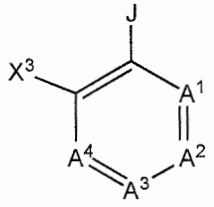
673-684 (2012)). Accordingly, there is an ongoing medical need to develop new drugs to treat these indications.

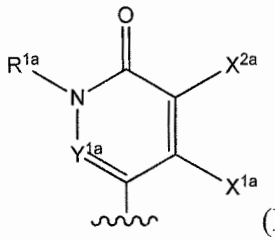
SUMMARY

In one aspect, the present ~~invention~~ disclosure relates to compounds of Formula (I) or a pharmaceutically acceptable salt thereof,

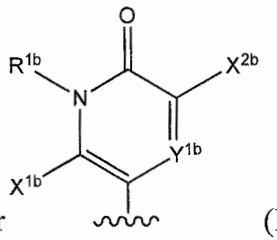


I

Wherein J is a group of formula IIa or IIb:



(IIa) or



(IIb);

wherein

R^{1a} is C_1-C_3 alkyl, C_2-C_3 alkylene-OH, or C_1-C_3 haloalkyl;

Y^{1a} is N or CR^{xa}, wherein R^{xa} is H, halo, C_1-C_3 alkyl, -O-C_1-C_3 alkyl, C_1-C_3 haloalkyl, -O-C_1-C_3 haloalkyl, aryl, aryl-C_1-C_3alkylene-OH, aryl-C_1-C_3alkylene-heterocycloalkyl, $C(O)NR^{10}R^{12}$, wherein heterocycloalkyl of aryl-C_1-C_3alkylene-heterocycloalkyl may be substituted with one to three C_1-C_3alkyl,

R^{1b} is H, C_1-C_3 alkyl, C_2-C_3 alkylene-OH, or C_1-C_3 haloalkyl;

Y^{1b} is N or CR^{xb}, wherein R^{xb} is heteroaryl, H, halo, C_1-C_3 alkyl, -O-C_1-C_3 alkyl, C_1-C_3 haloalkyl, -O-C_1-C_3 haloalkyl, aryl, aryl-C_1-C_3alkylene-OH, aryl-C_1-C_3alkylene-heterocycloalkyl, $C(O)NR^{10}R^{12}$, wherein heterocycloalkyl of aryl-C_1-C_3alkylene-heterocycloalkyl may be substituted with one to three C_1-C_3alkyl; wherein said heteroaryl may be substituted with one to three groups selected from the group consisting of: C_1-C_6 alkyl, C_1-C_3alkylene-aryl, C_1-C_3alkylene-heteroaryl, C_1-C_3alkylene-heterocycloalkyl, COOH, and COO-C_1-C_4alkyl,

In another aspect, the present ~~invention~~ disclosure relates to pharmaceutical compositions comprising a pharmaceutically acceptable exicipient and a therapeutically effective amount of a compound of formula I, or a pharmaceutically acceptable salt thereof.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating cancer in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable acceptable salt thereof, to a subject in need thereof. In certain embodiments, the cancer is selected from the group consisting of: acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia (monocytic, myeloblastic, adenocarcinoma, angiosarcoma, astrocytoma, myelomonocytic and promyelocytic), acute t-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, diffuse large B-cell lymphoma, dysproliferative changes (dysplasias and metaplasias), embryonal carcinoma, endometrial cancer, endotheliosarcoma, ependymoma, epithelial carcinoma, erythroleukemia, esophageal cancer, estrogen-receptor positive breast cancer, essential thrombocythemia, Ewing's tumor, fibrosarcoma, follicular lymphoma, germ cell testicular cancer, glioma, glioblastoma, gliosarcoma, heavy chain disease, hemangioblastoma, hepatoma, hepatocellular cancer, hormone insensitive prostate cancer, leiomyosarcoma, leukemia, liposarcoma, lung cancer, lymphagioendotheliosarcoma, lymphangiosarcoma, lymphoblastic leukemia, lymphoma (Hodgkin's and non-Hodgkin's), malignancies and hyperproliferative disorders of the bladder, breast, colon, lung, ovaries, pancreas, prostate, skin and uterus, lymphoid malignancies of T-cell or B-cell origin, leukemia, lymphoma, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, multiple myeloma, myelogenous leukemia, myeloma, myxosarcoma, neuroblastoma, NUT midline carcinoma (NMC), non-small cell lung cancer, oligodendroglioma, oral cancer, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rectal cancer, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, sebaceous gland carcinoma, seminoma, skin cancer, small cell lung carcinoma, solid tumors (carcinomas and sarcomas), small cell lung cancer, stomach cancer, squamous cell carcinoma, synovioma, sweat gland carcinoma, thyroid cancer, Waldenström's macroglobulinemia, testicular tumors, uterine cancer and Wilms' tumor. In

certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating a disease or condition in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable acceptable salt thereof, to a subject in need thereof, wherein said disease or condition is selected from the group consisting of: Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, chronic obstructive pulmonary disease (COPD), Crohn's disease, dermatitis, eczema, giant cell arteritis, glomerulonephritis, hepatitis, hypophysitis, inflammatory bowel disease, Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis, myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating a chronic kidney disease or condition in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof, wherein said disease or condition is selected from the group consisting of: diabetic nephropathy, hypertensive nephropathy, HIV-associated nephropathy, glomerulonephritis, lupus nephritis, IgA nephropathy, focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, polycystic kidney disease and tubular interstitial nephritis. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating an acute kidney injury or disease or condition in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof, wherein said acute kidney injury or disease or condition is selected from the group consisting of: ischemia-reperfusion induced, cardiac and major

surgery induced, percutaneous coronary intervention induced, radio-contrast agent induced, sepsis induced, pneumonia induced, and drug toxicity induced. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating AIDS in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable acceptable salt thereof, to a subject in need thereof. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating obesity in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable acceptable salt thereof, to a subject in need thereof. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating type II diabetes in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable acceptable salt thereof, to a subject in need thereof. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of preventing conception by inhibiting spermatogenesis in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

A further aspect of the ~~invention~~ disclosure provides the use of a compound of formula (I), alone or in combination with a second active pharmaceutical agent, in the manufacture of a medicament for treating or preventing conditions and disorders disclosed herein, with or without a pharmaceutically acceptable carrier.

Pharmaceutical compositions comprising a compound of formula (I), or a pharmaceutically acceptable salt, alone or in combination with a second active pharmaceutical agent, are also provided.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered to a subject in need thereof

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating a disease or condition , wherein said disease or condition is selected from the group consisting of: Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, chronic obstructive pulmonary disease (COPD), Crohn's disease,dermatitis, eczema,giant cell arteritis, glomerulonephritis, hepatitis, hypophysitis, inflammatory bowel disease,), Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis,myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis, wherein the medicament is to be administered to a subject in need thereof.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating AIDS, wherein the medicament is to be administered to a subject in need thereof.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating obesity, wherein the medicament is to be administered to a subject in need thereof.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating type II diabetes, wherein the medicament is to be administered to a subject in need thereof.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an acute kidney disease or condition, wherein said acute kidney disease or condition is selected from the group consisting of:

ischemia-reperfusion induced kidney disease, cardiac and major surgery induced kidney disease, percutaneous coronary intervention induced kidney disease, radio-contrast agent induced kidney disease, sepsis induced kidney disease, pneumonia induced kidney disease, and drug toxicity induced kidney disease, wherein the medicament is to be administered to a subject in need thereof.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a chronic kidney disease or condition, wherein said disease or condition is selected from the group consisting of: diabetic nephropathy, hypertensive nephropathy, HIV-associated nephropathy, glomerulonephritis, lupus nephritis, IgA nephropathy, focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, polycystic kidney disease and tubular interstitial nephritis, wherein the medicament is to be administered to a subject in need thereof.

N-[4-(2,4-difluorophenoxy)-3-(5-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl]ethanesulfonamide;

N-[4-(2,4-difluorophenoxy)-3-(5-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl]acetamide;

N-{4-[(4,4-difluorocyclohexyl)oxy]-3-(5-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl}methanesulfonamide; and

N-{4-[(4,4-difluorocyclohexyl)oxy]-3-(5-methyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl}ethanesulfonamide.

30. A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) according to claim 1, or a pharmaceutically acceptable acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

31. ~~A method for treating cancer in a subject comprising administering~~Use of a therapeutically effective amount of a compound of formula (I) according to claim 1, or a pharmaceutically acceptable acceptable salt thereof, ~~to a subject in need thereof~~in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered to a subject in need thereof.

32. The ~~method~~ use of claim 31, wherein the cancer is selected from the group consisting of: acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia (monocytic, myeloblastic, adenocarcinoma, angiosarcoma, astrocytoma, myelomonocytic and promyelocytic), acute t-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, diffuse large B-cell lymphoma, dysproliferative changes (dysplasias and metaplasias), embryonal carcinoma, endometrial cancer, endotheliosarcoma, ependymoma, epithelial carcinoma, erythroleukemia, esophageal cancer, estrogen-receptor positive breast cancer, essential thrombocythemia, Ewing's tumor, fibrosarcoma, follicular lymphoma, germ cell testicular cancer, glioma, glioblastoma, gliosarcoma, heavy chain disease, hemangioblastoma, hepatoma, hepatocellular cancer, hormone insensitive prostate cancer, leiomyosarcoma, leukemia, liposarcoma, lung cancer, lymphagioendotheliosarcoma, lymphangiosarcoma, lymphoblastic leukemia, lymphoma (Hodgkin's and non-Hodgkin's), malignancies and hyperproliferative disorders of the bladder, breast, colon, lung, ovaries, pancreas, prostate, skin and uterus, lymphoid malignancies of T-cell or B-cell origin, leukemia, lymphoma, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, multiple myeloma, myelogenous

leukemia, myeloma, myxosarcoma, neuroblastoma, NUT midline carcinoma (NMC), non-small cell lung cancer, oligodendroglioma, oral cancer, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rectal cancer, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, sebaceous gland carcinoma, seminoma, skin cancer, small cell lung carcinoma, solid tumors (carcinomas and sarcomas), small cell lung cancer, stomach cancer, squamous cell carcinoma, synovioma, sweat gland carcinoma, thyroid cancer, Waldenström's macroglobulinemia, testicular tumors, uterine cancer and Wilms' tumor.

33. The ~~method~~ use of claim 32, ~~further comprising administering~~wherein a therapeutically effective amount of at least one additional therapeutic agent is to be further administered.

34. ~~A method for treating a disease or condition in a subject comprising administering~~Use of a therapeutically effective amount of a compound of formula (I) according to claim 1, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating a disease or condition ~~to a subject in need thereof~~, wherein said disease or condition is selected from the group consisting of: Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, chronic obstructive pulmonary disease (COPD), Crohn's disease,dermatitis, eczema,giant cell arteritis, glomerulonephritis, hepatitis, hypophysitis, inflammatory bowel disease,), Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis,myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis, wherein the medicament is to be administered to a subject in need thereof.

35. The ~~method~~ use of claim 34, ~~further comprising administering~~wherein a therapeutically effective amount of at least one additional therapeutic agent is to be further administered.

36. ~~A method for treating AIDS in a subject comprising administering~~Use of a therapeutically effective amount of a compound of formula (I) according to claim 1, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating AIDS, wherein the medicament is to be administered to a subject in need thereof.

37. The ~~method~~ use of claim 36, ~~further comprising administering~~wherein a therapeutically effective amount of at least one additional therapeutic agent is to be further administered.

38. ~~A method for treating obesity in a subject comprising administering~~Use of a therapeutically effective amount of a compound of formula (I) according to claim 1, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating obesity, wherein the medicament is to be administered to a subject in need thereof.

39. The ~~method~~ use of claim 38, ~~further comprising administering~~wherein a therapeutically effective amount of at least one additional therapeutic agent is to be further administered.

40. ~~A method for treating type II diabetes in a subject comprising administering~~Use of a therapeutically effective amount of a compound of formula (I) according to claim 1, or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for treating type II diabetes, wherein the medicament is to be administered to a subject in need thereof.

41. The ~~method~~ use of claim 40, ~~further comprising administering~~wherein a therapeutically effective amount of at least one additional therapeutic agent is to be further administered.

42. ~~A method for treating an acute kidney disease or condition in a subject comprising administering~~Use of a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an acute kidney disease or condition ~~to a subject in need thereof~~, wherein said acute kidney disease or condition is selected from the group consisting of: ischemia-reperfusion induced kidney disease, cardiac and major surgery induced kidney disease, percutaneous coronary intervention induced kidney disease, radio-contrast agent induced kidney disease, sepsis induced kidney disease, pneumonia induced kidney disease, and drug toxicity induced kidney disease, wherein the medicament is to be administered to a subject in need thereof.

43. The ~~method~~ use of claim 42, ~~further comprising administering~~wherein a therapeutically effective amount of at least one additional therapeutic agent is to be further administered.

44. ~~A method of treating a chronic kidney disease or condition in a subject comprising administering~~ Use of a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a chronic kidney disease or condition ~~to a subject in need thereof~~, wherein said disease or condition is selected from the group consisting of: diabetic nephropathy, hypertensive nephropathy, HIV-associated nephropathy, glomerulonephritis, lupus nephritis, IgA nephropathy, focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, polycystic kidney disease and tubular interstitial nephritis, wherein the medicament is to be administered to a subject in need thereof.

45. The ~~method~~ use of claim 44, ~~further comprising administering~~wherein a therapeutically effective amount of at least one additional therapeutic agent is to be further administered.