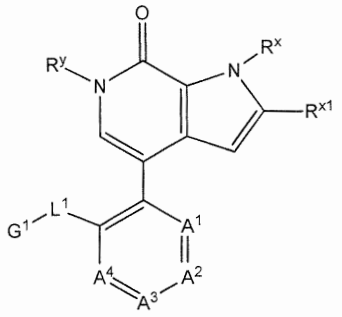
Accordingly, there is an ongoing medical need to develop new drugs to treat these indications.

SUMMARY

In one aspect the present ~~invention~~ disclosure provides for compounds of formula (I) or pharmaceutically acceptable salt thereof,



(I)

wherein

R^x is hydrogen or C_1-C_3 alkyl;

R^y is hydrogen or C_1-C_3 alkyl;

A^1 is N or CR^1, A^2 is N or CR^2, A^3 is N or CR^3; and A^4 is N or CR^4; wherein zero, one, two, or three of A^1, A^2, A^3, and A^4 are N;

R^1 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, CN, or NO_2;

R^2 is hydrogen, $-S(O)_2R^{2a}$, $-S(O)_2NR^{2b}R^{2c}$, $-N(R^{2b})S(O)_2R^{2a}$, or -(C_1-C_6 alkylenyl)-$S(O)_2R^{2a}$; wherein R^{2a} is C_1-C_6 alkyl or C_1-C_6 haloalkyl; and R^{2b} and R^{2c} are each independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl;

L^1 is O, N(H), or OCH_2 wherein the CH_2 moiety of OCH_2 is attached to G^1;

R^{x1}, G^1, R^3, and R^4, are selected from (i), (ii), (iii), or (iv);

(i) R^{x1} is –CN, $-G^{x1}$-G^{x2}, -(C_1-C_6 alkylenyl)-G^{x1}-G^{x2}, $-C(O)N(R^{xa})(R^{xb})$, C_1-C_6 alkyl substituted with one substituent selected from the group consisting of –CN, $-OR^{xb}$, $-SR^{xb}$, $-S(O)R^{xb}$, $-S(O)_2R^{xb}$, $-NR^{xa}R^{xb}$, $-C(O)R^{xb}$, $-C(O)OR^{xb}$, $-C(O)NR^{xa}R^{xb}$, and $-S(O)_2NR^{xa}R^{xb}$; C_2-C_6 alkenyl, or C_2-C_6 alkynyl; wherein the C_2-C_6 alkenyl and C_2-C_6 alkynyl are each independently substituted with one substituent selected from the group consisting of -CN, $-OR^{xc}$, $-SR^{xc}$, $-S(O)R^{xc}$, $-S(O)_2R^{xc}$, $-NR^{xa}R^{xc}$, $-C(O)R^{xc}$, $-C(O)OR^{xc}$, $-C(O)NR^{xa}R^{xc}$, $-S(O)_2NR^{xa}R^{xc}$, and G^{x1};

$-C(O)NR^jR^k$, $-NR^jR^k$, $-N(R^h)C(O)R^i$, $-N(R^h)S(O)_2R^i$, $-N(R^h)C(O)O(R^i)$, $-N(R^h)C(O)NR^jR^k$, $-(C_1\text{-}C_6$ alkylenyl)-OR^h, $-(C_1\text{-}C_6$ alkylenyl)-$OC(O)R^i$, $-(C_1\text{-}C_6$ alkylenyl)-$OC(O)NR^jR^k$, $-(C_1\text{-}C_6$ alkylenyl)-SR^h, $-(C_1\text{-}C_6$ alkylenyl)-$S(O)_2R^h$, $-(C_1\text{-}C_6$ alkylenyl)-$S(O)_2NR^jR^k$, $-(C_1\text{-}C_6$ alkylenyl)-$C(O)R^h$, $-(C_1\text{-}C_6$ alkylenyl)-$C(O)OR^h$, $-(C_1\text{-}C_6$ alkylenyl)-$C(O)NR^jR^k$, $-(C_1\text{-}C_6$ alkylenyl)-NR^jR^k, $-(C_1\text{-}C_6$ alkylenyl)-$N(R^h)C(O)R^i$, $-(C_1\text{-}C_6$ alkylenyl)-$N(R^h)S(O)_2R^i$, $-(C_1\text{-}C_6$ alkylenyl)-$N(R^h)C(O)O(R^i)$, $-(C_1\text{-}C_6$ alkylenyl)-$N(R^h)C(O)NR^jR^k$, or $-(C_1\text{-}C_6$ alkylenyl)-CN;

R^h, R^j, R^k, at each occurrence, are each independently hydrogen, $C_1\text{-}C_6$ alkyl, or $C_1\text{-}C_6$ haloalkyl; and

R^i, at each occurrence, is independently $C_1\text{-}C_6$ alkyl or $C_1\text{-}C_6$ haloalkyl.

In another aspect, the present ~~invention~~ disclosure provides for methods for treating or preventing disorders that are ameliorated by inhibition of BET. Such methods comprise of administering to the subject a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, alone, or in combination with a pharmaceutically acceptable carrier.

Some of the methods are directed to treating or preventing an inflammatory disease or cancer or AIDS.

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 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 certain embodiments, the additional therapeutic agent is selected from the group consisting of cytarabine, bortezomib, and 5-azacitidine.

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 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, cardiac myopathy, cardiac hypertrophy, chronic obstructive pulmonary disease (COPD), Crohn's disease, dermatitis, eczema, giant cell arteritis, glomerulonephritis, heart failure, 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 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 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 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 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, 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 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 at least one additional therapeutic agent, in the manufacture of a medicament for treating or preventing conditions and disorders disclosed herein, and 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 at least one additional therapeutic agent, are also provided.

In one aspect, there is provided the use of a therapeutically effective amount 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 one aspect, there is provided the use of a therapeutically effective amount 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 Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, cardiac myopathy, cardiac hypertrophy, chronic obstructive pulmonary disease (COPD), Crohn's disease,dermatitis, eczema,giant cell arteritis, glomerulonephritis, heart failure, 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 one aspect, there is provided the use of a therapeutically effective amount 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: 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 one aspect, there is provided the use of a therapeutically effective amount 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 one aspect, there is provided the use of a therapeutically effective amount 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

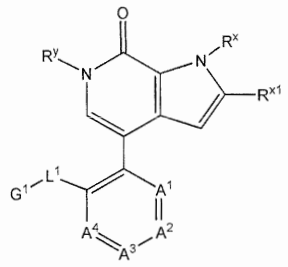
neuropathy.

In one aspect, there is provided the use of a therapeutically effective amount 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, 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.

In one aspect, there is provided the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a chronic kidney disease or condition in a subject, 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.

DETAILED DESCRIPTION

Disclosed herein are compounds of formula (I)



(I)

wherein R^x, R^y, R^{x1}, A^1, A^2, A^3, A^4, L^1 and G^1 are defined above in the Summary of the Invention and below in the Detailed Description. Further, compositions comprising such compounds and methods for treating conditions and disorders using such compounds and compositions are also disclosed.

Compounds disclosed herein may contain one or more variable(s) that occur more than one time in any substituent or in the formulae herein. Definition of a variable on each occurrence is independent of its definition at another occurrence. Further, combinations of substituents are permissible only if such combinations result in stable compounds. Stable compounds are compounds, which can be isolated from a reaction mixture.

Definitions

It is noted that, as used in this specification and the intended claims, the singular form "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a compound" includes a single compound as well as one or more of the same or different compounds, reference to "optionally a pharmaceutically acceptable carrier" refers to a single optional pharmaceutically acceptable carrier as well as one or more pharmaceutically acceptable carriers, and the like.

27. The compound of claim 22 or a pharmaceutically acceptable salt thereof, wherein the compound is

N-[3-cyclopropyl-4-(2,4-difluorophenoxy)-5-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide.

28. 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.

29. ~~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 salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for treating cancer in a subject.

30. The ~~method~~ use of claim 29 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.

31. ~~A method~~ Use of a therapeutically effective amount 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 in a subject ~~comprising administering a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically 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, cardiac myopathy, cardiac hypertrophy, chronic obstructive pulmonary disease (COPD), Crohn's disease,dermatitis, eczema,giant cell arteritis, glomerulonephritis, heart failure, 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.

32. ~~A method~~ Use of a therapeutically effective amount 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 in a subject ~~comprising administering a therapeutically effective amount of a compound of formula (I) according to claim 1 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.

33. ~~A method~~ Use of a therapeutically effective amount 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) in a subject ~~comprising administering a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, to a subject in need thereof~~.

34. ~~A method~~ Use of a therapeutically effective amount 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 in a subject ~~comprising administering a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, to 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.

35. A method of contraception in a male subject comprising administering 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.

36. ~~A method~~ Use of a therapeutically effective amount 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 in a subject ~~comprising administering a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, 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.

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

38. ~~A method of~~ Use of a therapeutically effective amount 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 chronic kidney disease or condition in a subject ~~comprising administering a therapeutically effective amount of a compound of formula (I) according to claim 1 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.

39. The ~~method~~ use of claim 38, wherein the medicament further comprises~~ing administering~~ a therapeutically effective amount of at least one additional therapeutic agent.