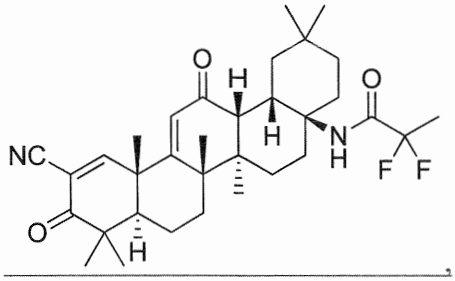
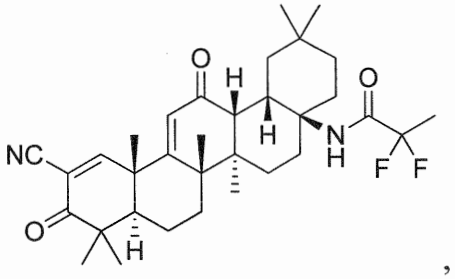
SUMMARY ~~OF THE INVENTION~~

In one aspect, there is provided a compound of the formula:



or a pharmaceutically acceptable salt thereof.

In some ~~aspects~~ embodiments of the present disclosure~~invention~~, there is provided a compound of the formula (also referred to herein as RTA 408, 63415, or PP415):

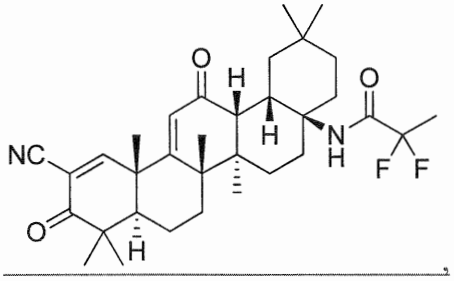


or a pharmaceutically acceptable salt thereof.

In some embodiments, the compound is in the form of a pharmaceutically acceptable salt. In some embodiments, the compound is not in the form of a salt.

~~In another aspect of the present invention, there are provided p~~Polymorphic forms of the above compound are provided.

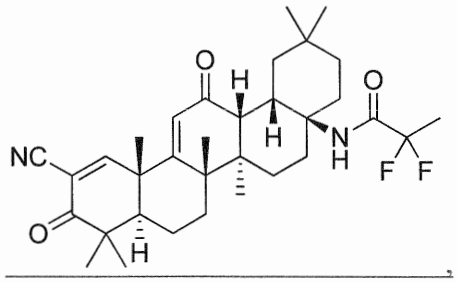
In one aspect, there is provided a polymorphic form of a compound having the formula:



wherein the polymorphic form has an X-ray powder diffraction pattern (CuKα) comprising a halo peak at about 14 °2θ.

In some embodiments, the polymorphic form has an X-ray powder diffraction pattern (CuKα) comprising a halo peak at about 14 °2θ. In some embodiments, the X-ray powder diffraction pattern (CuKα) further comprises a shoulder peak at about 8 °2θ. In some embodiments, the X-ray powder diffraction pattern (CuKα) is substantially as shown in FIG. 59. In some embodiments, the polymorphic form has a T_g from about 150 °C to about 155 °C, including for example, a T_g of about 153 °C or a T_g of about 150 °C. In some embodiments, the polymorphic form has a differential scanning calorimetry (DSC) curve comprising an endotherm centered from about 150 °C to about 155 °C. In some embodiments, the endotherm is centered at about 153 °C. In some embodiments, the endotherm is centered at about 150 °C. In some embodiments, the differential scanning calorimetry (DSC) curve is substantially as shown in FIG. 62.

In one aspect, there is provided a polymorphic form of a compound having the formula:



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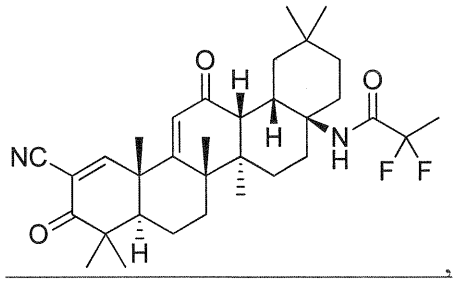
wherein the polymorphic form is a solvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 5.6, 7.0, 10.6, 12.7, and 14.6 °2θ.

In some embodiments, the polymorphic form is a solvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 5.6, 7.0, 10.6, 12.7, and 14.6 °2θ. In some embodiments, the X-ray powder diffraction pattern (CuKα) is substantially as shown in FIG. 75, top pattern.

In one aspect, there is provided a polymorphic form of a compound having the formula:

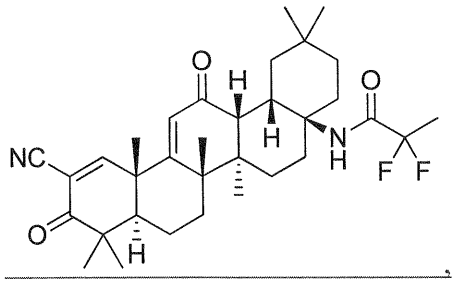


,

wherein the polymorphic form is a solvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 7.0, 7.8, 8.6, 11.9, 13.9 (double peak), 14.2, and 16.0 °2θ.

In some embodiments, the polymorphic form is a solvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 7.0, 7.8, 8.6, 11.9, 13.9 (double peak), 14.2, and 16.0 °2θ. In some embodiments, the X-ray diffraction pattern (CuKα) is substantially as shown in FIG. 75, second pattern from top.

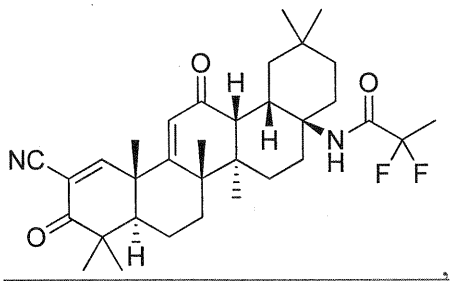
In one aspect, there is provided a polymorphic form of a compound having the formula:



wherein the polymorphic form is an acetonitrile hemisolvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 7.5, 11.4, 15.6, and 16.6 °2θ.

In some embodiments, the polymorphic form is an acetonitrile hemisolvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 7.5, 11.4, 15.6 and 16.6 °2θ. In some embodiments, the X-ray diffraction pattern (CuKα) is substantially as shown in FIG. 75, second pattern from bottom. In some embodiments, the polymorphic form has a T_g of about 196 °C. In some embodiments, the polymorphic form has a differential scanning calorimetry (DSC) curve comprising an endotherm centered at about 196 °C. In some embodiments, the differential scanning calorimetry (DSC) curve is substantially as shown in FIG. 116.

In one aspect, there is provided a polymorphic form of a compound having the formula:



wherein the polymorphic form is a solvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 6.8, 9.3, 9.5, 10.5, 13.6, and 15.6 °2θ.

In some embodiments, the polymorphic form is a solvate having an X-ray powder diffraction pattern (CuKα) comprising peaks at about 6.8, 9.3, 9.5, 10.5, 13.6,

and 15.6 °2θ. In some embodiments, the X-ray diffraction pattern (CuKα) is substantially as shown in FIG. 75, bottom pattern.

In one aspect, there is provided the compound as described herein or the polymorphic form as described herein for use in a medicament.

In one aspect, there is provided a pharmaceutical composition comprising:

an active ingredient consisting of a compound as described herein or a polymorphic form as described herein, and

a pharmaceutically acceptable carrier.

In another ~~aspect~~ embodiment of the present disclosure~~invention~~, there are provided pharmaceutical compositions comprising an active ingredient consisting of the above compound or a polymorphic form thereof (such as, *e.g.*, any one of the polymorphic forms described herein above and below), and a pharmaceutically acceptable carrier. In some embodiments, the pharmaceutical composition is formulated for administration: orally, intraadiposally, intraarterially, intraarticularly, intracranially, intradermally, intralesionally, intramuscularly, intranasally, intraocularly, intrapericardially, intraperitoneally, intrapleurally, intraprostatically, intrarectally, intrathecally, intratracheally, intratumorally, intraumbilically, intravaginally, intravenously, intravesicularlly, intravitreally, liposomally, locally, mucosally, parenterally, rectally, subconjunctival, subcutaneously, sublingually, topically, transbuccally, transdermally, vaginally, in crèmes, in lipid compositions, via a catheter, via a lavage, via continuous infusion, via infusion, via inhalation, via injection, via local delivery, or via localized perfusion. In some embodiments, the pharmaceutical composition is formulated for oral, intraarterial, intravenous, or topical administration. In some embodiments, the pharmaceutical composition is formulated for oral administration.

In some embodiments, the pharmaceutical composition is formulated as a hard or soft capsule, a tablet, a syrup, a suspension, an emulsion, a solution, a solid dispersion, a wafer, or an elixir. In some embodiments, the pharmaceutical composition according to the disclosure~~invention~~ further comprises an agent that enhances solubility and dispersibility. (For example, agents that enhance solubility and dispersibility include, but are not limited to, PEGs, cyclodextrans, and cellulose

derivatives.) In some embodiments, the compound or polymorphic form is suspended in sesame oil.

In other embodiments, the pharmaceutical composition is formulated for topical administration. In other embodiments, the pharmaceutical composition is formulated as a lotion, a cream, a gel, an oil, an ointment, a salve, an emulsion, a solution, or a suspension. In some embodiments, the pharmaceutical composition is formulated as a lotion, as a cream, or as a gel. In some embodiments, the amount of the active ingredient is from about 0.01% to about 5% by weight, about 0.01% to about 3% by weight, or 0.01%, 0.1%, 1%, or 3% by weight.

In one aspect, there is provided use of the compound as described herein, the polymorphic forms as described herein, or the pharmaceutical composition as described herein in the manufacture of a medicament for treating or preventing a condition associated with inflammation or oxidative stress in a patient.

In another ~~aspect~~ embodiment of the present ~~invention~~ disclosure there are provided methods of treating or preventing a condition associated with inflammation or oxidative stress in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of the pharmaceutical composition as described above or below.

In one aspect, there is provided the compound as described herein or the polymorphic form as described herein or the pharmaceutical composition as described herein for use in treating or preventing a condition associated with inflammation or oxidative stress.

The disclosure~~invention~~ likewise relates to the compound *N*-((4a*S*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-octadecahydropicen-4a-yl)-2,2-difluoropropanamide (or RTA 408) or a pharmaceutically acceptable salt thereof, or a polymorphic form of that compound (such as, e.g., any one of the polymorphic forms described herein above or below), or a pharmaceutical composition comprising any of the aforementioned entities and a pharmaceutically acceptable carrier (including, e.g., the pharmaceutical compositions described above), for use in treating or preventing a condition associated with inflammation or oxidative stress. The disclosure~~invention~~ also relates to the use of the aforementioned compound, polymorphic form or pharmaceutical composition for the preparation of a medicament for the treatment or prevention of a condition associated with inflammation or oxidative stress. In some embodiments,

the condition is associated with inflammation. In other embodiments, the condition is associated with oxidative stress. In some embodiments, the condition is a skin disease or disorder, sepsis, dermatitis, osteoarthritis, cancer, inflammation, an autoimmune disease, inflammatory bowel disease, a complication from localized or total-body exposure to ionizing radiation, mucositis, acute or chronic organ failure, liver disease, pancreatitis, an eye disorder, a lung disease or diabetes.

The present disclosure~~invention~~ furthermore relates to the compound *N*-((4a*S*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-octadecahydropicen-4a-yl)-2,2-

difluoropropanamide (or RTA 408) or a pharmaceutically acceptable salt thereof, or a polymorphic form of that compound (such as, e.g., any one of the polymorphic forms described herein above or below), or a pharmaceutical composition comprising any of the aforementioned entities and a pharmaceutically acceptable carrier (including, e.g., the pharmaceutical compositions described above), for use in treating or preventing a condition selected from a skin disease or disorder, sepsis, dermatitis, osteoarthritis, cancer, inflammation, an autoimmune disease, inflammatory bowel disease, a complication from localized or total-body exposure to ionizing radiation, mucositis, acute or chronic organ failure, liver disease, pancreatitis, an eye disorder, a lung disease, or diabetes. Accordingly, the disclosure~~invention~~ relates to the use of the aforementioned compound, polymorphic form or pharmaceutical composition for the preparation of a medicament for the treatment or prevention of a condition selected from a skin disease or disorder, sepsis, dermatitis, osteoarthritis, cancer, inflammation, an autoimmune disease, inflammatory bowel disease, a complication from localized or total-body exposure to ionizing radiation, mucositis, acute or chronic organ failure, liver disease, pancreatitis, an eye disorder, a lung disease, or diabetes. The disclosure~~invention~~ also relates to a method of treating or preventing a condition selected from a skin disease or disorder, sepsis, dermatitis, osteoarthritis, cancer, inflammation, an autoimmune disease, inflammatory bowel disease, a complication from localized or total-body exposure to ionizing radiation, mucositis, acute or chronic organ failure, liver disease, pancreatitis, an eye disorder, a lung disease, or diabetes in a patient in need thereof, the method comprising administering to the patient a therapeutically effective amount of the aforementioned compound, polymorphic form or pharmaceutical composition. In some embodiments, the condition is a skin disease or disorder such as dermatitis, a thermal or chemical burn, a chronic wound, acne, alopecia, other disorders of the hair follicle, epidermolysis bullosa, sunburn, complications of sunburn, disorders of skin pigmentation, an aging-related skin condition; a post-surgical wound, a scar from a skin injury or burn, psoriasis, a dermatological manifestation of an autoimmune disease or a graft-versus host disease, skin cancer, or a disorder involving hyperproliferation of skin cells. In some embodiments, the skin disease or disorder is dermatitis. In some embodiments, the dermatitis is allergic dermatitis, atopic dermatitis, dermatitis due to chemical exposure, or radiation-induced dermatitis. In other embodiments, the skin disease or disorder is a chronic wound. In some embodiments, the chronic wound is a diabetic

neurodegenerative disease is MS, such as primary progressive, relapsing-remitting secondary progressive or progressive relapsing MS. In some embodiments, the subject may be, for example, a primate. In some embodiments, the subject may be a human.

In particular embodiments of methods of treating or preventing a neurodegenerative disease in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure, the treatment suppresses the demyelination of neurons in the subject's brain or spinal cord. In certain embodiments, the treatment suppresses inflammatory demyelination. In certain embodiments, the treatment suppresses the transection of neuron axons in the subject's brain or spinal cord. In certain embodiments, the treatment suppresses the transection of neurites in the subject's brain or spinal cord. In certain embodiments, the treatment suppresses neuronal apoptosis in the subject's brain or spinal cord. In certain embodiments, the treatment stimulates the remyelination of neuron axons in the subject's brain or spinal cord. In certain embodiments, the treatment restores lost function after an MS attack. In certain embodiments, the treatment prevents a new MS attack. In certain embodiments, the treatment prevents a disability resulting from an MS attack.

One general ~~aspect~~ embodiment of the present disclosure contemplates a method of treating or preventing a disorder characterized by overexpression of iNOS genes in a subject, comprising administering to the subject a pharmaceutically effective amount of RTA 408, polymorphic forms, or a pharmaceutical composition of the present disclosure.

Another general embodiment~~aspect~~ of the present disclosure contemplates a method of inhibiting IFN-γ-induced nitric oxide production in cells of a subject, comprising administering to said subject a pharmaceutically effective amount of RTA 408, polymorphic forms, or a pharmaceutical composition of the present disclosure.

Yet another general method of the present disclosure contemplates a method of treating or preventing a disorder characterized by overexpression of COX-2 genes in a subject, comprising administering to the subject a pharmaceutically effective amount of RTA 408, polymorphic forms, or a pharmaceutical composition of the present disclosure.

Methods of treating renal/kidney disease (RKD) in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure are also contemplated. See U.S. Patent 8,129,429, which is

incorporated by reference herein. The RKD may result from, for example, a toxic insult. The toxic insult may result from but not limited to, for example, an imaging agent or a drug. The drug may be a chemotherapeutic, for example. The RKD may result from ischemia/reperfusion injury, in certain embodiments. In certain embodiments, the RKD results from diabetes or hypertension. In some embodiments, the RKD may result from an autoimmune disease. The RKD may be further defined as chronic RKD or acute RKD.

In certain methods of treating renal/kidney disease (RKD) in a subject, comprising administering to the subject a pharmaceutically effective amount of a compound of the present disclosure, the subject has undergone or is undergoing dialysis. In certain embodiments, the subject has undergone or is a candidate to undergo kidney transplant. The subject may be a primate. The primate may be a human. The subject in this or any other method may be, for example, a cow, horse, dog, cat, pig, mouse, rat or guinea pig.

Also contemplated by the present disclosure is a method for improving glomerular filtration rate or creatinine clearance in a subject, comprising administering to the subject a pharmaceutically effective amount of RTA 408, polymorphic forms, or a pharmaceutical composition of the present disclosure.

In some embodiments, the pharmaceutical composition is administered in a single dose per day. In other embodiments, the pharmaceutical composition is administered in more than one dose per day. In some embodiments, the pharmaceutical composition is administered in a pharmaceutically effective amount.

In some embodiments, the dose is from about 1 mg/kg to about 2000 mg/kg. In other embodiments, the dose is from about 3 mg/kg to about 100 mg/kg. In other embodiments, the dose is about 3, 10, 30, or 100 mg/kg.

In other embodiments, the pharmaceutical composition is administered topically. In some embodiments, the topical administration is administered to the skin. In other embodiments, the topical administration is administered to the eye.

In other embodiments, the pharmaceutical composition is administered orally. In other embodiments, the pharmaceutical composition is administered intraocularly.

Other objects, features and advantages of the present disclosure will become apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating specific embodiments of the disclosure~~invention~~, are given by way of illustration only, since various

changes and modifications within the spirit and scope of the disclosure~~invention~~ will become apparent to those skilled in the art from this detailed description. Note that simply because a particular compound is ascribed to one particular generic formula does not mean that it cannot also belong to another generic formula.

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34. The pharmaceutical composition of claim 33, wherein pharmaceutical composition is formulated as a lotion, a cream, a gel, an oil, an ointment, a salve, an emulsion, a solution, or a suspension.

35. The pharmaceutical composition of claim 34, wherein the pharmaceutical composition is formulated as a lotion.

36. The pharmaceutical composition of claim 34, wherein the pharmaceutical composition is formulated as a cream.

37. The pharmaceutical composition of claim 34, wherein the pharmaceutical composition is formulated as a gel.

38. The pharmaceutical composition of any one of claims 26-36, wherein the amount of the active ingredient is from about 0.01% to about 5% by weight.

39. The pharmaceutical composition of claim 38, wherein the amount of the active ingredient is from about 0.01% to about 3% by weight.

40. The pharmaceutical composition of claim 39, wherein the amount of the active ingredient is about 0.01% by weight.

41. The pharmaceutical composition of claim 39, wherein the amount of the active ingredient is about 0.1% by weight.

42. The pharmaceutical composition of claim 39, wherein the amount of the active ingredient is about 1% by weight.

43. The pharmaceutical composition of claim 39, wherein the amount of the active ingredient is about 3% by weight.

44. Use of the compound according to claim 1-3, the polymorphic forms of claims 4-24, or the pharmaceutical composition according to any one of claims 26 to 43 in the manufacture of a medicament for ~~A method of~~ treating or preventing a condition associated with inflammation or oxidative stress in a patient ~~in need thereof, comprising administering to the patient a therapeutically effective amount of the compound according to claim 1-3, the polymorphic forms of claims 4-24, or the pharmaceutical composition according to any one of claims 26 to 43~~.

45. The compound according to any one of claims 1-3 or the polymorphic form according to any one of claims 4-24 or the pharmaceutical composition according to any one of claims 26-43 for use in treating or preventing a condition associated with inflammation or oxidative stress.

~~46. Use of the compound according to any one of claims 1-3 or the polymorphic form according to any one of claims 4-24 or the pharmaceutical composition according to any one of claims 26-43 for the preparation of a medicament for the treatment or prevention of a condition associated with inflammation or oxidative stress.~~

~~47.~~46. The use ~~method~~ of claim 44 or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45~~, or the use of claim 46~~, wherein the condition is associated with inflammation.

~~48.~~47. The use ~~method~~ of claim 44 or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45~~, or the use of claim 46~~, wherein the condition is associated with oxidative stress.

~~49.~~48. The use ~~method~~ according to ~~any one of~~ claims~~s~~ 44, ~~and 47~~ or the compound, the polymorphic form, or the pharmaceutical composition for use according to ~~any one of~~ claims~~s~~ 45 ~~and 47~~-48, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to ~~of~~ any one of claims 46-47~~48~~, wherein the condition is a skin disease or disorder, sepsis, dermatitis, osteoarthritis, cancer, inflammation, an autoimmune disease, inflammatory bowel disease, a complication from localized or total-body exposure to ionizing radiation, mucositis, acute or chronic organ failure, liver disease, pancreatitis, an eye disorder, a lung disease, or diabetes.

~~50.~~49. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 4948, ~~or the use of claim 49,~~ wherein the condition is a skin disease or disorder.

~~51.~~50. ~~The method of claim 50 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 5049, ~~or the use of claim 50,~~ wherein the skin disease or disorder is dermatitis, a thermal or chemical burn, a chronic wound, acne, alopecia, other disorders of the hair follicle, epidermolysis bullosa, sunburn, complications of sunburn, a disorder of skin pigmentation, an aging-related skin condition, a post-surgical wound, a scar from a skin injury or burn,

psoriasis, a dermatological manifestation of an autoimmune disease or a graft-versus host disease, skin cancer, or a disorder involving hyperproliferation of skin cells.

~~52.~~51. ~~The method of claim 51 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~51~~50, ~~or the use of claim 51,~~ wherein the skin disease or disorder is dermatitis.

~~53.~~52. ~~The method of claim 52 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~52~~51, ~~or the use of claim 52,~~ wherein the dermatitis is allergic dermatitis, atopic dermatitis, dermatitis due to chemical exposure, or radiation-induced dermatitis.

~~54.~~53. ~~The method of claim 51 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~51~~50, ~~or the use of claim 51,~~ wherein the skin disease or disorder is a chronic wound.

~~55.~~54. ~~The method of claim 54 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~54~~53, ~~or the use of claim 54,~~ wherein the chronic wound is a diabetic ulcer, a pressure sore, or a venous ulcer.

~~56.~~55. ~~The method of claim 51 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~51~~50, ~~or the use of claim 51,~~ wherein the skin disease or disorder is alopecia.

~~57.~~56. ~~The method of claim 56 or t~~ The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~56~~55, ~~or the use of claim 56,~~ wherein the alopecia is baldness or drug-induced alopecia.

~~58.~~57. ~~The method of claim 51 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~51~~50, ~~or the use of claim 51,~~ wherein the skin disease or disorder is a disorder of skin pigmentation.

~~59.~~58. ~~The method of claim 58 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~58~~57, ~~or the use of claim 58,~~ wherein the disorder of skin pigmentation is vitiligo.

60.59. ~~The method of claim 51 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~51~~50, ~~or the use of claim 51,~~ wherein the skin disease or disorder is a disorder involving hyperproliferation of skin cells.

61.60. ~~The method of claim 60 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~60~~59, ~~or the use of claim 60,~~ wherein the disorder involving hyperproliferation of skin cells is hyperkeratosis.

62.61. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~49~~48, ~~or the use of claim 49,~~ wherein the condition is an autoimmune disease.

63.62. ~~The method of claim 62 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~62~~61, ~~or the use of claim 62,~~ wherein the autoimmune disease is rheumatoid arthritis, lupus, Crohn's disease, or psoriasis.

64.63. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~49~~48, ~~or the use of claim 49,~~ wherein the condition is a liver disease.

65.64. ~~The method of claim 64 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~64~~63, ~~or the use of claim 64,~~ wherein the liver disease is fatty liver disease or hepatitis.

66.65. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~49~~48, ~~or the use of claim 49,~~ wherein the condition is an eye disorder.

67.66. ~~The method of claim 63 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~66~~65, ~~or the use of claim 66,~~ wherein the eye disorder is uveitis, macular degeneration, glaucoma, diabetic macular edema, blepharitis, diabetic retinopathy, a disease or disorder of the corneal endothelium, post-surgical inflammation, dry eye, allergic conjunctivitis, or a form of conjunctivitis.

68.67. The method of claim 67 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 6766, or the use of claim 67, wherein the eye disorder is macular degeneration.

69.68. The method of claim 68 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 6867, or the use of claim 68, wherein the macular degeneration is the dry form.

70.69. The method of claim 68 or t The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 6867, or the use of claim 68, wherein the macular degeneration is the wet form.

71.70. The method of claim 67 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 6766, or the use of claim 67, wherein the disease or disorder of the corneal endothelium is Fuchs endothelial corneal dystrophy.

72.71. The method of claim 49 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 4948, or the use of claim 49, wherein the condition is a lung disease.

73.72. The method of claim 72 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 7271, or the use of claim 72, wherein the lung disease is pulmonary inflammation, pulmonary fibrosis, COPD, asthma, cystic fibrosis, or idiopathic pulmonary fibrosis.

74.73. The method of claim 73 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 7372, or the use of claim 73, wherein the lung disease is pulmonary inflammation.

75.74. The method of claim 73 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 7372, or the use of claim 73, wherein the lung disease is pulmonary fibrosis.

76.75. The method of claim 73 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 7372, or the use of claim 73, wherein the lung disease is COPD.

~~77.~~76. ~~The method of claim 76 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~76~~75, ~~or the use of claim 76,~~ wherein the COPD is induced by cigarette smoke.

~~78.~~77. ~~The method of claim 73 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~73~~72, ~~or the use of claim 73,~~ wherein the lung disease is asthma.

~~79.~~78. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~49~~48, ~~or the use of claim 49,~~ wherein the condition is sepsis.

~~80.~~79. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~49~~48, ~~or the use of claim 49,~~ wherein the condition is mucositis resulting from radiation therapy or chemotherapy.

~~81.~~80. ~~The method of claim 80 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~80~~79, ~~or the use of claim 80,~~ wherein the mucositis is oral mucositis.

~~82.~~81. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~49~~48, ~~or the use of claim 49,~~ wherein the condition is a complication from localized or total-body exposure to ionizing radiation.

~~83.~~82. ~~The method of claim 82 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~82~~81, ~~or the use of claim 82,~~ wherein the exposure to ionizing radiation leads to dermatitis.

~~84.~~83. ~~The method according to any one of claims 82-83 or t~~ The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims ~~82-83~~81-82, ~~or the use of any one of claims 82-83,~~ wherein the exposure to ionizing radiation is acute.

~~85.~~84. ~~The method according to any one of claims 82-83 or t~~ The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims 81-82~~82-~~

~~83~~, ~~or the use of any one of claims 82-83,~~ wherein the exposure to ionizing radiation is fractionated.

~~86.~~85. ~~The method of claim 49 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~49~~48, ~~or the use of claim 49,~~ wherein the condition is cancer.

~~87.~~86. ~~The method of claim 86 or t~~ The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~86~~85, ~~or the use of claim 86,~~ wherein the cancer is a carcinoma, sarcoma, lymphoma, leukemia, melanoma, mesothelioma, multiple myeloma, or seminoma.

~~88.~~87. ~~The method of claim 86 or t~~ The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~86~~85, ~~or the use of claim 86,~~ wherein the cancer is of the bladder, blood, bone, brain, breast, central nervous system, cervix, colon, endometrium, esophagus, gall bladder, genitalia, genitourinary tract, head, kidney, larynx, liver, lung, muscle tissue, neck, oral or nasal mucosa, ovary, pancreas, prostate, skin, spleen, small intestine, large intestine, stomach, testicle, or thyroid.

~~89.~~88. The use ~~method~~ according to ~~any one of~~ claim~~s~~ 44, ~~88~~ or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims ~~46~~45-~~87~~88, ~~or the use of any one of claims 46-88~~, wherein the compound or the pharmaceutical composition is administered in a single dose per day.

~~90.~~89. The use ~~method~~ according to ~~any one of~~ claim~~s~~ 44, ~~88~~ or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims ~~46~~45-~~87~~88, ~~or the use of any one of claims 46-88~~, wherein the compound or the pharmaceutical composition is administered in more than one dose per day.

~~91.~~90. The use ~~method~~ according to ~~any one of~~ claim~~s~~ 44, ~~90~~ or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims ~~45-88~~46-89, ~~or the use of any one of claims 46-88~~, wherein the pharmaceutical composition is administered in a unit dose from about 1 mg/kg to about 2000 mg/kg.

92.91. The method of claim 91 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 9190, or the use of claim 91, wherein the dose is from about 3 mg/kg to about 100 mg/kg.

93.92. The method of claim 92 or t The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 9291, or the use of claim 92, wherein the dose is about 3 mg/kg.

94.93. The method of claim 92 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 9291, or the use of claim 92, wherein the dose is about 10 mg/kg.

95.94. The method of claim 92 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 9291, or the use of claim 92, wherein the dose is about 30 mg/kg.

96.95. The method of claim 92 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 9291, or the use of claim 92, wherein the dose is about 100 mg/kg.

97.96. The use method according to any one of claims 44-96 or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims 45-9646-95, or the use of any one of claims 46-96, wherein the compound or the pharmaceutical composition is administered topically.

98.97. The method of claim 97 or t The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 9796, or the use of claim 97, wherein the topical administration is administered to the skin.

99.98. The method of claim 97 or tThe use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 9796, or the use of claim 97, wherein the topical administration is administered to the eye.

100.99. The use method according to any one of claims 44,-96 or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims 45-9646-95, or the use of any one of claims 46-96, wherein the compound or the pharmaceutical composition is administered orally.

~~101.~~100. The use ~~method~~ according to ~~any one of~~ claims ~~44, 96~~ or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims ~~45-96~~46-95~~, or the use of any one of claims 46-96~~, wherein the compound or the pharmaceutical composition is administered intraocularly.

~~102.~~101. The use ~~method~~ according to ~~any one of~~ claims ~~44, 101~~ or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims ~~45-101~~46-100~~, or the use of any one of claims 46-101~~, wherein the pharmaceutical composition is administered before or immediately after a subject is treated with a radiation therapy or a chemotherapy, wherein the chemotherapy does not comprise the active ingredient of claim 26.

~~103.~~102. ~~The method of claim 102 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~102~~101, ~~or the use of claim 102,~~ wherein the pharmaceutical composition is administered both before and after the subject is treated with the radiation therapy or the chemotherapy.

~~104.~~103. ~~The method according to either claims 102 or 103 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to either claims ~~102~~-101 or ~~103~~102, ~~or the use of either claims 102 or 103,~~ wherein the treatment reduces a side effect of the radiation therapy or the chemotherapy.

~~105.~~104. ~~The method of claim 104 or t~~The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim ~~104~~103, ~~or the use of claim 104,~~ wherein the side effect is mucositis and dermatitis.

~~106.~~105. ~~The method according to any one of claims 102-105 or t~~ The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims 101-104~~102-105~~, ~~or the use of any one of claims 102-105,~~ wherein the treatment enhances the efficacy of the radiation therapy or the chemotherapy.

~~107.~~106. ~~The method according to any one of claims 102-105 or t~~ The use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims 101-104~~102-105~~, ~~or the use of any one of claims 102-105,~~ wherein the chemotherapy comprises the administering to the patient a therapeutically effective amount of 5-fluorouracil or docetaxel.

~~108.~~107. The use ~~method~~ according to ~~any one of~~ claims 44~~-107~~, or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims 46-106, wherein the patient is a human.

~~109.~~108. The use ~~method~~ according to ~~any one of~~ claims ~~44-107~~, or the compound, the polymorphic form, or the pharmaceutical composition for use according to claim 45, or the use or the compound, the polymorphic form, or the pharmaceutical composition for use according to any one of claims 46-106, wherein the patient is a non-human mammal.