SOLID STATE FORMS OF AN FGFR INHIBITOR

CROSS-REFERENCE TO RELATED APPLICATION

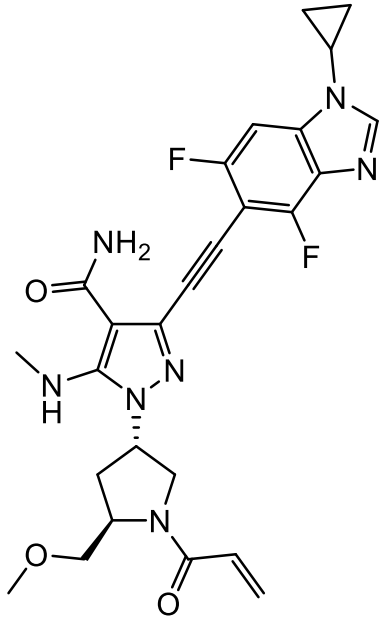
[0001] This application claims the benefit of U.S. Patent Application No. 63/287,212, filed on December 8, 2021, which is hereby incorporated by reference in its entirety.

BACKGROUND

[0002] Fibroblast growth factor receptors (FGFRs) are a subfamily of receptor tyrosine kinases (RTKs) that bind to members of the fibroblast growth factor family of proteins. Deregulation of the fibroblast growth factor/FGF receptor network occurs frequently in tumors. Accordingly, therapies that target aberrant FGFR kinase activity are desired for use in the treatment of cancer and other disorders. One such modulator of FGFR kinase is 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide.

SUMMARY

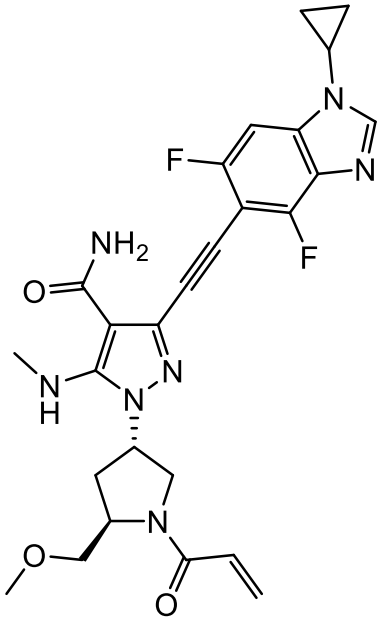
[0002a] In an aspect of the present disclosure, there is provided a solid form of 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide, depicted below as Compound 1,



Compound 1.

[0002b] In another aspect of the present disclosure, there is provided a solid form of 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide, wherein the solid form is crystalline.

[0003] The present disclosure relates to solid state forms of 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide, herein after known as Compound 1. The molecular structure of Compound 1 is shown below:



Compound 1

1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide

[0004] Disclosed herein is a solid form of 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide (Compound 1).

[0005] Disclosed herein is a solid form of 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide, wherein the solid form is crystalline.

[0006] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.8°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.9°±0.3 and 13.7°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.5°±0.3, 18.9°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.9°±0.3, 20.5°±0.3, and 22.3°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 20.8°±0.3, 25.7°±0.3, and 26.3°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 4. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 193.1 ℃ ± 5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 5. In some examples, the solid form exhibits less than 1.1 %

± 0.5 weight loss up to 200 °C ± 10.0 as determined by thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 5. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0007] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.7°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.0°±0.3 and 12.8°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 23.9°±0.3 and 24.3°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.5°±0.3, 20.3°±0.3, and 21.2°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.6°±0.3, 15.9°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 5.0°±0.3, 8.7°±0.3, 11.5°±0.3, 11.6°±0.3, 12.8°±0.3, 15.8°±0.3, 20.3°±0.3, 21.2°±0.3, 23.9°±0.3, 24.3°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 5.0°±0.3, 8.7°±0.3, 11.5°±0.3, 11.6°±0.3, 12.8°±0.3, 15.8°±0.3, 20.3°±0.3, 21.2°±0.3, 23.9°±0.3, 24.3°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 5.0°±0.3, 8.7°±0.3, 11.5°±0.3, 11.6°±0.3, 12.8°±0.3, 15.8°±0.3, 20.3°±0.3, 21.2°±0.3, 23.9°±0.3, 24.3°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 5.0°±0.3, 8.7°±0.3, 11.5°±0.3, 11.6°±0.3, 12.8°±0.3, 15.8°±0.3, 20.3°±0.3, 21.2°±0.3, 23.9°±0.3, 24.3°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 5.0°±0.3, 8.7°±0.3, 11.5°±0.3, 11.6°±0.3, 12.8°±0.3, 15.8°±0.3, 20.3°±0.3, 21.2°±0.3, 23.9°±0.3, 24.3°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 5.0°±0.3, 8.7°±0.3, 11.5°±0.3, 11.6°±0.3, 12.8°±0.3, 15.8°±0.3, 20.3°±0.3, 21.2°±0.3, 23.9°±0.3, 24.3°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 7. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising endothermic peaks at 164.0°C ±5.0 and 190.6°C ±5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 8. In some examples, the solid form exhibits less than 2.9 % ± 0.5 weight

loss up to 205 °C ± 10.0 as determined by thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 8. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0008] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.1°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.2°±0.3 and 8.6°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.2°±0.3 and 17.3°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 6.4°±0.3, 13.4°±0.3, and 15.3°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.8°±0.3, and 26.0°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 5.1°±0.3, 6.4°±0.3, 8.6°±0.3, 10.2°±0.3, 12.2°±0.3, 13.4°±0.3, 15.3°±0.3, 15.8°±0.3, 17.3°±0.3, and 26.0°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.6°±0.3, 10.2°±0.3, 12.2°±0.3, 13.4°±0.3, 15.3°±0.3, 15.8°±0.3, 17.3°±0.3, and 26.0°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.6°±0.3, 10.2°±0.3, 12.2°±0.3, 13.4°±0.3, 15.3°±0.3, 15.8°±0.3, 17.3°±0.3, and 26.0°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.6°±0.3, 10.2°±0.3, 12.2°±0.3, 13.4°±0.3, 15.3°±0.3, 15.8°±0.3, 17.3°±0.3, and 26.0°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.6°±0.3, 10.2°±0.3, 12.2°±0.3, 13.4°±0.3, 15.3°±0.3, 15.8°±0.3, 17.3°±0.3, and 26.0°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.6°±0.3, 10.2°±0.3, 12.2°±0.3, 13.4°±0.3, 15.3°±0.3, 15.8°±0.3, 17.3°±0.3, and 26.0°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 9. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising endothermic peaks at 66.2°C ±5.0, 106.4°C ±5.0, and 193.6°C ±5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 10. In some examples, the solid form exhibits less than 2.9 % ± 0.5 weight loss up to 94 °C ± 10.0 as determined by

thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 10. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0009] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.1°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.4°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 6.4°±0.3 and 25.6°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.7°±0.3, 11.9°±0.3, and 15.6°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 13.5°±0.3, and 25.8°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 5.1°±0.3, 6.4°±0.3, 8.7°±0.3, 10.4°±0.3, 11.9°±0.3, 13.5°±0.3, 15.6°±0.3, 25.8°±0.3, and 25.6°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.7°±0.3, 10.4°±0.3, 11.9°±0.3, 13.5°±0.3, 15.6°±0.3, 25.8°±0.3, and 25.6°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.7°±0.3, 10.4°±0.3, 11.9°±0.3, 13.5°±0.3, 15.6°±0.3, 25.8°±0.3, and 25.6°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.7°±0.3, 10.4°±0.3, 11.9°±0.3, 13.5°±0.3, 15.6°±0.3, 25.8°±0.3, and 25.6°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.7°±0.3, 10.4°±0.3, 11.9°±0.3, 13.5°±0.3, 15.6°±0.3, 25.8°±0.3, and 25.6°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 5.1°±0.3, 6.4°±0.3, 8.7°±0.3, 10.4°±0.3, 11.9°±0.3, 13.5°±0.3, 15.6°±0.3, 25.8°±0.3, and 25.6°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 11. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 105.8 °C ± 5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 12. In some examples, the solid form exhibits less than 2.1 % ± 0.5 weight loss up to 101 °C ± 10.0 as determined by thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in

Figure 12. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0010] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.5°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.2°±0.3 and 23.7°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.7°±0.3, 10.2°±0.3, and 19.5°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 6.5°±0.3, 15.5°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.4°±0.3, 15.0°±0.3, 19.0°±0.3, and 24.7°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 5.2°±0.3, 5.7°±0.3, 6.5°±0.3, 7.4°±0.3, 9.5°±0.3, 10.2°±0.3, 15.0°±0.3, 15.5°±0.3, 19.0°±0.3, 19.5°±0.3, 23.7°±0.3, 24.7°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 5.2°±0.3, 5.7°±0.3, 6.5°±0.3, 7.4°±0.3, 9.5°±0.3, 10.2°±0.3, 15.0°±0.3, 15.5°±0.3, 19.0°±0.3, 19.5°±0.3, 23.7°±0.3, 24.7°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 5.2°±0.3, 5.7°±0.3, 6.5°±0.3, 7.4°±0.3, 9.5°±0.3, 10.2°±0.3, 15.0°±0.3, 15.5°±0.3, 19.0°±0.3, 19.5°±0.3, 23.7°±0.3, 24.7°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 5.2°±0.3, 5.7°±0.3, 6.5°±0.3, 7.4°±0.3, 9.5°±0.3, 10.2°±0.3, 15.0°±0.3, 15.5°±0.3, 19.0°±0.3, 19.5°±0.3, 23.7°±0.3, 24.7°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 5.2°±0.3, 5.7°±0.3, 6.5°±0.3, 7.4°±0.3, 9.5°±0.3, 10.2°±0.3, 15.0°±0.3, 15.5°±0.3, 19.0°±0.3, 19.5°±0.3, 23.7°±0.3, 24.7°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 5.2°±0.3, 5.7°±0.3, 6.5°±0.3, 7.4°±0.3, 9.5°±0.3, 10.2°±0.3, 15.0°±0.3, 15.5°±0.3, 19.0°±0.3, 19.5°±0.3, 23.7°±0.3, 24.7°±0.3, and 26.8°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 13. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising endothermic peaks at 112.3°C ±5.0 and 193.7°C ±5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 14. In some examples, the solid form exhibits less than 4.3 % ± 0.5 weight loss up to 126 °C ± 10.0

as determined by thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 14. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0011] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.4°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.8°±0.3 and 23.4°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.0°±0.3 and 15.2°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.1°±0.3, 13.6°±0.3, and 26.7°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.1°±0.3, 25.6°±0.3, and 27.2°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 5.0°±0.3, 5.4°±0.3, 9.1°±0.3, 9.8°±0.3, 10.1°±0.3, 13.6°±0.3, 15.2°±0.3, 23.4°±0.3, 25.6°±0.3, 26.7°±0.3, and 27.2°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 5.0°±0.3, 5.4°±0.3, 9.1°±0.3, 9.8°±0.3, 10.1°±0.3, 13.6°±0.3, 15.2°±0.3, 23.4°±0.3, 25.6°±0.3, 26.7°±0.3, and 27.2°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 5.0°±0.3, 5.4°±0.3, 9.1°±0.3, 9.8°±0.3, 10.1°±0.3, 13.6°±0.3, 15.2°±0.3, 23.4°±0.3, 25.6°±0.3, 26.7°±0.3, and 27.2°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 5.0°±0.3, 5.4°±0.3, 9.1°±0.3, 9.8°±0.3, 10.1°±0.3, 13.6°±0.3, 15.2°±0.3, 23.4°±0.3, 25.6°±0.3, 26.7°±0.3, and 27.2°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 5.0°±0.3, 5.4°±0.3, 9.1°±0.3, 9.8°±0.3, 10.1°±0.3, 13.6°±0.3, 15.2°±0.3, 23.4°±0.3, 25.6°±0.3, 26.7°±0.3, and 27.2°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 5.0°±0.3, 5.4°±0.3, 9.1°±0.3, 9.8°±0.3, 10.1°±0.3, 13.6°±0.3, 15.2°±0.3, 23.4°±0.3, 25.6°±0.3, 26.7°±0.3, and 27.2°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 15. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising endothermic peaks at 120.8 ℃ ± 5.0 and 195.1 ℃ ± 5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 16. In some examples, the solid form exhibits less than 3.9 % ± 0.5 weight

loss up to 119°C ± 10.0 as determined by thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 16. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0012] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.8°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.2°±0.3 and 15.2°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.0°±0.3 and 10.1 °±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.4°±0.3, 9.8°±0.3, and 23.4°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.4°±0.3, 14.2°±0.3, and 25.5°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 5.0°±0.3, 5.2°±0.3, 5.8°±0.3, 8.4°±0.3, 9.8°±0.3, 10.1°±0.3, 10.4°±0.3, 14.2°±0.3, 15.2°±0.3, 23.4°±0.3, and 25.5°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 5.0°±0.3, 5.2°±0.3, 5.8°±0.3, 8.4°±0.3, 9.8°±0.3, 10.1°±0.3, 10.4°±0.3, 14.2°±0.3, 15.2°±0.3, 23.4°±0.3, and 25.5°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 5.0°±0.3, 5.2°±0.3, 5.8°±0.3, 8.4°±0.3, 9.8°±0.3, 10.1°±0.3, 10.4°±0.3, 14.2°±0.3, 15.2°±0.3, 23.4°±0.3, and 25.5°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 5.0°±0.3, 5.2°±0.3, 5.8°±0.3, 8.4°±0.3, 9.8°±0.3, 10.1°±0.3, 10.4°±0.3, 14.2°±0.3, 15.2°±0.3, 23.4°±0.3, and 25.5°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 5.0°±0.3, 5.2°±0.3, 5.8°±0.3, 8.4°±0.3, 9.8°±0.3, 10.1°±0.3, 10.4°±0.3, 14.2°±0.3, 15.2°±0.3, 23.4°±0.3, and 25.5°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 5.0°±0.3, 5.2°±0.3, 5.8°±0.3, 8.4°±0.3, 9.8°±0.3, 10.1°±0.3, 10.4°±0.3, 14.2°±0.3, 15.2°±0.3, 23.4°±0.3, and 25.5°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 17. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising endothermic peaks at 108.7°C ± 5.0 and 195.1 °C ± 5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 18. In some examples, the solid form exhibits less than 7.4 % ± 0.5 weight

loss up to 140 °C ± 10.0 as determined by thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 18. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0013] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is crystalline. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.3°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 6.1°±0.3 and 13.4°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.9°±0.3 and 10.5°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.8°±0.3, 25.0 °±0.3, and 25.7°±0.3. In some examples, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 18.6°±0.3, 23.0°±0.3, and 25.2°±0.3. In some examples, the solid form exhibits at least one X-ray powder diffraction reflection selected from 6.1°±0.3, 7.9°±0.3, 10.5°±0.3, 11.8°±0.3, 12.3°±0.3, 13.4°±0.3, 18.6°±0.3, 23.0°±0.3, 25.0°±0.3, 25.2°±0.3, and 25.7°±0.3. In some examples, the solid form exhibits at least two X-ray powder diffraction reflections selected from 6.1°±0.3, 7.9°±0.3, 10.5°±0.3, 11.8°±0.3, 12.3°±0.3, 13.4°±0.3, 18.6°±0.3, 23.0°±0.3, 25.0°±0.3, 25.2°±0.3, and 25.7°±0.3. In some examples, the solid form exhibits at least three X-ray powder diffraction reflections selected from 6.1°±0.3, 7.9°±0.3, 10.5°±0.3, 11.8°±0.3, 12.3°±0.3, 13.4°±0.3, 18.6°±0.3, 23.0°±0.3, 25.0°±0.3, 25.2°±0.3, and 25.7°±0.3. In some examples, the solid form exhibits at least four X-ray powder diffraction reflections selected from 6.1°±0.3, 7.9°±0.3, 10.5°±0.3, 11.8°±0.3, 12.3°±0.3, 13.4°±0.3, 18.6°±0.3, 23.0°±0.3, 25.0°±0.3, 25.2°±0.3, and 25.7°±0.3. In some examples, the solid form exhibits at least five X-ray powder diffraction reflections selected from 6.1°±0.3, 7.9°±0.3, 10.5°±0.3, 11.8°±0.3, 12.3°±0.3, 13.4°±0.3, 18.6°±0.3, 23.0°±0.3, 25.0°±0.3, 25.2°±0.3, and 25.7°±0.3. In some examples, the solid form exhibits at least six X-ray powder diffraction reflections selected from 6.1°±0.3, 7.9°±0.3, 10.5°±0.3, 11.8°±0.3, 12.3°±0.3, 13.4°±0.3, 18.6°±0.3, 23.0°±0.3, 25.0°±0.3, 25.2°±0.3, and 25.7°±0.3. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 19. In some examples, the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 179.3 °C ± 5.0. In some examples, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 20. In some examples, the solid form exhibits less than 2.9 % ± 0.5 weight

loss up to 245 °C ± 10.0 as determined by thermogravimetric analysis. In some examples, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 20. In some examples, the solid form is substantially free of other crystalline or amorphous forms. In some examples, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some examples, the solid form is substantially free of impurities. In some examples, the amount of impurities is 2% or less.

[0014] Disclosed herein is a solid crystalline form of Compound 1 wherein the solid form is amorphous. In some examples, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 1.

[0015] Disclosed herein is a pharmaceutical composition comprising the solid form of any one of the solid forms provided herein and a pharmaceutically acceptable excipient. In some examples, the pharmaceutical composition further comprises a disintegrating agent.

[0016] Disclosed herein is a method of treating cancer in a patient in need thereof, comprising administering to the patient a composition comprising the solid form of any one of the solid forms provided herein and at least one pharmaceutically acceptable excipient.

[0017] Disclosed herein is a method of treating cancer in a patient in need thereof, comprising administering to the patient the solid form of any of the solid forms provided herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] The features of the invention are set forth with particularity in the appended claims. A better understanding of the features of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0019] Figure 1 shows an X-ray diffraction pattern of amorphous Compound 1;

[0020] Figure 2 shows an X-ray diffraction pattern of crystalline Form I of Compound 1;

[0021] Figure 3 shows a differential scanning calorimetry and thermogravimetric analysis of Form I of Compound 1;

[0022] Figure 4 shows an X-ray diffraction pattern of crystalline Form II of Compound 1;

[0023] Figure 5 shows a Differential scanning calorimetry and thermogravimetric analysis of Form II of Compound 1;

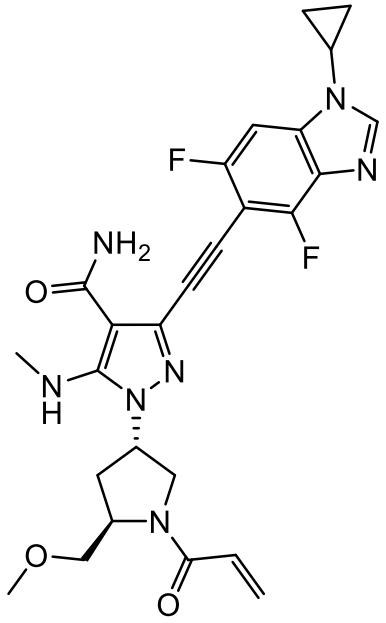
[0024] Figure 6 shows a Dynamic Vapor Sorption isotherm plot and mass plot of crystalline Form II of Compound 1;

[0025] Figure 7 shows an X-ray diffraction pattern of crystalline Form III of Compound 1;

[0026] Figure 8 shows a differential scanning calorimetry and thermogravimetric analysis of Form III of Compound 1;

CLAIMS

1. A solid form of 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide, depicted below as Compound 1,



Compound 1.

2. A solid form of 1-((3S,5R)-1-acryloyl-5-(methoxymethyl)pyrrolidin-3-yl)-3-((1-cyclopropyl-4,6-difluoro-1H-benzo[d]imidazol-5-yl)ethynyl)-5-(methylamino)-1H-pyrazole-4-carboxamide, wherein the solid form is crystalline.
3. The solid form of claim 2, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.8°±0.3.
4. The solid form of claim 3, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.9°±0.3 and 13.7°±0.3.
5. The solid form of any one of claims 3 or 4, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.5°±0.3, 18.9°±0.3, and 26.8°±0.3.
6. The solid form of any one of claims 3 to 5, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.9°±0.3, 20.5°±0.3, and 22.3°±0.3.
7. The solid form of any one of claims 3 to 6, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 20.8°±0.3, 25.7°±0.3, and 26.3°±0.3.
8. The solid form of claim 2, wherein the solid form exhibits at least one X-ray powder diffraction reflection selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3.

9. The solid form of claim 8, wherein the solid form exhibits at least two X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3.
10. The solid form of claim 9, wherein the solid form exhibits at least three X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3.
11. The solid form of claim 10, wherein the solid form exhibits at least four X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3.
12. The solid form of claim 11, wherein the solid form exhibits at least five X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3.
13. The solid form of claim 12, wherein the solid form exhibits at least six X-ray powder diffraction reflections selected from 7.9°±0.3, 9.5°±0.3, 11.8°±0.3, 13.7°±0.3, 15.9°±0.3, 18.9°±0.3, 20.5°±0.3, 20.8°±0.3, 22.3°±0.3, 25.7°±0.3, and 26.3°±0.3.
14. The solid form of claim 2, wherein the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 4.
15. The solid form of any one of claims 3 to 14, wherein the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 193.1 ℃ ± 5.0.
16. The solid form of any one of claims 3 to 15, wherein the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 5.
17. The solid form of any one of claims 3 to 16, wherein the solid form exhibits less than 1.1 % ± 0.5 weight loss up to 200 °C ± 10.0 as determined by thermogravimetric analysis.
18. The solid form of any one of claims 3 to 17, wherein the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 5.
19. The solid form of any one of claims 3 to 18, wherein the solid form is substantially free of other crystalline or amorphous forms.
20. The solid form of claim 19, wherein the amount of other crystalline or amorphous forms is 5 % (w/w) or less.
21. The solid form of any one of claims 3 to 20, wherein the solid form is substantially free of impurities.
22. The solid form of claim 21, wherein the amount of impurities is 2% or less.
23. The solid form of claim 2, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.0°±0.3.

24. The solid form of claim 23, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.1°±0.3 and 17.1°±0.3.

25. The solid form of any one of claims 23 or 24, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.5°±0.3, 24.8°±0.3, and 25.8°±0.3.

26. The solid form of any one of claims 23 to 25, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.3°±0.3, 13.0°±0.3, and 16.4°±0.3.

27. The solid form of any one of claims 23 to 26, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.1°±0.3 and 15.2°±0.3.

28. The solid form of claim 2, wherein the solid form exhibits at least one X-ray powder diffraction reflection selected from 5.0°±0.3, 8.5°±0.3, 9.3°±0.3, 10.1°±0.3, 12.1°±0.3, 13.0°±0.3, 15.2°±0.3, 16.4°±0.3, 17.1°±0.3, 24.8°±0.3, and 25.8°±0.3.

29. The solid form of claim 28, wherein the solid form exhibits at least two X-ray powder diffraction reflections selected from 5.0°±0.3, 8.5°±0.3, 9.3°±0.3, 10.1°±0.3, 12.1°±0.3, 13.0°±0.3, 15.2°±0.3, 16.4°±0.3, 17.1°±0.3, 24.8°±0.3, and 25.8°±0.3.

30. The solid form of claim 29, wherein the solid form exhibits at least three X-ray powder diffraction reflections selected from 5.0°±0.3, 8.5°±0.3, 9.3°±0.3, 10.1°±0.3, 12.1°±0.3, 13.0°±0.3, 15.2°±0.3, 16.4°±0.3, 17.1°±0.3, 24.8°±0.3, and 25.8°±0.3.

31. The solid form of claim 30, wherein the solid form exhibits at least four X-ray powder diffraction reflections selected from 5.0°±0.3, 8.5°±0.3, 9.3°±0.3, 10.1°±0.3, 12.1°±0.3, 13.0°±0.3, 15.2°±0.3, 16.4°±0.3, 17.1°±0.3, 24.8°±0.3, and 25.8°±0.3.

32. The solid form of claim 31, wherein the solid form exhibits at least five X-ray powder diffraction reflections selected from 5.0°±0.3, 8.5°±0.3, 9.3°±0.3, 10.1°±0.3, 12.1°±0.3, 13.0°±0.3, 15.2°±0.3, 16.4°±0.3, 17.1°±0.3, 24.8°±0.3, and 25.8°±0.3.

33. The solid form of claim 32, wherein the solid form exhibits at least six X-ray powder diffraction reflections selected from 5.0°±0.3, 8.5°±0.3, 9.3°±0.3, 10.1°±0.3, 12.1°±0.3, 13.0°±0.3, 15.2°±0.3, 16.4°±0.3, 17.1°±0.3, 24.8°±0.3, and 25.8°±0.3.

34. The solid form of claim 2, wherein the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 2.

35. The solid form of any one of claims 23 to 34, wherein the solid form exhibits a differential scanning calorimetry thermogram comprising endothermic peaks at 53.5°C ±10.0, 106.5°C ±5.0, and 193.7°C ±5.0.

36. The solid form of any one of claims 23 to 35, wherein the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 3.

37. The solid form of any one of claims 23 to 36, wherein the solid form exhibits less than 4.9 % ±0.5 weight loss up to 76°C ±10.0 as determined by thermogravimetric analysis.

38. The solid form of any one of claims 23 to 37, wherein the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 3.

39. The solid form of any one of claims 23 to 38, wherein the solid form is substantially free of other crystalline or amorphous forms.

40. The solid form of claim 39, wherein the amount of other crystalline or amorphous forms is 5 % (w/w) or less.

41. The solid form of any one of claims 23 to 40, wherein the solid form is substantially free of impurities.

42. The solid form of claim 41, wherein the amount of impurities is 2% or less.