cs_2CO_3 , 1,3-dibromopropane, DMF, rt; (g) isopropylamine, DMF, rt.

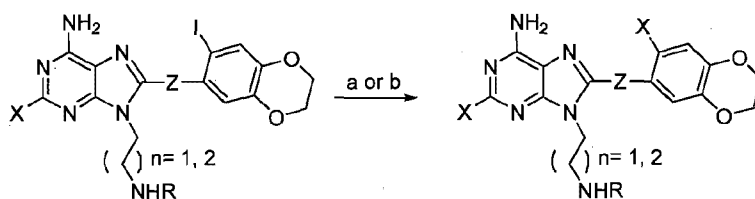
Scheme 17.

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Reagents and conditions: (a) Ac_2O , CH_2Cl_2 , rt; (b) Br_2 , AcOH , 10°C ; (c) CrO_3 , $\text{AcOH}/\text{H}_2\text{O}$, $50\text{--}55^\circ\text{C}$; (d) NaI , CuI , $\text{N,N'$ -dimethylethylenediamine, dioxane, 110°C ; (e) 6M HCl (aq.), reflux; (f) 8-mercaptoadenine, neocuproine, CuI , NaOtBu , DMF , 115°C ; (g) KI , NaNO_2 , HCl , $<5^\circ\text{C}$; (h) Cs_2CO_3 , 1,3-dibromopropane, DMF , rt; (i) isopropylamine, DMF , rt.

Scheme 18.



PU-RK11 X=H, Z=S, n=2, R=isopropyl
 PU-HT165 X=H, Z=S, n=1, R=isobutyl
 DZ3-73 X=F, Z= CH_2 , n=1, R=isobutyl

PU-HJP18 X=H, Z=S, n=2, R=isopropyl, X=2-furanyl
 PU-HJP19 X=H, Z=S, n=2, R=isopropyl, X=3-pyrazolyl
 PU-HJP23 X=H, Z=S, n=1, R=isobutyl, X=2-furanyl
 TT-VI-53A X=F, Z= CH_2 , n=1, R=isobutyl, X=2-furanyl
 TT-VI-54A X=F, Z= CH_2 , n=1, R=isobutyl, X=3-pyrazolyl
 PU-HJP20 X=H, Z=S, n=2, R=isopropyl, X=2-oxazolyl

Reagents or conditions: (a) boronic acid, $\text{PdCl}_2(\text{PPh}_3)_2$, NaHCO_3 , H_2O , DMF ; (b) $\text{XSn}(\text{Bu})_3$, LiCl , $\text{Pd}(\text{PPh}_3)_4$, DMF , 90°C .

Scheme 19. Cross-coupling reactions of PU-RK11, PU-HT165 and DZ3-73.

8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-

(isopropylamino)propyl)-9H-purin-6-amine [HJP18]. 2-Furanylboronic acid (8 mg, 0.0712 mmol) was added to **PU-RK11** (25 mg, 0.0475 mmol) and NaHCO₃ (12 mg, 0.1425 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (6.7 mg, 0.0095 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 12 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 10.2 mg (45%) of **HJP18**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.29 (s, 1H), 7.47 (s, 1H), 7.26 (d, *J* = 3.8 Hz, 1H), 6.89 (s, 1H), 6.73 (d, *J* = 3.9 Hz, 1H), 6.46 (m, 1H), 4.25 (m, 4H), 4.16 (t, *J* = 6.2 Hz, 2H), 2.67 (m, 1H), 2.47 (t, *J* = 7.1 Hz, 2H), 1.86 (m, 2H), 1.01 (d, *J* = 6.2 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 154.4, 152.8, 151.7, 151.0, 146.7, 144.2, 143.7, 142.2, 126.6, 122.1, 119.9, 119.3, 117.6, 111.5, 109.5, 64.4, 64.3, 48.6, 43.8, 41.6, 30.1, 22.8; MS (ESI) *m/z* 467.14 [M+H]⁺.

8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-

(isopropylamino)propyl)-9H-purin-6-amine [HJP19]. 1H-Pyrazole-3-boronic acid (6.4 mg, 0.057 mmol) was added to **PU-RK11** (20 mg, 0.038 mmol) and NaHCO₃ (9.8 mg, 0.117 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (5.3 mg, 0.0076 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 12 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 15:1) to give 7.6 mg (43%) of **HJP19**. Additionally, 15.9 mg of unreacted PU-RK11 was recovered for an actual yield of 86%. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.18 (s, 1H), 7.53 (d, *J* = 2.4 Hz, 1H), 7.15 (s, 1H), 7.14 (s, 1H), 6.36 (d, *J* = 2.4 Hz, 1H), 4.29 (m, 4H), 4.19 (t, *J* = 6.6 Hz, 2H), 2.75 (septet, *J* = 6.1 Hz, 1H), 2.52 (t, *J* = 6.6 Hz, 2H), 1.93 (m, 2H), 1.06 (d, *J* = 6.1 Hz, 6H); MS (ESI) *m/z* 468.0 [M+H]⁺.

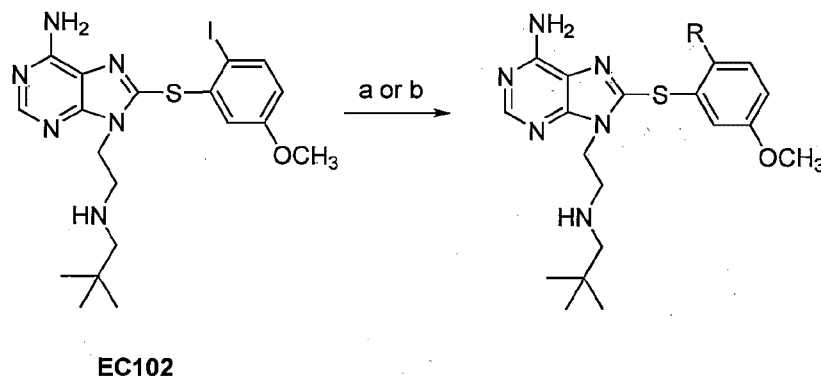
8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [HJP23]. 2-Furanylboronic acid (5.4 mg, 0.0486 mmol) was added to **PU-HT165** (9 mg, 0.0171 mmol) and NaHCO₃ (5.7 mg, 0.0684 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (2.4 mg, 0.0034 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 12 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 1.8 mg (23%) of **HJP23**. ¹H NMR (500 MHz, CDCl₃) δ 8.29 (s, 1H), 7.48 (d, *J* = 1.8 Hz, 1H), 7.26 (s, 1H), 6.90 (s, 1H), 6.74 (d, *J* = 3.2 Hz, 1H), 6.47 (m, 1H), 5.63 (br s, 2H), 4.20-4.30 (m, 6H), 2.90 (t, *J* = 6.0 Hz, 2H), 2.38 (d, *J* = 6.8 Hz, 2H), 1.65 (m, 1H), 0.85 (d, *J* = 6.9 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₇N₆O₃S, 467.1865; found 467.1884.

2-fluoro-8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [TT-VI-53A]. 2-Furanylboronic acid (8 mg, 0.0712 mmol) was added to **DZ3-73** (25 mg, 0.0475 mmol) and NaHCO₃ (12 mg, 0.1425 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.1 mL) and Pd(PPh₃)₂Cl₂ (6.7 mg, 0.0095 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 12 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 20.9 mg (94%) of **TT-VI-53A**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 7.45 (d, *J* = 1.8 Hz, 1H), 7.13 (s, 1H), 6.60 (s, 1H), 6.44 (dd, *J* = 1.8, 3.3 Hz, 1H), 6.35 (d, *J* = 3.3 Hz, 1H), 4.34 (s, 2H), 4.26 (s, 4H), 4.05 (t, *J* = 6.4 Hz, 2H), 2.85 (t, *J* = 6.4 Hz, 2H), 2.35 (d, *J* = 6.9 Hz, 2H), 1.67 (m, 1H), 0.85 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 158.8 (d, *J* = 209.1 Hz), 156.3 (d, *J* = 19.5 Hz), 152.8, 152.2, 143.9, 142.9, 142.2, 126.0, 124.1, 118.7, 117.7, 117.6, 116.3, 111.6, 108.2, 64.6, 57.5, 48.6, 43.1, 31.8, 28.2, 20.6; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₄H₂₈FN₆O₃, 467.2207; found 467.2203; HPLC: method A R_t = 7.05, method B R_t = 8.74.

8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine [TT-VI-54A]. 1H-Pyrazole-3-boronic acid (26 mg, 0.228 mmol) was added to **DZ3-73** (30 mg, 0.0570 mmol) and NaHCO₃ (29 mg, 0.342 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H₂O (0.2 mL) and Pd(PPh₃)₂Cl₂ (8 mg, 0.0114 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 12 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 15:1) to give 11.3 mg (42%) of **TT-VI-54A**. Additionally, 15.9 mg of unreacted **DZ3-73** was recovered for an actual yield of 90%. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 7.60 (d, *J* = 2.1 Hz, 1H), 7.02 (s, 1H), 6.82 (s, 1H), 6.33 (d, *J* = 2.1 Hz, 1H), 4.32 (t, *J* = 6.8 Hz, 2H), 4.29 (s, 2H), 4.28 (s, 4H), 2.96 (t, *J* = 6.8 Hz, 2H), 2.59 (d, *J* = 7.0 Hz, 2H), 1.92 (m, 1H), 0.96 (d, *J* = 6.7 Hz, 6H); ¹³C NMR (125 MHz, CDCl₃/MeOH-*d*₄) δ 158.2 (d, *J* = 210.1 Hz), 156.5 (d, *J* = 19.9 Hz), 152.6, 152.2, 152.1, 144.0, 143.0, 126.5, 119.1, 118.9, 115.94, 115.91, 105.4, 64.65, 64.56, 56.5, 47.7, 41.0, 31.1, 27.2, 20.3; HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₈FN₈O₂, 467.2319; found 467.2323; HPLC: method A R_t = 6.39, method B R_t = 7.03.

9-(3-(isopropylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine [HJP20]. 2-(Tributyltin)oxazole (54 mg, 0.1518 mmol) was added to **PU-RK11** (20 mg, 0.038 mmol) and LiCl (3.2 mg, 0.076 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then Pd(PPh₃)₄ (6.7 mg, 0.0095 mmol) was added and the reaction mixture was heated under nitrogen at 90°C for 12 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 4.7 mg (27%) of **HJP20**. Additionally, 7 mg of unreacted **PU-RK11** was recovered for an actual yield of 45%. ¹H NMR (500 MHz, CDCl₃) δ 8.32 (s, 1H), 7.70 (s, 1H), 7.54 (s, 1H), 7.26 (s, 1H), 6.59 (s, 1H), 5.79 (br s, 2H), 4.20-4.34 (m, 6H), 2.67 (m, *J* = 6.1 Hz, 1H), 2.50 (t, *J* =

6.8 Hz, 2H), 1.93 (m, $J = 7.1$ Hz, 2H), 0.99 (d, $J = 6.4$ Hz, 6H); MS (ESI) m/z 468.15 $[M+H]^+$.



Reagents or conditions: (a) $RB(OH)_2$, $PdCl_2(PPh_3)_2$, $NaHCO_3$, H_2O , DMF; (b) CuI , $PdCl_2(PPh_3)_2$, trimethylsilylacetylene, Et_3N , DMF, $90^\circ C$.

Scheme 20. Cross-coupling reactions of **EC102**.

8-(2-(furan-2-yl)-5-methoxyphenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [TT-V-138]. 2-Furanylboronic acid (8.2 mg, 0.0732 mmol) was added to **EC102** (25 mg, 0.0488 mmol) and $NaHCO_3$ (12.3 mg, 0.1464 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.1 mL) and $Pd(PPh_3)_2Cl_2$ (6.8 mg, 0.00976 mmol) were added and the reaction mixture was heated under nitrogen at $90^\circ C$ for 5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 20:1) to give 20.7 mg (94%) of **TT-V-138**. ^1H NMR (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.62 (d, $J = 8.7$ Hz, 1H), 7.50 (d, $J = 1.8$ Hz, 1H), 6.86 (dd, $J = 2.6, 8.7$ Hz, 1H), 6.70-6.73 (m, 2H), 6.49 (dd, $J = 1.8, 3.3$ Hz, 1H), 5.98 (br s, 2H), 4.26 (t, $J = 6.2$ Hz, 2H), 3.70 (s, 3H), 2.89 (t, $J = 6.2$ Hz, 2H), 2.28 (s, 2H), 0.84 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 154.8, 153.2, 151.6, 151.2, 145.4, 142.0, 130.9, 130.2, 124.3, 120.1, 116.5, 113.4, 111.4, 109.1, 61.8, 55.3, 49.6, 43.9,

31.5, 27.6; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{23}H_{29}N_6O_2S$, 453.2073; found 453.2071; HPLC: method A R_t = 6.76, method B R_t = 7.29.

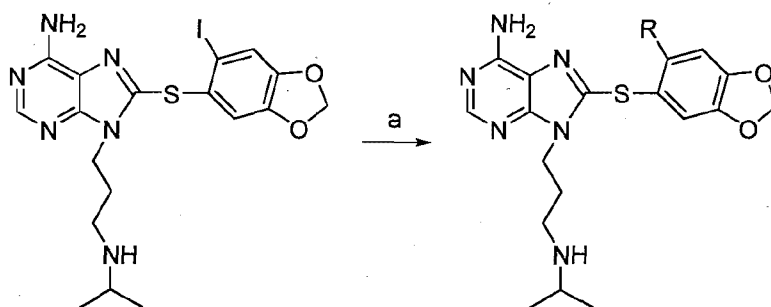
8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [TT-V-139]. 2-Thiopheneboronic acid (18.8 mg, 0.147 mmol) was added to **EC102** (25 mg, 0.0488 mmol) and $NaHCO_3$ (24.6 mg, 0.293 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.25 mL) and $Pd(PPh_3)_2Cl_2$ (10.4 mg, 0.0148 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 5 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 20:1) to give 16.2 mg (71%) of **TT-V-139**. ^1H NMR (500 MHz, $CDCl_3$ /MeOH- d_4) δ 8.19 (s, 1H), 7.45 (d, J = 8.5 Hz, 1H), 7.30-7.33 (m, 1H), 6.99-7.04 (m, 3H), 6.97 (dd, J = 2.6, 8.5 Hz, 1H), 4.24 (t, J = 6.1 Hz, 2H), 3.82 (s, 3H), 2.97 (t, J = 6.1 Hz, 2H), 2.41 (s, 2H), 0.91 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$ /MeOH- d_4) δ 159.9, 154.6, 152.4, 150.9, 147.6, 140.4, 133.2, 130.8, 129.3, 127.6, 127.1, 126.2, 119.5, 118.9, 114.6, 61.4, 55.6, 49.3, 43.3, 31.3, 27.6; HRMS (ESI) m/z $[M+H]^+$ calcd. for $C_{23}H_{29}N_6OS_2$, 469.1844; found 469.1830; HPLC: method A R_t = 6.84, method B R_t = 7.48.

8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [TT-V-140]. 1H-Pyrazole-3-boronic acid (26.2 mg, 0.234 mmol) was added to **EC102** (30 mg, 0.0585 mmol) and $NaHCO_3$ (29.5 mg, 0.351 mmol). DMF (1 mL) was added and the reaction mixture was evacuated and back filled with nitrogen. This was repeated four times then nitrogen was bubbled through the reaction mixture for 10 minutes. Then H_2O (0.2 mL) and $Pd(PPh_3)_2Cl_2$ (8.2 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for 7 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 15:1) to give 6.2 mg (23%) of **TT-V-140**. Additionally, 16.4 mg of unreacted **EC102** was recovered for an actual yield of 52%. ^1H NMR (500 MHz, $CDCl_3$ /MeOH- d_4) δ 8.19 (s, 1H), 7.58 (d, J = 2.1 Hz, 1H), 7.50 (d, J = 8.5 Hz, 1H), 7.03 (d, J = 2.4 Hz, 1H), 6.99 (dd, J = 2.6, 8.6 Hz, 1H), 6.40 (d, J = 2.1 Hz, 1H), 4.42 (t, J = 6.1 Hz, 2H), 3.81 (s, 3H), 3.02 (t, J = 6.1 Hz, 2H), 2.52 (s, 2H),

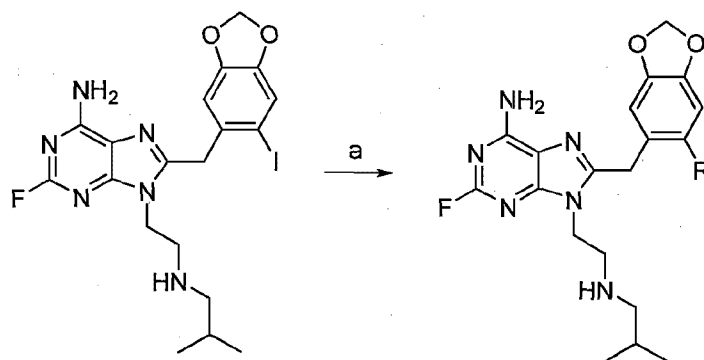
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0.98 (s, 9H); ^{13}C NMR (125 MHz, $\text{CDCl}_3/\text{MeOH}-d_4$) δ 154.6, 152.3, 150.8, 149.4, 148.6, 148.5, 120.1, 119.2, 114.5, 110.9, 106.0, 102.3, 61.2, 49.1, 42.5, 31.1, 27.5; HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{22}\text{H}_{29}\text{N}_8\text{OS}$, 453.2185; found 453.2186; HPLC: method A R_t = 6.61, method B R_t = 6.82.

8-((2-ethynyl-5-methoxyphenyl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine (PU-WS31). Following the procedure to make PU-WS8, PU-WS31 was obtained from EC102 as a white solid. ^1H NMR (CDCl_3 , 500 MHz) δ : 8.35 (s, 1H), 7.46 (d, J = 8.4 Hz, 1H), 6.75 (m, 2H), 5.65 (br, 2H), 4.35 (t, J = 6.3 Hz, 2H), 3.72 (s, 3H), 3.30 (s, 1H), 2.97 (t, J = 6.3 Hz, 2H), 2.31 (s, 2H), 0.87 (s, 9H); MS (ESI) m/z 411.3 ($\text{M}+\text{H}$) $^+$.



PU-H71



PU-DZ13

Reagents and conditions: (a) $\text{RSn}(\text{Bu})_3$, LiCl , $\text{Pd}(\text{PPh}_3)_4$, DMF, 90°C .

Scheme 21. Stille coupling of PU-H71 and PU-DZ13.

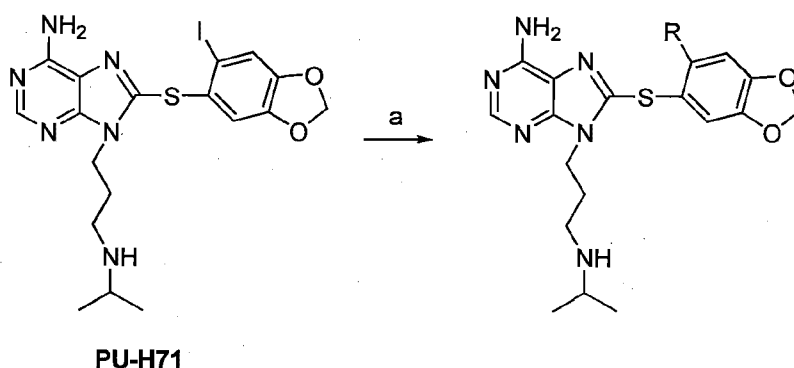
9-(3-(isopropylamino)propyl)-8-(6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ4-20]. A mixture of **PU-H71** (30 mg, 0.0585 mmol), 2-(tri-*n*-butylstannyl)oxazole (83.8 mg, 49 μ l, 0.234 mmol), LiCl (5 mg, 0.117 mmol) and Pd(PPh₃)₄ (6.7 mg, 0.0058 mmol) in DMF (1 mL) was evacuated and back filled with nitrogen. This was repeated four times then the reaction mixture was heated under nitrogen at 90°C for 18 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 20.8 mg (78%) of **DZ4-20**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.25 (s, 1H), 7.75 (s, 1H), 7.46 (s, 1H), 7.27 (s, 1H), 6.71 (s, 1H), 6.06 (s, 2H), 4.26 (t, *J* = 6.9 Hz, 2H), 2.75 (septet, *J* = 6.3 Hz, 1H), 2.53 (t, *J* = 6.9 Hz, 2H), 1.98 (m, 2H), 1.06 (d, *J* = 6.3 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₁H₂₄N₇O₃S, 454.1661; found 454.1650; HPLC: method A R_t = 5.77, method B R_t = 5.28.

9-(3-(isopropylamino)propyl)-8-(6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine [DZ4-21]. A mixture of **PU-H71** (30 mg, 0.0585 mmol), 2-(tri-*n*-butylstannyl)thiazole (87.6 mg, 72.4 μ l, 0.234 mmol), LiCl (5 mg, 0.117 mmol) and Pd(PPh₃)₄ (6.7 mg, 0.0058 mmol) in DMF (1 mL) was evacuated and back filled with nitrogen. This was repeated four times then the reaction mixture was heated under nitrogen at 90°C for 18 h. Then additional 2-(tri-*n*-butylstannyl)thiazole (21.9 mg, 18 μ l, 0.0585 mmol) was added and the reaction mixture was heated under nitrogen at 90°C for an additional 18 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5) to give 17.6 mg (64%) of **DZ4-21**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.20 (s, 1H), 7.87 (d, *J* = 3.3 Hz, 1H), 7.45 (s, 1H), 7.44 (d, *J* = 3.3 Hz, 1H), 6.98 (s, 1H), 6.11 (s, 2H), 4.21 (t, *J* = 6.9 Hz, 2H), 2.78 (septet, *J* = 6.3 Hz, 1H), 2.55 (t, *J* = 6.9 Hz, 2H), 1.98 (m, 2H), 1.09 (d, *J* = 6.3 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₁H₂₄N₇O₂S₂, 470.1433; found 470.1438; HPLC: method A R_t = 5.86, method B R_t = 5.66.

2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine [DZ4-23]. A mixture of **PU-DZ13** (20 mg, 0.039 mmol), 2-(tri-*n*-butylstannyl)oxazole (55.9 mg, 32.7 μ l, 0.156 mmol), LiCl (3.3 mg, 0.078 mmol) and Pd(PPh₃)₄ (4.5 mg, 0.0039 mmol) in DMF (1 mL) was evacuated and back filled with nitrogen. This was repeated four times then the reaction mixture was heated under nitrogen at 90°C for 18 h. Then additional LiCl (3.3 mg, 0.078 mmol) and Pd(PPh₃)₄ (4.5 mg, 0.0039 mmol) were added and the reaction mixture was heated under nitrogen at 90°C for an additional 18 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC two times (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5 then CH₂Cl₂:MeOH-NH₃ (7N), 20:1) to give 5.5 mg (31%) of **DZ4-23**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 7.68 (s, 1H), 7.53 (s, 1H), 7.12 (s, 1H), 6.84 (s, 1H), 6.07 (s, 2H), 4.74 (s, 2H), 4.41 (t, *J* = 6.4 Hz, 2H), 3.15 (t, *J* = 6.4 Hz, 2H), 2.59 (d, *J* = 6.9 Hz, 2H), 1.88 (m, 1H), 0.96 (d, *J* = 6.8 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₅FN₇O₃, 454.2003; found 454.1995; HPLC: method A R_t = 6.61, method B R_t = 7.58.

2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine [DZ4-24]. A mixture of **PU-DZ13** (20 mg, 0.039 mmol), 2-(tri-*n*-butylstannyl)thiazole (58.3 mg, 48.2 μ l, 0.156 mmol), LiCl (3.3 mg, 0.078 mmol) and Pd(PPh₃)₄ (9 mg, 0.0078 mmol) in DMF (1 mL) was evacuated and back filled with nitrogen. This was repeated four times then the reaction mixture was heated under nitrogen at 90°C for 18 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC two times (hexane:CH₂Cl₂:EtOAc:MeOH-NH₃ (7N), 2:2:1:0.5 and CH₂Cl₂:MeOH:AcOH, 20:1:0.5) to give 10.2 mg (56%) of **DZ4-24**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 7.77 (d, *J* = 3.3 Hz, 1H), 7.36 (d, *J* = 3.3 Hz, 1H), 7.17 (s, 1H), 6.80 (s, 1H), 6.05 (s, 2H), 4.58 (s, 2H), 4.15 (t, *J* = 6.6 Hz, 2H), 2.85 (t, *J* = 6.6 Hz, 2H), 2.35 (d, *J* = 6.8 Hz, 2H), 1.64 (m, 1H), 0.86 (d, *J* = 6.8 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₅FN₇O₂S, 470.1774; found 470.1770; HPLC: method A R_t = 6.68, method B R_t = 7.79.

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Reagents and conditions: (a) alkene (R), Pd(PPh₃)₄, *i*-Pr₂NEt, NMP, 55-100°C.

Scheme 22. Heck coupling of PU-H71.

8-(6-(cyclopent-2-enyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [TT-VI-116]. A solution of PU-H71 (30 mg, 0.0585 mmol) in NMP (1 mL) was evacuated and back filled with nitrogen. This was repeated four times, then DIEA (15.1 mg, 21 μ L, 0.117 mmol), cyclopentene (80 mg, 103 μ L, 1.171 mmol) and Pd(PPh₃)₄ (6.8 mg, 0.00586 mmol) were added and the reaction mixture was heated under nitrogen at 100°C for 20 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC two times (CH₂Cl₂:MeOH-NH₃ (7N), 15:1 then CH₂Cl₂:MeOH, 7:3) to give 9.2 mg (35%) of TT-VI-116. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.16 (s, 1H), 6.99 (s, 1H), 6.82 (s, 1H), 6.01 (s, 2H), 5.98 (m, 1H), 5.63 (m, 1H), 4.41 (t, *J* = 6.4 Hz, 2H), 3.39 (m, 1H), 3.34 (septet, *J* = 6.6 Hz, 1H), 2.95 (t, *J* = 6.4 Hz, 2H), 2.22-2.52 (m, 5H), 1.50-1.59 (m, 1H), 1.44 (d, *J* = 6.6 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₃H₂₉N₆O₂S, 453.2073; found 453.2064; HPLC: method A R_t = 6.51, method B R_t = 7.79.

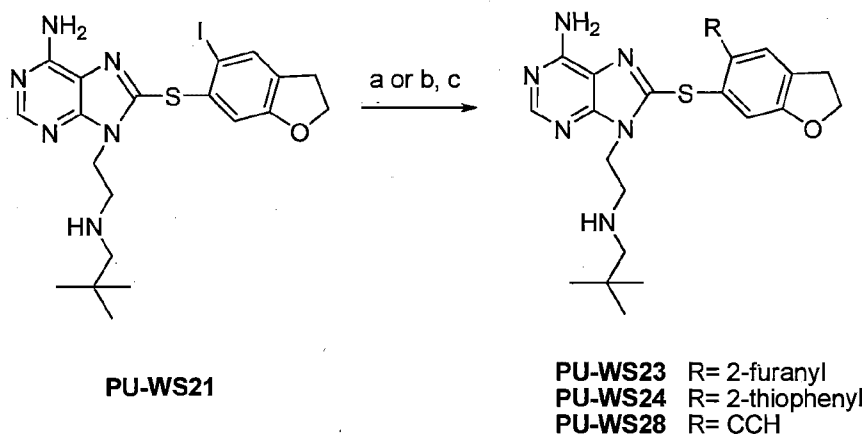
8-(6-(2,5-dihydro-1H-pyrrol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-141]. A solution of PU-H71 (30 mg, 0.0585 mmol) and N-Boc-2,3-dihydro-1H-pyrrole (19.8 mg, 20.2 μ L, 0.117 mmol) in NMP (1.5 mL) was evacuated and back filled with nitrogen. This was repeated four times, then DIEA (15.1 mg, 21 μ L, 0.117 mmol) and Pd(PPh₃)₄ (13.5 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 100°C for 20 h. Solvent was removed

under reduced pressure and the resulting residue was purified by preparatory TLC (CH_2Cl_2 :MeOH- NH_3 (7N), 15:1) and the resulting residue was dissolved into 2 mL of CH_2Cl_2 :TFA (4:1) and stirred for 1 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 6.0 mg (23%) of **DZ3-141**. ^1H NMR (500 MHz, CDCl_3 /MeOH- d_4) δ 8.19 (s, 1H), 6.98 (s, 2H), 6.04 (m, 1H), 6.01 (s, 2H), 5.74 (m, 1H), 5.62 (d, $J = 2.0$ Hz, 1H), 4.31 (t, $J = 6.9$ Hz, 2H), 3.81-3.88 (m, 1H), 3.89-3.95 (m, 1H), 2.87 (septet, $J = 6.3$ Hz, 1H), 2.68 (t, $J = 6.7$ Hz, 2H), 2.14 (m, 2H), 1.15 (d, $J = 6.3$ Hz, 6H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{22}\text{H}_{28}\text{N}_7\text{O}_2\text{S}$, 454.2025; found 454.2046; HPLC: method A $R_t = 5.27$, method B $R_t = 2.72$.

8-(6-(2,3-dihydrofuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-142]. A solution of **PU-H71** (30 mg, 0.0585 mmol) in NMP (1.5 mL) was evacuated and back filled with nitrogen. This was repeated four times, then DIEA (15.1 mg, 21 μL , 0.117 mmol), 2,3-dihydrofuran (82 mg, 88 μL , 1.17 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (13.5 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 55°C for 20 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC two times (hexane:EtOAc: CH_2Cl_2 :MeOH- NH_3 (7N), 2:1:2:0.5, then CH_2Cl_2 :MeOH- NH_3 (7N), 15:1) to give 7.0 mg (26%) of **DZ3-142**. ^1H NMR (500 MHz, CDCl_3) δ 8.23 (s, 1H), 7.06 (s, 1H), 6.96 (s, 1H), 6.43 (m, 1H), 6.01 (s, 2H), 5.94 (dd, $J = 8.1$, 10.8 Hz, 1H), 5.72 (br s, 2H), 4.93 (m, 1H), 4.35 (t, $J = 6.8$ Hz, 2H), 2.95-3.55 (m, 2H), 2.70 (t, $J = 6.5$ Hz, 2H), 2.39-2.47 (m, 1H), 2.22 (m, 2H), 1.25 (d, $J = 6.2$ Hz, 6H); HRMS (ESI) m/z $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{22}\text{H}_{27}\text{N}_6\text{O}_3\text{S}$, 455.1865; found 455.1865; HPLC: method A $R_t = 6.07$, method B $R_t = 6.49$.

8-(6-(2,3-dihydrofuran-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine [DZ3-143]. A solution of **PU-H71** (30 mg, 0.0585 mmol) in NMP (1.5 mL) was evacuated and back filled with nitrogen. This was repeated four times, then DIEA (15.1 mg, 21 μL , 0.117 mmol), 2,5-dihydrofuran (82 mg, 88 μL , 1.17 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (13.5 mg, 0.0117 mmol) were added and the reaction mixture was heated under nitrogen at 55°C for 20 h. Solvent was removed under reduced pressure and the resulting residue was purified by preparatory TLC two times (CH_2Cl_2 :MeOH- NH_3 (7N), 10:1, then

hexane:EtOAc:CH₂Cl₂:MeOH-NH₃ (7N), 2:1:2:0.5) to give 5.0 mg (19%) of **DZ3-143**. ¹H NMR (500 MHz, CDCl₃/MeOH-*d*₄) δ 8.18 (s, 1H), 7.02 (s, 1H), 7.00 (s, 1H), 6.55 (m, 1H), 6.04 (s, 2H), 4.99 (m, 1H), 4.64-4.69 (m, 1H), 4.45 (m, 1H), 4.31 (t, *J* = 6.8 Hz, 2H), 4.05 (dd, *J* = 6.2, 9.2 Hz, 1H), 3.40 (m, 1H), 2.67 (t, *J* = 6.4 Hz, 2H), 2.14 (m, 2H), 1.16 (d, *J* = 6.1 Hz, 6H); HRMS (ESI) *m/z* [M+H]⁺ calcd. for C₂₂H₂₇N₆O₃S, 455.1865; found 455.1862; HPLC: method A R_t = 6.04, method B R_t = 6.32.



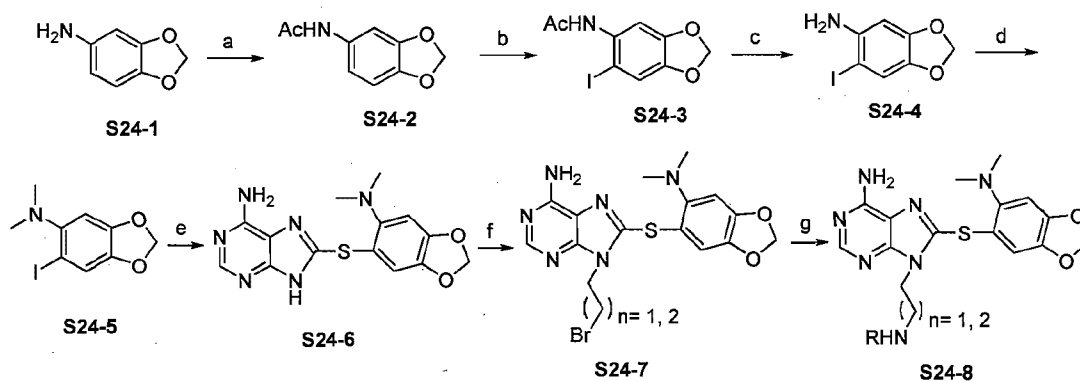
Reagents and conditions: (a) RB(OH)₂, PdCl₂(PPh₃)₂, NaHCO₃, H₂O, DMF, 90°C; (b) CuI, PdCl₂(PPh₃)₂, trimethylsilylacetylelene, Et₃N, DMF, 90°C; (c) KOH, MeOH, rt.

Scheme 23. Cross coupling reactions of PU-WS21.

8-(5-(furan-2-yl)-2,3-dihydrobenzofuran-6-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [PU-WS23]. Following the procedure to make **PU-DZ3-4**, compound **PU-WS23** was obtained as a white solid. ¹H NMR (500 MHz, CDCl₃) δ 8.31 (s, 1H), 7.49 (s, 2H), 6.68 (d, *J* = 3.4 Hz, 1H), 6.58 (s, 1H), 6.49 (m, 1H), 5.60 (br s, 2H), 4.58 (t, *J* = 8.7 Hz, 2H), 4.25 (m, 2H), 3.22 (t, *J* = 8.7 Hz, 2H), 2.86 (m, 2H), 2.25 (s, 2H), 0.86 (s, 9H); HRMS (*m/z*): [M+H]⁺ calcd for C₂₄H₂₉N₆O₂ 465.2073; found 465.2077.

9-(2-(neopentylamino)ethyl)-8-(5-(thiophen-2-yl)-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-6-amine [PU-WS24]. Following the procedure to make PU-DZ2-395, compound PU-WS24 was obtained as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 8.31 (s, 1H), 7.32 (m, 1H), 7.27 (s, 1H), 7.03-7.07 (m, 2H), 6.67 (s, 1H), 5.59 (br s, 2H), 4.58 (t, $J = 8.7$ Hz, 2H), 4.15 (m, 2H), 3.21 (t, $J = 8.7$ Hz, 2H), 2.86 (m, 2H), 2.25 (s, 2H), 0.83 (s, 9H); HRMS (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{29}\text{N}_6\text{O}_2$ 481.1844; found 481.1825.

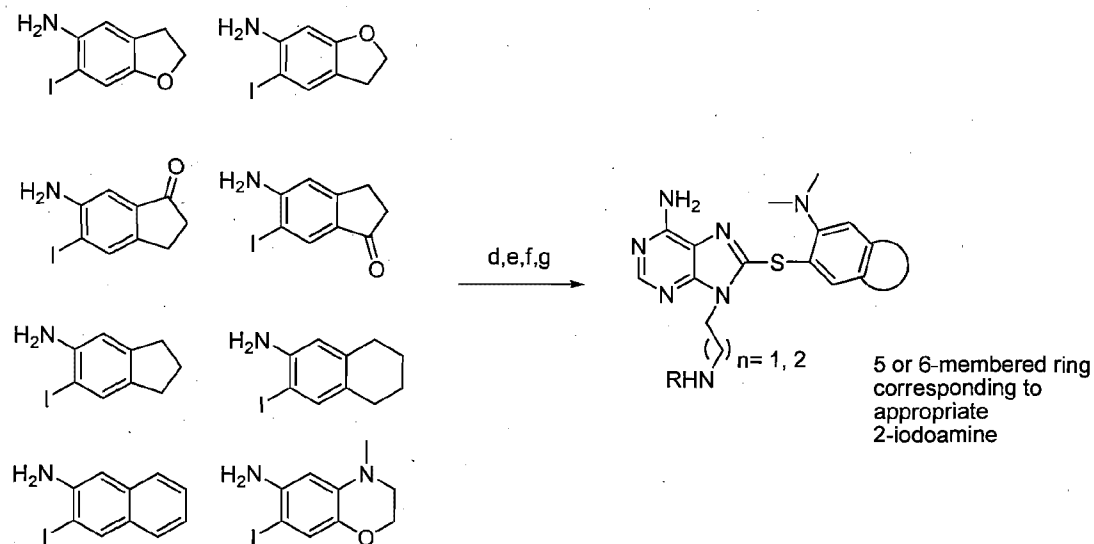
8-(5-ethynyl-2,3-dihydrobenzofuran-6-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine [PU-WS28]. Following the procedure to make PU-WS8, compound PU-WS28 was obtained as a white solid. ^1H NMR (500 MHz, CDCl_3 , δ): 8.33 (s, 1H), 7.36 (s, 1H), 6.59 (s, 1H), 5.70 (br, 2H), 4.58 (t, $J = 8.7$ Hz, 2H), 4.41 (m, 2H), 3.33 (t, $J = 8.7$ Hz, 2H), 3.49 (m, 2H), 3.02 (s, 2H), 2.44 (s, 2H), 0.91 (s, 9H); HRMS (m/z): $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{27}\text{N}_6\text{OS}$ 423.1967; found 423.1968.



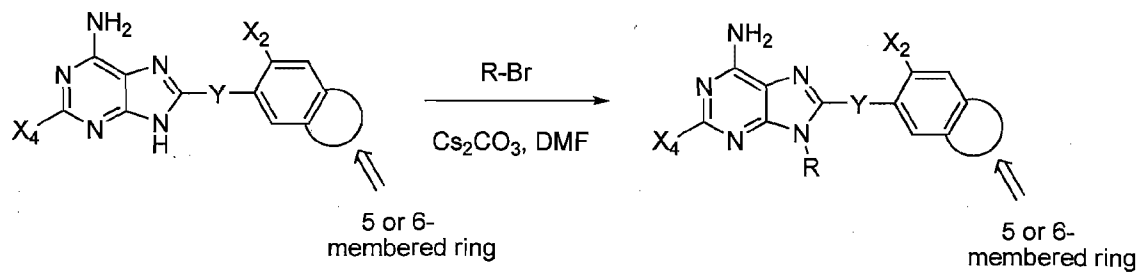
Reagents and conditions: (a) Ac_2O , AcOH , rt; (b) ICl , CH_2Cl_2 , AcOH , rt; (c) NaOH , EtOH , H_2O , reflux; (d) paraformaldehyde, NaBH_3CN , MeOH , 50°C ; (e) 8-mercaptadenine, neocuproine, CuI , NaOtBu , DMF , 115°C ; (f) Cs_2CO_3 , 1,3-dibromopropane or 1,2-dibromoethane, DMF , rt; (g) amine, DMF , rt.

Scheme 24.

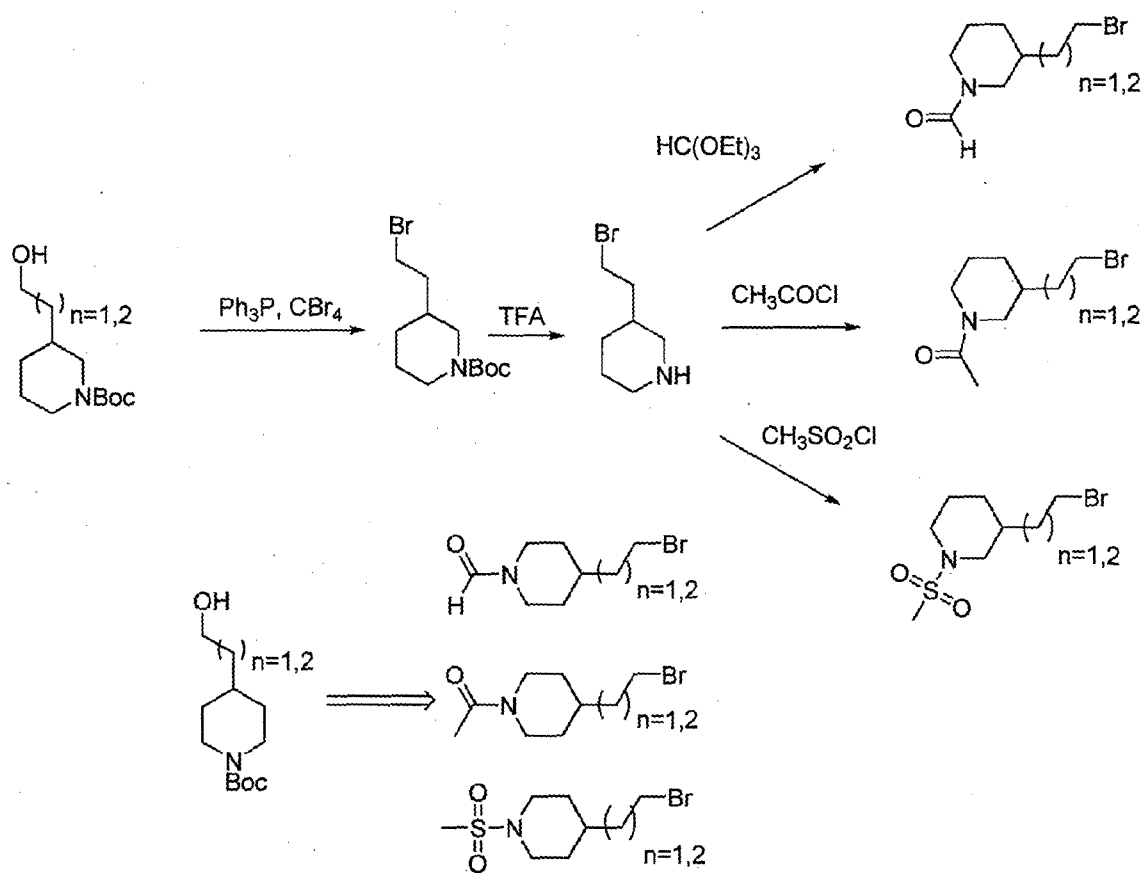
Similarly,



Scheme 25. Synthesis of various bromides required for alkylation of the purine skeleton.



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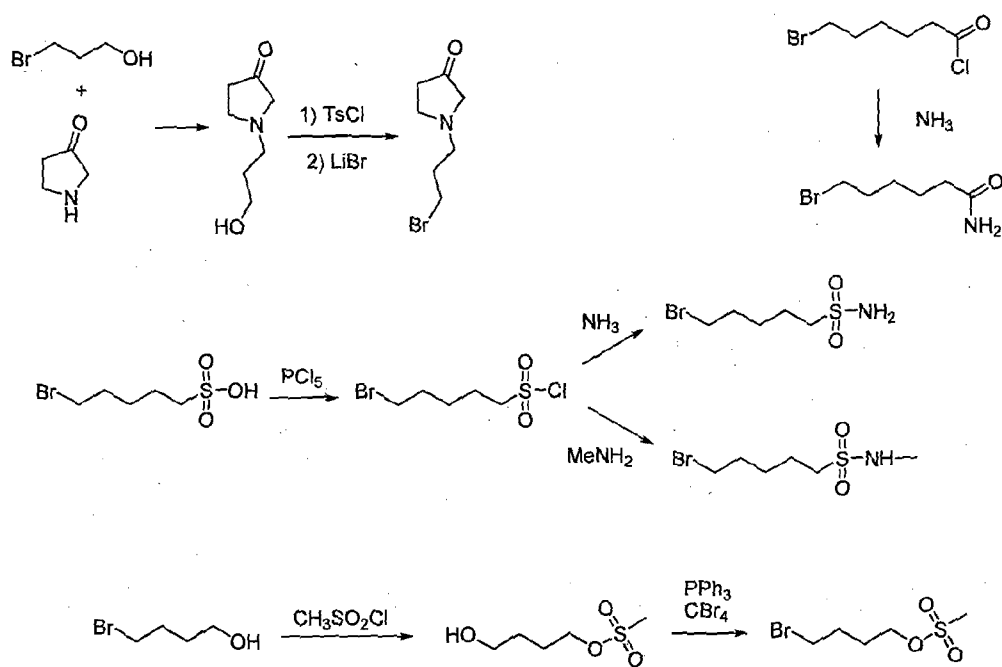
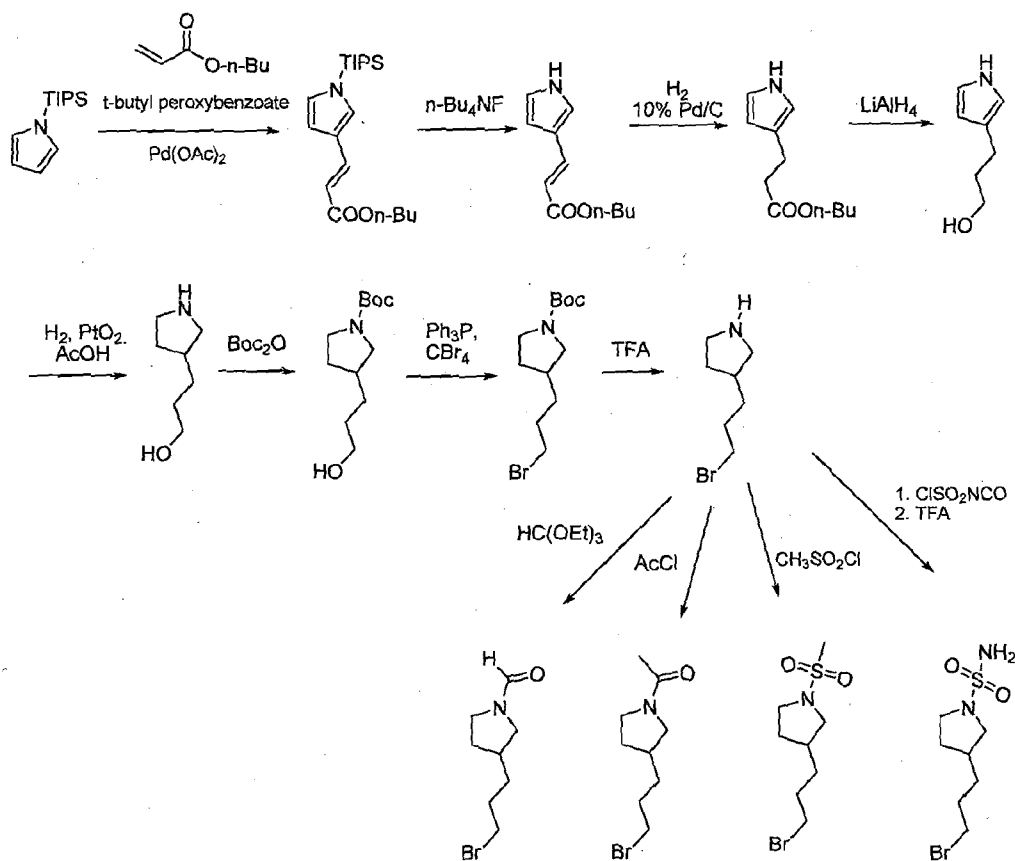


Table 1A

No.	Name
1A-1	PU-WS10 8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1A-2	8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1A-3	1-(6-amino-8-(6-iodo-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol
1A-4	2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1A-5	2-chloro-8-((6-(furan-2-yl)-2,3-dihydrobenzofuran-5-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1A-6	2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1A-7	8-((6-(furan-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1A-8	8-((6-ethynyl-2,3-dihydrobenzofuran-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1A-9	5-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-2,3-dihydrobenzofuran-6-carbonitrile
1A-10	8-((6-(aziridin-1-yl)-2,3-dihydrobenzofuran-5-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1A-11	8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1A-12	3-(2-(6-amino-8-(6-(5-methylfuran-2-yl)-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)ethyl)piperidine-1-sulfonamide
1A-13	1-(3-(2-(8-(6-(1H-pyrazol-3-yl)-2,3-dihydrobenzofuran-5-ylthio)-6-amino-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1A-14	4-(3-(6-amino-8-(6-ethynyl-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)propyl)piperidine-1-carbaldehyde
1A-15	1-(3-(2-(6-amino-2-fluoro-8-((6-(furan-2-yl)-2,3-dihydrobenzofuran-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1A-16	N-(2-((2-(6-amino-8-((6-(furan-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1A-17	3-((2-(6-amino-8-((6-(furan-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
1A-18	2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine

1A-19	2-chloro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1A-20	9-(2-aminoethyl)-2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9H-purin-6-amine
1A-21	9-(3-aminopropyl)-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
1A-22	9-(2-aminoethyl)-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
1A-23	9-(3-(tert-butylamino)propyl)-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
1A-24	1-(6-amino-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
1A-25	1-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1A-26	1-(3-(6-amino-8-(6-iodo-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1A-27	5-(6-amino-8-(6-iodo-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
1A-28	1-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
1A-29	8-((6-ethynyl-2,3-dihydrobenzofuran-5-yl)methyl)-2-fluoro-9-(5-(methylsulfonyl)pentyl)-9H-purin-6-amine
1A-30	2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9-(2-(1-(methylsulfonyl)pyrrolidin-3-yl)ethyl)-9H-purin-6-amine
1A-31	N-(4-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydrobenzofuran-5-yl)methyl)-9H-purin-9-yl)butyl)methanesulfonamide
1A-32	1-(6-amino-8-((6-ethynyl-2,3-dihydrobenzofuran-5-yl)methyl)-2-fluoro-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
1A-33	6-(6-amino-8-((6-ethynyl-2,3-dihydrobenzofuran-5-yl)methyl)-2-fluoro-9H-purin-9-yl)hexanamide
1A-34	1-(4-(2-(6-amino-8-((6-ethynyl-2,3-dihydrobenzofuran-5-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1A-35	8-((6-ethynyl-2,3-dihydrobenzofuran-5-yl)methyl)-2-fluoro-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
	9-(3-(isopropylamino)propyl)-8-((6-(5-methylfuran-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
	9-(3-(tert-butylamino)propyl)-8-((6-(5-methylfuran-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
	9-(3-(tert-butylamino)propyl)-8-((6-

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	(dimethylamino)-2,3-dihydrobenzofuran-5-yl)thio)- 9H-purin-6-amine
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	1-(4-(2-(6-amino-8-((6-(dimethylamino)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1A-40	8-((6-(dimethylamino)-2,3-dihydrobenzofuran-5-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1A-41	4-(3-(6-amino-8-(6-(aziridin-1-yl)-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)propyl)piperidine-1-carbaldehyde
1A-42	8-((6-(furan-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1A-43	8-((6-(dimethylamino)-2,3-dihydrobenzofuran-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1A-44	8-((6-(dimethylamino)-2,3-dihydrobenzofuran-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1A-45	9-(3-(tert-butylamino)propyl)-8-((6-(oxazol-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
1A-46	1-(3-(2-(6-amino-8-(6-(oxazol-2-yl)-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1A-47	4-(3-(6-amino-8-(6-(oxazol-2-yl)-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)propyl)piperidine-1-carbaldehyde
1A-48	9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-8-((6-(oxazol-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
1A-49	1-(2-(3-(6-amino-8-(6-iodo-2,3-dihydrobenzofuran-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-1-yl)ethanone
1A-50	9-(3-(tert-butylamino)propyl)-8-((6-(5-methyloxazol-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
1A-51	9-(3-(tert-butylamino)propyl)-8-((6-(thiazol-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine
1A-52	9-(3-(tert-butylamino)propyl)-8-((6-(5-methylthiazol-2-yl)-2,3-dihydrobenzofuran-5-yl)thio)-9H-purin-6-amine

Table 1B

No.	Name
1B-1	PU-WS9 8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1B-2	PU-WS4 8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine

1B-3	PU-WS17 2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1B-4	PU-WS18 2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1B-5	2-chloro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1B-6	8-((5-(furan-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1B-7	8-((5-(dimethylamino)-2,3-dihydrobenzofuran-6-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1B-8	8-((5-(1H-pyrazol-3-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1B-9	8-((5-cyclopentyl-2,3-dihydrobenzofuran-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1B-10	8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1B-11	6-(((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-2,3-dihydrobenzofuran-5-carbonitrile
1B-12	2-chloro-9-(3-(isopropylamino)propyl)-8-((5-(5-methylfuran-2-yl)-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-6-amine
1B-13	4-(2-(6-amino-8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1B-14	1-(4-(2-(6-amino-2-fluoro-8-((5-(furan-2-yl)-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1B-15	N-(2-((2-(6-amino-8-((5-(furan-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1B-16	3-((2-(6-amino-8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
1B-17	9-(2-(isobutylamino)ethyl)-8-((5-(thiophen-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-18	3-(3-(6-amino-8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)propyl)-2-oxoimidazolidine-1-carbaldehyde
1B-19	2-chloro-8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1B-20	6-(((6-amino-2-chloro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-2,3-dihydrobenzofuran-5-carbonitrile
1B-21	2-chloro-8-((5-(dimethylamino)-2,3-dihydrobenzofuran-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1B-22	8-((5-cyclopentyl-2,3-dihydrobenzofuran-6-yl)thio)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1B-23	1-(3-(6-amino-8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1B-24	PU-WS21 8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1B-25	PU-WS22 2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine

1B-26	PU-WS23 8-((5-(furan-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1B-27	PU-WS24 9-(2-(neopentylamino)ethyl)-8-((5-(thiophen-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-28	PU-WS28 8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1B-29	9-(3-aminopropyl)-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-30	9-(2-aminoethyl)-2-fluoro-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)methyl)-9H-purin-6-amine
1B-31	9-(2-aminoethyl)-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-32	9-(3-(tert-butylamino)propyl)-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-33	2-fluoro-8-((5-(5-methylfuran-2-yl)-2,3-dihydrobenzofuran-6-yl)methyl)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1B-34	1-(3-(6-amino-8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)propyl)-4-hydroxypyrrolidin-2-one
1B-35	N-(3-(6-amino-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
1B-36	1-(3-(6-amino-8-(5-ethynyl-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1B-37	8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9-(2-(1-(methylsulfonyl)pyrrolidin-3-yl)ethyl)-9H-purin-6-amine
1B-38	N-(3-(6-amino-8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
1B-39	1-(4-(2-(6-amino-8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone

1B-40	8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1B-41	5-(6-amino-8-(5-ethynyl-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
1B-42	1-(4-(2-(6-amino-8-((5-(furan-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1B-43	8-(5-(5-methylfuran-2-yl)-2,3-dihydrobenzofuran-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1B-44	2-(3-(6-amino-8-(5-(5-methylfuran-2-yl)-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidine-1-carbaldehyde
1B-45	N-(2-(6-amino-8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl) N'-methyl-sulfuric diamide
1B-46	9-(3-(tert-butylamino)propyl)-8-((5-(oxazol-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-47	9-(3-(tert-butylamino)propyl)-8-((5-ethynyl-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-48	9-(3-(tert-butylamino)propyl)-8-((5-(dimethylamino)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-49	1-(6-amino-8-((5-iodo-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
1B-50	1-(4-(2-(6-amino-8-((5-(oxazol-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1B-51	9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-8-((5-(oxazol-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-52	3-(3-(6-amino-8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidine-1-sulfonamide
1B-53	9-(3-(tert-butylamino)propyl)-8-((5-(5-methyloxazol-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-54	9-(3-(tert-butylamino)propyl)-8-((5-(thiazol-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-55	9-(3-(tert-butylamino)propyl)-8-((5-(5-methylthiazol-2-yl)-2,3-dihydrobenzofuran-6-yl)thio)-9H-purin-6-amine
1B-56	6-(6-amino-8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)hexanamide
1B-57	5-(6-amino-8-(5-iodo-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
1B-58	3-(6-amino-8-(5-ethynyl-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-9-yl)propyl sulfamate

Table 1C

No.	Name
1C-1	8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1C-2	8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1C-3	8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1C-4	2-fluoro-8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)methyl)-9-(2-

	(isobutylamino)ethyl)-9H-purin-6-amine
1C-5	2-chloro-8-((6-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1C-6	8-((6-(1H-imidazol-4-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)methyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1C-7	8-((6-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1C-8	8-((6-ethynyl-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1C-9	5-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-2,3-dihydrobenzo[b]thiophene-6-carbonitrile
1C-10	8-((6-(aziridin-1-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1C-11	8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1C-12	1-(4-(2-(6-amino-8-((6-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1C-13	4-(2-(8-((6-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-6-amino-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1C-14	4-(2-(6-amino-8-((6-ethynyl-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1C-15	1-(4-(2-(6-amino-2-fluoro-8-((6-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1C-16	N-(2-((2-(6-amino-8-((6-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1C-17	3-((2-(6-amino-8-((6-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
1C-18	9-(3-aminopropyl)-8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9H-purin-6-amine
1C-19	9-(2-aminoethyl)-2-fluoro-8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)methyl)-9H-purin-6-amine
1C-20	9-(2-aminoethyl)-8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9H-purin-6-amine
1C-21	9-(3-(tert-butylamino)propyl)-8-((6-iodo-2,3-dihydrobenzo[b]thiophen-5-yl)thio)-9H-purin-6-amine

Table 1D

No.	Name
1D-1	8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1D-2	8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1D-3	2-fluoro-8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1D-4	2-fluoro-8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1D-5	8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1D-6	8-((5-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9-(3-

	(isopropylamino)propyl)-9H-purin-6-amine
1D-7	8-((5-(dimethylamino)-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1D-8	8-((5-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1D-9	8-((5-cyclopentyl-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1D-10	8-((5-ethynyl-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1D-11	6-((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-2,3-dihydrobenzo[b]thiophene-5-carbonitrile
1D-12	2-chloro-8-((5-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1D-13	4-(2-(6-amino-8-((5-ethynyl-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1D-14	1-(4-(2-(6-amino-2-fluoro-8-((5-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1D-15	N-(2-((2-(6-amino-8-((5-(furan-2-yl)-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1D-16	3-((2-(6-amino-8-((5-ethynyl-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide

1D-17	2-chloro-8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1D-18	9-(3-aminopropyl)-8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9H-purin-6-amine
1D-19	9-(2-aminoethyl)-2-fluoro-8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)methyl)-9H-purin-6-amine
1D-20	9-(2-aminoethyl)-8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9H-purin-6-amine
1D-21	9-(3-(tert-butylamino)propyl)-8-((5-iodo-2,3-dihydrobenzo[b]thiophen-6-yl)thio)-9H-purin-6-amine

Table 1E

No.	Name
1E-1	1-(6-amino-8-(6-iodo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol
1E-2	PU-WS26 8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1E-3	1-(3-(6-amino-8-(6-iodo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1E-4	2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1E-5	2-chloro-8-((6-(furan-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1E-6	2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1E-7	8-((6-(furan-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1E-8	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1E-9	6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-2,3-dihydro-1H-indene-5-carbonitrile
1E-10	8-((6-(azetidin-1-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1E-11	9-(3-(isopropylamino)propyl)-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine
1E-12	1-(3-(2-(6-amino-8-(6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone

1E-13	3-(2-(8-(6-(1H-pyrazol-3-yl)-2,3-dihydro-1H-inden-5-ylthio)-6-amino-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1E-14	1-(3-(2-(6-amino-8-(6-ethynyl-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1E-15	2-fluoro-9-(3-(1-(methylsulfonyl)pyrrolidin-3-yl)propyl)-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-6-amine
1E-16	N-(2-((2-(6-amino-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1E-17	3-(2-(6-amino-8-(6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
1E-18	1-(3-(3-(6-amino-8-(6-iodo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-1-yl)ethanone
1E-19	1-(3-(3-(6-amino-8-(6-ethynyl-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-1-yl)ethanone
1E-20	2-chloro-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1E-21	PU-WS25 8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1E-22	PU-WS27 8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1E-23	PU-WS29 8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1E-24	9-(3-aminopropyl)-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine
1E-25	9-(2-aminoethyl)-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine
1E-26	9-(3-(tert-butylamino)propyl)-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine
1E-27	9-(3-(isopropylamino)propyl)-8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine
1E-28	1-(4-(3-(6-amino-8-(6-(dimethylamino)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)piperidin-1-yl)ethanone
1E-29	1-(3-(2-(6-amino-2-fluoro-8-((6-(4-methylthiazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1E-30	8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1E-31	9-(3-aminopropyl)-8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine
1E-32	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(4-methylthiazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-6-amine
1E-33	8-((6-(1H-pyrazol-3-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9-(3-(tert-butylamino)propyl)-2-fluoro-9H-purin-6-amine
1E-34	8-(6-(aziridin-1-yl)-2,3-dihydro-1H-inden-5-ylthio)-9-(3-(1-(methylsulfonyl)pyrrolidin-3-yl)propyl)-9H-purin-6-amine
1E-35	1-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1E-36	8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1E-37	1-(6-amino-8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-

	yl)-3-(isopropylamino)propan-2-ol
1E-38	5-(6-amino-8-(6-iodo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)-N-methylpentane-1-sulfonamide
1E-39	5-(6-amino-8-(6-iodo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
1E-40	5-(6-amino-8-(6-ethynyl-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
1E-41	1-(2-(4-(6-amino-8-(6-(5-methylfuran-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)butyl)pyrrolidin-1-yl)ethanone
1E-42	1-(3-(6-amino-8-(6-iodo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-ol
1E-43	6-(6-amino-8-(6-iodo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)hexanamide
1E-44	1-(3-(3-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-1-yl)ethanone
1E-45	5-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)-N-methylpentane-1-sulfonamide
1E-46	5-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)pentane-1-sulfonamide
1E-47	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-6-amine
1E-48	2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1E-49	1-(4-(3-(6-amino-8-(6-ethynyl-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)piperidin-1-yl)ethanone
1E-50	1-(3-(2-(6-amino-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1E-51	9-(3-(tert-butylamino)propyl)-8-(6-ethynyl-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-6-amine
1E-52	9-(3-(tert-butylamino)propyl)-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9H-purin-6-amine
1E-53	6-(6-amino-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9H-purin-9-yl)hexanamide
1E-54	1-(3-(6-amino-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9H-purin-9-yl)propyl)pyrrolidin-3-one
1E-55	4-(6-amino-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9H-purin-9-yl)butane-1-sulfonamide
1E-56	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1E-57	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
1E-58	1-acetyl-3-(3-(6-amino-8-(6-ethynyl-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)imidazolidin-2-one
1E-59	9-(3-(tert-butylamino)propyl)-8-(6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-6-amine
1E-60	9-(3-(tert-butylamino)propyl)-8-(6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-6-amine
1E-61	8-(6-(1H-pyrazol-3-yl)-2,3-dihydro-1H-inden-5-ylthio)-9-(3-(tert-butylamino)propyl)-9H-purin-6-amine
1E-62	1-(3-(2-(6-amino-8-(6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone

1E-63	6-(6-amino-8-(6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)hexanamide
1E-64	1-(3-(6-amino-8-(6-(4-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1E-65	6-(6-amino-2-fluoro-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)hexanamide
1E-66	1-(3-(6-amino-2-fluoro-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1E-67	5-(6-amino-2-fluoro-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)pentane-1-sulfonamide
1E-68	8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine
1E-69	8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine
1E-70	8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1E-71	3-(2-(6-amino-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-sulfonamide
1E-72	2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine
1E-73	2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine
1E-74	2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1E-75	3-(2-(6-amino-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-sulfonamide
1E-76	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-iodo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-6-amine
1E-77	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine
1E-78	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine
1E-79	3-(2-(6-amino-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidine-1-sulfonamide
1E-80	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1E-81	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine
1E-82	8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine
1E-83	9-(3-(tert-butylamino)propyl)-8-(6-(4-methylthiazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-6-amine
1E-84	2-fluoro-9-(2-(1-methylpiperidin-2-yl)ethyl)-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-6-amine
1E-85	2-fluoro-9-(2-(1-methylpiperidin-3-yl)ethyl)-8-((6-(oxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-6-amine

Table 1F

No.	Name
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1F-1	8-((6-iodoindolin-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1F-2	2-fluoro-8-((6-iodoindolin-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1F-3	8-((6-(1H-pyrazol-3-yl)indolin-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1F-4	8-((6-ethynylindolin-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1F-5	8-((6-(1H-pyrrol-3-yl)indolin-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1F-6	5-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)indoline-6-carbonitrile

1F-7	8-((6-(furan-2-yl)-1-methylindolin-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1F-8	8-((6-(cyclobutyl-1-methylindolin-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1F-9	1-(5-((6-amino-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-8-yl)methyl)-6-(aziridin-1-yl)indolin-1-yl)ethanone
1F-10	1-(4-(2-(6-amino-8-((6-(furan-2-yl)indolin-5-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1F-11	4-(2-(8-((6-(1H-pyrazol-3-yl)indolin-5-yl)thio)-6-amino-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1F-12	4-(2-(6-amino-8-((6-ethynyl-1-methylindolin-5-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1F-13	1-(4-(2-(6-amino-2-fluoro-8-((6-(furan-2-yl)indolin-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1F-14	N-(2-((2-(6-amino-8-((6-(furan-2-yl)indolin-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1F-15	3-((2-(6-amino-8-((6-(furan-2-yl)indolin-5-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
1F-16	2-chloro-8-((6-iodoindolin-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1F-17	9-(3-aminopropyl)-8-((6-iodoindolin-5-yl)thio)-9H-purin-6-amine
1F-18	9-(2-aminoethyl)-8-((6-iodoindolin-5-yl)thio)-9H-purin-6-amine
1F-19	9-(3-(tert-butylamino)propyl)-8-((6-iodoindolin-5-yl)thio)-9H-purin-6-amine
1F-20	8-((6-iodoindolin-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine

Table 1G

No.	Name
1G-1	1-(6-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)-5-iodoindolin-1-yl)ethanone
1G-2	2-fluoro-8-((5-iodoindolin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1G-3	8-((5-(1H-pyrazol-3-yl)indolin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1G-4	8-((5-ethynylindolin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1G-5	8-((5-(1H-pyrrol-3-yl)indolin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine

1G-6	6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)indoline-5-carbonitrile
1G-7	8-((5-(furan-2-yl)-1-methylindolin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1G-8	8-((5-cyclobutyl-1-methylindolin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
1G-9	1-(6-((6-amino-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-8-yl)methyl)-5-(aziridin-1-yl)indolin-1-yl)ethanone
1G-10	1-(4-(2-(6-amino-8-((5-(furan-2-yl)indolin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1G-11	8-(5-(1H-pyrazol-3-yl)indolin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
1G-12	3-(2-(6-amino-8-(1-ethyl-5-ethynylindolin-6-ylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1G-13	1-(3-(2-(6-amino-2-fluoro-8-((1-methyl-5-(5-methylfuran-2-yl)indolin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
1G-14	N-(2-((2-(6-amino-8-((5-(furan-2-yl)indolin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1G-15	3-(2-(6-amino-8-(5-(5-methylfuran-2-yl)indolin-6-ylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
1G-16	1-(3-(4-(6-amino-8-(5-iodo-1-methylindolin-6-ylthio)-9H-purin-9-yl)butyl)pyrrolidin-1-yl)ethanone
1G-17	9-(3-aminopropyl)-8-((5-iodoindolin-6-yl)thio)-9H-purin-6-amine
1G-18	9-(2-aminoethyl)-8-((5-iodoindolin-6-yl)thio)-9H-purin-6-amine
1G-19	9-(3-(tert-butylamino)propyl)-8-(1-ethyl-5-iodoindolin-6-ylthio)-9H-purin-6-amine
1G-20	8-(5-iodo-1-methylindolin-6-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
1G-21	1-(3-(6-amino-8-(5-iodo-1-methylindolin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one

Table 1H

No.	Name
1H-1	6-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-2	6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-3	6-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-4	6-((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-5	6-(6-amino-9-(2-hydroxy-3-(isopropylamino)propyl)-9H-purin-8-ylthio)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-6	6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-5-(furan-2-yl)-2,3-dihydro-1H-inden-1-one
1H-7	6-((6-amino-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-8-yl)methyl)-5-(dimethylamino)-2,3-dihydro-1H-inden-1-one
1H-8	6-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)-5-(1H-pyrazol-3-yl)-2,3-dihydro-1H-inden-1-one
1H-9	6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-5-cyclopropyl-2,3-

	dihydro-1H-inden-1-one
1H-10	6-(((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)-5-ethynyl-2,3-dihydro-1H-inden-1-one
1H-11	6-(((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-1-oxo-2,3-dihydro-1H-indene-5-carbonitrile
1H-12	6-(((6-amino-2-chloro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-5-(furan-2-yl)-2,3-dihydro-1H-inden-1-one
1H-13	4-(2-(6-amino-8-(((6-ethynyl-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
1H-14	6-((9-(2-(1-acetylpiperidin-3-yl)ethyl)-6-amino-2-fluoro-9H-purin-8-yl)methyl)-5-(5-methylfuran-2-yl)-2,3-dihydro-1H-inden-1-one
1H-15	N-(2-(((2-(6-amino-8-(((6-(furan-2-yl)-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
1H-16	3-((2-(6-amino-8-(((6-ethynyl-3-oxo-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
1H-17	6-(((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)-5-iodo-2,3-dihydro-1H-indene-1-thione
1H-18	6-(((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-5-iodo-2,3-dihydro-1H-indene-1-thione
1H-19	6-(((6-amino-9-(3-aminopropyl)-9H-purin-8-yl)thio)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-20	6-(((6-amino-9-(2-aminoethyl)-2-fluoro-9H-purin-8-yl)methyl)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-21	6-(((6-amino-9-(2-aminoethyl)-9H-purin-8-yl)thio)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-22	6-(((6-amino-9-(3-(tert-butylamino)propyl)-9H-purin-8-yl)thio)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-23	3-(2-(6-amino-8-(6-iodo-3-oxo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)ethyl)pyrrolidine-1-carbaldehyde
1H-24	6-(6-amino-9-(2-(1-(methylsulfonyl)pyrrolidin-3-yl)ethyl)-9H-purin-8-ylthio)-5-iodo-2,3-dihydro-1H-inden-1-one
1H-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)methanesulfonamide
1H-26	6-(((6-amino-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-8-yl)thio)-5-(1H-pyrazol-3-yl)-2,3-dihydro-1H-inden-1-one
1H-27	6-(((6-amino-9-(3-(tert-butylamino)propyl)-9H-purin-8-yl)thio)-5-(5-methylfuran-2-yl)-2,3-dihydro-1H-inden-1-one
1H-28	6-(((6-amino-9-(3-(tert-butylamino)propyl)-9H-purin-8-yl)thio)-5-(5-methylthiazol-2-yl)-2,3-dihydro-1H-inden-1-one
1H-29	6-(((6-amino-9-(3-(tert-butylamino)propyl)-9H-purin-8-yl)thio)-5-(thiophen-2-yl)-2,3-dihydro-1H-inden-1-one
1H-30	2-(3-(6-amino-8-(6-iodo-3-oxo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)azetidine-1-carbaldehyde
1H-31	6-(((6-amino-9-(3-(tert-butylamino)propyl)-2-fluoro-9H-purin-8-yl)methyl)-5-ethynyl-2,3-dihydro-1H-inden-1-one
1H-32	6-(((6-amino-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-8-yl)thio)-5-(dimethylamino)-2,3-dihydro-1H-inden-1-one
1H-33	6-(((6-amino-9-(3-(tert-butylamino)propyl)-2-fluoro-9H-purin-8-yl)methyl)-5-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-1-one
1H-34	6-((9-(2-(1-acetylpiperidin-4-yl)ethyl)-6-amino-2-fluoro-9H-purin-8-yl)methyl)-5-

	(5-methylthiazol-2-yl)-2,3-dihydro-1H-inden-1-one
1H-35	N-(3-(6-amino-2-fluoro-8-((6-(5-methyloxazol-2-yl)-3-oxo-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-9-yl)propyl)methanesulfonamide
1H-36	1-(3-(6-amino-8-(6-iodo-3-oxo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
1H-37	1-(3-(6-amino-8-(6-iodo-3-oxo-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-2-one

Table 2A

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
1B-1	PU-WS9	5.5	ND
1B-2	PU-WS4	8.0-14	ND
1A-1	PU-WS10	132.9-346	ND

Table 2B

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
1B-3	PU-WS17	17.3	ND
1B-4	PU-WS18	33.3	ND
1B-24	PU-WS21	10.8	ND
1B-25	PU-WS22	8.0	ND

Table 2C

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
1B-26	PU-WS23	12.2	ND
1B-27	PU-WS24	25.4	ND

Table 2D

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
1B-28	PU-WS28	8.1	ND

Table 2E

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
1E-2	PU-WS26	3.6	ND
1E-21	PU-WS25	7.2	ND
1E-23	PU-WS29	4.5	ND

Table 2F

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
1E-22	PU-WS27	15	ND

Table 2G

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
4A-1	DZ2-388	270	645
4A-2	DZ2-390	2,666	6,240
4A-3	DZ2-391	>100,000	>100,000
4A-4	TT-V-47B	8,287	15,010
4A-5	DZ2-392	1,388	2,520
4A-6	DZ3-3	438	1,030
4A-7	DZ3-6	732	1,385
4A-8	DZ3-50	2,333	>3000
4C-1	DZ3-4	11	22
4C-2	DZ3-27	48	86
4C-3	DZ3-25	3.9	5.2
4C-4	DZ3-26	14	26
4C-5	TT5-53A	5.3	6.5
4C-6	DZ3-33	56	141
4C-7	DZ3-34	82	142
4C-8	DZ3-35	23	37
4C-9	DZ3-36	6.0	12
4C-10	DZ3-49	>300	>300
4C-11	DZ3-51	153	185
4C-14	DZ3-60	ND	10.1
4C-16	DZ3-56	ND	10.2
4C-38	DZ4-20	ND	7.9
4C-39	DZ4-23	ND	11.4
4C-40	DZ3-142	ND	509
4C-41	DZ3-143	ND	2,081
4D-1	DZ2-395	43	80
4D-2	DZ3-48	24	59
4D-3	DZ3-58	ND	18.5
4D-16	DZ4-21	ND	47
4D-17	DZ4-24	ND	19.7
4F-1	DZ3-5	4,120	9,620

Table 2H

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
4B-1	PU-WS8	19.1	ND
4B-2	PU-WS6	403	ND
4B-3	PU-WS7	731	ND
4B-4	PU-WS16	13.7	ND
4B-13	PU-WS19	8.6	ND
4B-14	PU-WS20	<200	ND

Table 2I

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
4E-1	PU-WS3	218.8	ND
4E-2	PU-WS5	285	ND
4E-3	DZ3-39	542	1126
4E-4	DZ3-40	46	93

Table 2J

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
4I-12	TT-VI-116	ND	394

Table 2K

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
4G-1	DZ3-30	374	1024
4G-2	DZ3-32	107	128
4G-3	DZ3-43	2.6	7.2
4G-4	DZ3-44	>300	>300
4G-5	DZ3-45	>300	>300
4G-6	DZ3-46	4.0	5.5
4G-9	DZ3-61	ND	5.5

Table 2L

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
4H-1	DZ3-29	309	740
4H-2	DZ3-31	89	121
4H-3	DZ3-41	57	161
4H-4	DZ3-59	ND	24.6
4H-6	DZ3-38	23	47
4H-7	DZ3-141	ND	26,653

Table 2M

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
5A-1	PU-RK11	ND	34.5
5A-2	PU-HT165	ND	34.6
5A-3	PU-HT175	ND	34.8
5A-4	PU-RK12	ND	62.8
5A-5	DZ3-73	ND	9.4
5A-6	DZ4-84	45.1	ND

Table 2N

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
5B-1	HJP18	ND	6.9
5B-7	TT-VI-53A	ND	5.3
5B-33	HJP23	46.3	ND
5B-34	HJP20	ND	3.5

Table 2O

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
5D-2	HJP19	ND	11.2
5D-4	TT-VI-54A	ND	7.7

Table 2P

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
6B-25	DZ4-52-N9	ND	97.0

Table 2Q

Compound #	Name	EC ₅₀ ; binding to JNPL3 brain Hsp90 (nM)	EC ₅₀ ; binding to SKBr3 cell Hsp90 (nM)
7A-20	PU-WS31	<200	ND
7C-13	TT-V-138	ND	84
7D-3	TT-V-139	ND	240
7E-6	TT-V-140	ND	32

Table 3A

No.	Name
3A-1	2-fluoro-8-((5-(furan-2-yl)benzofuran-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3A-2	2-fluoro-8-((5-iodo-1H-indol-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3A-3	N-(2-((2-(6-amino-8-((5-(furan-2-yl)benzo[b]thiophen-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
3A-4	3-((2-(8-((1-acetyl-5-(furan-2-yl)-1H-indol-6-yl)thio)-6-amino-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
3A-5	8-((5-(azetidin-1-yl)benzofuran-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3A-6	8-((5-iodobenzo[b]thiophen-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3A-7	8-((5-(1H-pyrazol-3-yl)-1H-indol-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
3A-8	8-((5-ethynyl-1H-indol-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3A-9	6-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)-1-methyl-1H-indole-5-carbonitrile
3A-10	9-(3-aminopropyl)-8-((5-iodobenzofuran-6-yl)thio)-9H-purin-6-amine
3A-11	9-(2-aminoethyl)-8-((5-iodobenzofuran-6-yl)thio)-9H-purin-6-amine
3A-12	9-(3-(tert-butylamino)propyl)-8-((5-iodobenzofuran-6-yl)thio)-9H-purin-6-amine
3A-13	2-fluoro-8-((5-iodobenzofuran-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3A-14	1-(4-(2-(6-amino-2-fluoro-8-((5-(5-methylfuran-2-yl)benzofuran-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
3A-15	9-(3-(tert-butylamino)propyl)-8-((5-ethynylbenzofuran-6-yl)thio)-9H-purin-6-amine
3A-16	2-fluoro-8-((5-(5-methyloxazol-2-yl)benzofuran-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3A-17	9-(3-(tert-butylamino)propyl)-8-((5-(dimethylamino)benzofuran-6-yl)thio)-9H-purin-6-amine
3A-18	8-((5-iodobenzofuran-6-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
3A-19	8-((5-(1H-pyrazol-3-yl)benzofuran-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3A-20	N-(3-(6-amino-8-((5-(aziridin-1-yl)benzofuran-6-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
3A-21	3-(6-amino-8-((5-iodobenzofuran-6-yl)thio)-9H-purin-9-yl)propyl sulfamate
3A-22	9-(3-(tert-butylamino)propyl)-8-((5-(oxazol-2-yl)benzofuran-6-yl)thio)-9H-purin-6-amine
3A-23	8-((5-ethynylbenzofuran-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3A-24	1-(6-amino-8-((5-iodobenzofuran-6-yl)thio)-9H-purin-9-yl)-3-(tert-

	butylamino)propan-2-ol
3A-25	8-((5-iodobenzofuran-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
3A-26	9-(3-(tert-butylamino)propyl)-8-((5-(5-methylthiazol-2-yl)benzofuran-6-yl)thio)-9H-purin-6-amine

Table 3B

No.	Name
3B-1	5-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)benzofuran-6-carbonitrile
3B-2	8-((6-iodobenzofuran-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-3	8-((6-(furan-2-yl)benzofuran-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-4	N-(2-((2-(6-amino-8-((6-(furan-2-yl)benzofuran-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
3B-5	3-((2-(6-amino-8-((6-(furan-2-yl)benzofuran-5-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
3B-6	2-fluoro-8-((6-(furan-2-yl)-1H-indol-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3B-7	8-((6-(azetidin-1-yl)-1H-indol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-8	9-(2-(isobutylamino)ethyl)-8-((6-(pyrrolidin-1-yl)-1H-indol-5-yl)thio)-9H-purin-6-amine
3B-9	8-((6-(furan-2-yl)-1-methyl-1H-indol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
3B-10	2-fluoro-8-((6-iodo-1-isopropyl-1H-indol-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-11	2-fluoro-8-((6-(furan-2-yl)benzo[b]thiophen-5-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
3B-12	2-fluoro-8-((6-iodobenzo[b]thiophen-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3B-13	8-((6-(1H-pyrrol-3-yl)benzo[b]thiophen-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-14	8-((6-ethynylbenzo[b]thiophen-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-15	2-chloro-8-((6-ethynylbenzo[b]thiophen-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-16	8-((6-(azetidin-1-yl)-1H-indol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-17	8-((6-(aziridin-1-yl)-1H-indol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3B-18	9-(3-aminopropyl)-8-((6-iodobenzofuran-5-yl)thio)-9H-purin-6-amine
3B-19	9-(2-aminoethyl)-8-((6-iodobenzofuran-5-yl)thio)-9H-purin-6-amine
3B-20	9-(3-(tert-butylamino)propyl)-8-((6-iodobenzofuran-5-yl)thio)-9H-purin-6-amine
3B-21	1-(4-(2-(6-amino-2-fluoro-8-((6-(5-methylfuran-2-yl)benzofuran-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
3B-22	9-(3-(tert-butylamino)propyl)-8-((6-ethynylbenzofuran-5-yl)thio)-9H-

	purin-6-amine
3B-23	2-fluoro-8-(((6-(5-methyloxazol-2-yl)benzofuran-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3B-24	9-(3-(tert-butylamino)propyl)-8-(((6-(dimethylamino)benzofuran-5-yl)thio)-9H-purin-6-amine
3B-25	8-(((6-iodobenzofuran-5-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
3B-26	8-(((6-(1H-pyrazol-3-yl)benzofuran-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3B-27	N-(3-(6-amino-8-(((6-(aziridin-1-yl)benzofuran-5-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
3B-28	3-(6-amino-8-(((6-iodobenzofuran-5-yl)thio)-9H-purin-9-yl)propyl sulfamate
3B-29	9-(3-(tert-butylamino)propyl)-8-(((6-(oxazol-2-yl)benzofuran-5-yl)thio)-9H-purin-6-amine
3B-30	8-(((6-ethynylbenzofuran-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3B-31	1-(6-amino-8-(((6-iodobenzofuran-5-yl)thio)-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol
3B-32	8-(((6-iodobenzofuran-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
3B-33	9-(3-(tert-butylamino)propyl)-8-(((6-(5-methylthiazol-2-yl)benzofuran-5-yl)thio)-9H-purin-6-amine
3B-34	1-(3-(6-amino-8-(6-iodobenzofuran-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-ol
3B-35	1-(3-(6-amino-8-(6-iodobenzofuran-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one

Table 3C

No.	Name
3C-1	6-(((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)benzo[d]oxazole-5-carbonitrile
3C-2	8-(((5-(furan-2-yl)benzo[d]thiazol-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3C-3	2-fluoro-8-(((5-(furan-2-yl)benzo[d]oxazol-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3C-4	8-(((5-(azetidin-1-yl)benzo[d]oxazol-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3C-5	9-(2-(isobutylamino)ethyl)-8-(((5-(pyrrolidin-1-yl)benzo[d]thiazol-6-yl)thio)-9H-purin-6-amine
3C-6	8-(((5-ethynylbenzo[d]thiazol-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3C-7	N-(2-(((2-(6-amino-8-(((5-iodobenzo[d]oxazol-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
3C-8	3-(((2-(6-amino-8-(((5-(furan-2-yl)benzo[d]oxazol-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide

Table 3D

No.	Name
3D-1	5-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)-1H-benzo[d]imidazole-6-carbonitrile
3D-2	8-((6-(furan-2-yl)-1H-benzo[d]imidazol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3D-3	2-fluoro-8-((6-(furan-2-yl)-1H-benzo[d]imidazol-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3D-4	8-((6-(azetidin-1-yl)-1H-benzo[d]imidazol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3D-5	9-(2-(isobutylamino)ethyl)-8-((6-(pyrrolidin-1-yl)-1H-benzo[d]imidazol-5-yl)thio)-9H-purin-6-amine
3D-6	8-((6-ethynyl-1-methyl-1H-benzo[d]imidazol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3D-7	N-(2-((2-(8-((1-acetyl-6-iodo-1H-benzo[d]imidazol-5-yl)thio)-6-amino-9H-purin-9-yl)ethyl)amino)ethyl)methanesulfonamide
3D-8	3-((2-(6-amino-8-((6-(furan-2-yl)-1H-benzo[d]imidazol-5-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
3D-9	5-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)benzo[d]oxazole-6-carbonitrile
3D-10	8-((6-iodobenzo[d]oxazol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3D-11	5-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)benzo[d]thiazole-6-carbonitrile
3D-12	8-((6-(furan-2-yl)benzo[d]thiazol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3D-13	2-fluoro-8-((6-(furan-2-yl)benzo[d]oxazol-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3D-14	8-((6-(azetidin-1-yl)benzo[d]oxazol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3D-15	9-(2-(isobutylamino)ethyl)-8-((6-(pyrrolidin-1-yl)benzo[d]thiazol-5-yl)thio)-9H-purin-6-amine
3D-16	8-((6-ethynylbenzo[d]thiazol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine

Table 3E

No.	Name
3E-1	6-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)benzo[d][1,2,3]oxadiazole-5-carbonitrile
3E-2	8-((5-(furan-2-yl)benzo[d][1,2,3]thiadiazol-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3E-3	2-fluoro-8-((5-(furan-2-yl)benzo[d][1,2,3]oxadiazol-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3E-4	8-((5-(azetidin-1-yl)benzo[d][1,2,3]oxadiazol-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3E-5	9-(2-(isobutylamino)ethyl)-8-((5-(pyrrolidin-1-yl)benzo[d][1,2,3]thiadiazol-6-yl)thio)-9H-

	purin-6-amine
3E-6	8-((5-ethynylbenzo[d][1,2,3]thiadiazol-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3E-7	N-(2-((2-(6-amino-8-((5-iodobenzo[d][1,2,3]oxadiazol-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
3E-8	3-((2-(6-amino-8-((5-(furan-2-yl)benzo[d][1,2,3]oxadiazol-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
3E-9	5-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)-3H-indazole-6-carbonitrile
3E-10	8-((6-(furan-2-yl)-3H-indazol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3E-11	2-fluoro-8-((6-(furan-2-yl)-3H-indazol-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3E-12	8-(6-(azetidin-1-yl)-3H-indazol-5-ylthio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine

Table 3F

No.	Name
3F-1	5-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)benzo[d][1,2,3]oxadiazole-6-carbonitrile
3F-2	8-((6-(1H-pyrazol-3-yl)benzo[d][1,2,3]oxadiazol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3F-3	2-fluoro-8-((6-(furan-2-yl)-1H-benzo[d][1,2,3]triazol-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3F-4	8-((6-(azetidin-1-yl)benzo[d][1,2,3]thiadiazol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3F-5	9-(2-(isobutylamino)ethyl)-8-((5-(pyrrolidin-1-yl)-3H-indazol-6-yl)thio)-9H-purin-6-amine
3F-6	8-((6-ethynyl-1-methyl-1H-benzo[d][1,2,3]triazol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3F-7	N-(2-((2-(6-amino-8-((6-iodobenzo[d][1,2,3]oxadiazol-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
3F-8	3-((2-(6-amino-8-((5-(furan-2-yl)-3H-indazol-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
3F-9	6-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)-3H-indazole-5-carbonitrile
3F-10	8-((6-iodobenzo[d][1,2,3]oxadiazol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3F-11	5-((6-amino-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)thio)benzo[d][1,2,3]thiadiazole-6-carbonitrile
3F-12	8-((6-(furan-2-yl)benzo[d][1,2,3]thiadiazol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3F-13	2-fluoro-8-((6-(furan-2-yl)benzo[d][1,2,3]oxadiazol-5-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
3F-14	8-((6-(azetidin-1-yl)benzo[d][1,2,3]oxadiazol-5-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
3F-15	9-(2-(isobutylamino)ethyl)-8-((6-(pyrrolidin-1-yl)benzo[d][1,2,3]thiadiazol-5-yl)thio)-9H-purin-6-amine
3F-16	8-((5-ethynyl-3H-indazol-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine

Table 4A

No.	Name
4A-1	DZ2-388 9-(3-(isopropylamino)propyl)-8-(6-phenylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
4A-2	DZ2-390 8-(6-(4-tert-butylphenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4A-3	DZ2-391 8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4A-4	TT-V-47B N1-(3-(6-amino-8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)hexane-1,6-diamine
4A-5	DZ2-392 8-(6-(4-(dimethylamino)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4A-6	DZ3-3 9-(3-(isopropylamino)propyl)-8-(6-(4-methoxyphenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
4A-7	DZ3-6 8-(6-(4-bromophenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4A-8	DZ3-50 4-(6-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)benzo[d][1,3]dioxol-5-yl)benzaldehyde
4A-9	4-(2-(6-amino-8-(6-phenylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
4A-10	1-(4-(2-(6-amino-2-fluoro-8-((6-phenylbenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4A-11	N-(2-((2-(6-amino-8-((6-phenylbenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
4A-12	3-(2-(6-amino-8-(6-phenylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
4A-13	9-(3-aminopropyl)-8-(6-phenylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine

Table 4B

No.	Name
4B-1	PU-WS8 8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4B-2	PU-WS6 8-(6-(3,3-dimethylbut-1-ynyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4B-3	PU-WS7 9-(3-(isopropylamino)propyl)-8-(6-(phenylethynyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine

4B-4	PU-WS16 8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
4B-5	1-(3-(2-(6-amino-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4B-6	8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
6B-7	1-(3-(4-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-9-yl)butyl)pyrrolidin-1-yl)ethanone
4B-8	5-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-9-yl)pentane-1-sulfonamide
4B-9	3-(2-(6-amino-2-chloro-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
4B-10	3-(2-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidine-1-sulfonamide
4B-11	N-(2-((2-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
4B-12	3-(2-(6-amino-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
4B-13	PU-WS19 8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
4B-14	PU-WS20 8-(((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
4B-15	9-(3-aminopropyl)-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
4B-16	9-(2-aminoethyl)-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
4B-17	9-(3-(tert-butylamino)propyl)-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
4B-18	1-(3-(6-amino-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
4B-19	3-(2-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-sulfonamide
4B-20	6-(6-amino-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)hexanamide
4B-21	1-(6-amino-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol
4B-22	6-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-9-yl)hexanamide
4B-23	1-(2-((2-(6-amino-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethylamino)methyl)pyrrolidin-1-yl)ethanone
4B-24	5-(6-amino-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
4B-25	1-(3-(2-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4B-26	8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-

	(neopentylamino)ethyl)-9H-purin-6-amine
4B-27	8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4B-28	9-(3-(tert-butylamino)propyl)-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-6-amine
4B-29	8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
4B-30	1-(3-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-9-yl)propyl)pyrrolidin-3-one
4B-31	8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine
4B-32	8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine
4B-33	1-(2-((2-(6-amino-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-9-yl)ethylamino)methyl)pyrrolidin-1-yl)ethanone
4B-34	8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine
4B-35	8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine

Table 4C

No.	Name
4C-1	DZ3-4 8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4C-2	DZ3-27 8-((6-(furan-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4C-3	DZ3-25 2-fluoro-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
4C-4	DZ3-26 2-fluoro-8-((6-(furan-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
4C-5	TT5-53A 8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
4C-6	DZ3-33 5-(6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)benzo[d][1,3]dioxol-5-yl)furan-2-carbaldehyde
4C-7	DZ3-34 5-(6-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)benzo[d][1,3]dioxol-5-yl)furan-2-carbaldehyde
4C-8	DZ3-35 9-(3-(isopropylamino)propyl)-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4C-9	DZ3-36 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-

	yl)methyl)-9H-purin-6-amine
4C-10	DZ3-49 9-(3-(isopropylamino)propyl)-8-((6-(isoxazol-4-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4C-11	DZ3-51 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(isoxazol-4-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
4C-12	8-((6-(5-(aminomethyl)furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
4C-13	8-((6-(5-(aminomethyl)furan-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
4C-14	DZ3-60 8-((6-(furan-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
4C-15	8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
4C-16	DZ3-56 8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
4C-17	1-(3-(6-amino-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one
4C-18	8-((6-(5-(aminomethyl)furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
4C-19	1-(3-(2-(6-amino-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-20	8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
4C-21	1-(3-(2-(6-amino-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-22	4-(2-(6-amino-2-fluoro-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
4C-23	1-(3-(6-amino-8-(6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
4C-24	6-(6-amino-8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)hexanamide
4C-25	6-(6-amino-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)hexanamide
4C-26	1-(4-(2-(6-amino-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-27	1-(4-(2-(6-amino-2-chloro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-28	1-(3-(2-(6-amino-8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-29	1-(3-(2-(6-amino-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-30	3-(2-(6-amino-2-chloro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-sulfonamide
4C-31	1-(4-(2-(6-amino-8-((6-(5-(aminomethyl)furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-32	1-(3-(2-(6-amino-8-((6-(5-(aminomethyl)oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-

	2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4C-33	5-(6-amino-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)pentane-1-sulfonamide
	2-fluoro-9-(3-(isopropylamino)propyl)-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
	N-(2-((2-(6-amino-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl) sulfamide
	3-(2-(6-amino-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
	DZ4-20 9-(3-(isopropylamino)propyl)-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
	DZ4-23 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
	DZ3-142 8-((6-(2,3-dihydrofuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
	DZ3-143 8-((6-(2,3-dihydrofuran-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
	9-(3-aminopropyl)-8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
	9-(2-aminoethyl)-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine

	9-(3-(tert-butylamino)propyl)-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
	9-(3-(tert-butylamino)propyl)-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
	1-(4-(2-(6-amino-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
	8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
	9-(3-(tert-butylamino)propyl)-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
	1-(6-amino-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol
	1-(6-amino-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
	2-(3-(6-amino-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)aziridine-1-carbaldehyde
	5-(6-amino-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
	5-(6-amino-8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide

	8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(1-(methylsulfonyl)pyrrolidin-3-yl)propyl)-9H-purin-6-amine
	1-(3-(6-amino-8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
	5-(6-amino-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)pentane-1-sulfonamide
	6-(6-amino-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)hexanamide
	2-fluoro-9-(3-(isopropylamino)propyl)-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
	9-(3-aminopropyl)-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
	9-(3-aminopropyl)-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine

Table 4D

No.	Name
4D-1	DZ2-395 9-(3-(isopropylamino)propyl)-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-2	DZ3-48 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
4D-3	DZ3-58 9-(2-(neopentylamino)ethyl)-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-4	9-(3-(isopropylamino)propyl)-8-((6-(thiophen-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-5	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(thiophen-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
4D-6	9-(2-(neopentylamino)ethyl)-8-((6-(thiophen-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-7	1-(4-(2-(6-amino-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4D-8	4-(2-(6-amino-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
4D-9	1-(4-(2-(6-amino-2-fluoro-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4D-10	4-(2-(6-amino-2-fluoro-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
4D-11	4-(2-(6-amino-8-((6-(thiophen-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
4D-12	4-(2-(6-amino-2-fluoro-8-((6-(thiophen-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6D-13	4-(2-(6-amino-2-chloro-8-((6-(thiophen-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
4D-14	N-(2-((2-(6-amino-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
4D-15	3-((2-(6-amino-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
4D-16	DZ4-21 9-(3-(isopropylamino)propyl)-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-17	DZ4-24 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
4D-18	9-(3-aminopropyl)-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-19	9-(3-(tert-butylamino)propyl)-8-((6-(thiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-20	9-(3-(tert-butylamino)propyl)-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-21	9-(3-(tert-butylamino)propyl)-8-((6-(5-methylthiophen-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine
4D-22	9-(3-(tert-butylamino)propyl)-8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-

	yl)thio)-9H-purin-6-amine
4D-23	1-(3-(2-(6-amino-8-(6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
4D-24	1-(6-amino-8-((6-(5-methylthiophen-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
4D-25	1-(6-amino-8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
4D-26	6-(6-amino-8-(6-(5-methylthiophen-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)hexanamide
4D-27	5-(6-amino-8-(6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
4D-28	9-(3-(1-(methylsulfonyl)pyrrolidin-3-yl)propyl)-8-(6-(5-methylthiophen-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
4D-29	2-(2-(6-amino-8-(6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)pyrrolidine-1-carbaldehyde
4D-30	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(5-methylthiophen-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
4D-31	8-((6-(5-methylthiophen-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
4D-32	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine
4D-33	8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine

Table 4E

No.	Name
4E-1	PU-WS3 6-((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)benzo[d][1,3]dioxole-5-carbonitrile
4E-2	PU-WS5 6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)benzo[d][1,3]dioxole-5-carbonitrile
4E-3	DZ3-39 2-(6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)benzo[d][1,3]dioxol-5-yl)acetonitrile
4E-4	DZ3-40 2-(6-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)benzo[d][1,3]dioxol-5-yl)acetonitrile
6E-5	N-(2-((2-(6-amino-8-((6-(cyanomethyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
4E-6	3-((2-(6-amino-8-((6-(cyanobenzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
4E-7	6-((6-amino-2-chloro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)benzo[d][1,3]dioxole-5-carbonitrile

Table 4F

No.	Name
4F-1	DZ3-5

	9-(3-(isopropylamino)propyl)-8-(6-(pyridin-4-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine
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Table 5A

No.	Name
5A-1	PU-RK11 8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
5A-2	PU-HT165 8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
	PU-HT175 8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
	PU-RK12 9-(3-(1H-imidazol-1-yl)propyl)-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
	PU-DZ3-73 2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
	PU-DZ4-84 9-(2-(tert-butylamino)ethyl)-2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
	9-(3-aminopropyl)-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
	9-(2-aminoethyl)-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
	9-(3-(tert-butylamino)propyl)-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
	1-(6-amino-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
	5-(6-amino-8-(7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide

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	1-(3-(6-amino-8-(7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
	6-(6-amino-8-(7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)hexanamide
	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
	1-(3-(4-(6-amino-8-(7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)butyl)pyrrolidin-1-yl)ethanone
	2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
	1-(3-(6-amino-2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one
	6-(6-amino-2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)hexanamide
	5-(6-amino-2-fluoro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)pentane-1-sulfonamide

Table 5B

No.	Name
5B-1	HJP18 8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
5B-2	1-(3-(6-amino-8-(7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
5B-3	9-(3-(isopropylamino)propyl)-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-

	yl)thio)-9H-purin-6-amine
5B-4	6-(6-amino-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)hexanamide
5B-5	6-(6-amino-8-(7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)hexanamide
5B-6	2-fluoro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5B-7	TT-VI-53A 2-fluoro-8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5B-8	1-(3-(2-(6-amino-2-fluoro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-9	8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5B-10	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5B-11	1-(3-(6-amino-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one
5B-12	8-((7-(5-(aminomethyl)furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5B-13	8-(7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5B-14	1-(3-(2-(6-amino-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-15	8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5B-16	8-((7-(isoxazol-4-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5B-17	1-(3-(2-(6-amino-8-(7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-18	8-((7-(5-(aminomethyl)furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5B-19	5-(6-amino-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
5B-20	5-(6-amino-8-(7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
5B-21	1-(4-(2-(6-amino-2-chloro-8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-22	1-(4-(2-(6-amino-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-23	1-(4-(2-(6-amino-2-fluoro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-24	1-(3-(6-amino-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
5B-25	9-(3-(tert-butylamino)propyl)-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine
5B-26	2-chloro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-(1-(methylsulfonyl)pyrrolidin-3-yl)ethyl)-9H-purin-6-amine
5B-27	1-(3-(2-(6-amino-8-(7-(5-(aminomethyl)furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone

5B-28	1-(3-(2-(6-amino-8-((7-(5-(aminomethyl)furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-29	5-(6-amino-2-fluoro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)pentane-1-sulfonamide
5B-30	4-(2-(6-amino-2-chloro-8-((7-(isoxazol-4-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5B-31	N-(2-((2-(6-amino-8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
5B-32	3-((2-(6-amino-8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
5B-33	HJP23 8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5B-34	HJP20 9-(3-(isopropylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5B-35	9-(3-aminopropyl)-2-fluoro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5B-36	9-(3-aminopropyl)-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine
5B-37	9-(3-(tert-butylamino)propyl)-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine
5B-38	9-(3-aminopropyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5B-39	9-(3-(tert-butylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5B-40	9-(3-(tert-butylamino)propyl)-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5B-41	1-(4-(2-(6-amino-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5B-42	8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5B-43	1-(6-amino-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
5B-44	1-(6-amino-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
5B-45	6-(6-amino-2-fluoro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)hexanamide
5B-46	N-(3-(6-amino-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
5B-47	1-(2-(4-(6-amino-8-(7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)butyl)pyrrolidin-1-yl)ethanone
5B-48	9-(3-aminopropyl)-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5B-49	2-fluoro-9-(3-(isopropylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5B-50	2-fluoro-9-(3-(isopropylamino)propyl)-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5B-51	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine

5B-52	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5B-53	6-(6-amino-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)hexanamide
5B-54	5-(6-amino-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)pentane-1-sulfonamide
5B-55	1-(3-(6-amino-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one
5B-56	1-(3-(6-amino-2-fluoro-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)propyl)pyrrolidin-3-one

Table 5C

No.	Name
5C-1	9-(3-(isopropylamino)propyl)-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-2	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5C-3	9-(2-(neopentylamino)ethyl)-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-4	9-(3-(isopropylamino)propyl)-8-((7-(thiophen-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-5	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(thiophen-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5C-6	9-(2-(neopentylamino)ethyl)-8-((7-(thiophen-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-7	1-(4-(2-(6-amino-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5C-8	4-(2-(6-amino-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5C-9	1-(4-(2-(6-amino-2-fluoro-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5C-11	4-(2-(6-amino-8-((7-(thiophen-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5C-13	4-(2-(6-amino-2-chloro-8-((7-(thiophen-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5C-14	N-(2-((2-(6-amino-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
5C-15	3-(2-(6-amino-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
5C-16	9-(3-aminopropyl)-8-((7-(thiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-17	9-(3-(isopropylamino)propyl)-8-((7-(5-methylthiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-18	1-(6-amino-8-((7-(5-methylthiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
5C-19	1-(2-(3-(6-amino-8-((7-(5-methylthiazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl)pyrrolidin-1-yl)ethanone

5C-20	9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-8-((7-(5-methylthiazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-21	1-(6-amino-8-((7-(5-methylthiazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
5C-22	9-(3-(tert-butylamino)propyl)-8-((7-(thiazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5C-23	9-(3-(tert-butylamino)propyl)-8-((7-(5-methylthiophen-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine

Table 5D

No.	Name
5D-1	8-((7-(1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
5D-2	HJP19 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
5D-3	8-((7-(1H-pyrazol-4-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5D-4	TT-VI-54A 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5D-5	1-(3-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-6-amino-9H-purin-9-yl)propyl)pyrrolidin-3-one
5D-6	8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5D-7	1-(4-(2-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-6-amino-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5D-8	8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-aminoethyl)-2-fluoro-9H-purin-6-amine
5D-9	1-(4-(2-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-amino-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5D-10	1-(3-(2-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-amino-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5D-11	8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5D-12	1-(3-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-amino-2-fluoro-9H-purin-9-yl)propyl)pyrrolidin-3-one
5D-13	8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5D-14	N-(2-((2-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-6-amino-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
5D-15	3-((2-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-6-amino-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
5D-16	8-((7-(1H-imidazol-4-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
5D-17	8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-aminopropyl)-9H-purin-6-amine
5D-18	8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(tert-butylamino)propyl)-9H-purin-6-amine

5D-19	8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(3-(tert-butylamino)propyl)-2-fluoro-9H-purin-6-amine
5D-20	9-(3-(isopropylamino)propyl)-8-((7-(5-methyl-1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5D-21	8-((7-(5-methyl-1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5D-22	9-(3-(tert-butylamino)propyl)-2-fluoro-8-((7-(5-methyl-1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5D-23	1-(8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-6-amino-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
5D-24	1-(8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-amino-2-fluoro-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol
5D-25	5-(8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-amino-2-fluoro-9H-purin-9-yl)pentane-1-sulfonamide
5D-26	6-(8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-amino-2-fluoro-9H-purin-9-yl)hexanamide
5D-27	5-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-6-amino-9H-purin-9-yl)pentane-1-sulfonamide
5D-28	6-(8-(7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-6-amino-9H-purin-9-yl)hexanamide

Table 5E

No.	Name
5E-1	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
5E-2	3-(3-(6-amino-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidine-1-carbaldehyde
5E-3	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5E-4	9-(2-aminoethyl)-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine
5E-5	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5E-6	9-(2-aminoethyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5E-7	1-(3-(2-(6-amino-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5E-8	8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5E-9	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5E-10	1-(3-(2-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5E-11	3-(2-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5E-12	1-(3-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)propyl)pyrrolidine-3-one
5E-13	6-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)hexanamide

5E-14	N-(2-((2-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
5E-15	3-((2-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
5E-16	9-(3-aminopropyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5E-17	6-(6-amino-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)hexanamide
5E-18	5-(6-amino-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
5E-19	1-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol
5E-20	1-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
5E-21	5-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)pentane-1-sulfonamide
5E-22	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
5E-23	9-(3-(tert-butylamino)propyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-6-amine
5E-24	9-(3-aminopropyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-6-amine
5E-25	9-(3-(tert-butylamino)propyl)-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine
5E-26	8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine
5E-27	8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine
5E-28	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(1-methylpiperidin-2-yl)ethyl)-9H-purin-6-amine
5E-29	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(1-methylpiperidin-3-yl)ethyl)-9H-purin-6-amine

Table SF

No.	Name
5F-1	7-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile
5F-2	7-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile
5F-3	7-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile
5F-4	7-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile
5F-5	7-((6-amino-9-(2-(neopentylamino)ethyl)-9H-purin-8-yl)thio)-2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile
5F-6	7-((6-amino-9-(2-(neopentylamino)ethyl)-9H-purin-8-yl)thio)-2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile
5F-7	2-(7-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)acetonitrile

5F-8	N-(2-((2-(6-amino-8-((7-(cyanomethyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)sulfamide
5F-9	3-((2-(6-amino-8-((7-(cyanomethyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
5F-10	7-((6-amino-2-chloro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)-2,3-dihydrobenzo[b][1,4]dioxine-6-carbonitrile

Table 5G

No.	Name
5G-1	8-((7-(aziridin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5G-2	8-((7-(azetidin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5G-3	9-(2-(isobutylamino)ethyl)-8-((7-(pyrrolidin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5G-4	8-((7-(aziridin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5G-5	8-((7-(azetidin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5G-6	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(pyrrolidin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5G-7	2-chloro-9-(2-(isobutylamino)ethyl)-8-((7-(pyrrolidin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5G-8	1-(4-(2-(6-amino-8-((7-(aziridin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5G-9	1-(3-(2-(6-amino-8-(7-(azetidin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5G-10	4-(2-(6-amino-2-chloro-8-((7-(pyrrolidin-1-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5G-11	8-((7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5G-12	8-((7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5G-13	1-(3-(2-(6-amino-8-(7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5G-14	1-(3-(2-(6-amino-8-(7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5G-15	8-(7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5G-16	8-((7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5G-17	8-((7-(ethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5G-18	1-(3-(2-(6-amino-8-(7-(ethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5G-19	8-(7-(ethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5G-20	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(isopropylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine
5G-21	8-(7-(isopropylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5G-22	1-(3-(2-(6-amino-2-fluoro-8-((7-(isopropylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5G-23	8-((7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine

5G-24	8-((7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5G-25	5-(6-amino-8-(7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
5G-26	6-(6-amino-8-(7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)hexanamide
5G-27	9-(3-(tert-butylamino)propyl)-8-((7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5G-28	1-(3-(6-amino-8-(7-(dimethylamino)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one

Table 5H

No.	Name
5H-1	8-((7-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5H-2	8-((7-cyclobutyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5H-3	8-((7-cyclopentyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5H-4	8-((7-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
5H-5	8-((7-cyclobutyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5H-6	8-((7-cyclopentyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
5H-7	1-(4-(2-(6-amino-8-((7-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5H-8	1-(4-(2-(6-amino-8-((7-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5H-9	1-(4-(2-(6-amino-2-chloro-8-((7-cyclobutyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
5H-10	4-(2-(6-amino-8-((7-cyclobutyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5H-11	4-(2-(6-amino-8-((7-cyclopentyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
5H-12	3-(6-amino-8-((7-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)propyl sulfamate
5H-13	8-((7-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5H-14	9-(3-(tert-butylamino)propyl)-8-((7-cyclopropyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine
5H-15	2-(3-(6-amino-8-(7-cyclobutyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidine-1-sulfonamide
5H-16	3-(2-(6-amino-8-(7-cyclopentyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)ethyl)pyrrolidine-1-sulfonamide
5H-17	8-(7-cyclopentyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
5H-18	9-(3-(tert-butylamino)propyl)-8-(7-cyclopentyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-

	purin-6-amine
5H-19	1-(6-amino-8-(7-cyclopentyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol

Table 6A

No.	Name
6A-1	8-((7-iodo-2,3-dihydrobenzo[b][1,4]oxathiin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-2	8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-3	8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]oxathiin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-4	4-(2-(6-amino-8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-5	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(pyrrolidin-1-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-6-yl)methyl)-9H-purin-6-amine
6A-6	8-((7-(aziridin-1-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6A-7	8-((6-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-7-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-8	8-((6-ethynyl-2,3-dihydrobenzo[b][1,4]oxathiin-7-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-9	4-(2-(6-amino-8-((6-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-7-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-10	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(pyrrolidin-1-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-7-yl)methyl)-9H-purin-6-amine
6A-11	8-((6-(aziridin-1-yl)-2,3-dihydrobenzo[b][1,4]oxathiin-7-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6A-12	8-((7-(furan-2-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6A-13	8-((4-methyl-7-(1H-pyrazol-3-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6A-14	8-((7-ethynyl-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6A-15	2-fluoro-8-((7-(furan-2-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)methyl)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6A-16	4-(2-(6-amino-8-((7-(furan-2-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]thiazin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-17	8-((6-(furan-2-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-18	9-(3-(isopropylamino)propyl)-8-((4-methyl-6-(thiophen-2-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-6-amine
6A-19	4-(2-(6-amino-8-((6-(furan-2-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-20	4-(2-(6-amino-8-((6-ethynyl-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-21	8-((6-(azetidin-1-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine

6A-22	8-((6-(furan-2-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]thiazin-7-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-23	8-((6-iodochroman-7-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-24	8-((6-(furan-2-yl)chroman-7-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-25	8-((6-ethynylthiochroman-7-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-26	4-(2-(6-amino-8-((6-(furan-2-yl)thiochroman-7-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-27	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((1-methyl-6-(pyrrolidin-1-yl)-1,2,3,4-tetrahydroquinolin-7-yl)methyl)-9H-purin-6-amine
6A-28	4-(2-(6-amino-8-((6-(furan-2-yl)-1,2,3,4-tetrahydroquinolin-7-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-29	8-((7-iodochroman-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-30	8-((7-(furan-2-yl)chroman-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-31	8-((7-ethynylthiochroman-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6A-32	4-(2-(6-amino-8-((7-(furan-2-yl)thiochroman-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-33	2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(pyrrolidin-1-yl)-1,2,3,4-tetrahydroquinolin-6-yl)methyl)-9H-purin-6-amine
6A-34	4-(2-(6-amino-8-((7-(furan-2-yl)-1-methyl-1,2,3,4-tetrahydroquinolin-6-yl)thio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
6A-35	2-chloro-8-((7-iodo-2,3-dihydrobenzo[b][1,4]oxathiin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6A-36	2-chloro-8-((6-iodo-2,3-dihydrobenzo[b][1,4]oxathiin-7-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6A-37	2-chloro-8-((6-iodochroman-7-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6A-38	9-(3-(tert-butylamino)propyl)-8-((6-iodochroman-7-yl)thio)-9H-purin-6-amine
6A-39	N-(3-(6-amino-8-((6-iodochroman-7-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
6A-40	3-(6-amino-8-((6-iodochroman-7-yl)thio)-9H-purin-9-yl)propyl sulfamate
6A-41	1-(6-amino-8-((6-iodochroman-7-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
6A-42	9-(3-(tert-butylamino)propyl)-8-((6-ethynylchroman-7-yl)thio)-9H-purin-6-amine
6A-43	N-(3-(6-amino-8-((6-ethynylchroman-7-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
6A-44	3-(6-amino-8-((6-(furan-2-yl)chroman-7-yl)thio)-9H-purin-9-yl)propyl sulfamate
6A-45	1-(6-amino-8-((6-(5-methyloxazol-2-yl)chroman-7-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
6A-46	9-(3-(tert-butylamino)propyl)-8-((6-iodo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-6-amine
6A-47	N-(3-(6-amino-8-((6-iodo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
6A-48	3-(6-amino-8-((6-iodo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-9-yl)propyl sulfamate
6A-49	1-(6-amino-8-((6-iodo-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
6A-50	9-(3-(tert-butylamino)propyl)-8-((6-ethynyl-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-6-amine
6A-51	N-(3-(6-amino-8-((6-ethynyl-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-9-yl)propyl)methanesulfonamide
6A-52	3-(6-amino-8-((6-(furan-2-yl)-4-methyl-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-

	9H-purin-9-yl)propyl sulfamate
6A-53	1-(6-amino-8-((4-methyl-6-(5-methyloxazol-2-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
6A-54	9-(3-(tert-butylamino)propyl)-8-((4-methyl-6-(5-methyloxazol-2-yl)-3,4-dihydro-2H-benzo[b][1,4]oxazin-7-yl)thio)-9H-purin-6-amine

Table 6B

No.	Name
6B-1	8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-2	8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6B-3	8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6B-4	2-fluoro-8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6B-5	2-chloro-8-((3-(furan-2-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-6	2-fluoro-8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-7	8-((3-(furan-2-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-8	8-((3-ethynyl-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-9	3-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)-5,6,7,8-tetrahydronaphthalene-2-carbonitrile
6B-10	8-((3-(azetidin-1-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6B-11	8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6B-12	6-(6-amino-8-(3-(oxazol-2-yl)-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-purin-9-yl)hexanamide
6B-13	1-(3-(2-(8-(3-(1H-pyrazol-3-yl)-5,6,7,8-tetrahydronaphthalen-2-ylthio)-6-amino-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
6B-14	1-(3-(2-(6-amino-8-(3-ethynyl-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
6B-15	1-(3-(2-(6-amino-2-fluoro-8-((3-(5-methylfuran-2-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
6B-16	N-(2-((2-(6-amino-8-((3-(furan-2-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9H-purin-9-yl)ethyl)amino)ethyl)methanesulfonamide
6B-17	3-((2-(6-amino-8-((3-(furan-2-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9H-purin-9-yl)ethyl)amino)-N-hydroxypropanamide
6B-18	9-(3-aminopropyl)-8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9H-purin-6-amine
6B-19	9-(3-(isopropylamino)propyl)-8-((3-(oxazol-2-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9H-purin-6-amine
6B-20	9-(3-(tert-butylamino)propyl)-8-((3-iodo-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9H-purin-6-amine
6B-21	1-(3-(2-(6-amino-8-(3-(5-methylfuran-2-yl)-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-

	purin-9-yl)ethyl)piperidin-1-yl)ethanone
6B-22	1-(3-(2-(6-amino-8-(3-(oxazol-2-yl)-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
6B-23	8-((3-(dimethylamino)-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6B-24	9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-8-((3-(5-methylthiazol-2-yl)-5,6,7,8-tetrahydronaphthalen-2-yl)thio)-9H-purin-6-amine
6B-25	DZ4-52-N9 8-((3-iodonaphthalen-2-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-26	8-((3-(dimethylamino)naphthalen-2-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
6B-27	1-(3-(2-(6-amino-8-(3-(5-methylfuran-2-yl)naphthalen-2-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
6B-28	9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-8-((3-(5-methylthiazol-2-yl)naphthalen-2-yl)thio)-9H-purin-6-amine
6B-29	8-((3-ethynynaphthalen-2-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-30	8-((3-(1H-pyrazol-3-yl)naphthalen-2-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
6B-31	1-(6-amino-8-((3-iodonaphthalen-2-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
6B-32	5-(6-amino-8-(3-ethynynaphthalen-2-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
6B-33	9-(3-(tert-butylamino)propyl)-8-((3-iodonaphthalen-2-yl)thio)-9H-purin-6-amine
6B-34	8-((3-(5-methyloxazol-2-yl)naphthalen-2-yl)thio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
6B-35	2-fluoro-8-((3-iodonaphthalen-2-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
6B-36	1-(3-(2-(6-amino-8-(3-(aziridin-1-yl)naphthalen-2-ylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
6B-37	6-(6-amino-8-(3-(5-methyloxazol-2-yl)-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-purin-9-yl)hexanamide
6B-38	6-(6-amino-8-(3-iodo-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-purin-9-yl)hexanamide
6B-39	5-(6-amino-8-(3-iodo-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-purin-9-yl)pentane-1-sulfonamide
6B-40	1-(3-(6-amino-8-(3-iodo-5,6,7,8-tetrahydronaphthalen-2-ylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one

Table 7A

No.	Name
7A-1	8-(2-ethynyl-5-methoxyphenylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7A-2	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(prop-1-ynyl)phenylthio)-9H-purin-6-amine
7A-3	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(phenylethynyl)phenylthio)-9H-purin-6-amine
7A-4	8-(2-ethynyl-5-methoxyphenylthio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
7A-5	1-(4-(2-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7A-6	4-(2-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde

7A-7	1-(4-(2-(6-amino-8-(2-ethynyl-5-methoxybenzyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7A-8	4-(2-(6-amino-8-(2-ethynyl-5-methoxybenzyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7A-9	1-(4-(2-(6-amino-2-chloro-8-(2-ethynyl-5-methoxybenzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7A-10	4-(2-(6-amino-2-chloro-8-(2-ethynyl-5-methoxybenzyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7A-11	N-(2-(2-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)ethylamino)ethyl)sulfamide
7A-12	3-(2-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
7A-13	8-(5-ethoxy-2-ethynylphenylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7A-14	1-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
7A-15	8-(2-ethynyl-5-methoxyphenylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
7A-16	N-(3-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)propyl)methanesulfonamide
7A-17	2-(3-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)propyl)pyrrolidine-1-carbaldehyde
7A-18	8-(2-ethynyl-5-methoxybenzyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7A-19	1-(3-(6-amino-8-(2-ethynyl-5-methoxyphenylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
7A-20	PU-WS31 8-((2-ethynyl-5-methoxyphenyl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine

Table 7B

No.	Name
7B-1	2-((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-4-methoxybenzonitrile
7B-2	2-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)-4-methoxybenzonitrile
7B-3	2-(2-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)-4-methoxyphenyl)acetonitrile
7B-4	2-(2-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)-4-methoxyphenyl)acetonitrile
7B-5	2-(9-(2-(1-acetylpiperidin-4-yl)ethyl)-6-amino-9H-purin-8-ylthio)-4-methoxybenzonitrile
7B-6	2-((6-amino-2-fluoro-9-(2-(1-formylpiperidin-4-yl)ethyl)-9H-purin-8-yl)methyl)-4-methoxybenzonitrile
7B-7	2-((9-(2-(1-acetylpiperidin-4-yl)ethyl)-6-amino-2-chloro-9H-purin-8-yl)methyl)-4-methoxybenzonitrile
7B-8	2-(2-(6-amino-9-(2-(1-formylpiperidin-4-yl)ethyl)-9H-purin-8-ylthio)-4-methoxyphenyl)acetonitrile
7B-9	2-(2-((9-(2-(1-acetylpiperidin-4-yl)ethyl)-6-amino-2-fluoro-9H-purin-8-yl)methyl)-4-methoxyphenyl)acetonitrile
7B-10	2-((6-amino-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)methyl)-4-methoxybenzonitrile

7B-11	N-(2-(2-(6-amino-8-(2-cyano-5-methoxyphenylthio)-9H-purin-9-yl)ethylamino)ethyl)methanesulfonamide
7B-12	3-(2-(6-amino-8-(2-cyano-5-methoxyphenylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide

Table 7C

No.	Name
7C-1	8-(2-(furan-2-yl)-5-methoxyphenylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7C-2	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(5-methylfuran-2-yl)phenylthio)-9H-purin-6-amine
7C-3	9-(3-(isopropylamino)propyl)-8-(2-(isoxazol-4-yl)-5-methoxyphenylthio)-9H-purin-6-amine
7C-4	8-(2-(5-(aminomethyl)furan-2-yl)-5-methoxyphenylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7C-5	2-fluoro-8-(2-(furan-2-yl)-5-methoxybenzyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
7C-6	2-fluoro-8-(2-(furan-3-yl)-5-methoxybenzyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
7C-7	2-fluoro-9-(2-(isobutylamino)ethyl)-8-(5-methoxy-2-(5-methylfuran-2-yl)benzyl)-9H-purin-6-amine
7C-8	2-fluoro-9-(2-(isobutylamino)ethyl)-8-(2-(isoxazol-4-yl)-5-methoxybenzyl)-9H-purin-6-amine
7C-9	8-(2-(5-(aminomethyl)furan-2-yl)-5-methoxybenzyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
7C-10	1-(3-(6-amino-8-(5-methoxy-2-(5-methylfuran-2-yl)phenylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
7C-11	8-(5-methoxy-2-(5-methylfuran-2-yl)phenylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
7C-12	5-(6-amino-8-(5-methoxy-2-(oxazol-2-yl)phenylthio)-9H-purin-9-yl)pentane-1-sulfonamide
7C-13	TT-V-138 8-(2-(furan-2-yl)-5-methoxyphenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7C-14	8-(2-(furan-3-yl)-5-methoxyphenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7C-15	8-(5-methoxy-2-(5-methylfuran-2-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7C-16	8-(2-(isoxazol-4-yl)-5-methoxyphenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7C-17	6-(6-amino-8-(5-methoxy-2-(5-methylfuran-2-yl)phenylthio)-9H-purin-9-yl)hexanamide
7C-18	8-(2-(5-(aminomethyl)furan-2-yl)-5-methoxyphenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7C-19	1-(3-(2-(6-amino-8-(5-methoxy-2-(oxazol-2-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7C-20	1-(3-(2-(6-amino-2-fluoro-8-(5-methoxy-2-(oxazol-2-yl)benzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7C-21	3-(2-(6-amino-2-chloro-8-(5-methoxy-2-(5-methylfuran-2-yl)benzyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7C-22	1-(3-(2-(6-amino-8-(5-methoxy-2-(5-methylfuran-2-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone

7C-23	1-(4-(2-(6-amino-2-fluoro-8-(5-methoxy-2-(5-methylfuran-2-yl)benzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7C-24	1-(3-(6-amino-8-(5-methoxy-2-(thiazol-2-yl)phenylthio)-9H-purin-9-yl)propyl)pyrrolidin-3-one
7C-25	9-(3-aminopropyl)-8-(5-methoxy-2-(5-methylfuran-2-yl)phenylthio)-9H-purin-6-amine
7C-26	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(oxazol-2-yl)phenylthio)-9H-purin-6-amine
7C-27	1-(4-(2-(6-amino-8-(2-(5-(aminomethyl)furan-2-yl)-5-methoxyphenylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7C-28	1-(4-(2-(6-amino-8-(2-(5-(aminomethyl)furan-2-yl)-5-methoxybenzyl)-2-fluoro-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7C-29	4-(2-(6-amino-8-(2-(isoxazol-4-yl)-5-methoxyphenylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7C-30	4-(2-(6-amino-2-chloro-8-(2-(isoxazol-4-yl)-5-methoxybenzyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7C-31	N-(2-(2-(6-amino-8-(2-(furan-2-yl)-5-methoxyphenylthio)-9H-purin-9-yl)ethylamino)ethyl)sulfamide
7C-32	3-(2-(6-amino-8-(2-(furan-2-yl)-5-methoxyphenylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
7C-33	8-(5-ethoxy-2-(furan-2-yl)phenylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7C-34	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(oxazol-2-yl)phenylthio)-9H-purin-6-amine
7C-35	9-(3-(tert-butylamino)propyl)-8-(2-(furan-2-yl)-5-methoxyphenylthio)-9H-purin-6-amine

Table 7D

No.	Name
7D-1	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9H-purin-6-amine
7D-2	2-fluoro-9-(2-(isobutylamino)ethyl)-8-(5-methoxy-2-(thiophen-2-yl)benzyl)-9H-purin-6-amine
7D-3	TT-V-139 8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7D-4	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(thiophen-3-yl)phenylthio)-9H-purin-6-amine
7D-5	N-(3-(6-amino-8-(5-methoxy-2-(thiazol-2-yl)phenylthio)-9H-purin-9-yl)propyl)methanesulfonamide
7D-6	8-(5-methoxy-2-(thiophen-3-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7D-7	1-(4-(2-(6-amino-8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7D-8	4-(2-(6-amino-8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7D-9	1-(4-(2-(6-amino-2-fluoro-8-(5-methoxy-2-(thiophen-2-yl)benzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7D-10	1-(6-amino-8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
7D-11	8-(5-methoxy-2-(5-methylthiophen-2-yl)phenylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
7D-12	N-(2-(2-(6-amino-8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9H-purin-9-yl)ethylamino)ethyl)sulfamide
7D-13	3-(2-(6-amino-8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
7D-14	8-(5-ethoxy-2-(thiophen-2-yl)benzyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
7D-15	9-(3-aminopropyl)-8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9H-purin-6-amine
7D-16	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(thiazol-2-yl)phenylthio)-9H-purin-6-amine

Table 7E

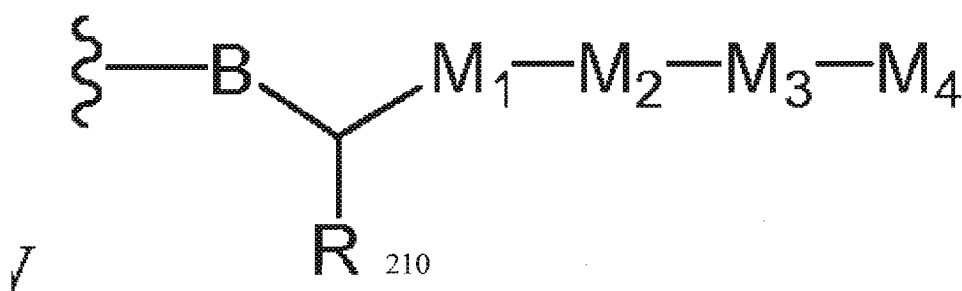
No.	Name
7E-1	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(1H-pyrazol-4-yl)phenylthio)-9H-purin-6-amine
7E-2	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-6-amine
7E-3	2-fluoro-9-(2-(isobutylamino)ethyl)-8-(5-methoxy-2-(1H-pyrazol-4-yl)benzyl)-9H-purin-6-amine
7E-4	2-fluoro-9-(2-(isobutylamino)ethyl)-8-(5-methoxy-2-(1H-pyrazol-3-yl)benzyl)-9H-purin-6-amine
7E-5	1-(3-(2-(6-amino-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-9-yl)ethyl)pyrrolidin-1-yl)ethanone
7E-6	TT-V-140 8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7E-7	1-(4-(2-(6-amino-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7E-8	4-(2-(6-amino-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7E-9	1-(4-(2-(6-amino-2-fluoro-8-(5-methoxy-2-(1H-pyrazol-3-yl)benzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7E-10	4-(2-(6-amino-2-fluoro-8-(5-methoxy-2-(1H-pyrazol-3-yl)benzyl)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7E-11	1-(4-(2-(6-amino-2-chloro-8-(5-methoxy-2-(1H-pyrazol-3-yl)benzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7E-12	4-(2-(6-amino-8-(5-methoxy-2-(1H-pyrazol-4-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7E-13	1-(6-amino-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol
7E-14	N-(2-(2-(6-amino-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-9-yl)ethylamino)ethyl)sulfamide
7E-15	3-(2-(6-amino-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
7E-16	8-(5-ethoxy-2-(1H-pyrazol-3-yl)phenylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7E-17	8-(5-ethoxy-2-(1H-pyrazol-3-yl)benzyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
7E-18	9-(3-(tert-butylamino)propyl)-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-6-amine
7E-19	9-(3-aminopropyl)-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-6-amine
7E-20	8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
7E-21	N-(3-(6-amino-8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9H-purin-9-yl)propyl)methanesulfonamide
7E-22	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(5-methyl-1H-pyrazol-3-yl)phenylthio)-9H-purin-6-amine

Table 7F

No.	Name
7F-1	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-6-amine
7F-2	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(1H-pyrrol-2-yl)phenylthio)-9H-purin-6-amine
7F-3	2-fluoro-9-(2-(isobutylamino)ethyl)-8-(5-methoxy-2-(1H-pyrrol-3-yl)benzyl)-9H-purin-6-amine
7F-4	8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9-(2-(1-(methylsulfonyl)pyrrolidin-2-yl)ethyl)-9H-purin-6-amine
7F-5	8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine
7F-6	9-(3-(isopropylamino)propyl)-8-(5-methoxy-2-(5-methyl-1H-pyrrol-3-yl)phenylthio)-9H-purin-6-amine
7F-7	4-(3-(6-amino-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-9-yl)propyl)piperidine-1-carbaldehyde
7F-8	4-(2-(6-amino-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-9-yl)ethyl)piperidine-1-carbaldehyde
7F-9	1-(4-(2-(6-amino-2-fluoro-8-(5-methoxy-2-(1H-pyrrol-3-yl)benzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7F-10	1-(4-(3-(6-amino-2-fluoro-8-(5-methoxy-2-(1H-pyrrol-3-yl)benzyl)-9H-purin-9-yl)propyl)piperidin-1-yl)ethanone
7F-11	1-(4-(2-(6-amino-2-chloro-8-(5-methoxy-2-(1H-pyrrol-3-yl)benzyl)-9H-purin-9-yl)ethyl)piperidin-1-yl)ethanone
7F-12	N-(3-(6-amino-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-9-yl)propyl)methanesulfonamide
7F-13	8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9-(2-(1-(methylsulfonyl)piperidin-3-yl)ethyl)-9H-purin-6-amine
7F-14	N-(2-(2-(6-amino-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-9-yl)ethylamino)ethyl)sulfamide
7F-15	3-(2-(6-amino-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-9-yl)ethylamino)-N-hydroxypropanamide
7F-16	8-(5-ethoxy-2-(1H-pyrrol-3-yl)phenylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine
7F-17	8-(5-ethoxy-2-(1H-pyrrol-3-yl)benzyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine
7F-18	9-(3-(tert-butylamino)propyl)-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-6-amine
7F-19	9-(3-aminopropyl)-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-6-amine
7F-20	1-(6-amino-8-(5-methoxy-2-(1H-pyrrol-3-yl)phenylthio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol

Table 8
Options for R.

1. R is hydrogen, a C₁ to C₁₀ alkyl, alkenyl, alkynyl, or an alkoxyalkyl group, optionally including heteroatoms such as N or O, or a targeting moiety connected to N9 via a linker,
2. R is hydrogen, straight- or branched-, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, in which one or more methylenes can be interrupted or terminated by O, S, S(O), SO₂, N(R₂₁₈), C(O), substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclic; substituted or unsubstituted cycloalkyl; or



B is a linker; R₂₁₀ is selected from the group consisting of hydrogen, N(R₂)COR₄,

N(R₂)CON(R₃)R₄, N(R₂)COOR₄, N(R₂)S(O)_nR₃, N(R₂)S(O)_nN(R₃)R₄; where R₂ and R₃ are independently selected from hydrogen, aliphatic or substituted aliphatic; R₄ is selected from the group consisting of: aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, and substituted or unsubstituted -C₁-C₆ alkyl, -C₂-C₆ alkenyl, or -C₂-C₆ alkynyl each containing O, 1, 2, or 3 heteroatoms selected from O, S or N; n is 1 or 2;

M₁ is absent or selected from substituted or unsubstituted -C₁-C₆ alkyl, -C₂-C₆ alkenyl, or -C₂-C₆ alkynyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

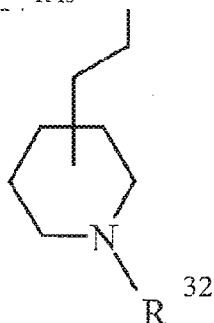
M₂ is absent, O, S, SO, SO₂, N(R₂) or CO;

M₃ is absent, O, S, SO, SO₂, N(R₂), CO, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, cycloalkyl, heterocyclic, aryl, or heteroaryl;

M₄ is hydrogen, NR₅R₆, CF₃, OR₄, halogen, substituted or unsubstituted -C₁-C₆ alkyl, -C₂-C₆ alkenyl, or -C₂-C₆ alkynyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl or substituted heteroaryl; where R₅ and R₆ are independently selected from the group consisting of hydrogen, aliphatic, substituted aliphatic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkyl or substituted cycloalkyl; provided that -R and -M₁-M₂-M₃-M₄ cannot be both hydrogen.

Table 8 cont'd

3. R is

wherein R^{32} is

(a) hydro;

(b) C_1 - C_6 alkyl optionally substituted with 1, 2, 3, 4, or 5 substituents each independently chosen from the group of halo, hydroxyl, amino, cyano, and $-C(=O)R^{31}$ wherein R^{31} is amino;(c) $-C(=O)R^{33}$, wherein R^{33} is selected from the group consisting of:

(1) hydro,

(2) C_1 - C_{10} (e.g., C_1 - C_6) alkyl optionally substituted with 1, 2, 3, 4, or 5 substituents each independently chosen from the group of (A) halo, (B) hydroxyl, (C) thiol, (D) cyano, (E) C_1 - C_6 haloalkyl (e.g., trifluoromethyl), (F) C_1 - C_6 alkoxy (e.g., methoxy) optionally substituted with C_1 - C_6 alkoxy (e.g., methoxy), (G) C-amido, (H) N-amido, (I) sulfonyl, (J) $-N(R^{22})(R^{23})$ wherein R^{22} and R^{23} are independently hydro, C_1 - C_6 alkyl, sulfonyl, and C-carboxy,(3) C_1 - C_6 cycloalkyl optionally substituted with 1, 2, 3, 4, or 5 substituents each independently chosen from the group of halo, hydroxyl, amino, cyano, and C_1 - C_6 haloalkyl (e.g., trifluoromethyl), and(4) C_1 - C_6 alkoxy optionally substituted with 1, 2, 3, 4, or 5 substituents each independently chosen from halo, hydroxyl, amino, cyano, and C_1 - C_6 haloalkyl (e.g., trifluoromethyl),(f) heterocycle or heterocyclalkyl, optionally substituted with 1, 2, 3, 4, or 5 substituents independently chosen from halo, hydroxyl, amino, cyano, trihalomethyl, and C_1 - C_4 alkyl optionally substituted with 1, 2, 3, or 4 substituents independently chosen from halo, hydroxyl, amino, cyano, C_1 - C_6 haloalkyl (e.g., trifluoromethyl) (e.g., tetrazole-5-yl optionally substituted with 1, 2, 3, or 4 C_1 - C_4 alkyl);

(g) sulfonyl; and

(h) optionally substituted heteroaryl

Table 8, cont'd

4. R is $-R^{54}-R^{55}$, wherein

R^{54} is $-(CH_2)_n-$ wherein $n=0-3$, $-C(O)$, $-C(S)$, $-SO_2-$, or $-SO_2N-$; and

R^{55} is alkyl, aromatic, heteroaromatic, alicyclic, or heterocyclic, each of which is optionally bi- or tri-cyclic, and optionally substituted with H, halogen, lower alkyl, lower alkenyl, lower alkynyl, lower aryl, lower alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, perhaloalkyl, perhaloalkyloxy, perhaloacyl, $-N_3$, $-SR^{58}$, $-OR^{58}$, $-CN$, $-CO_2R^{59}$, $-NO_2$, or $-NR^{58}R^{510}$,

R^{58} is hydrogen, lower alkyl, lower aryl, or $-C(O)R^{59}$;

R^{59} is lower alkyl, lower aryl, lower heteroaryl, $-NR^{510}R^{510}$ or $-OR^{511}$;

R^{510} is independently hydrogen or lower alkyl; and

R^{511} is _____

5. R is selected from the group consisting of H, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted alicyclic, optionally substituted aralkyl, optionally substituted aryloxyalkyl, optionally substituted alkoxyalkyl, alkylaminoalkyl, alkylcarbonylaminoalkyl, alkylcarbonyloxyalkyl, optionally substituted heterocyclic, hydroxyalkyl, haloalkyl, perhaloalkyl, $C(O)R^{62}$, $S(O)_2R^{62}$, $C(O)NHR^{62}$, and $C(O)OR^{62}$; where R^{62} is _____

6. R is H, SR_{71} , SOR_{71} , SO_2R_{71} , OR_{71} , $COOR_{71}$, $CONR_{71}R_{72}$, $-CN$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $-R_{7A}OR_{7B}-$, $-R_{7A}NR_{7B}$, $-R_{7A}NR_{71}R_{7B}$, $-R_{7A}SR_{7B}$, $-R_{7A}SOR_{7B}$ or $-R_{7A}SO_2R_{7B}$, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, $NR_{71}R_{72}$, $-OSO_2N(R_{7C})_2$, $-N(R_{7C})SO_2OH$, $-N(R_{7C})SO_2R_{7C}$, $-R_{7A}OSO_2N(R_{7C})_2$, or $-R_{7A}N(R_{7C})OSO_2R_{7C}$;

R_{71} and R_{72} are independently selected from the group consisting of H, $COOR_{7B}$, $CON(R_{7C})_2$, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, $-R_{7A}OR_{7B}-$, $-R_{7A}NR_{7B}$, $-R_{7A}NR_{71}R_{7B}$, $-R_{7A}SR_{7B}$, $-R_{7A}SOR_{7B}$ or $-R_{7A}SO_2R_{7B}$, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, and heteroarylalkyl;

each R_{7A} is independently C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, alkylheteroarylalkyl, or heteroarylalkyl; and

each R_{7B} is independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, heteroarylalkyl, $-SO_2OH$, $-SO_2N(R_{7A})_2$, $-SO_2NHR_{7A}$ or $-SO_2NH_2$; and

each $R_{sub.C}$ is independently H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, cycloalkyl, heteroalkyl, heterocycloalkyl, aryl, heteroaryl, alkylaryl, arylalkyl, alkylheteroaryl, or heteroarylalkyl;

7A. R is hydrogen, straight- or branched-, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, which one or more methylenes can be interrupted or terminated by O, S, $S(O)$, SO_2 , $N(R_{88})$, $C(O)$, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclic; substituted or unsubstituted cycloalkyl; where R_{88} is hydrogen, acyl, aliphatic or substituted aliphatic.

7B. R is $-M_1-M_2-M_3-M_4$, wherein

M_1 is absent, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, aryl or heteroaryl;

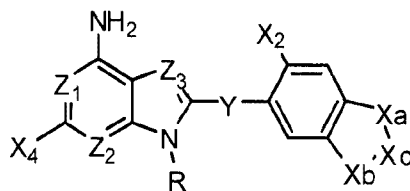
M_2 is absent, O, S, SO, SO_2 , $N(R_{88})$, or $C=O$;

M_3 is absent, $C=O$, O, S, SO, SO_2 or $N(R_{88})$; and

M_4 is hydrogen, halogen, CN, N_3 , hydroxy, substituted hydroxy, amino, substituted amino, CF_3 , C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, cycloalkyl, heterocyclic, aryl or heteroaryl.

WHAT IS CLAIMED IS:

1. A compound of the formula:



wherein

- (a) each of Z₁, Z₂ and Z₃ is N;
- (b) X_a and X_b are O and X_c is CH₂;
- (c) Y is -CH₂- or -S-;
- (d) X₄ is hydrogen or halogen; and
- (e) X₂ is an aryl, an alkynyl, a cycloalkyl, or a cycloalkenyl group, each of which is optionally substituted, and R is:

- (a) hydrogen; or
- (b) a straight-chain- or branched- C₁ to C₁₀ alkyl, C₂ to C₆ alkenyl, or C₂ to C₆ alkynyl, which is unsubstituted or substituted with -OH, -OR', halogen, -C₅ to C₁₀ aryl, -SR', C₂ to C₁₀ heterocyclic, or C₃ to C₁₀ carbocyclic, wherein R' is C₁ to C₁₀ alkyl, C₂ to C₆ alkenyl, or C₂ to C₆ alkynyl; or
- (c) straight-chain- or branched- amino-alkyl, secondary or tertiary alkyl-amino-alkyl, or trialkylammonioalkyl.

2. The compound of claim 1, wherein X₂ is optionally substituted alkynyl.
3. The compound of claim 2, wherein the compound is selected from the group consisting of: 8-[6-(3,3-dimethyl-but-1-ynyl)-benzo[1,3]dioxol-5-ylthio]9-(3-isopropylaminopropyl)-9H-purin-6-ylamine, 9-(3-isopropylamino-propyl)-8-(6-phenylethynyl-benzo[1,3]dioxol-5-ylthio)-9H-purin-6-ylamine, 8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; 8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-

fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; 9-(3-aminopropyl)-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine; 9-(2-aminoethyl)-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-(6-ethynylbenzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine; 8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; and 9-(3-(tert-butylamino)propyl)-8-((6-ethynylbenzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9H-purin-6-amine.

4. The compound of claim 1, wherein X₂ is an optionally substituted heteroaryl group.
5. The compound of claim 4, wherein X₂ is optionally substituted furanyl.
6. The compound of claim 5, wherein the compound is selected from the group consisting of: 8-(6-(furan-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 2-fluoro-8-((6-(furan-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, 8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 5-(6-((6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-yl)thio)benzo[d][1,3]dioxol-5-yl)furan-2-carbaldehyde; 9-(3-(isopropylamino)propyl)-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine; 8-((6-(5-(aminomethyl)furan-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine; 1-(6-amino-8-(6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol; 2-fluoro-8-((6-(furan-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; 5-(6-((6-amino-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-8-yl)methyl)benzo[d][1,3]dioxol-5-yl)furan-2-carbaldehyde; 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; 8-((6-(5-(aminomethyl)furan-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-

(isobutylamino)ethyl)-9H-purin-6-amine; 2-fluoro-9-(3-(isopropylamino)propyl)-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; and 9-(3-aminopropyl)-2-fluoro-8-((6-(5-methylfuran-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine.

7. The compound of claim 4, wherein X₂ is optionally substituted oxazolyl.

8. The compound of claim 7, wherein the compound is selected from the group consisting of: 8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 9-(3-(isopropylamino)propyl)-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine; 9-(3-aminopropyl)-8-(6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine; 1-(6-amino-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; 2-fluoro-9-(3-(isopropylamino)propyl)-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(oxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; and 9-(3-aminopropyl)-2-fluoro-8-((6-(5-methyloxazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine.

9. The compound of claim 4, wherein X₂ is optionally substituted pyrazolyl.

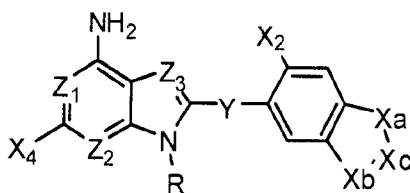
10. The compound of claim 9, wherein the compound is selected from the group consisting of: 8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 8-((6-(5-methyl-1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-

yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-aminopropyl)-9H-purin-6-amine; 8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(3-(tert-butylamino)propyl)-9H-purin-6-amine; 1-(8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)thio)-6-amino-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(5-methyl-1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; 8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(2-aminoethyl)-2-fluoro-9H-purin-6-amine; and 8-((6-(1H-pyrazol-3-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9-(3-(tert-butylamino)propyl)-2-fluoro-9H-purin-6-amine.

11. The compound of claim 4, wherein X₂ is optionally substituted furan, thiophene, 3-pyrazole, oxazole, or thiazolyl.

12. The compound of claim 11, wherein the compound is selected from the group consisting of: 9-(3-(isopropylamino)propyl)-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine; 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-((6-(thiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-6-amine; 1-(6-amino-8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-yl)methyl)-9H-purin-6-amine; and 8-((6-(5-methylthiazol-2-yl)benzo[d][1,3]dioxol-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine.

13. A compound of the formula:



wherein

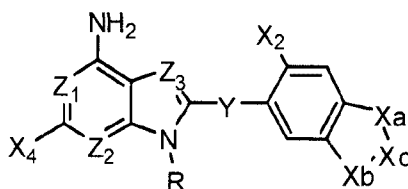
- (a) each of Z_1 , Z_2 and Z_3 is N;
 - (b) $X_a-X_c-X_b$ is $CH_2-CH_2-CH_2$, $CH=CH-CH_2$, or $CH_2-CH=CH$;
 - (c) Y is $-CH_2-$ or $-S-$;
 - (d) X_4 is hydrogen or halogen; and
 - (e) X_2 is selected from the group consisting of alkynyl, aryl, cycloalkyl, and cycloalkenyl, each of which is optionally substituted, and R is:
 - (a) hydrogen; or
 - (b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or
 - (c) straight-chain- or branched- amino-alkyl, secondary or tertiary alkyl-amino-alkyl, or trialkylammonioalkyl.
14. The compound of claim 13, wherein X_2 is optionally substituted aryl.
15. The compound of claim 13, wherein X_2 is optionally substituted alkynyl.
16. The compound of claim 15, wherein the compound is selected from the group consisting of: 8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-(6-ethynyl-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9H-purin-6-amine; 8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; and 8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)methyl)-2-fluoro-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine.
17. The compound of claim 13, wherein X_2 is optionally substituted heteroaryl.
18. The compound of claim 17, wherein the compound is selected from the group consisting of: 8-((6-(furan-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 9-(3-(isopropylamino)propyl)-8-((6-(oxazol-2-

yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine; 9-(3-(isopropylamino)propyl)-8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine; 9-(3-aminopropyl)-8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-(6-(4-methylthiazol-2-yl)-2,3-dihydro-1H-inden-5-ylthio)-9H-purin-6-amine; 8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 1-(6-amino-8-((6-(5-methyloxazol-2-yl)-2,3-dihydro-1H-inden-5-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 9-(3-(tert-butylamino)propyl)-2-fluoro-8-((6-(4-methylthiazol-2-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9H-purin-6-amine; and 8-((6-(1H-pyrazol-3-yl)-2,3-dihydro-1H-inden-5-yl)methyl)-9-(3-(tert-butylamino)propyl)-2-fluoro-9H-purin-6-amine.

19. The compound of claim 13, wherein X_2 is optionally substituted cycloalkyl.

20. The compound of claim 13, wherein X_2 is optionally substituted cycloalkenyl.

21. A compound of the formula:



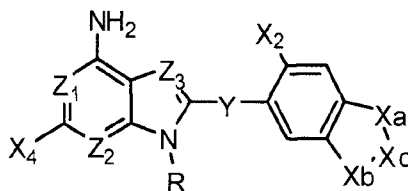
wherein

- (a) each of Z_1 , Z_2 and Z_3 is N;
- (b) one of X_a and X_b is O and X_c and the other of X_a and X_b are $-CH_2-$;
- (c) Y is $-CH_2-$ or $-S-$;
- (d) X_4 is hydrogen or halogen; and
- (e) X_2 is an aryl, an alkynyl, a cycloalkyl, or a cycloalkenyl group, each of which is optionally substituted, and R is:

- (a) hydrogen; or
- (b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or

(c) straight-chain- or branched- amino-alkyl, secondary or tertiary alkyl-amino-alkyl, or trialkylammonioalkyl.

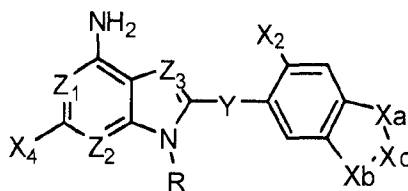
22. A compound of the formula:



wherein

- (a) each of Z_1 , Z_2 and Z_3 is N;
- (b) one of X_a and X_b is S, C(=O), C(=S), NH or substituted N, and X_c and the other of X_a and X_b are $-CH_2-$;
- (c) Y is $-CH_2-$ or $-S-$;
- (d) X_4 is hydrogen or halogen;
- (e) X_2 is selected from the group consisting of alkynyl, aryl, cycloalkyl, and cycloalkenyl, each of which is optionally substituted; and
- (f) R is:
 - (a) hydrogen; or
 - (b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or
 - (c) straight-chain- or branched- amino-alkyl, secondary or tertiary alkyl-amino-alkyl, or trialkylammonioalkyl.

23. A compound of the formula:



wherein

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

(b) $X_a-X_c-X_b$ is $CH=CH-O$, $CH=CH-NH$, $CH=CH-S$, $O-CH=CH$, $NH-CH=CH$, $S-CH=CH$, $N=CH-O$, $N=CH-S$, $NH-CH=N$, $O-CH=N$, $S-CH=N$, $N=N-O$, $N=N-S$, $N=N-CH_2$, $O-N=N$, $NH-N=N$, $S-N=N$, or $CH_2-N=N$;

(c) Y is $-CH_2-$ or $-S-$;

(d) X_4 is hydrogen or halogen;

(e) X_2 is selected from the group consisting of alkynyl, aryl, cycloalkyl and cycloalkenyl, each of which is optionally substituted; and

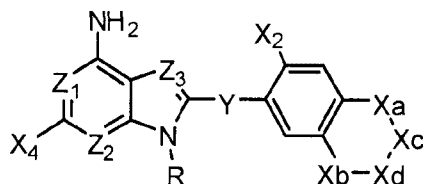
(f) R is:

(a) hydrogen; or

(b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or

(c) straight-chain- or branched- amino-alkyl, secondary or tertiary alkyl-amino-alkyl, or trialkylammonioalkyl.

24. A compound of the formula:



wherein

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

(b) X_a and X_b are O, and X_c and X_d are CH_2 ;

(c) Y is $-CH_2-$, $-O-$ or $-S-$;

(d) X_4 is hydrogen or halogen; and

(e) X_2 is selected from the group consisting of an aryl, an alkynyl, a cycloalkyl and a cycloalkenyl, each of which is optionally substituted, and R is:

(a) hydrogen; or

(b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or

(c) straight-chain- or branched- amino-alkyl, secondary or tertiary alkyl-amino-alkyl, or trialkylammonioalkyl.

25. The compound of claim 24, wherein X₂ is optionally substituted aryl.
26. The compound of claim 24, wherein X₂ is optionally substituted cycloalkyl.
27. The compound of claim 24, wherein X₂ is optionally substituted cycloalkenyl.
28. The compound of claim 24, wherein X₂ is optionally substituted heteroaryl.
29. The compound of claim 28, wherein X₂ is optionally substituted pyrazolyl.
30. The compound of claim 29, wherein the compound is selected from the group consisting of: 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-aminopropyl)-9H-purin-6-amine; 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(tert-butylamino)propyl)-9H-purin-6-amine; 9-(3-(isopropylamino)propyl)-8-((7-(5-methyl-1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine; 8-((7-(5-methyl-1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 1-(8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-6-amino-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(3-(tert-butylamino)propyl)-2-fluoro-9H-purin-6-amine; 1-(8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-6-amino-2-fluoro-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol; and 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-aminoethyl)-2-fluoro-9H-purin-6-amine.

31. The compound of claim 28, wherein X₂ is optionally substituted furanyl.

32. The compound of claim 31, wherein the compound is selected from the group consisting of: 8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, 8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 9-(3-(isopropylamino)propyl)-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine; 8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 8-((7-(5-(aminomethyl)furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 1-(6-amino-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 9-(3-aminopropyl)-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-(7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine; 2-fluoro-8-((7-(furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; 2-fluoro-9-(2-(isobutylamino)ethyl)-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine; 8-((7-(5-(aminomethyl)furan-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; and 9-(3-aminopropyl)-2-fluoro-8-((7-(5-methylfuran-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine.

33. The compound of claim 28, wherein X₂ is optionally substituted oxazolyl.

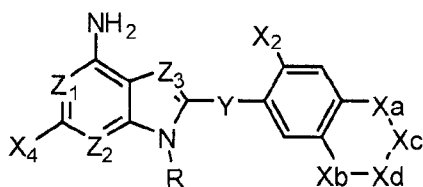
34. The compound of claim 33, wherein the compound is selected from the group consisting of: 8-(7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 1-(6-amino-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 9-(3-(tert-butylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine; 9-(3-aminopropyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine;; 9-(3-(isopropylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine; 2-fluoro-9-(3-

(isopropylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine; 2-fluoro-9-(3-(isopropylamino)propyl)-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-2-fluoro-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine; and 9-(3-aminopropyl)-2-fluoro-8-((7-(5-methyloxazol-2-yl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-9H-purin-6-amine.

35. The compound of claim 24, wherein X₂ is optionally substituted alkynyl.

36. The compound of claim 35, wherein the compound is selected from the group consisting of: 3-(3-(6-amino-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-9-yl)propyl)pyrrolidine-1-carbaldehyde; 8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine; 9-(2-aminoethyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine; 9-(3-aminopropyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-6-amine; 1-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)thio)-9H-purin-9-yl)-3-(isopropylamino)propan-2-ol; 9-(3-(tert-butylamino)propyl)-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine; 9-(2-aminoethyl)-8-(7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-ylthio)-9H-purin-6-amine; 8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine; 1-(6-amino-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-9-yl)-3-(tert-butylamino)propan-2-ol; 8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9-(3-(isopropylamino)propyl)-9H-purin-6-amine; 9-(3-(tert-butylamino)propyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-6-amine; and 9-(3-aminopropyl)-8-((7-ethynyl-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)methyl)-2-fluoro-9H-purin-6-amine.

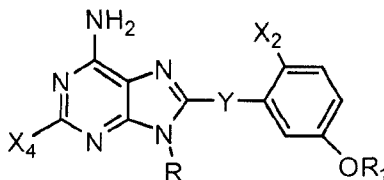
37. A compound of the formula:



wherein

- (a) each of Z₁, Z₂ and Z₃ is N;
- (b) X_a, X_c, X_d and X_b are all carbon connected by single or double bonds;
- (c) Y is -CH₂-, -O- or -S-;
- (d) X₄ is hydrogen or halogen;
- (e) X₂ is selected from the group consisting of alkynyl, aryl, cycloalkyl, and cycloalkenyl, each of which is optionally substituted; and
- (f) R is:
 - (a) hydrogen; or
 - (b) a straight-chain- or branched- C₁ to C₁₀ alkyl, C₂ to C₆ alkenyl, or C₂ to C₆ alkynyl, which is unsubstituted or substituted; or
 - (c) straight-chain- or branched- amino-alkyl, secondary or tertiary alkyl-amino-alkyl, or trialkylammonioalkyl.

38. A compound of the formula



wherein

- (a) R₁ is alkyl;
- (b) Y is -CH₂- or -S-;
- (c) X₄ is H or halogen;
- (d) X₂ is a cycloalkyl, a cycloalkenyl, an aryl, or an alkynyl group, each of which is optionally substituted; and

(e) R is hydrogen or linear or branched alkyl, alkenyl, or alkynyl, optionally including N, S, or O, and optionally part of an 8 to 10 member ring formed by joining the 2'-position X₂ and R.

39. The compound of claim 4, wherein the compound is selected from the group consisting of: 9-(3-(isopropylamino)propyl)-8-(6-(thiophen-2-yl)benzo [d] [1,3] dioxol-5-ylthio)-9H-purin-6-amine, 8-(6-(1H-pyrrol-3-yl) benzo [d] [1,3] dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 9-(3-(isopropylamino)propyl)-8-(6-(pyridin-4-yl) benzo [d] [1,3] dioxol-5-ylthio)-9H-purin-6-amine, 8-(6-(1H-pyrazol-4-yl) benzo [d] [1,3] dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 9-(3-(isopropylamino)propyl)-8-(6-(1-methyl-1H-pyrazol-5-yl)benzo [d] [1,3]dioxol-5-ylthio)-9H-purin-6-amine, 9-(3-(isopropylamino)propyl)-8-(6-(isoxazol-4-yl)benzo[d] [1,3] dioxol-5-ylthio)-9H-purin-6-amine, 8-(((6-(1H-pyrrol-2-yl)benzo [d] [1,3] dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, 8-(((6-(1H-pyrazol-4-yl) benzo [d] [1,3] dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, 8-(((6-(1H-pyrrol-3-yl) benzo [d] [1,3] dioxol-5-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, 2-fluoro-9-(2-(isobutylamino)ethyl)-8-(((6-(1-methyl-1H-pyrazol-5-yl)benzo[d] [1,3]dioxol-5-yl)methyl)-9H-purin-6-amine, 2-fluoro-9-(2-(isobutylamino)ethyl)-8-(((6-(thiophen-2-yl)benzo [d] [1,3] dioxol-5-yl)methyl)-9H-purin-6-amine, 2-fluoro-9-(2-(isobutylamino)ethyl)-8-(((6-(isoxazol-4-yl) benzo [d] [1,3] dioxol-5-yl)methyl)-9H-purin-6-amine, 9-(2-(neopentylamino)ethyl)-8-(6-(thiophen-2-yl) benzo [d] [1,3] dioxol-5-ylthio)-9H-purin-6-amine, 8-(6-(1H-pyrrol-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine, and 8-(6-(furan-3-yl) benzo [d] [1,3] dioxol-5-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine.

40. The compound of claim 1, wherein X₂ is optionally substituted aryl.

41. The compound of claim 40, wherein the compound is selected from the group consisting of: 9-(3-(isopropylamino)propyl)-8-(6-phenylbenzo [d] [1,3] dioxol-5-ylthio)-9H-purin-6-amine, 8-(6-(4-tert-butylphenyl)benzo [d] [1,3] dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo [d] [1,3] dioxol-5-

ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 8-(6-(4-(dimethylamino)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 9-(3-(isopropylamino)propyl)-8-(6-(4-methoxyphenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-6-amine, 8-(6-(4-bromophenyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 4-(6-(6-amino-9-(3-(isopropylamino)propyl)-9H-purin-8-ylthio)benzo[d][1,3]dioxol-5-yl)benzaldehyde, tert-Butyl 6-(3-(6-amino-8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propylamino)hexylcarbamate, and N-(3-(6-amino-8-(6-(3,5-bis(trifluoromethyl)phenyl)benzo[d][1,3]dioxol-5-ylthio)-9H-purin-9-yl)propyl)hexane-1,6-diamine.

42. The compound of claim 1, wherein X₂ is optionally substituted cycloalkenyl.

43. The compound of claim 42, wherein the compound is 8-(6-(cyclopent-2-enyl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine.

44. A compound, wherein the compound is 8-(6-(2,5-dihydro-1H-pyrrol-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 8-(6-(2,3-dihydrofuran-2-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, or 8-(6-(2,3-dihydrofuran-3-yl)benzo[d][1,3]dioxol-5-ylthio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine.

45. The compound of claim 21, wherein the compound is 8-(5-(furan-2-yl)-2,3-dihydrobenzofuran-6-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine, 9-(2-(neopentylamino)ethyl)-8-(5-(thiophen-2-yl)-2,3-dihydrobenzofuran-6-ylthio)-9H-purin-6-amine, or 8-(5-ethynyl-2,3-dihydrobenzofuran-6-ylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine.

46. The compound of claim 15, wherein the compound is 8-((6-ethynyl-2,3-dihydro-1H-inden-5-yl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine.

47. The compound of claim 24, wherein the compound is 8-((7-(furan-2-yl)-2,3-dihydrobenzo [b] [1,4] dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo[b] [1,4]dioxin-6-yl)thio)-9-(3-(isopropylamino)propyl)-9H-purin-6-amine, 8-((7-(furan-2-yl)-2,3-dihydrobenzo [b] [1,4]dioxin-6-yl)thio)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, 2-fluoro-8-((7-(furan-2-yl)-2,3-dihydrobenzo [b] [1,4] dioxin-6-yl)methyl)-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, 8-((7-(1H-pyrazol-3-yl)-2,3-dihydrobenzo [b] [1,4] dioxin-6-yl)methyl)-2-fluoro-9-(2-(isobutylamino)ethyl)-9H-purin-6-amine, or 9-(3-(isopropylamino)propyl)-8-((7-(oxazol-2-yl)-2,3-dihydrobenzo [b] [1,4] dioxin-6-yl)thio)-9H-purin-6-amine.
48. The compound of claim 38, wherein the compound is 8-(2-(furan-2-yl)-5-methoxyphenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine, 8-(5-methoxy-2-(thiophen-2-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine, 8-(5-methoxy-2-(1H-pyrazol-3-yl)phenylthio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine, or 8-((2-ethynyl-5-methoxyphenyl)thio)-9-(2-(neopentylamino)ethyl)-9H-purin-6-amine.
49. The compound of claim 1, wherein Y is S, X₄ is H, and X₂ is acetylenyl, 2-furanyl, 3-furanyl, 5-methyl-2-furanyl, 2-thiophene, 3-thiophene, 2-pyrazolyl, 3-pyrazolyl, 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl, 5-methyl-2-oxazolyl, or optionally substituted imidazole.
50. The compound of any one of claims 1, 2, 4, 5, 7, 9, 11, 13, 15, 17, 21-24, 28, 29, 31, 33, 35, 37, 38, 40, 42, or 49 wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 2-(hydroxyethyl(isopropyl)amino)ethyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(hydroxyethyl(isopropyl)amino)propyl, 3-(methyl(propargyl)amino)propyl, 2-(methyl(propargyl)amino)ethyl, 3-(allyl(methyl)amino)propyl, or 2-(methyl(isobutyl)amino)ethyl.
51. The compound of claim 50, wherein R is 3-(isopropyl-amino)propyl.

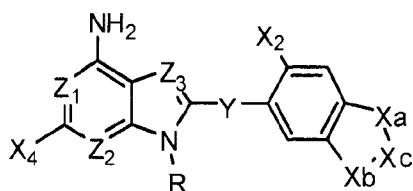
52. The compound of claim 50, wherein Y is S, X₄ is H, and X₂ is acetylenyl, 2-furanyl, 3-furanyl, 5-methyl-2-furanyl, 2-pyrazolyl, 3-pyrazolyl, 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl, or 5-methyl-2-oxazolyl.
53. The compound of any one of claims 1, 2, 4, 5, 7, 9, 11, 13, 15, 17, 21-24, 28, 29, 31, 33, 35, 37, 38, 40, or 42, wherein R is secondary or tertiary alkyl-amino-alkyl.
54. A pharmaceutical composition comprising the compound of any one of claims 1 to 53 and a pharmaceutically acceptable carrier.
55. Use of the compound according to any one of claims 1 to 53 for the inhibition of Hsp90.
56. Use of the compound according to any one of claims 1 to 53 in the manufacture of a medicament for the inhibition of Hsp90.
57. The compound according to any one of claims 1 to 53 for use in the inhibition of Hsp90.
58. Use of the pharmaceutical composition according to claim 54 for the inhibition of Hsp90.
59. The pharmaceutical composition according to claim 54 for use in the inhibition of Hsp90.
60. Use of the compound according to any one of claims 1 to 53 for the treatment of a cancer or a neurodegenerative disease.
61. Use of the compound according to any one of claims 1 to 53 in the manufacture of a medicament for the treatment of a cancer or a neurodegenerative disease.

62. The compound according to any one of claims 1 to 53 for use in the treatment of a cancer or a neurodegenerative disease.

63. Use of the pharmaceutical composition according to claim 54 for the treatment of a cancer or a neurodegenerative disease.

64. The pharmaceutical composition according to claim 54 for use in the treatment of a cancer or a neurodegenerative disease.

65. A compound of the formula:



wherein

- (a) each of Z_1 , Z_2 and Z_3 is independently N;
- (b) X_a and X_b are O and X_c is CH_2 ;
- (c) Y is $-CH_2-$ or $-S-$;
- (d) X_4 is hydrogen or halogen; and
- (e) X_2 is an aryl, an alkynyl, a cycloalkyl, or a cycloalkenyl group, each of which is optionally substituted, and R is:

- (a) hydrogen; or
- (b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or
- (c) aryl, heteroaryl, heterocyclic, cycloalkyl, alkylaryl, or arylalkyl, which is unsubstituted or substituted.

66. The compound of claim 65, wherein Y is S, X_4 is H, and X_2 is acetylenyl, 2-furanyl, 3-furanyl, 5-methyl-2-furanyl, 2-thiophene, 3-thiophene, 2-pyrazolyl, 3-pyrazolyl, 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl, 5-methyl-2-oxazolyl, or optionally substituted imidazole.

67. The compound of claim 65, wherein Y is S, X₄ is H, and X₂ is acetylenyl, 2-furanyl, 3-furanyl, 5-methyl-2-furanyl, 2-pyrazolyl, 3-pyrazolyl, 2-thiazolyl, 5-methyl-2-thiazolyl, 2-oxazolyl, or 5-methyl-2-oxazolyl.

68. The compound of claim 65, wherein X₂ is optionally substituted alkynyl.

69. The compound of claim 68, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 2-(hydroxyethyl(isopropyl)amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(hydroxyethyl(isopropyl)amino)propyl, 3-(methyl(propargyl)amino)propyl, 2-(methyl(propargyl)amino)ethyl, 3-(allyl(methyl)amino)propyl, 3-(propyl(cyclopropyl)methyl-amino)propyl, 3-(hydroxyethyl(cyclohexyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

70. The compound of claim 69, wherein R is 3-(isopropyl-amino)propyl.

71. The compound of claim 65, wherein X₂ is an optionally substituted heteroaryl group.

72. The compound of claim 71, wherein X₂ is optionally substituted furanyl.

73. The compound of claim 71, wherein X₂ is optionally substituted oxazolyl.

74. The compound of claim 71, wherein X₂ is optionally substituted pyrazolyl.

75. The compound of claim 71, wherein X₂ is optionally substituted thiazolyl.

76. The compound of claim 71, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 2-(hydroxyethyl(isopropyl)amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(hydroxyethyl(isopropyl)amino)propyl, 3-(methyl(propargyl)amino)propyl, 2-(methyl(propargyl)amino)ethyl, 3-(allyl(methyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 3-(hydroxyethyl(cyclohexyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

77. The compound of claim 76, wherein R is 3-(isopropyl-amino)propyl.

78. The compound of claim 65, wherein X₂ is optionally substituted aryl.

79. The compound of claim 65, wherein X₂ is optionally substituted cycloalkenyl.

80. The compound of claim 65, wherein R is a secondary or tertiary alkyl-amino-alkyl.

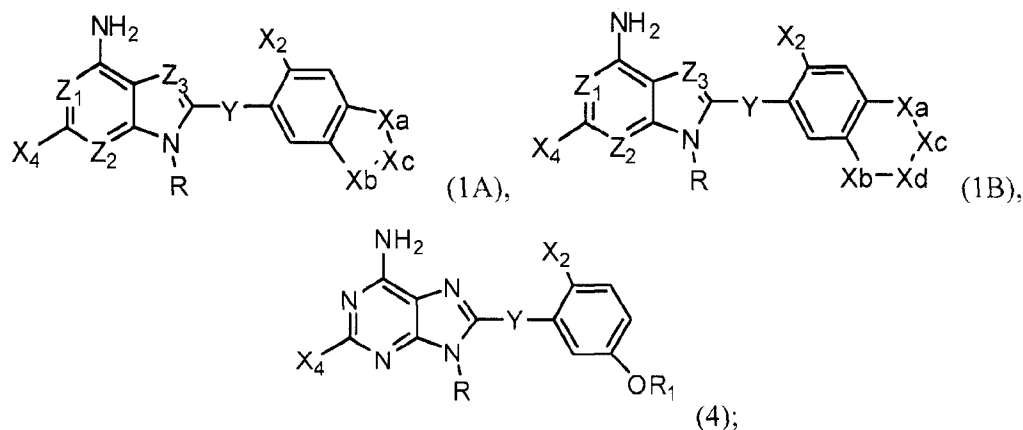
81. The compound of claim 80, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 2-(hydroxyethyl(isopropyl)amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(hydroxyethyl(isopropyl)amino)propyl, 3-(methyl(propargyl)amino)propyl, 2-(methyl(propargyl)amino)ethyl, 3-(allyl(methyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 3-(hydroxyethyl(cyclohexyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

82. The compound of claim 81, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

83. The compound of claim 82, wherein X₂ is acetylene.

84. The compound of claim 82, wherein X₂ is optionally substituted furan, thiophene, oxazole, or pyrazole.

85. A compound of the formula (1A), (1B), or (4):



wherein the variable substituents of the formula (1A) are selected from one of the following groups (A)-(D), the variable substituents of the formula (1B) are selected from groups (E) and (F), and the variable substituents of the formula (4) are described in group (G):

- (A) (a) each of Z₁, Z₂ and Z₃ is independently N;
 (b) X_a-X_c-X_b is CH₂-CH₂-CH₂, CH=CH-CH₂, or CH₂-CH=CH;
 (c) Y is -CH₂- or -S-;
 (d) X₄ is hydrogen or halogen; and

(c) X_2 is alkynyl, aryl, cycloalkyl, or cycloalkenyl, each of which is optionally substituted, and R is:

(a) hydrogen; or

(b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or

(c) aryl, heteroaryl, heterocyclic, cycloalkyl, alkylaryl, or arylalkyl, which is unsubstituted or substituted;

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

(b) one of X_a and X_b is O and X_c and the other of X_a and X_b are $-CH_2-$;

(c) Y is $-CH_2-$ or $-S-$;

(d) X_4 is hydrogen or halogen; and

(e) X_2 is an aryl, an alkynyl, a cycloalkyl, or a cycloalkenyl, each of which is optionally substituted, and R is:

(a) hydrogen; or

(b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or

(c) aryl, heteroaryl, heterocyclic, cycloalkyl, alkylaryl, or arylalkyl, which is unsubstituted or substituted;

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

(b) one of X_a and X_b is S, $C(=O)$, $C(=S)$, NH or substituted N, and X_c and the other of X_a and X_b are $-CH_2-$;

(c) Y is $-CH_2-$ or $-S-$;

(d) X_4 is hydrogen or halogen;

(e) X_2 is alkynyl, aryl, cycloalkyl, or cycloalkenyl, each of which is optionally substituted; and

(f) R is:

(a) hydrogen; or

(b) a straight-chain- or branched- C_1 to C_{10} alkyl, C_2 to C_6 alkenyl, or C_2 to C_6 alkynyl, which is unsubstituted or substituted; or

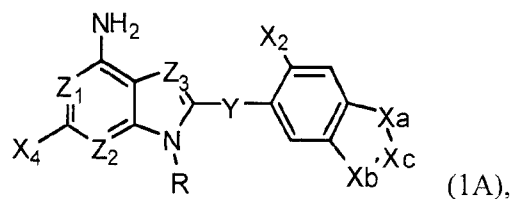
(c) aryl, heteroaryl, heterocyclic, cycloalkyl, alkylaryl, or arylalkyl, which is unsubstituted or substituted;

- (D) (a) each of Z_1 , Z_2 and Z_3 is independently N;
- (b) $X_a-X_c-X_b$ is CH=CH-O, CH=CH-NH, CH=CH-S, O-CH=CH, NH-CH=CH, S-CH=CH, N=CH-O, N=CH-S, NH-CH=N, O-CH=N, S-CH=N, N=N-O, N=N-S, N=N-CH₂, O-N=N, NH-N=N, S-N=N, or CH₂-N=N;
- (c) Y is -CH₂- or -S-;
- (d) X_4 is hydrogen or halogen;
- (e) X_2 is alkynyl, aryl, cycloalkyl, or cycloalkenyl, each of which is optionally substituted; and
- (f) R is:
- (a) hydrogen; or
- (b) a straight-chain- or branched- C₁ to C₁₀ alkyl, C₂ to C₆ alkenyl, or C₂ to C₆ alkynyl, which is unsubstituted or substituted; or
- (c) aryl, heteroaryl, heterocyclic, cycloalkyl, alkylaryl, or arylalkyl, which is unsubstituted or substituted;
- (E) (a) each of Z_1 , Z_2 and Z_3 is independently N;
- (b) X_a and X_b are O, and X_c and X_d are CH₂;
- (c) Y is -CH₂-, -O- or -S-;
- (d) X_4 is hydrogen or halogen; and
- (e) X_2 is aryl, alkynyl, cycloalkyl or cycloalkenyl, each of which is optionally substituted, and R is:
- (a) hydrogen; or
- (b) a straight-chain- or branched- C₁ to C₁₀ alkyl, C₂ to C₆ alkenyl, or C₂ to C₆ alkynyl, which is unsubstituted or substituted; or
- (c) aryl, heteroaryl, heterocyclic, cycloalkyl, alkylaryl, or arylalkyl, which is unsubstituted or substituted;
- (F) (a) each of Z_1 , Z_2 and Z_3 is independently N;
- (b) X_a , X_c , X_d and X_b are all carbon connected by single or double bonds;
- (c) Y is -CH₂-, -O- or -S-;
- (d) X_4 is hydrogen or halogen;
- (e) X_2 is alkynyl, aryl, cycloalkyl, or cycloalkenyl, each of which is optionally substituted; and

- (f) R is:
- (a) hydrogen; or
 - (b) a straight-chain- or branched- C₁ to C₁₀ alkyl, C₂ to C₆ alkenyl, or C₂ to C₆ alkynyl, which is unsubstituted or substituted; or
 - (c) aryl, heteroaryl, heterocyclic, cycloalkyl, alkylaryl, or arylalkyl, which is unsubstituted or substituted;
- (G) (a) R₁ is alkyl;
- (b) Y is -CH₂- or -S-;
 - (c) X₄ is H or halogen;
 - (d) X₂ is cycloalkyl, cycloalkenyl, aryl, or alkynyl, each of which is optionally substituted; and
 - (e) R is hydrogen or linear, branched, or cyclic alkyl, alkenyl, or alkynyl, optionally including N, S, or O, and optionally part of an 8 to 10 member ring formed by joining the 2'-position X₂ and R.

86. The compound of claim 85, wherein R is a secondary or tertiary alkyl-amino-alkyl.

87. The compound of claim 86, wherein the compound is of the formula (1A)



- (a) each of Z₁, Z₂ and Z₃ is independently N;
- (b) X_a-X_c-X_b is CH₂-CH₂-CH₂, CH=CH-CH₂, or CH₂-CH=CH; or one of X_a and X_b is O and X_c and the other of X_a and X_b are -CH₂-;
- (c) Y is -CH₂- or -S-;
- (d) X₄ is hydrogen or halogen; and
- (e) X₂ is alkynyl, aryl, cycloalkyl, or cycloalkenyl, each of which is optionally substituted.

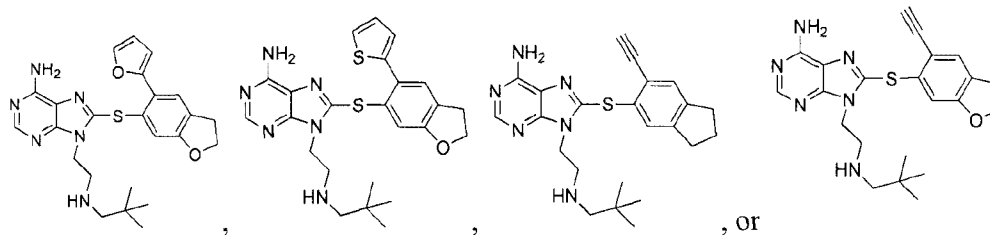
88. The compound of claim 87, wherein X₂ is alkynyl or heteroaryl, each of which is optionally substituted.

89. The compound of claim 88, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 2-(hydroxyethyl(isopropyl)amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(hydroxyethyl(isopropyl)amino)propyl, 3-(methyl(propargyl)amino)propyl, 2-(methyl(propargyl)amino)ethyl, 3-(allyl(methyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 3-(hydroxyethyl(cyclohexyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

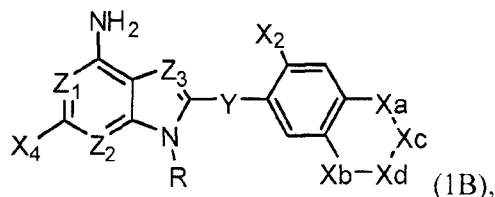
90. The compound of claim 89, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

91. The compound of claim 90, wherein X₂ is acetylene, furan, or thiophene.

92. The compound of claim 91, wherein the compound is



93. The compound of claim 86, wherein the compound is of the formula (1B)



- (a) each of Z_1 , Z_2 and Z_3 is independently N;
- (b) X_a and X_b are O, and X_c and X_d are CH_2 ;
- (c) Y is $-CH_2-$ or $-S-$;
- (d) X_4 is hydrogen or halogen; and
- (e) X_2 is alkynyl, aryl, cycloalkyl, or cycloalkenyl, each of which is optionally substituted.

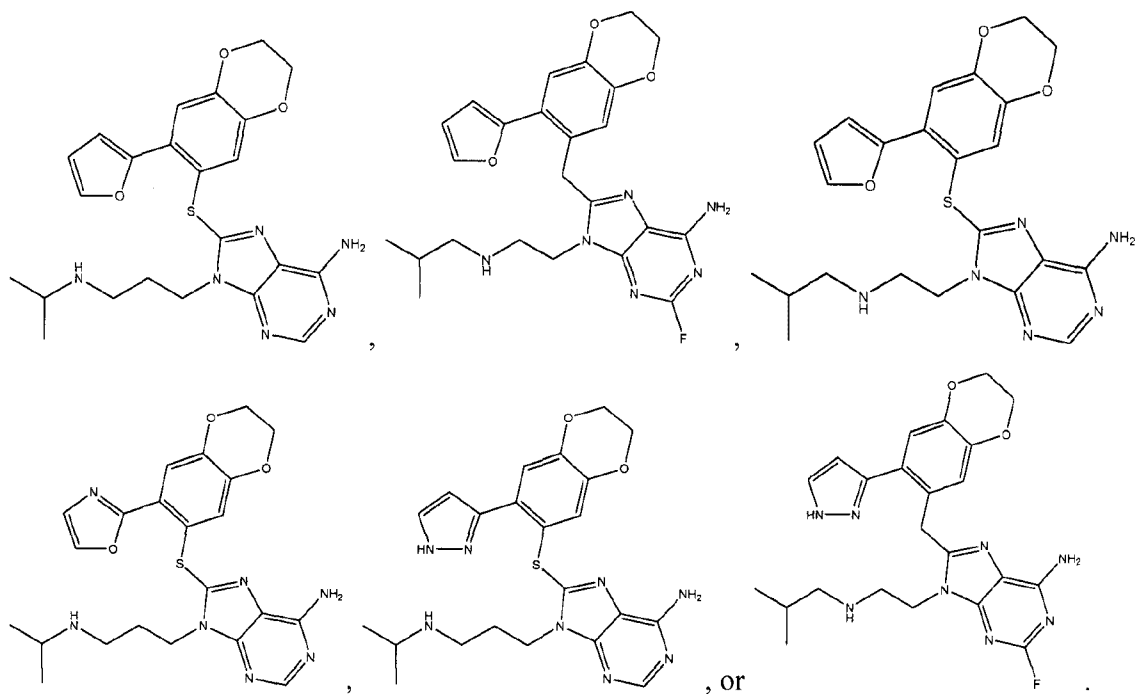
94. The compound of claim 93, wherein X_2 is alkynyl or heteroaryl, each of which is optionally substituted.

95. The compound of claim 94, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 2-(hydroxyethyl(isopropyl)amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(hydroxyethyl(isopropyl)amino)propyl, 3-(methyl(propargyl)amino)propyl, 2-(methyl(propargyl)amino)ethyl, 3-(allyl(methyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 3-(hydroxyethyl(cyclohexyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

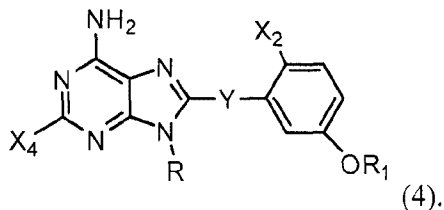
96. The compound of claim 95, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

97. The compound of claim 96, wherein X₂ is acetylene, furan, oxazole, or pyrazole.

98. The compound of claim 97, wherein the compound is



99. The compound of claim 86, wherein the compound is of the formula (4)



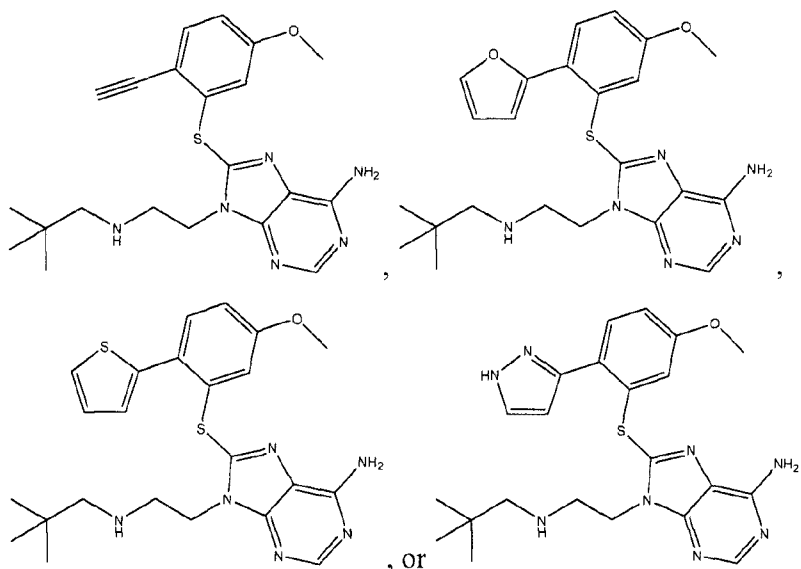
100. The compound of claim 99, wherein X₂ is alkynyl or heteroaryl, each of which is optionally substituted.

101. The compound of claim 100, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 2-(hydroxyethyl(isopropyl)amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(hydroxyethyl(isopropyl)amino)propyl, 3-(methyl(propargyl)amino)propyl, 2-(methyl(propargyl)amino)ethyl, 3-(allyl(methyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 3-(hydroxyethyl(cyclohexyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

102. The compound of claim 101, wherein R is 2-(methyl(t-butyl)amino)ethyl, 2-(methyl(isopropyl)amino)ethyl, 3-(neopentyl-amino)propyl, 2-(isobutyl-amino)ethyl, 2-(ethyl(isopropyl)amino)ethyl, 3-(isopropyl-amino)propyl, 3-(t-butyl-amino)propyl, 2-(isopropyl-amino)ethyl, 3-(cyclopentylamino)propyl, 3-(cyclopentyl(methyl)amino)propyl, 3-(ethylamino)propyl, 3-(ethyl(methyl)amino)propyl, 2-(neopentyl-amino)ethyl, 3-(methyl(isopropyl)amino)propyl, 3-(ethyl(isopropyl)amino)propyl, 3-(propyl(cyclopropylmethyl)amino)propyl, 2-(cyclopropylmethyl-amino)ethyl, or 2-(methyl(isobutyl)amino)ethyl.

103. The compound of claim 102, wherein X₂ is acetylene, furan, thiophene, or pyrazole.

104. The compound of claim 103, wherein the compound is



105. A pharmaceutical composition comprising the compound of any one of claims 65 to 104 and a pharmaceutically acceptable carrier.

106. Use of the compound according to any one of claims 65 to 104 for the inhibition of Hsp90.

107. Use of the compound according to any one of claims 65 to 104 in the manufacture of a medicament for the inhibition of Hsp90.

108. The compound according to any one of claims 65 to 104 for use in the inhibition of Hsp90.

109. Use of the pharmaceutical composition according to claim 105 for the inhibition of Hsp90.

110. The pharmaceutical composition according to claim 105 for use in the inhibition of Hsp90.

111. Use of the compound according to any one of claims 65 to 104 for the treatment of a cancer or a neurodegenerative disease.
112. Use of the compound according to any one of claims 65 to 104 in the manufacture of a medicament for the treatment of a cancer or a neurodegenerative disease.
113. The compound according to any one of claims 65 to 104 for use in the treatment of a cancer or a neurodegenerative disease.
114. Use of the pharmaceutical composition according to claim 105 for the treatment of a cancer or a neurodegenerative disease.
115. The pharmaceutical composition according to claim 105 for use in the treatment of a cancer or a neurodegenerative disease.

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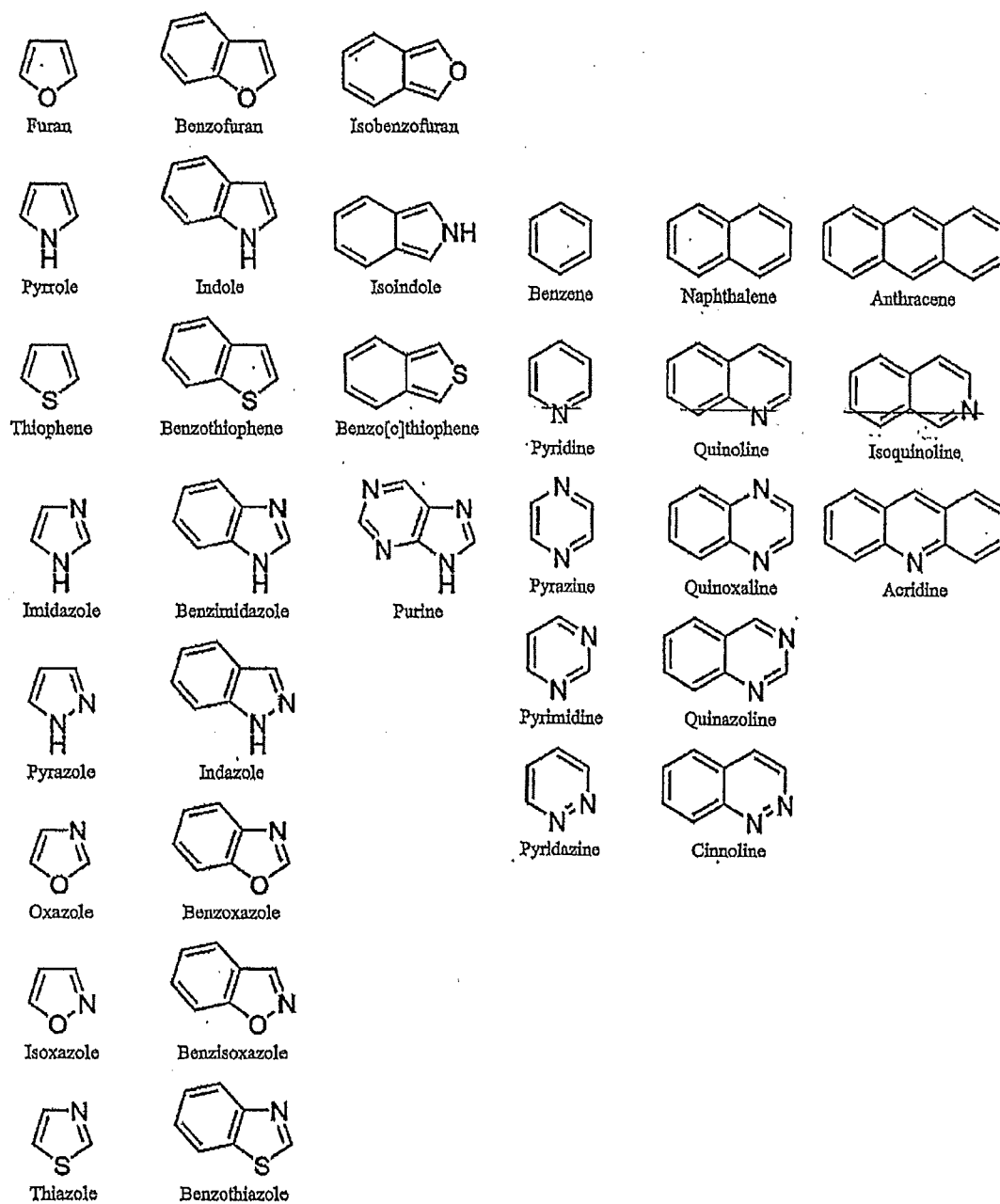


Fig. 1

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Heterocycles

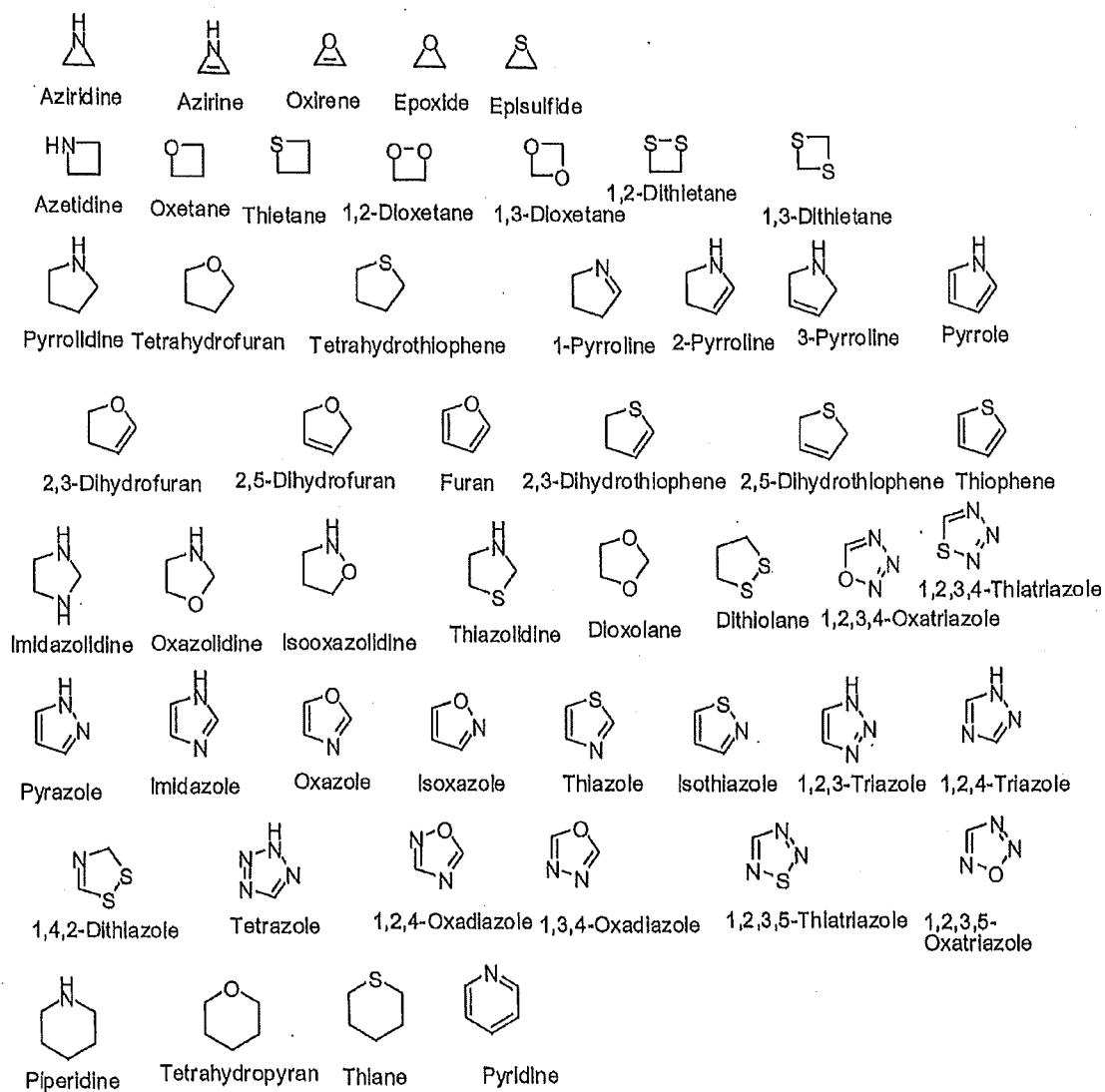
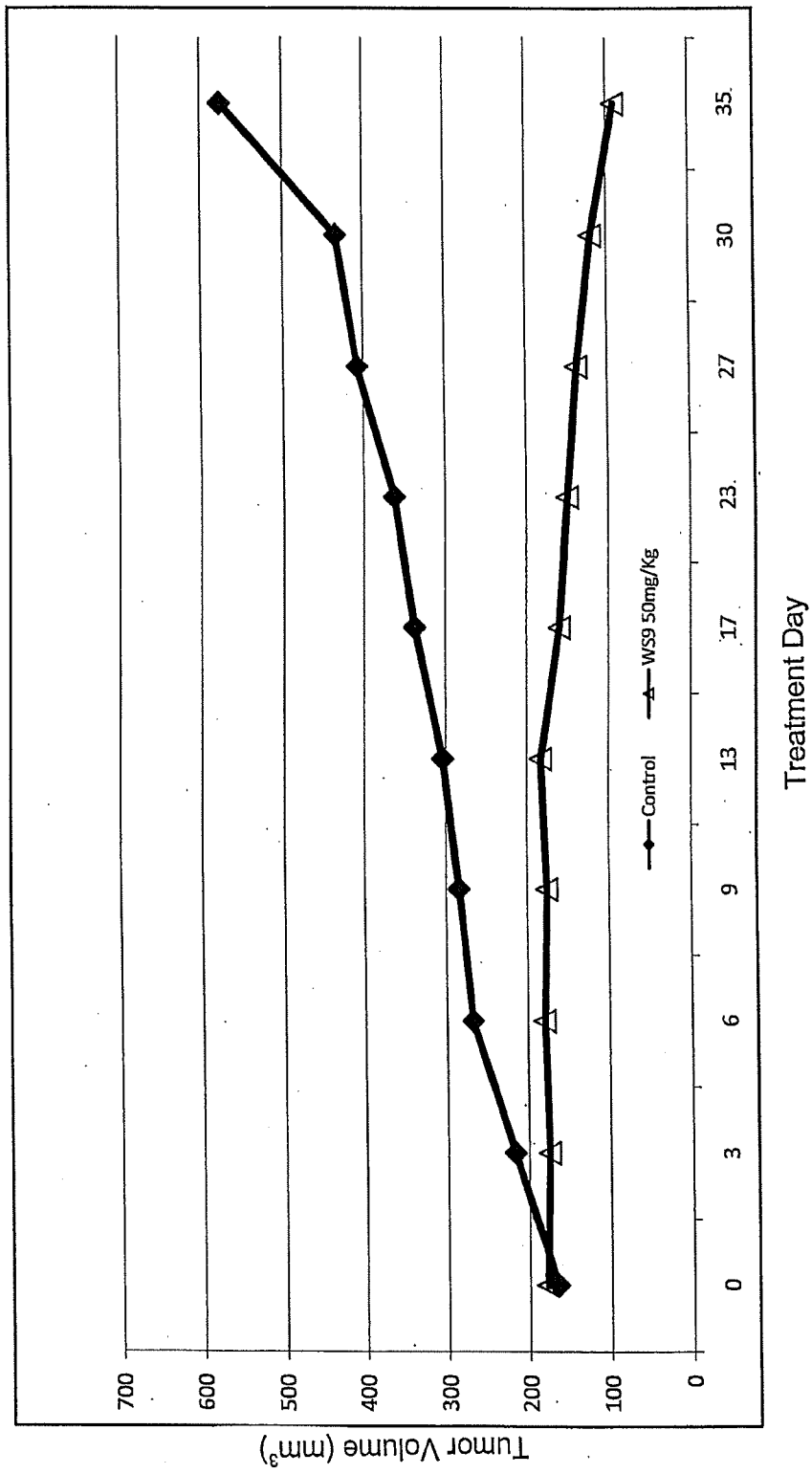
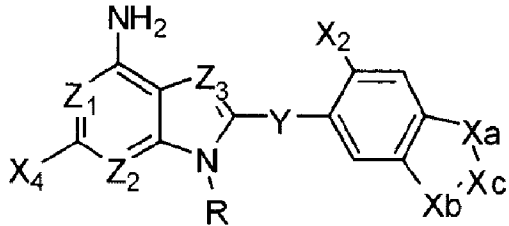


Fig. 2

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Fig. 3





or

