

[0005] Polymorphic forms of a compound are known in the pharmaceutical arts to affect, for example, the solubility, stability, flowability, fractability, and compressibility of the compound, as well as the safety and efficacy of drug products comprising it. See, e.g., Knapman, K. *Modern Drug Discoveries*, 2000, 53. Therefore, the discovery of new polymorphs of a drug can provide a variety of advantages.

[0006] The present disclosure provides new polymorphic forms of Compound 1, including several crystalline forms of an anhydrous form, a hydrate form, several solvate forms, and physical forms thereof, pharmaceutical compositions, and a method of treating a disease mediated by KRAS G12C inhibition. The new polymorphic forms can further the development of formulations for the treatment of these chronic illnesses, and may yield numerous formulation, manufacturing and therapeutic benefits.

SUMMARY

[0007] The present disclosure provides crystalline and amorphous forms of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one, including several anhydrous, hydrate and solvate forms, and solid state forms thereof, pharmaceutical compositions, and methods of treating a disease mediated by KRAS G12C inhibition.

[0007a] In one aspect, the present disclosure provides a compound, wherein the compound is a crystalline anhydrous form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (Compound 1/AMG 510) and wherein the compound is characterized by an x-ray powder diffraction pattern comprising a peak at 9.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å or an atropisomer thereof. In another aspect, the present disclosure provides a compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510), wherein the compound is characterized by an x-ray powder diffraction pattern comprising peaks at 9.0, 12.0, 12.6, and 19.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å. In another aspect, the present disclosure provides a compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510), wherein the compound is characterized by an x-ray powder diffraction pattern comprising at least three peaks selected from 8.8, 9.0, 10.8, 12.0, 12.6, 12.8, 13.6, 14.2, 15.0, 15.4, 18.0, 18.6, 18.7, 19.0, 19.9, 20.0, 22.9, and 25.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å. In another aspect, the present disclosure provides a compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510), wherein the compound is characterized by a differential scanning calorimetry thermogram comprising an endotherm with an onset of about 293°C.

[0007b] In another aspect, the present disclosure provides a pharmaceutical composition comprising the compound as described herein and a pharmaceutically acceptable excipient.

[0007c] In another aspect, the present disclosure provides a compound as described herein or the pharmaceutical composition as described herein for use as a medicament. In yet another aspect, the present disclosure provides a use of a compound as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament for treating cancer having a KRAS G12C mutation.

~~**[0007d]** In still another aspect, the present disclosure provides a compound, wherein the compound is an amorphous form of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-~~

propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (Compound 1) or an atropisomer thereof.

[0007e] — In a further aspect, the present disclosure provides a pharmaceutical composition comprising the compound as described herein, or any mixtures thereof; and a pharmaceutically acceptable excipient.

[0007d] — In yet another aspect, the present disclosure provides a compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510), wherein the compound is characterized by a thermogravimetric analysis thermogram comprising a weight loss of about 0.2% when heated from about 25 °C to about 275 °C. In yet another aspect, the present disclosure provides a compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510), wherein the compound is characterized by ¹³C solid state NMR comprising at least three peaks selected from peaks at approximately 12, 13, 16, 21, 23, 31, 33, 38, 42, 44, 47, 50, 54, 107, 110, 111, 123, 124, 127, 128, 132, 145, 146, 150, 154, 156, 158, 160, 162, 166, 167.7, and 168 ppm. In a still further aspect, the present disclosure provides a compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510), wherein the compound is characterized by ¹⁹F solid state NMR comprising peaks at approximately -109 and -120 ppm.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] Figure 1 shows XRPD data for an amorphous form of Compound 1. The powder X-ray pattern is characteristic of amorphous material with a broad amorphous halo and no distinct compound related diffraction peaks from 5-40° 2-theta.

[0009] Figure 2 shows DSC data for an amorphous form of Compound 1.

[0010] Figure 3 shows TGA data for an amorphous form of Compound 1.

[0011] Figure 4 shows ¹⁹F solid state NMR (SSNMR) for an amorphous form of Compound 1.

[0012] Figure 5 shows XRPD data for the crystalline anhydrous form I of Compound 1. The powder X-ray diffraction pattern of the anhydrous forms I-III of Compound 1 is characteristic of crystalline material with distinct diffraction peaks between 3° 2-theta to 40° 2-theta.

CLAIMS

What is claimed is:

1. A compound, wherein the compound is a crystalline anhydrous form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510Compound 1) ~~or an atropisomer thereof.~~ and wherein the compound is characterized by an x-ray powder diffraction pattern comprising a peak at 9.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

~~2. The compound of Claim 1, wherein the compound is the M atropisomer of Compound 1.~~

~~3. The compound of Claim 1 or 2, wherein the compound is a crystalline anhydrous form of Compound 1.~~

~~4. The compound of Claim 3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising a peak at 9.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

5.2. A compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510)~~The compound of any one of Claims 1-3,~~ wherein the compound is characterized by an powder x-ray powder diffraction pattern comprising peaks at 9.0, 12.0, 12.6, and 19.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

6.3. A compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510).~~The compound of any one of Claims 1-3,~~ wherein the compound is characterized by an powder x-ray powder diffraction pattern comprising at least three peaks selected from 8.8, 9.0, 10.8, 12.0,

12.6, 12.8, 13.6, 14.2, 15.0, 15.4, 18.0, 18.6, 18.7, 19.0, 19.9, 20.0, 22.9, and 25.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

~~7.4.~~ The compound of ~~Claim 3~~~~any one of Claims 1-3~~, wherein the compound is characterized by an ~~an powder~~-x-ray ~~powder~~ diffraction pattern comprising at least five peaks selected from 8.8, 9.0, 10.8, 12.0, 12.6, 12.8, 13.6, 14.2, 15.0, 15.4, 18.0, 18.6, 18.7, 19.0, 19.9, 20.0, 22.9, and 25.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

~~8.5.~~ The compound of ~~Claim 3~~~~any one of Claims 1-3~~, wherein the compound is characterized by an ~~an powder~~-x-ray ~~powder~~ diffraction pattern comprising at least seven peaks selected from 8.8, 9.0, 10.8, 12.0, 12.6, 12.8, 13.6, 14.2, 15.0, 15.4, 18.0, 18.6, 18.7, 19.0, 19.9, 20.0, 22.9, and 25.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

~~9.6.~~ The compound of ~~Claim 3~~~~any one of Claims 1-3~~, wherein the compound is characterized by an ~~an powder~~-x-ray ~~powder~~ diffraction pattern comprising peaks at 8.8, 9.0, 10.8, 12.0, 12.6, 12.8, 13.6, 14.2, 15.0, 15.4, 18.0, 18.6, 18.7, 19.0, 19.9, 20.0, 22.9, and 25.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

~~10.7.~~ The compound of ~~Claim 3~~~~any one of Claims 1-3~~, wherein the compound is characterized by ~~anthe powder~~-x-ray ~~powder~~ diffraction pattern substantially as shown in Figure 5 as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

~~11.8.~~ A compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510)~~The compound of any one of Claims 1-10~~, wherein the compound is characterized by a differential scanning calorimetry thermogram comprising an endotherm with an onset of about 293°C.

~~12.9.~~ A compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510)~~The compound of any one of Claims 1-11~~, wherein the compound is characterized by a

thermogravimetric analysis thermogram comprising a weight loss of about 0.2% when heated from about 25 °C to about 275 °C.

~~13.10.~~ A compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propenyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510)The compound of any one of Claims 1-12, wherein the compound is characterized by ¹³C solid state NMR comprising at least three peaks selected from peaks at approximately 12, 13, 16, 21, 23, 31, 33, 38, 42, 44, 47, 50, 54, 107, 110, 111, 123, 124, 127, 128, 132, 145, 146, 150, 154, 156, 158, 160, 162, 166, 167.7, and 168 ppm.

~~14.11.~~ The compound of ~~Claim 10~~any one of Claims 1-12, wherein the compound is characterized by ¹³C solid state NMR comprising at least five peaks selected from peaks at approximately 12, 13, 16, 21, 23, 31, 33, 38, 42, 44, 47, 50, 54, 107, 110, 111, 123, 124, 127, 128, 132, 145, 146, 150, 154, 156, 158, 160, 162, 166, 167.7, and 168 ppm.

~~15.12.~~ The compound of ~~Claim 10~~any one of Claims 1-12, wherein the compound is characterized by ¹³C solid state NMR comprising at least seven peaks selected from peaks at approximately 12, 13, 16, 21, 23, 31, 33, 38, 42, 44, 47, 50, 54, 107, 110, 111, 123, 124, 127, 128, 132, 145, 146, 150, 154, 156, 158, 160, 162, 166, 167.7, and 168 ppm.

~~16.13.~~ The compound of ~~Claim 10~~any one of Claims 1-12, wherein the compound is characterized by ¹³C solid state NMR comprising peaks at approximately 12, 13, 16, 21, 23, 31, 33, 38, 42, 44, 47, 50, 54, 107, 110, 111, 123, 124, 127, 128, 132, 145, 146, 150, 154, 156, 158, 160, 162, 166, 167.7, and 168 ppm.

~~17.14.~~ The compound of ~~Claim 10~~any one of Claims 1-12, wherein the compound is characterized by ¹³C solid state NMR substantially as depicted in Figure 8.

~~15.~~ A compound, wherein the compound is a crystalline form of the M atropisomer of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propenyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (AMG 510)The compound of any one of Claims 1-17, wherein the compound is characterized by ¹⁹F solid state

NMR comprising peaks at approximately ~~-49, -60, -79, -90, -109~~ and, -120, ~~-138, -150, -168,~~
~~and -179~~ ppm.

~~18.16.~~ The compound of Claim 15, wherein the compound is characterized by ¹⁹F solid state NMR comprising peaks at approximately -49, -60, -79, -90, -109, -120, -138, -150, -168, and -179 ppm.

~~19.17.~~ The compound of Claim 15~~any one of Claims 1-17~~, wherein the compound is characterized by ¹⁹F solid state NMR substantially as depicted in Figure 9.

~~20.18.~~ The compound of any one of Claims 1-~~17~~19, wherein the compound is substantially pure.

~~21.19.~~ A pharmaceutical composition comprising the compound of any one of Claims 1-~~20~~18 and a pharmaceutically acceptable excipient.

~~22.20.~~ The pharmaceutical composition of Claim ~~21~~19, wherein the pharmaceutical composition is a dosage form for oral administration.

~~23.21.~~ The pharmaceutical composition of Claim ~~21~~19 or ~~20~~22, wherein the dosage form is a solid dosage form.

~~24.22.~~ The pharmaceutical composition of Claim ~~23~~21, wherein the solid dosage form is a tablet.

~~25.23.~~ The pharmaceutical composition of any one of Claims ~~21-24~~19-22, wherein the pharmaceutical composition comprises 120 mg of the compound.

~~26.24.~~ ~~Use of a~~A compound of any one of Claims 1-~~20~~18 or the pharmaceutical composition of any one of Claims ~~21-25~~19-23 for use as a medicament.

~~27.25.~~ Use of a compound of any one of Claims 1-~~20~~18 or the pharmaceutical composition of any one of Claims ~~21-25~~19-23 in the manufacture of a medicament for treating cancer having a KRAS G12C mutation.

~~28.26.~~ The use of Claim ~~2725~~, wherein the cancer having a KRAS G12C mutation is non-small cell lung cancer, small intestine cancer, appendix cancer, colorectal cancer, endometrial cancer, pancreatic cancer, skin cancer, gastric cancer, nasal cavity cancer, bile duct cancer.

~~29.27.~~ The use of Claim ~~2725~~, wherein the cancer having a KRAS G12C mutation is non-small cell lung cancer.

~~30.28.~~ The use of Claim ~~2527~~, wherein the cancer having a KRAS G12C mutation is pancreatic cancer.

~~31.29.~~ The use of Claim ~~2527~~, wherein the cancer having a KRAS G12C mutation is colorectal cancer.

~~32.30.~~ The use of any one of Claims ~~26-3125-29~~, wherein the compound is to be administered at a total daily dose of 5 mg to 1000 mg.

~~33.31.~~ The use of any one of Claims ~~26-3224-30~~, wherein the compound is to be administered at a total daily dose of 960 mg.

~~34.32.~~ The use of any one of Claims ~~26-3324-31~~, wherein the compound is to be administered to an adult.

~~35.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising peaks at 7.3, 9.8, 10.1, 11.3, 13.3, and 17.2 $\pm$ 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~36.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least three peaks selected from 7.3, 9.8, 10.1, 10.4, 11.3, 11.5, 11.9, 13.3, 14.3, 14.7, 17.2, and 18.4 $\pm$ 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~37.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least five peaks selected from 7.3, 9.8, 10.1,~~

~~10.4, 11.3, 11.5, 11.9, 13.3, 14.3, 14.7, 17.2, and 18.4 ± 0.2 degrees 2 theta as measured by x ray powder diffraction using an x ray wavelength of 1.54 Å.~~

~~38.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x ray diffraction pattern comprising at least seven peaks selected from 7.3, 9.8, 10.1, 10.4, 11.3, 11.5, 11.9, 13.3, 14.3, 14.7, 17.2, and 18.4 ± 0.2 degrees 2 theta as measured by x ray powder diffraction using an x ray wavelength of 1.54 Å.~~

~~39.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x ray diffraction pattern comprising peaks at 7.3, 9.8, 10.1, 10.4, 11.3, 11.5, 11.9, 13.3, 14.3, 14.7, 17.2, and 18.4 ± 0.2 degrees 2 theta as measured by x ray powder diffraction using an x ray wavelength of 1.54 Å.~~

~~40.—The compound of any one of Claims 1-3, wherein the compound is characterized by the powder x ray diffraction pattern substantially as shown in Figure 10 as measured by x ray powder diffraction using an x ray wavelength of 1.54 Å.~~

~~41.—The compound of any one of Claims 1-3 and 35-40, wherein the compound is characterized by a differential scanning calorimetry thermogram comprising an endotherm with an onset of about 193 °C.~~

~~42.—The compound of any one of Claims 1-3 and 35-41, wherein the compound is characterized by having a thermogravimetric analysis thermogram comprising a weight loss of about 1% to about 1.8% when heated from about 25 °C to about 250 °C.~~

~~43.—The compound of any one of Claims 1-3 and 35-42, wherein the compound is characterized by ¹³C solid state NMR comprising peaks at approximately 16, 18, 19, 20, 23, 25, 31, 32, 38, 40, 43, 46, 51, 57, 105, 107, 110, 117, 120, 123, 124, 125, 128, 132, 149, 152, 155, 158, 159, 163, and 166 ppm.~~

~~44.—The compound of any one of Claims 1-3 and 35-42, wherein the compound is characterized by ¹³C solid state NMR substantially as depicted in Figure 13.~~

~~45.—The compound of any one of Claims 1-3 and 35-44, wherein the compound is characterized by ¹⁹F solid state NMR, comprising peaks at approximately 59, 62, 89, 92, 119, 122, 148, 151, 179 and 181 ppm.~~

~~46.—The compound of any one of Claims 1-3 and 35-44, wherein the compound is characterized by ¹⁹F solid state NMR substantially as depicted in Figure 14.~~

~~47.—The compound of any one of Claims 35-46, wherein the compound is substantially pure.~~

~~48.—A pharmaceutical composition comprising the compound of any one of Claims 35-47 and a pharmaceutically acceptable excipient.~~

~~49.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising peaks at 6.3, 8.4, 9.5, and 16.0 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~50.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least three peaks selected from 6.3, 8.4, 9.5, 10.4, 14.9, 15.4, 15.5, 16.0, and 17.6 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~51.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least five peaks selected from 6.3, 8.4, 9.5, 10.4, 14.9, 15.4, 15.5, 16.0, and 17.6 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~52.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least seven peaks selected from 6.3, 8.4, 9.5, 10.4, 14.9, 15.4, 15.5, 16.0, and 17.6 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~53.—The compound of any one of Claims 1-3, wherein the compound is characterized by a powder x-ray diffraction pattern comprising peaks at 6.3, 8.4, 9.5, 10.4, 14.9, 15.4, 15.5, 16.0, and 17.6 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~54.—The compound of any one of Claims 1-3, wherein the compound is characterized by the powder x-ray diffraction pattern substantially as shown in Figure 15 as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~55.—The compound of any one of Claims 1-3 and 49-54, wherein the compound is characterized by a differential scanning calorimetry thermogram comprising an endotherm with an onset of about 194 °C.~~

~~56.—The compound of any one of Claims 1-3 and 49-55, wherein the compound is characterized by having an approximate negligible weight loss when heated from about 25 °C to about 250 °C.~~

~~57.—The compound of any one of Claims 49-56, wherein the compound is substantially pure.~~

~~58.—A pharmaceutical composition comprising the compound of any one of Claims 49-57 and a pharmaceutically acceptable excipient.~~

~~59.—The compound of Claim 1 or 2, wherein the compound is a crystalline hydrate form of Compound 1.~~

~~60.—The compound of any one of Claims 1, 2, and 59, wherein the compound is characterized by a powder x-ray diffraction pattern comprising peaks at 6.9, 8.0, 9.6, 12.4, and 13.1 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~61.—The compound of any one of Claims 1, 2, and 59, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least three peaks selected from 4.0, 4.4, 4.8, 6.9, 8.0, 8.8, 9.6, 11.3, 12.4, 13.0, 13.1, 14.6, 14.9, 15.2, 16.6, 17.3, 17.4, 17.9, and 19.5 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~62.—The compound of any one of Claims 1, 2, and 59, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least five peaks selected from 4.0, 4.4, 4.8, 6.9, 8.0, 8.8, 9.6, 11.3, 12.4, 13.0, 13.1, 14.6, 14.9, 15.2, 16.6, 17.3, 17.4, 17.9, and 19.5 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~63.—The compound of any one of Claims 1, 2, and 59, wherein the compound is characterized by a powder x-ray diffraction pattern comprising at least seven peaks selected from 4.0, 4.4, 4.8, 6.9, 8.0, 8.8, 9.6, 11.3, 12.4, 13.0, 13.1, 14.6, 14.9, 15.2, 16.6, 17.3, 17.4, 17.9, and 19.5 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.~~

~~64.—The compound of any one of Claims 1, 2, and 59, wherein the compound is characterized by a powder x-ray diffraction pattern comprising peaks at 4.0, 4.4, 4.8, 6.9, 8.0,~~

8.8, 9.6, 11.3, 12.4, 13.0, 13.1, 14.6, 14.9, 15.2, 16.2, 16.4, 16.6, 17.3, 17.4, 17.9, and 19.5 ± 0.2 degrees 2 theta as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

65. — The compound of any one of Claims 1, 2, and 59, wherein the compound is characterized by the powder x-ray diffraction pattern substantially as shown in Figure 18 as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

66. — The compound of any one of Claims 1, 2, and 59-65, wherein the compound is characterized by a differential scanning calorimetry thermogram comprising an endotherm with an onset of about 91°C.

67. — The compound of any one of Claims 1, 2, and 59-66, wherein the compound is characterized by having a thermogravimetric analysis thermogram comprising an approximate 11% weight loss when heated from about 39 °C to about 160 °C.

68. — The compound of any one of Claims 59-67, wherein the compound is substantially pure.

69. — A pharmaceutical composition comprising the compound of any one of Claims 59-68 and a pharmaceutically acceptable excipient.

70. — The compound of Claim 1 or 2, wherein the compound is a crystalline solvate form of Compound 1.

71. — The compound of Claim 70, wherein the compound is a solvate with tetrahydrofuran, acetonitrile, methyl ethylketone, ethyl acetate, dichloromethane, acetone, p-dioxane, methanol, isopropyl alcohol, or ethanol.

72. — A compound, wherein the compound is an amorphous form of 6-fluoro-7-(2-fluoro-6-hydroxyphenyl)-1-(4-methyl-2-(2-propanyl)-3-pyridinyl)-4-((2S)-2-methyl-4-(2-propenoyl)-1-piperazinyl)pyrido[2,3-d]pyrimidin-2(1H)-one (Compound 1) or an atropisomer thereof.

73. — The compound of Claim 72, wherein the compound is the M-atropisomer of Compound 1.

74. — The compound of Claims 72 or 73, wherein the compound is characterized by the powder x-ray diffraction pattern substantially as shown in Figure 5 as measured by x-ray powder diffraction using an x-ray wavelength of 1.54 Å.

~~75.—The compound of any one of Claims 72-74, wherein the compound is characterized by a differential scanning calorimetry thermogram comprising an endotherm with an onset of about 144 °C.~~

~~76.—The compound of any one of Claims 72-75, wherein the compound is characterized by a thermogravimetric analysis thermogram comprising a weight loss of about 1.5% when heated from about 25 °C to about 275 °C.~~

~~77.—The compound of any one of Claims 72-76, wherein the compound is characterized by ¹⁹F solid state NMR comprising peaks at approximately 86, 96, 116, 127, 146, and 156 ppm.~~

~~78.—The compound of any one of Claims 72-77, wherein the compound is characterized by ¹⁹F solid state NMR substantially as depicted in Figure 4.~~

~~79.—The compound of any one of Claims 72-78, wherein the compound is substantially pure.~~

~~80.—A pharmaceutical composition comprising the compound of any one of Claims 72-79 and a pharmaceutically acceptable excipient.~~

~~81.—A pharmaceutical composition comprising (1) the compound of any one of Claims 5-19, (2) the compound of any one of claims 35-46, (3) the compound of any one of Claims 49-56, (4) the compound of any one of Claims 59-67, or (5) the compound of any one of Claims 72-78, or any mixtures thereof, and a pharmaceutically acceptable excipient.~~