

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.

5 In another aspect, the present invention relates to methods of treating obesity, dyslipidemia, hypercholesterolemia, Alzheimer's disease, metabolic syndrome, hepatic steatosis, type II diabetes, insulin resistance, diabetic retinopathy or diabetic neuropathy 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
10 amount of at least one additional therapeutic agent.

In another aspect, the present invention 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
15 administering a therapeutically effective amount of at least one additional therapeutic agent.

A further aspect of the invention 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.

20 In another aspect, there is provided the use of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer in a subject in need thereof.

In another aspect, there is provided the use of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof, in a manufacture of a medicament for
25 treating a disease or condition in 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
30 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 another aspect, there is provided the use of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or condition in 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 another aspect, there is provided the use of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an acute kidney disease or condition in a subject in need thereof, wherein said acute kidney 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 another aspect, there is provided the use of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an acquired immunodeficiency syndrome (AIDS) in a subject.

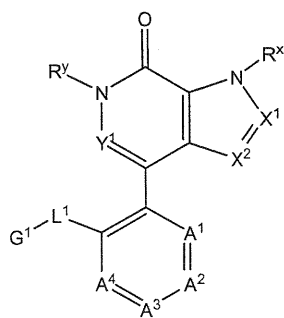
In another aspect, there is provided the use of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or condition in a subject, wherein said disease or condition is selected from the group consisting of: obesity, dyslipidemia, hypercholesterolemia, Alzheimer's disease, metabolic syndrome, hepatic steatosis, type II diabetes, insulin resistance, diabetic retinopathy and diabetic neuropathy.

In another aspect, there is provided the use of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable acceptable salt thereof, in the manufacture of a medicament for contraception in a male subject.

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.

DETAILED DESCRIPTION

Disclosed herein are compounds of formula (I)



(I)

wherein A¹, A², A³, A⁴, X¹, X², Y¹, L¹, G¹, R^x, and R^y are defined above in the Summary of the Invention and below in the Detailed Description. Further, compositions comprising such

R^x is hydrogen;

R^y is methyl;

Y^1 is CR^u wherein R^u is hydrogen;

X^1 is CR^{x1} wherein R^{x1} is hydrogen;

X^2 is CR^{x2} wherein R^{x2} is hydrogen;

L^1 is $(CH_2)_mN(R^z)$ wherein m is 0 and R^z is hydrogen;

G^1 is $-(C_1-C_6 \text{ alkylenyl})-G^{1a}$, wherein G^{1a} is optionally substituted cycloalkyl; and

R^2 is $-S(O)_2R^{2d}$, $-S(O)_2NR^{2b}R^{2c}$, $-N(R^{2e})S(O)_2R^{2d}$, or $-(C_1-C_6 \text{ alkylenyl})-S(O)_2R^{2d}$.

54. The compound of claim 53 or a pharmaceutically acceptable salt thereof, wherein A^1 is CR^1 , A^2 is CR^2 , A^3 is CR^3 , and A^4 is CR^4 .

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

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

57. The ~~method~~ use of claim 56 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.

58. ~~The method use of claim 56, further comprising administering wherein the medicament is to be administered with~~ a therapeutically effective amount of at least one additional therapeutic agent, wherein the additional therapeutic agent is selected from the group consisting of cytarabine, bortezomib, and 5-azacitidine.

59. ~~A method for treating a disease or condition in a subject comprising administering a therapeutically effective amount of~~ Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, in a manufacture of a medicament for treating a disease or condition ~~into~~ 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.

60. ~~A method for treating a disease or condition in a subject comprising administering a therapeutically effective amount~~ Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or condition ~~into~~ 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.

61. ~~A method for treating an acute kidney disease or condition in a subject comprising administering a therapeutically effective amount~~ Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an acute kidney disease or condition ~~into a subject in need thereof, wherein said acute kidney 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.~~

~~6062. A method for treating an acquired immunodeficiency syndrome (AIDS) in a subject comprising administering a therapeutically effective amount~~ Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating an acquired immunodeficiency syndrome (AIDS) ~~into a subject in need thereof.~~

~~6263. A method for treating a disease or condition in a subject comprising administering a therapeutically effective amount~~ Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or condition ~~into a subject in need thereof, wherein said disease or condition is selected from the group consisting of: obesity, dyslipidemia, hypercholesterolemia, Alzheimer's disease, metabolic syndrome, hepatic steatosis, type II diabetes, insulin resistance, diabetic retinopathy and diabetic neuropathy.~~

~~6364. A method of contraception in a male subject comprising administering a therapeutically effective amount~~ Use of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for contraception in a male subject ~~to a male subject in need thereof.~~