

SUMMARY

In one aspect the present ~~invention~~ disclosure relates to an isolated crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, wherein the crystalline form has a powder X-ray diffraction pattern comprising three or more 2θ peak values ± 0.2 selected from the group consisting of: 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In one aspect the present invention relates to an isolated crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, wherein the crystalline form has a powder X-ray diffraction pattern comprising the following 2θ peak values ± 0.2 : 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises the following 2θ peak values ± 0.2 : 6.2° , 9.0° , 11.0° , 12.3° , 12.6° , 13.1° , 14.1° , 15.6° , 16.4° , 16.5° , 16.9° , 17.8° , 18.1° , 18.3° , 18.9° , 20.4° , 21.1° , 21.6° , 21.8° , 22.1° , 22.9° , 23.2° , 24.4° , 24.7° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises three, four, five, or six 2θ peak values ± 0.2 selected from the group consisting of 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises six 2θ peak values ± 0.2 selected from the group consisting of 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises five 2θ peak values ± 0.2 selected from the group consisting of 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises four 2θ peak values ± 0.2 selected from the group consisting of 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises three 2θ peak values ± 0.2 selected from the group consisting of 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises the following 2θ peak values ± 0.2 : 6.2° , 9.0° , 12.3° , 12.6° , 15.6° , 22.1° , 25.6° , 26.3° , 27.0° , and 27.3° . In certain embodiments, the powder X-ray diffraction pattern comprises the following 2θ

peak values ± 0.2 : 6.2°, 9.0°, 12.3°, 12.6°, and 15.6°. In certain embodiments, the powder X-ray diffraction pattern comprises the following 2 θ peak values ± 0.2 : 22.1°, 25.6°, 26.3°, 27.0°, and 27.3°. In certain embodiments, the powder X-ray diffraction pattern comprises peak values ± 0.2 at 2 θ positions 6.2°, 9.0°, 12.3°, 12.6°, 13.1°, 14.1°, 16.4°, 16.5°, 16.9°, 17.8°, 18.1°, 18.3°, and 18.9°. In certain embodiments, the powder X-ray diffraction pattern comprises peak values ± 0.2 at 2 θ positions 6.2°, 9.0°, 12.3°, 12.6°, 13.1°, 14.1°, 18.1°, and 18.9°. In certain embodiments, the powder X-ray diffraction pattern comprises peak values ± 0.2 at 2 θ positions 6.2°, 9.0°, 12.3°, 12.6°, 13.1°, and 18.1°. In certain embodiments, the powder X-ray diffraction pattern comprises peak values ± 0.2 at 2 θ positions 9.0°, 12.3°, 12.6°, 13.1°, and 18.1°. In certain embodiments, crystalline form II has a differential scanning calorimetry thermogram endotherm between 240 and 242 °C. In certain embodiments, crystalline form II has a differential scanning calorimetry thermogram endotherm at approximately 241 °C. In certain embodiments, the endotherm is determined using DSC at a heating rate of 10°C/min. In certain embodiments, the powder X-ray diffraction pattern comprises peak values ± 0.2 at 2 θ positions 6.2°, 9.0°, 11.0°, 12.2°, 12.6°, 13.1°, 14.1°, 15.5°, 16.3°, 16.5°, 16.9°, 17.8°, 18.0°, 18.3°, 18.9°, 20.4°, 21.0°, 21.6°, 21.8°, 22.1°, 22.9°, 23.2°, 24.4°, 24.6°, 25.5°, 26.3°, 26.9°, and 27.2°. In certain embodiments, the powder X-ray diffraction pattern comprises peak values ± 0.2 at 2 θ positions ± 0.2 selected from the group consisting of: 6.2°, 9.0°, 12.2°, 12.6°, 15.5°, 22.1°, 25.5°, 26.3°, 26.9°, and 27.2°.

In another aspect the present ~~invention~~ disclosure relates to pharmaceutical compositions comprising crystalline form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, and at least one pharmaceutically acceptable carrier. In certain embodiments, the pharmaceutical composition is a solid dosage form.

In another aspect the present ~~invention~~ disclosure relates to methods for treating cancer in a subject comprising administering a therapeutically effective amount of a pharmaceutical composition comprising crystalline form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide and at least

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 a method of treating a disease or condition in a subject comprising administering a therapeutically effective amount of a crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide 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 method further comprises administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~-disclosure relates to a method of treating a chronic kidney disease or condition in a subject comprising administering a therapeutically effective amount of a crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide 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 method further comprises administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to a method of treating an acute kidney injury or disease or condition in a subject comprising administering a therapeutically effective amount of a crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide 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 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 certain embodiments, the method further comprises 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 crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide to a subject in need thereof. In certain embodiments, the method further comprises administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to a method 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 crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide to a subject in need thereof. In certain embodiments, the method further comprises administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to a methods of contraception in a male subject comprising administering a therapeutically effective amount of a crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide to a subject in need thereof. In certain embodiments, the method further comprises administering a therapeutically effective amount of at least one additional therapeutic agent.

A further aspect of the ~~invention~~-disclosure provides the use of a crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, 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, with or without a pharmaceutically acceptable carrier.

In certain embodiments, the ~~invention~~-disclosure provides the use of a crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, alone or in combination with at least one additional therapeutic agent, in the manufacture of a medicament for treating cancer, with or without a pharmaceutically acceptable carrier.

As mentioned above, crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide may provide advantages in formulating pharmaceutical compositions. Accordingly, one aspect of the present invention relates to a pharmaceutical composition comprising the N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide in crystalline form, and a pharmaceutically acceptable carrier. In a further embodiment, the composition according to the present invention comprises N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide Form II as described above, alone or in combination with a second therapeutic agent, and a pharmaceutically acceptable carrier.

Another aspect relates to a process for preparing crystalline Form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide.

In another aspect the present ~~invention~~-disclosure relates to methods of making a pharmaceutical composition comprising N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide and a pharmaceutically acceptable carrier, comprising: mixing an isolated crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, wherein the crystalline form has a powder X-ray diffraction pattern comprising three or more 2 θ peak values $\pm$ 0.2 selected from the group

consisting of: 6.2°, 9.0°, 12.3°, 12.6°, 15.6°, 22.1°, 25.6°, 26.3°, 27.0°, and 27.3°, with a pharmaceutically acceptable carrier.

In another aspect the present ~~invention~~ disclosure relates to compositions comprising greater than 90% (w/w) crystalline form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, wherein the crystalline form has a powder X-ray diffraction pattern comprising three or more 2θ peak values ± 0.2 selected from the group consisting of: 6.2°, 9.0°, 12.3°, 12.6°, 15.6°, 22.1°, 25.6°, 26.3°, 27.0°, and 27.3°. In certain embodiments, the composition comprises between 90-99% (w/w) crystalline form II.

In another aspect, there is provided the use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide as disclosed herein and at least one pharmaceutically acceptable carrier in the manufacture of a medicament for treating cancer in a subject.

In another aspect, there is provided the use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide as disclosed herein and at least one pharmaceutically acceptable carrier 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 another aspect, there is provided the use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide as disclosed herein and at least one pharmaceutically acceptable carrier in the manufacture of a medicament for treating a chronic kidney disease or condition in a subject, wherein said chronic kidney 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 therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide as disclosed herein and at least one pharmaceutically acceptable carrier 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 another aspect, there is provided the use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide as disclosed herein and at least one pharmaceutically acceptable carrier 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 therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide as disclosed herein and at least one pharmaceutically acceptable carrier 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.

DETAILED DESCRIPTION

N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide can be prepared as a crystalline form which is termed crystalline Form II. As used herein, a crystalline form of a compound refers to the same chemical entity, but in a different crystalline arrangement. N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide is an inhibitor of human BRD4, and of the proliferation of the breast cancer cell line MX-1.

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 “a pharmaceutically acceptable carrier” refers to a single pharmaceutically acceptable carrier as well as one or more pharmaceutically acceptable carriers, and the like.

When used in reference to crystalline form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, which is greater than about 90% pure. This means that the N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide crystal form II does not contain more than about 10% of any other compound and, in particular, does not contain more than about 10% of crystal form I. More preferably, the term “substantially pure” refers to crystalline Form II, which is greater than about 95% pure. This means that crystalline Form II does not contain more than about 5% of any other compound and, in particular, does not contain

16. A pharmaceutical composition comprising an isolated crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1, and at least one pharmaceutically acceptable carrier.

17. ~~A method for treating cancer in a subject comprising administering~~ Use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier in the manufacture of a medicament for treating cancer in a subject, ~~to a subject in need thereof.~~

18. The ~~method~~ use of claim 17 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.

19. A method of making a pharmaceutical composition comprising N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide and a pharmaceutically acceptable carrier, comprising:

mixing an isolated crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, wherein the crystalline form has a powder X-ray diffraction pattern comprising three or more 2θ peak values ± 0.2 selected from the group consisting of: 6.2°, 9.0°, 12.3°, 12.6°, 15.6°, 22.1°, 25.6°, 26.3°, 27.0°, and 27.3°, with a pharmaceutically acceptable carrier.

20. A composition comprising greater than 90% (w/w) crystalline form II of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide, wherein the crystalline form has a powder X-ray diffraction pattern comprising three or more 2θ peak values ± 0.2 selected from the group consisting of: 6.2°, 9.0°, 12.3°, 12.6°, 15.6°, 22.1°, 25.6°, 26.3°, 27.0°, and 27.3°.

21. ~~A method~~ Use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier 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 pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier, 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.

22. ~~A method~~ Use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier 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 pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier, to a subject in need thereof, wherein said chronic kidney 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.

23. ~~A method~~ Use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier in the manufacture of a medicament for treating a disease or condition in a subject comprising administering a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier, 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.

24. ~~A method Use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier in the manufacture of a medicament for treating an acquired immunodeficiency syndrome (AIDS) in a subject comprising administering a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier, to a subject in need thereof.~~

25. ~~A method Use of a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier in the manufacture of a medicament for treating a disease or condition in a subject comprising administering a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier, 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.~~

26. A method of contraception in a male subject comprising administering a therapeutically effective amount of a pharmaceutical composition comprising a crystalline form of N-[4-(2,4-difluorophenoxy)-3-(6-methyl-7-oxo-6,7-dihydro-1H-pyrrolo[2,3-c]pyridin-4-yl)phenyl]ethanesulfonamide according to claim 1 and at least one pharmaceutically acceptable carrier, to a subject in need thereof.