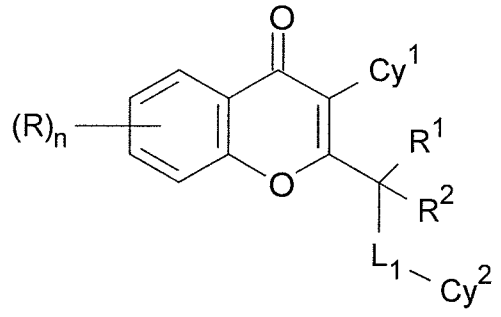
inhibitors. Accordingly, there still remains an unmet and dire need for small molecule kinase modulators in order to regulate and/or modulate transduction of kinases, particularly PI3K and related protein kinase for the treatment of diseases and disorders associated with kinases-mediated events.

SUMMARY

[25] The present disclosure is directed to compounds, which are useful as PI3K protein kinase modulators and in particular as PI3K inhibitors. In one embodiment, the compound of the present disclosure has the formula:



(I)

or a tautomer thereof, N-oxide thereof, pharmaceutically acceptable ester thereof, prodrug thereof, or pharmaceutically acceptable salt thereof, wherein

each occurrence of R is independently selected from hydrogen, halogen, $-OR^a$, CN, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted C_{3-8} cycloalkyl, and substituted or unsubstituted heterocyclic group;

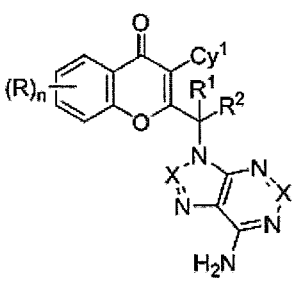
R^1 and R^2 may be the same or different and are independently selected from hydrogen, halogen, and substituted or unsubstituted C_{1-6} alkyl, or both R^1 and R^2 directly bound to a common atom, may be joined to form an oxo group (=O) or a substituted or unsubstituted saturated or unsaturated 3-10 member ring (including the carbon atom to which R^1 and R^2 are bound), which may optionally include one or more heteroatoms which may be the same or different and are selected from O, NR^a and S;

heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted heterocyclylalkyl ring, substituted or unsubstituted guanidine, –$COOR^x$, $-C(O)R^x$, $-C(S)R^x$, $-C(O)NR^xR^y$, $-C(O)ONR^xR^y$, $-NR^yR^z$, $-NR^xCONR^yR^z$, $-N(R^x)SOR^y$, $-N(R^x)SO_2R^y$, $-(=N-N(R^x)R^y)$, $-NR^xC(O)OR^y$, $-NR^xR^y$, $-NR^xC(O)R^y-$, $-NR^xC(S)R^y$ $-NR^xC(S)NR^yR^z$, $-SONR^xR^y-$, $-SO_2NR^xR^y-$, $-OR^x$, $-OR^xC(O)NR^yR^z$, $-OR^xC(O)OR^y-$, $-OC(O)R^x$, $-OC(O)NR^xR^y$, $-R^xNR^yC(O)R^z$, $-R^xOR^y$, $-R^xC(O)OR^y$, $-R^xC(O)NR^yR^z$, $-R^xC(O)R^x$, $-R^xOC(O)R^y$, $-SR^x$, $-SOR^x$, $-SO_2R^x$, and $-ONO_2$, wherein R^x, R^y and R^z in each of the above groups can be hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstituted heterocyclylalkyl ring, or substituted or unsubstituted amino, or any two of R^x, R^y and R^z may be joined to form a substituted or unsubstituted saturated or unsaturated 3-10 membered ring, which may optionally include heteroatoms which may be the same or different and are selected from O, NR^x (e.g., R^x can be hydrogen or substituted or unsubstituted alkyl) or S.

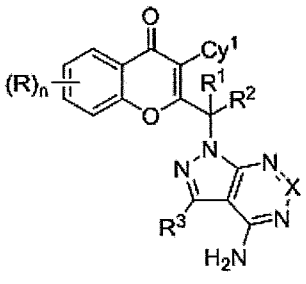
n is an integer from 1 to 4; and

q is 0, 1 or 2.

[42a] In one aspect, there is provided a compound of formula **(IA-I)** or **(IA-II)**:



(IA-I)



(IA-II)

or a tautomer thereof, N-oxide thereof, or pharmaceutically acceptable salt thereof, wherein

each occurrence of R is independently selected from hydrogen, halogen, -OR^a, CN, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted C_{3-8} cycloalkyl, and substituted or unsubstituted heterocyclic group;

R^1 and R^2 may be the same or different and are independently selected from hydrogen, halogen, and substituted or unsubstituted C_{1-6} alkyl, or both R^1 and R^2 directly bound to a common atom, may be joined to form an oxo group (=O) or a substituted or unsubstituted saturated or unsaturated 3-10 member ring (including the carbon atom to which R^1 and R^2 are bound), which may optionally include one or more heteroatoms which may be the same or different and are selected from O, NR^a and S;

Cy^1 is a monocyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclic group, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

each occurrence of R^a may be the same or different and is independently selected from hydrogen, halogen, hydroxy, cyano, substituted or unsubstituted (C_{1-6})alkyl, -NR^cR^d (wherein R^c and R^d are independently hydrogen, halogen, hydroxy, cyano, substituted or unsubstituted (C_{1-6})alkyl, and (C_{1-6})alkoxy) and -OR^c (wherein R^c is substituted or unsubstituted (C_{1-6})alkyl);

n is an integer from 1 to 4; and

each occurrence of X is independently selected from CR^3 or N, wherein

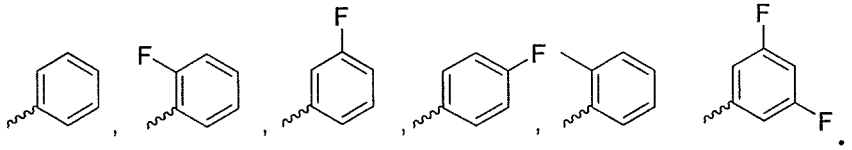
R^3 is hydrogen, hydroxy, halogen, NH_2, iodo, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and wherein the term substituted refers to a substitution selected from hydrogen, hydroxy, halogen, carboxyl, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, $COOR^x$, -$C(O)R^x$, -$C(S)R^x$, -$C(O)ONR^xR^y$, -$NR^xCONR^yR^z$, -$N(R^x)SOR^y$, -$N(R^x)SO_2R^y$, -(=N-$N(R^x)R^y$), - $NR^xC(O)OR^y$, -NR^xR^y, -$NR^xC(O)R^y$-, -

$NR^xC(S)R^y$ $-NR^xC(S)NR^yR^z$, $-SONR^xR^y-$, $-SO_2NR^xR^y-$, $-OR^x$, $-OR^xC(O)NR^yR^z$, $-OR^xC(O)OR^y-$, $-OC(O)R^x$, $-OC(O)NR^xR^y$, $-R^xNR^yC(O)R^z$, $-R^xOR^y$, $-R^xC(O)OR^y$, $-R^xC(O)NR^yR^z$, $-R^xC(O)R^x$, $-R^xOC(O)R^y$, $-SR^x$, $-SOR^x$, $-SO_2R^x$, and $-ONO_2$, wherein R^x, R^y and R^z in each of the above groups can be hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, or or any two of R^x, R^y and R^z together with a common atom to which they are attached may be joined to form a substituted or unsubstituted saturated or unsaturated 3-10 membered ring, which may optionally include heteroatoms which may be the same or different and are selected from O, NR^x or S wherein the substituents in the aforementioned "substituted" groups cannot be further substituted.

[43] Yet another embodiment is a compound having the formula **(IA-I), (IA-II), (IA-III)** or **(IA-IV)** wherein R is selected from hydrogen, halogen, substituted or unsubstituted C_{1-6} alkyl or OR^a.

[44] Yet another embodiment is a compound having the formula **(IA-I), (IA-II), (IA-III)** or **(IA-IV)** wherein R is selected from hydrogen, halogen or OR^a.

[45] Yet another embodiment is a compound having the formula **(IA-I), (IA-II), (IA-III)** or **(IA-IV)** wherein Cy^1 is selected from



[71] Yet another embodiment is a compound having the formula **(IA-VI)** wherein R^1 is ethyl and R^2 is hydrogen.

[72] Yet another embodiment is a compound having the formula **(IA-VI)** wherein R^1 and R^2 are hydrogen.

[73] Yet another embodiment is a compound having the formula **(IA-VI)** wherein each occurrence of X is independently selected from C-H, C-F, C-Cl, C-NH_2 or C-OH.

[74] Further preferred is a compound having the formula **(IA-VI)** wherein X is C-H.

[75] Representative compounds of the present disclosure include those specified below (including in Table 1) and pharmaceutically acceptable salts thereof. The present disclosure should not be construed to be limited to them.

2-[(6-Amino-9H-purin-9-yl) methyl]-6-bromo-3-phenyl-4H-chromen-4-one;

6-Bromo-2-(morpholinomethyl)-3-phenyl-4H-chromen-4-one;

6-Bromo-2-(morpholinomethyl)-3-phenyl-4H-chromen-4-one hydrochloride;

2-[(6-Amino-9H-purin-9-yl) methyl]-3-phenyl-4H-chromen-4-one;

2-(Morpholinomethyl)-3-phenyl-4H-chromen-4-one;

2-(Morpholinomethyl)-3-phenyl-4H-chromen-4-one hydrochloride;

2-[(1H-Benzo[d]imidazol-1-yl) methyl]-6-bromo-3-phenyl-4H-chromen-4-one;

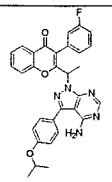
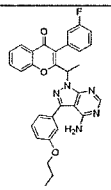
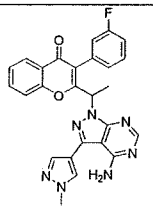
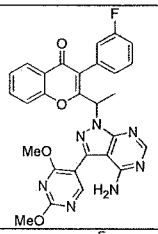
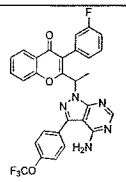
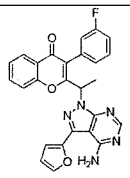
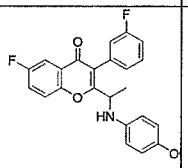
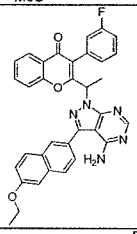
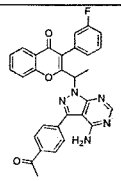
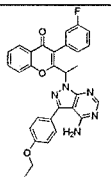
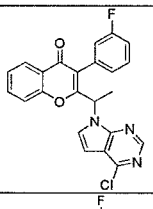
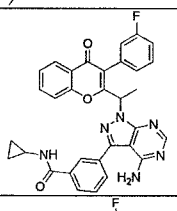
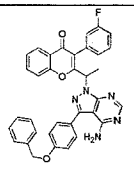
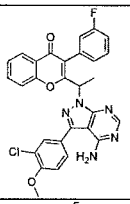
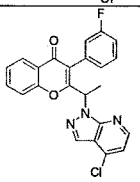
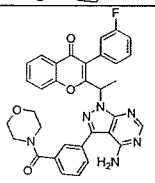
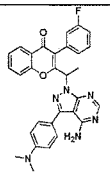
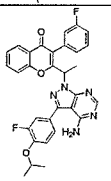
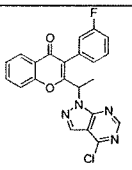
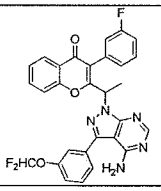
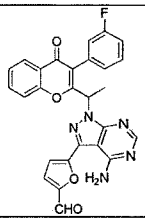
6-Bromo-2-[(4-methyl-1H-benzo[d]imidazol-1-yl) methyl]-3-phenyl-4H-chromen-4-one;

2-[(1H-benzo[d]imidazol-1-yl) methyl]-3-phenyl-4H-chromen-4-one;

2-[(4-methyl-1H-benzo[d]imidazol-1-yl)methyl]-3-phenyl-4H-chromen-4-one;

2-[(6-Chloro-9H-purin-9-yl)methyl]-3-phenyl-4H-chromen-4-one;

6-Bromo-2-[(6-chloro-9H-purin-9-yl)methyl]-3-phenyl-4H-chromen-4-one;

TABLE-1							
Ex.	Structure	Ex.	Structure	Ex.	Structure	Ex.	Structure
144		154		164		174	
145		155		165		175	
146		156		166		176	
147		157		167		177	
148		158		168		178	
179							

[76] Yet another embodiment of the present disclosure is a method for inhibiting PI3K in a patient by administering to the patient an effective amount of at least one compound of the present disclosure (for instance, a compound of formula **(I), (I-A), (I-B), (IA-I), (IA-II) (IA-III)**, **(IA-IV)**, **(IA-V)** or **(IA-VI)** as defined above).

[77] Yet another embodiment of the present disclosure is a method for treating a proliferative disease via modulation of a protein kinase (such as PI3K) by administering to a patient in need of such treatment an effective amount of at least one compound of the present

disclosure. In one embodiment, the compound of the present disclosure inhibits a protein kinase (such as PI3K).

[78] Yet another embodiment of the present disclosure is a method for treating a proliferative disease via modulation of a protein kinase (such as PI3K) by administering to a patient in need of such treatment an effective amount of at least one compound of the present disclosure, in combination (simultaneously or sequentially) with at least one other anti-cancer agent. In one embodiment, the compound of formula **(I), (I-A), (I-B), (IA-I), (IA-II), (IA-III), (IA-IV),(IA-V)** or **(IA-VI)** inhibits a protein kinase (such as PI3K).

[79] More particularly, the compounds of formula ((**I), (I-A), (I-B), (IA-I), (IA-II), (IA-III), (IA-IV), (IA-V)** or **(IA-VI)**and pharmaceutically acceptable esters or salts thereof can be administered for the treatment, prevention and/or amelioration of PI3K and related protein kinase mediated diseases or disorders, including but not limited to, cancer and other proliferative diseases or disorders.

[80] The compounds of the present disclosure are useful in the treatment of a variety of cancers, including, but not limited to, the following:

- carcinoma, including that of the bladder, breast, colon, kidney, liver, lung, including small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous cell carcinoma;
- hematopoietic tumors of lymphoid lineage, including leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkin's lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma;
- hematopoietic tumors of myeloid lineage, including acute and chronic myelogenous leukemias, myelodysplastic syndrome and promyelocytic leukemia;
- tumors of mesenchymal origin, including fibrosarcoma and rhabdomyosarcoma;

- tumors of the central and peripheral nervous system, including astrocytoma, neuroblastoma, glioma and schwannomas; and
- other tumors, including melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer and Kaposi's sarcoma.

[81] Due to the key role of protein kinases in the regulation of cellular proliferation in general, the protein kinase inhibitors of the present disclosure could act as reversible cytostatic agents which may be useful in the treatment of any disease process which features abnormal cellular proliferation, e.g., benign prostatic hyperplasia, familial adenomatosis polyposis, neuro-fibromatosis, atherosclerosis, pulmonary fibrosis, arthritis, psoriasis, glomerulonephritis, restenosis following angioplasty or vascular surgery, hypertrophic scar formation, inflammatory bowel disease, transplantation rejection, endotoxic shock, and fungal infections.

[82] The compounds of the present disclosure as modulators of apoptosis are useful in the treatment of cancer (including but not limited to those types mentioned herein above), viral infections (including but not limited to herpevirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus), prevention of AIDS development in HIV-infected individuals, autoimmune diseases (including but not limited to systemic lupus, erythematosus, autoimmune mediated glomerulonephritis, rheumatoid arthritis, psoriasis, inflammatory bowel disease, and autoimmune diabetes mellitus), neurodegenerative disorders (including but not limited to Alzheimer's disease, AIDS-related dementia, Parkinson's disease, amyotrophic lateral sclerosis, retinitis pigmentosa, spinal muscular atrophy and cerebellar degeneration), myelodysplastic syndromes, aplastic anemia, ischemic injury associated with myocardial infarctions, stroke and reperfusion injury, arrhythmia, atherosclerosis, toxin-induced or alcohol related liver diseases, hematological diseases (including but not limited to chronic anemia and aplastic anemia), degenerative diseases of the musculoskeletal system (including but not limited to osteoporosis and arthritis) aspirin-sensitive rhinosinusitis, cystic fibrosis, multiple sclerosis, kidney diseases and cancer pain.

[83] The compounds of present disclosure can modulate the level of cellular RNA and DNA synthesis. These agents are therefore useful in the treatment of viral

infections (including but not limited to HIV, human papilloma virus, herpesvirus, poxvirus, Epstein-Barr virus, Sindbis virus and adenovirus).

[84] The compounds of the present disclosure are useful in the chemoprevention of cancer. Chemoprevention is defined as inhibiting the development of invasive cancer by either blocking the initiating mutagenic event or by blocking the progression of pre-malignant cells that have already suffered an insult or inhibiting tumor relapse. The compounds are also useful in inhibiting tumor angiogenesis and metastasis. One embodiment of the disclosure is a method of inhibiting tumor angiogenesis or metastasis in a patient in need thereof by administering an effective amount of one or more compounds of the present disclosure.

[85] Another embodiment of the present disclosure is a method of treating an immune system-related disease (e.g., an autoimmune disease), a disease or disorder involving inflammation (e.g., asthma, chronic obstructive pulmonary disease, rheumatoid arthritis, inflammatory bowel disease, glomerulonephritis, neuroinflammatory diseases, multiple sclerosis, uveitis and disorders of the immune system), cancer or other proliferative disease, a hepatic disease or disorder, a renal disease or disorder. The method includes administering an effective amount of one or more compounds of the present disclosure.

[86] Examples of immune disorders include psoriasis, rheumatoid arthritis, vasculitis, inflammatory bowel disease, dermatitis, osteoarthritis, asthma, inflammatory muscle disease, allergic rhinitis, vaginitis, interstitial cystitis, scleroderma, osteoporosis, eczema, allogeneic or xenogeneic transplantation (organ, bone marrow, stem cells and other cells and tissues) graft rejection, graft-versus-host disease, lupus erythematosus, inflammatory disease, type I diabetes, pulmonary fibrosis, dermatomyositis, Sjogren's syndrome, thyroiditis (e.g., Hashimoto's and autoimmune thyroiditis), myasthenia gravis, autoimmune hemolytic anemia, multiple sclerosis, cystic fibrosis, chronic relapsing hepatitis, primary biliary cirrhosis, allergic conjunctivitis and atopic dermatitis.

[87] In one embodiment, the compounds described herein are used as immunosuppresants to prevent transplant graft rejections, allogeneic or xenogeneic transplantation rejection (organ, bone marrow, stem cells, other cells and tissues), and graft - versus - host disease. In other embodiments, transplant graft rejections result from tissue or organ transplants. In further embodiments, graft-versus-host disease results from bone marrow or stem cell transplantation. One embodiment is a method of preventing or

decreasing the risk of transplant graft rejection, allogeneic or xenogeneic transplantation rejection (organ, bone marrow, stem cells, other cells and tissues), or graft - versus - host disease by administering an effective amount of one or more compounds of the present disclosure.

[88] The compounds of the present disclosure are also useful in combination (administered together or sequentially) with known anti-cancer treatments such as radiation therapy or with cytostatic or cytotoxic or anticancer agents, such as for example, but not limited to, DNA interactive agents, such as cisplatin or doxorubicin; topoisomerase II inhibitors, such as etoposide; topoisomerase I inhibitors such as CPT-11 or topotecan; tubulin interacting agents, such as paclitaxel, docetaxel or the epothilones (for example ixabepilone), either naturally occurring or synthetic; hormonal agents, such as tamoxifen; thymidilate synthase inhibitors, such as 5-fluorouracil; and anti-metabolites, such as methotrexate, other tyrosine kinase inhibitors such as Iressa and OSI-774; angiogenesis inhibitors; EGF inhibitors; VEGF inhibitors; CDK inhibitors; SRC inhibitors; c-Kit inhibitors; Her1/2 inhibitors and monoclonal antibodies directed against growth factor receptors such as erbitux (EGF) and herceptin (Her2) and other protein kinase modulators as well.

[89] The compounds of the present disclosure are also useful in combination (administered together or sequentially) with one or more steroidal anti-inflammatory drugs, non-steroidal anti-inflammatory drugs (NSAIDs) or Immune Selective Anti-Inflammatory Derivatives (ImSAIDs).

[90] The disclosure further provides a pharmaceutical composition comprising one or more compounds of the present disclosure (such as a compound having formula **(I), (I-A), (I-B), (IA-I), (IA-II), (IA-III), (IA-IV), (IA-V)** or **(IA-VI)**) together with a pharmaceutically acceptable carrier. The pharmaceutical composition may further comprise one or more of the active ingredients identified above, such as other anti-cancer agents. In one embodiment, the pharmaceutical composition includes a therapeutically effective amount of one or more compounds of formula **(I), (I-A), (I-B), (IA-I), (IA-II) (IA-III), (IA-IV), (IA-V)** or **(IA-VI)**.

[90a] In another aspect, there is provided pharmaceutical composition, comprising a compound as defined herein and a pharmaceutically acceptable carrier.

[91] Yet another embodiment is a method of treating leukemia in a patient in need thereof by administering a therapeutically effective amount of a compound of the present disclosure. For example, the compounds of the present disclosure are effective for

treating chronic lymphocytic leukemia (CLL), non-Hodgkin lymphoma (NHL), acute myeloid leukemia (AML), multiple myeloma (MM), small lymphocytic lymphoma (SLL), and indolent non-Hodgkin's lymphoma (I-NHL).

[92] Yet another embodiment is a method of treating allergic rhinitis in a patient in need thereof by administering a therapeutically effective amount of a compound of the present disclosure.

[92a] In another aspect, there is provided a compound as defined herein for use in the treatment of a disease, disorder or condition selected from inflammation, glomerulonephritis, uveitis, hepatic diseases or disorders, renal diseases or disorders, chronic obstructive pulmonary disease, rheumatoid arthritis, inflammatory bowel disease, vasculitis, dermatitis, osteoarthritis, inflammatory muscle disease, allergic rhinitis, vaginitis, interstitial cystitis, scleroderma, osteoporosis, eczema, allogeneic or xenogeneic transplantation, graft rejection, graft-versus-host disease, lupus erythematosus, pulmonary fibrosis, dermatomyositis, thyroiditis, myasthenia gravis, autoimmune hemolytic anemia, cystic fibrosis, chronic relapsing hepatitis, primary biliary cirrhosis, allergic conjunctivitis, hepatitis, atopic dermatitis, asthma, Sjogren's syndrome, organ transplant rejection, multiple sclerosis, Guillain-Barre, autoimmune uveitis, autoimmune hemolytic anemia, pernicious anemia, autoimmune thrombocytopenia, temporal arteritis, anti-phospholipid syndrome, vasculitides such as Wegener's granulomatosis, Behcet's disease, psoriasis, dermatitis herpetiformis, pemphigus vulgaris, vitiligo, Crohn's disease, colitis, ulcerative colitis, primary biliary cirrhosis, autoimmune hepatitis, Type 1 or immune-mediated diabetes mellitus, Grave's disease, Hashimoto's thyroiditis, autoimmune oophoritis and orchitis, autoimmune disorder of the adrenal gland, systemic lupus erythematosus, polymyositis, dermatomyositis, ankylosing spondylitis, transplant rejection, skin graft rejection, arthritis, bone diseases associated with increased bone resorption, ileitis, Barrett's syndrome, adult respiratory distress syndrome, chronic obstructive airway disease; corneal dystrophy, trachoma, onchocerciasis, sympathetic ophthalmitis, endophthalmitis; gingivitis, periodontitis; tuberculosis; leprosy; uremic complications, nephrosis; sclerodermatitis, psoriasis, chronic demyelinating diseases of the nervous system, AIDS-related neurodegeneration, Alzheimer's disease, infectious meningitis, encephalomyelitis, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis viral or autoimmune encephalitis; autoimmune disorders,

immune-complex vasculitis, systemic lupus and erythematodes; systemic lupus erythematosus (SLE); cardiomyopathy, ischemic heart disease hypercholesterolemia, atherosclerosis, preeclampsia; chronic liver failure, brain and spinal cord trauma, cancer, hematopoietic tumors of lymphoid lineage, leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkin's lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma; hematopoietic tumors of myeloid lineage, acute myelogenous leukemias, chronic myelogenous leukemias, myelodysplastic syndrome, promyelocytic leukemia; carcinoma of the bladder, carcinoma of the breast, carcinoma of the colon, carcinoma of the kidney, carcinoma of the liver, carcinoma of the lung, small cell lung cancer, esophageal cancer, gall bladdercancer, ovarian cancer, pancreatic cancer, stomach cancer, cervical cancer, thyroid cancer, prostate cancer, skin cancer, squamous cell carcinoma; tumors of mesenchymal origin, fibrosarcoma, rhabdomyosarcoma; tumors of the central and peripheral nervous system, astrocytoma, neuroblastoma, glioma, schwannoma; melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer, Kaposi's sarcoma, chronic lymphocytic leukemia, multiple myelomas which includes smoldering multiple myeloma, nonsecretory myeloma, osteosclerotic myeloma, plasma cell leukemia, solitary plasmacytoma, extramedullary plasmacytoma, Chronic Lymphocytic Leukemia (CLL); Lymphoma Non-Hodgkin (NHL); Acute Myeloid Leukemia (AML); Multiple Myeloma (MM), Small Lymphocytic Lymphoma (SLL), or Indolent Non-Hodgkin's Lymphoma (I-NHL).

DETAILED DESCRIPTION

[93] As used herein the following definitions shall apply unless otherwise indicated. Further many of the groups defined herein can be optionally substituted. The listing of substituents in the definition is exemplary and is not to be construed to limit the substituents defined elsewhere in the specification.

[94] The term "alkyl" refers to a straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, containing no unsaturation, having from one to eight carbon atoms, and which is attached to the rest of the molecule by a single bond, e.g., methyl, ethyl, n-propyl, 1-methylethyl (isopropyl), n-butyl, n-pentyl, and 1,1-dimethylethyl (t-butyl). The term "(C_{1-6})alkyl" refers to an alkyl group as defined above having up to 6 carbon atoms.

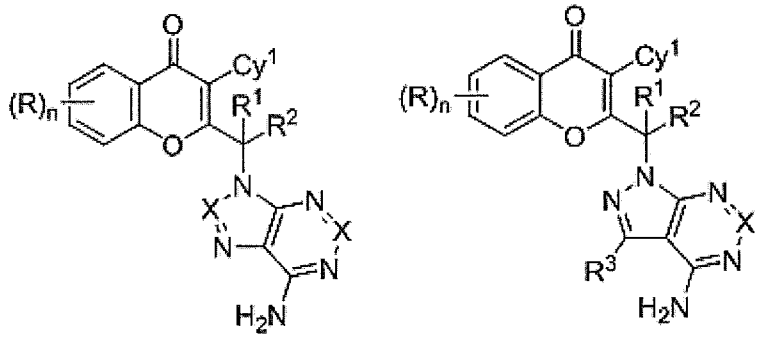
[95] The term "alkenyl" refers to an aliphatic hydrocarbon group containing a carbon-carbon double bond and which may be a straight or branched or branched chain having about 2 to about 10 carbon atoms, e.g., ethenyl, 1-propenyl, 2-propenyl (allyl), iso-propenyl, 2-methyl-1-propenyl, 1-butenyl, and 2-butenyl. The term "(C_{2-6})alkenyl" refers to an alkenyl group as defined above having up to 6 carbon atoms.

[96] The term "alkynyl" refers to a straight or branched chain hydrocarbyl radical having at least one carbon-carbon triple bond, and having in the range of 2 to up to 12 carbon atoms (with radicals having in the range of 2 to up to 10 carbon atoms presently being preferred) e.g., ethynyl, propynyl, and butnyl. The term "(C_{2-6}) alkynyl" refers to an alkynyl group as defined above having up to 6 carbon atoms.

[97] The term "alkoxy" denotes an alkyl, cycloalkyl, or cycloalkylalkyl group as defined above attached via an oxygen linkage to the rest of the molecule. The term

We claim:

1. A compound of formula **(IA-I)** or **(IA-II)**:



(IA-I) **(IA-II)**

or a tautomer thereof, N-oxide thereof, or pharmaceutically acceptable salt thereof, wherein

each occurrence of R is independently selected from hydrogen, halogen, $-OR^a$, CN, substituted or unsubstituted C_{1-6} alkyl, substituted or unsubstituted C_{2-6} alkenyl, substituted or unsubstituted C_{2-6} alkynyl, substituted or unsubstituted C_{3-8} cycloalkyl, and substituted or unsubstituted heterocyclic group;

R^1 and R^2 may be the same or different and are independently selected from hydrogen, halogen, and substituted or unsubstituted C_{1-6} alkyl, or both R^1 and R^2 directly bound to a common atom, may be joined to form an oxo group (=O) or a substituted or unsubstituted saturated or unsaturated 3-10 member ring (including the carbon atom to which R^1 and R^2 are bound), which may optionally include one or more heteroatoms which may be the same or different and are selected from O, NR^a and S;

Cy^1 is a monocyclic group selected from substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclic group, substituted or unsubstituted aryl and substituted or unsubstituted heteroaryl;

each occurrence of R^a may be the same or different and is independently selected from hydrogen, halogen, hydroxy, cyano, substituted or unsubstituted (C_{1-6})alkyl, $-NR^cR^d$ (wherein R^c and R^d are independently hydrogen, halogen, hydroxy, cyano, substituted or unsubstituted

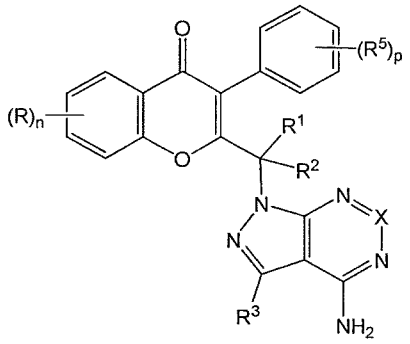
(C_{1-6})alkyl, and (C_{1-6})alkoxy) and -OR^c (wherein R^c is substituted or unsubstituted (C_{1-6})alkyl);

n is an integer from 1 to 4; and

each occurrence of X is independently selected from CR^3 or N, where in R^3 is hydrogen, hydroxy, halogen, NH_2, iodo, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, and wherein the term substituted refers to a substitution selected from hydrogen, hydroxy, halogen, carboxyl, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl,–$COOR^x$, -$C(O)R^x$, -$C(S)R^x$, -$C(O)ONR^xR^y$, -$NR^xCONR^yR^z$, -$N(R^x)SOR^y$, -$N(R^x)SO_2R^y$, -(=N-$N(R^x)R^y$), - $NR^xC(O)OR^y$, -NR^xR^y, -$NR^xC(O)R^y$-, -$NR^xC(S)R^y$ - $NR^xC(S)NR^yR^z$, -$SONR^xR^y$-, -$SO_2NR^xR^y$-, -OR^x, -$OR^xC(O)NR^yR^z$, -$OR^xC(O)OR^y$-, -$OC(O)R^x$, -$OC(O)NR^xR^y$, - $R^xNR^yC(O)R^z$, -R^xOR^y, -$R^xC(O)OR^y$, -$R^xC(O)NR^yR^z$, -$R^xC(O)R^x$, -$R^xOC(O)R^y$, -SR^x, -SOR^x, -SO_2R^x, and -ONO_2, wherein R^x, R^y and R^z in each of the above groups can be hydrogen atom, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted cycloalkenyl,

substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, or or any two of R^x, R^y and R^z together with a common atom to which they are attached may be joined to form a substituted or unsubstituted saturated or unsaturated 3-10 membered ring, which may optionally include heteroatoms which may be the same or different and are selected from O, NR^x or S wherein the substituents in the aforementioned "substituted" groups cannot be further substituted.

2. A compound of claim 1, wherein the compound has the formula (IA-V)



(IA-V)

or a pharmaceutically acceptable salt thereof,

wherein

R, R^1, R^2, R^3 and X are as defined in claim 1;

each occurrence of R^5 is hydrogen, C_{1-6} alkyl or halogen;

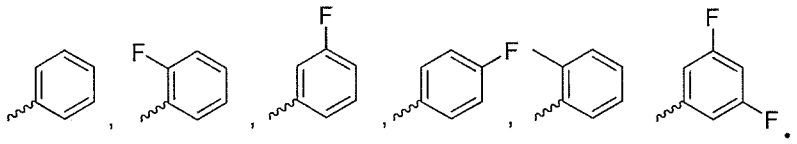
n is 0, 1, 2, 3 or 4; and

p is 0, 1, 2, 3, 4 or 5.

3. A compound of claim 1 or 2, wherein R is hydrogen, halogen, substituted or unsubstituted C_{1-6} alkyl, or OR^a.

4. A compound of claim 3, wherein R^a is alkyl.

5. A compound of claim 1, wherein Cy^1 is selected from:



6. A compound of any one of claims 1-5, wherein R^1 and R^2 represent hydrogen or substituted or unsubstituted C_{1-6} alkyl.

7. A compound of claim 1 or 2, wherein R^3 is iodo, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

8. A compound of claim 1 or 2, wherein X is CR^3 and each occurrence of R^3 is independently hydrogen, halogen, hydroxyl or NH_2.

9. A compound of claim 8, wherein R^3 is hydrogen.

10. A compound of any one of claims 1-9, wherein the compound is selected from:

2-[(6-Amino-9H-purin-9-yl) methyl]-6-bromo-3-phenyl-4H-chromen-4-one;

2-[(6-Amino-9H-purin-9-yl) methyl]-3-phenyl-4H-chromen-4-one;

2-((4-Amino-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)-6-bromo-3-phenyl-4H-chromen-4-one ;

2-[(6-Amino-9H-purin-9-yl)methyl]-6-bromo-3-(4-fluorophenyl)-4H-chromen-4-one ;

2-[(6-Amino-9H-purin-9-yl)methyl]-3-(4-fluorophenyl)-4H-chromen-4-one ;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-6-bromo-3-phenyl-4H-chromen-4-one;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-6-bromo-3-phenyl-4H-chromen-4-one ;

2-((6-Amino-9H-purin-9-yl)methyl)-6-methoxy-3-phenyl-4H-chromen-4-one;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-6-bromo-3-(2-fluorophenyl)-4H-chromen-4-one;

2-((6-Amino-9H-purin-9-yl)methyl)-6-bromo-3-(2-fluorophenyl)-4H-chromen-4-one ;

2-(1-(4-Amino-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-3-phenyl-4H-chromen-4-one ;

2-(1-(6-Amino-9H-purin-9-yl) propyl)-3-phenyl-4H-chromen-4-one;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((6-Amino-9H-purin-9-yl)methyl)-3-(2-fluorophenyl)-4H-chromen-4-one ;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-3-(2-fluorophenyl)-4H-chromen-4-one ;

2-(1-(6-Amino-9H-purin-9-yl)propyl)-3-(2-fluorophenyl)-4H-chromen-4-one;

2-(1-(6-amino-9H-purin-9-yl)propyl)-3-(3-fluorophenyl)-4H-chromen-4-one ;

2-(1-(6-Amino-9H-purin-9-yl)propyl)-3-(4-fluorophenyl)-4H-chromen-4-one ;

2-(1-(6-amino-9H-purin-9-yl)propyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-3-(4-fluorophenyl)-4H-chromen-4-one;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-(1-(4-Amino-3-(3-methoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-Amino-3-(3-hydroxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-3-o-tolyl-4H-chromen-4-one;

2-(1-(6-amino-9H-purin-9-yl)ethyl)-6-fluoro-3-(2-fluorophenyl)-4H-chromen-4-one;

2-(1-(6-Amino-9H-purin-9-yl)ethyl)-3-(3,5-difluorophenyl)-4H-chromen-4-one;

2-(1-(6-amino-9H-purin-9-yl)ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-Amino-3-(3-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-Amino-3-(3-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(3-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-Amino-3-iodo-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-iodo-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-iodo-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-iodo-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-iodo-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-iodo-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-iodo-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) propyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(pyridin-3-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(3-hydroxyprop-1-ynyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(1H-pyrazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(3-(hydroxymethyl) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(1H-indazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(3-fluorophenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one

2-((4-amino-3-(3-hydroxypropyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

N-(3-(4-amino-1-((4-oxo-3-phenyl-4H-chromen-2-yl) methyl)-1H-pyrazolo [3, 4-d] pyrimidin-3-yl) phenyl) acetamide;

2-((4-amino-3-(3-fluoro-5-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(3-fluoro-5-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1H-pyrazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(3-hydroxy-3-methylbut-1-ynyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(1H-pyrazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(3-fluoro-5-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1H-indazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 5-dimethyl-1H-pyrazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2-(hydroxymethyl) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-fluoro-3-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-fluoro-3-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-hydroxyprop-1-ynyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-fluoro-4-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-fluoro-4-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-chloro-5-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-chloro-5-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-(trifluoromethoxy) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((6-amino-9H-purin-9-yl) methyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-fluoro-2-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-fluoro-2-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3-aminophenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-((4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(2-aminopyrimidin-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1H-indol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-chloro-3-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-chloro-3-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2-chloro-5-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2-chloro-5-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 4-dimethoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 4-dihydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1H-indol-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-Amino-3-(3-methyl-1H-indol-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

tert-butyl-(5-(4-amino-1-(1-(3-(3-fluorophenyl)-4-oxo-4H-chromen-2-yl) ethyl)-1H-pyrazolo [3, 4-d] pyrimidin-3-yl) thiophen-2-yl) methylcarbamate

2-(1-(4-amino-3-(5-(aminomethyl) thiophen-2-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indazol-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

N-(4-(4-amino-1-(1-(3-(3-fluorophenyl)-4-oxo-4H-chromen-2-yl) ethyl)-1H-pyrazolo [3, 4-d] pyrimidin-3-yl) phenyl) acetamide;

2-(1-(4-amino-3-(4-aminophenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2, 3-dihydrobenzofuran-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-ethyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2-methoxypyrimidin-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

4-(4-amino-1-(1-(3-(3-fluorophenyl)-4-oxo-4H-chromen-2-yl) ethyl)-1H-pyrazolo [3, 4-d] pyrimidin-3-yl) thiophene-2-carbaldehyde;

2-(1-(4-amino-3-(5-(hydroxymethyl) thiophen-3-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2-methyl-1H-benzo[d]imidazol-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) propyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methyl-1H-indol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((6-amino-9H-purin-9-yl) methyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-((6-amino-9H-purin-9-yl) methyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3-fluoro-5-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3-fluoro-5-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(1H-pyrazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-6-fluoro-3-phenyl-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 5-difluoro-4-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 5-difluoro-4-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3, 5-difluoro-4-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

2-((4-amino-3-(3, 5-difluoro-4-hydroxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) methyl)-6-fluoro-3-(3-fluorophenyl)-4H-chromen-4-one;

(+)-2-(1-(4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

(-)-2-(1-(4-amino-3-(3-methyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 5-dimethoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-methoxy-3, 5-dimethylphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2-fluoro-5-isopropoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2, 3-dihydrobenzo[b] [1, 4] dioxin-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1-benzyl-1H-pyrazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2-methylpyridin-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 4-dihydro-2H-benzo[b] [1, 4] dioxepin-7-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(6-morpholinopyridin-3-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(dibenzo [b, d] furan-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-(benzyloxy)-3-chlorophenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-chloro-4-isopropoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-(dimethylamino) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-ethoxy-3-fluorophenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-isopropoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-(trifluoromethoxy) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(3-(4-acetylphenyl)-4-amino-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-(benzyloxy) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-(dimethylamino) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-(methylsulfonyl) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-ethoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(benzo[b]thiophen-2-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(5-chlorothiophen-2-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3, 5-dimethylisoxazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-propoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(furan-2-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(4-ethoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-chloro-4-methoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-fluoro-4-isopropoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(6-fluoropyridin-3-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(pyrimidin-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-(methoxymethyl) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(6-hydroxynaphthalen-2-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-isopropoxyphenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1-methyl-1H-pyrazol-4-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(1, 3-dimethyl-1H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2, 3-dimethyl-2H-indazol-6-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(6-methoxynaphthalen-2-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(benzo[b]thiophen-3-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(2, 4-dimethoxypyrimidin-5-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(6-ethoxynaphthalen-2-yl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

3-(4-amino-1-(1-(3-(3-fluorophenyl)-4-oxo-4H-chromen-2-yl) ethyl)-1H-pyrazolo [3, 4-d] pyrimidin-3-yl)-N-cyclopropylbenzamide;

2-(1-(4-amino-3-(3-(morpholine-4-carbonyl) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

2-(1-(4-amino-3-(3-(difluoromethoxy) phenyl)-1H-pyrazolo [3, 4-d] pyrimidin-1-yl) ethyl)-3-(3-fluorophenyl)-4H-chromen-4-one;

5-(4-amino-1-(1-(3-(3-fluorophenyl)-4-oxo-4H-chromen-2-yl) ethyl)-1H-pyrazolo [3, 4-d] pyrimidin-3-yl) furan-2-carbaldehyde;

2-[(6-Amino-9H-purin-9-yl)methyl]-6-bromo-3-o-tolyl-4H-chromen-4-one;

and pharmaceutically acceptable salts thereof.

11. A pharmaceutical composition, comprising a compound of any one of claims 1-10 and a pharmaceutically acceptable carrier.

12. The pharmaceutical composition of claim 11, further comprising one or more additional therapeutic agents selected from anti-cancer agents, anti-inflammatory agents, immunosuppressive agents, steroids, non-steroidal anti-inflammatory agents, antihistamines, analgesics, and mixtures thereof.

13. Compound of any one of claims 1-10 for use in the treatment of a disease, disorder or condition selected from inflammation, glomerulonephritis, uveitis, hepatic diseases or disorders, renal diseases or disorders, chronic obstructive pulmonary disease, rheumatoid arthritis, inflammatory bowel disease, vasculitis, dermatitis, osteoarthritis, inflammatory muscle disease, allergic rhinitis, vaginitis, interstitial cystitis, scleroderma, osteoporosis, eczema, allogeneic or xenogeneic transplantation, graft rejection, graft-versus-host disease, lupus erythematosus, pulmonary fibrosis, dermatomyositis, thyroiditis, myasthenia gravis, autoimmune hemolytic anemia, cystic fibrosis, chronic relapsing hepatitis, primary biliary cirrhosis, allergic conjunctivitis, hepatitis, atopic dermatitis, asthma, Sjogren's syndrome, organ transplant rejection, multiple sclerosis, Guillain-Barre, autoimmune uveitis, autoimmune hemolytic anemia, pernicious anemia, autoimmune thrombocytopenia, temporal arteritis, anti-phospholipid syndrome, vasculitides such as Wegener's granulomatosis, Behcet's disease, psoriasis, dermatitis herpetiformis, pemphigus vulgaris, vitiligo, Crohn's disease, colitis, ulcerative colitis, primary biliary cirrhosis, autoimmune hepatitis, Type 1 or immune-mediated diabetes mellitus, Grave's disease, Hashimoto's thyroiditis, autoimmune oophoritis and orchitis, autoimmune disorder of the adrenal gland, systemic lupus erythematosus, polymyositis, dermatomyositis, ankylosing spondylitis, transplant rejection, skin graft rejection, arthritis, bone diseases associated with increased bone resorption, ileitis, Barrett's syndrome, adult respiratory distress syndrome, chronic obstructive airway disease; corneal dystrophy, trachoma, onchocerciasis, sympathetic ophthalmitis, endophthalmitis; gingivitis, periodontitis; tuberculosis; leprosy; uremic complications, nephrosis; sclerodermatitis, psoriasis, chronic demyelinating diseases of the nervous system, AIDS-related neurodegeneration, Alzheimer's disease, infectious meningitis, encephalomyelitis, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis viral or autoimmune encephalitis; autoimmune disorders, immune-complex vasculitis, systemic lupus and erythematodes; systemic lupus erythematosus (SLE); cardiomyopathy, ischemic heart disease hypercholesterolemia, atherosclerosis, preeclampsia; chronic liver failure, brain and spinal cord trauma, cancer, hematopoietic tumors of lymphoid lineage, leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T-cell lymphoma, Hodgkin's lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma; hematopoietic tumors of myeloid lineage, acute myelogenous leukemias, chronic

myelogenous leukemias, myelodysplastic syndrome, promyelocytic leukemia; carcinoma of the bladder, carcinoma of the breast, carcinoma of the colon, carcinoma of the kidney, carcinoma of the liver, carcinoma of the lung, small cell lung cancer, esophageal cancer, gall bladdercancer, ovarian cancer, pancreatic cancer, stomach cancer, cervical cancer, thyroid cancer, prostate cancer, skin cancer, squamous cell carcinoma; tumors of mesenchymal origin, fibrosarcoma, rhabdomyosarcoma; tumors of the central and peripheral nervous system, astrocytoma, neuroblastoma, glioma, schwannoma; melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer, Kaposi's sarcoma, chronic lymphocytic leukemia, multiple myelomas which includes smoldering multiple myeloma, nonsecretory myeloma, osteosclerotic myeloma, plasma cell leukemia, solitary plasmacytoma, extramedullary plasmacytoma, Chronic Lymphocytic Leukemia (CLL); Lymphoma Non-Hodgkin (NHL); Acute Myeloid Leukemia (AML); Multiple Myeloma (MM), Small Lymphocytic Lymphoma (SLL), or Indolent Non-Hodgkin's Lymphoma (I-NHL).

14. The compound for use of claim 13, wherein the treatment of the disease is performed simultaneously or sequentially with at least one other anti-cancer agent, anti-inflammatory agent, immunosuppressive agent, steroid, non-steroidal anti-inflammatory agent, antihistamine, analgesic, or a mixture thereof.