SOLID STATE FORMS OF AN AKT1 INHIBITOR AND SALTS THEREOF

CROSS REFERENCE

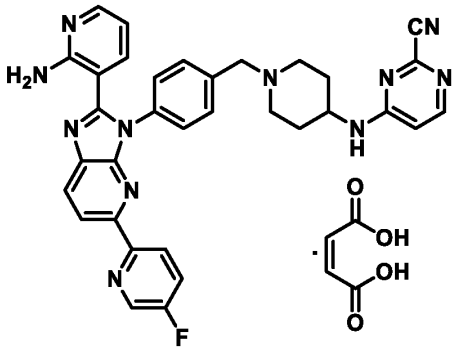
[0001] This Application claims the benefit of US Provisional Application No. 63/570,497, filed March 27, 2024, which is incorporated by reference in its entirety herein.

BACKGROUND OF THE INVENTION

[0002] AKT is a protein kinase and mediates cell survival and proliferation by inhibiting pathways which promote apoptosis. AKT signaling cascade dysfunction is observed in several cancer types and may be associated with tumor aggressiveness. Additionally, malfunction of AKT typically leads to enhanced proliferation, growth, survival, and resistance to apoptosis. Pharmaceutical agents with the ability to modulate AKT activity, particularly AKT1 activity, would be useful in the treatment of disease, such as cancer. One such modulator of AKT1 is 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile and pharmaceutically acceptable salts thereof.

SUMMARY OF THE INVENTION

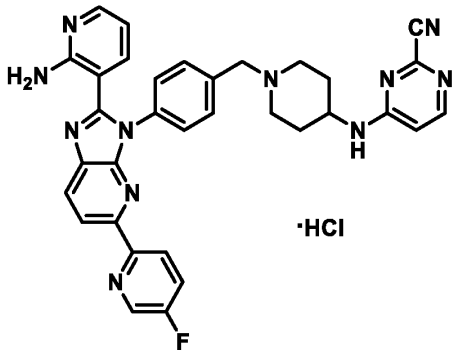
[0003] The present disclosure relates to crystalline forms I-X of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate, herein after known as Compound 1. The molecular structure of Compound 1 is shown below:



Compound 1

4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate

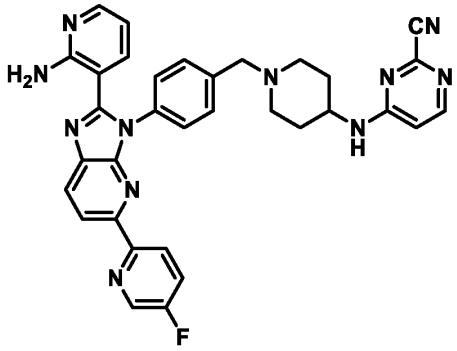
[0004] Also disclosed herein are crystalline forms I-III of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride, hereinafter known as Compound 2. The molecular structure of Compound 2 is shown below:



Compound 2

4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride

[0005] Also disclosed herein are crystalline forms of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile, hereinafter known as Compound 3. The molecular structure of Compound 3 is shown below:



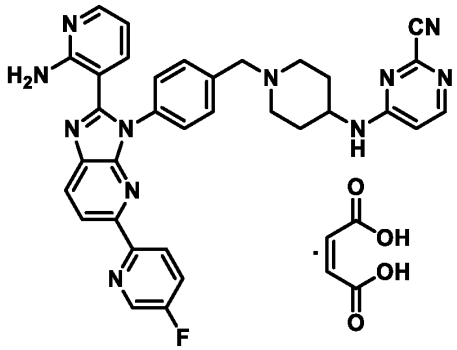
Compound 3

4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile

[0006] Provided herein are pharmaceutical compositions comprising solid state forms of Compound 1, Compound 2, Compound 3, or any combinations thereof, and a pharmaceutically acceptable excipient.

[0007] Also described herein is a method of inhibiting AKT1 protein kinase comprising administering to the subject with a condition in need thereof, the solid form of Compound 1, Compound 2, Compound 3, or any combinations thereof.

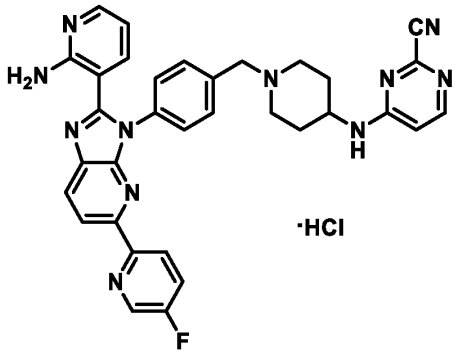
[0008] One embodiment provides a solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate, depicted below as Compound 1,



Compound 1

Wherein the solid form is crystalline.

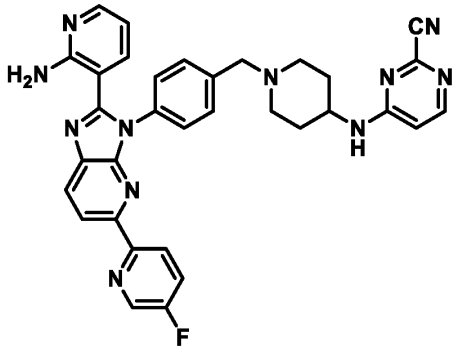
[0009] One embodiment provides a solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride, depicted below as Compound 2,



Compound 2

wherein the solid form is crystalline.

[0010] One embodiment provides a solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile, depicted below as Compound 3,



Compound 3

wherein the solid form is crystalline.

[0011] One embodiment provides a pharmaceutically acceptable salt of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile wherein the salt is selected from the group consisting of hydrochloride, maleate, citrate, sulfate, malate, mesylate, tosylate, besylate, fumarate, tartrate, phosphate, and succinate.

[0012] One embodiment provides a compound 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride.

[0013] One embodiment provides a compound 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate.

[0014] One embodiment provides a pharmaceutical composition comprising a solid form of any one of the compounds provided herein, and a pharmaceutically acceptable excipient.

[0015] One embodiment provides a method of treating a disease or disorder in a patient in need thereof, comprising administering a solid form of any one of the compounds provided herein. Another embodiment provides the method wherein the disease or disorder is cancer. Another embodiment provides the method wherein the disease or disorder is neoplastic disease.

[0016] One embodiment provides a method of treating a disease or disorder in a patient in need thereof, comprising administering a solid form of any one of the compounds provided herein and a pharmaceutically acceptable excipient. Another embodiment provides the method wherein the disease or disorder is cancer. Another embodiment provides the method wherein the disease or disorder is neoplastic disease.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] 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:

[0018] Figure 1 shows an X-ray diffraction pattern of crystalline Compound 1 Form I;

[0019] Figure 2 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form I;

[0020] Figure 3 shows an X-ray diffraction pattern of crystalline Compound 1 Form II;

[0021] Figure 4 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form II;

[0022] Figure 5 shows an X-ray diffraction pattern of crystalline Compound 1 Form III;

[0023] Figure 6 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form III;

[0024] Figure 7 shows an X-ray diffraction pattern of crystalline Compound 1 Form IV;

[0025] Figure 8 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form IV;

[0026] Figure 9 shows an X-ray diffraction pattern of crystalline Compound 1 Form V;

[0027] Figure 10 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form V;

[0028] Figure 11 shows an X-ray diffraction pattern of crystalline Compound 1 Form VI;

[0029] Figure 12 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form VI;

[0030] Figure 13 shows an X-ray diffraction pattern of crystalline Compound 1 Form VII;

[0031] Figure 14 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form VII;

[0032] Figure 15 shows X-ray diffraction patterns of crystalline Compound 1 Form VIII;

[0033] Figure 16 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form VIII;

[0034] Figure 17 shows an X-ray diffraction pattern of crystalline Compound 1 Form IX;

[0035] Figure 18 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form IX;

[0036] Figure 19 shows an X-ray diffraction pattern of crystalline Compound 1 Form X;

[0037] Figure 20 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 1 Form X;

[0038] Figure 21 shows an X-ray diffraction pattern of crystalline Compound 2 Form I;

[0039] Figure 22 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 2 Form I;

[0040] Figure 23 shows an X-ray diffraction pattern of crystalline Compound 2 Form II;

[0041] Figure 24 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 2 Form II;

[0042] Figure 25 shows an X-ray diffraction pattern of crystalline Compound 2 Form III;

[0043] Figure 26 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 2 Form III;

[0044] Figure 27 shows an X-ray diffraction pattern of crystalline Compound 3 Form I;

[0045] Figure 28 shows a differential scanning calorimetry and thermogravimetric analysis of crystalline Compound 3 Form I;

[0046] Figure 29 shows a ^{1}H NMR spectrum of crystalline Compound 1;

[0047] Figure 30 shows a ^{1}H NMR spectrum of crystalline Compound 2;

[0048] Figure 31 shows a ^{1}H NMR spectrum of crystalline Compound 3;

[0049] Figure 32 shows the Dynamic Vapor Sorption Isotherm Plot of Compound 1 Form I;

[0050] Figure 33 shows the Dynamic Vapor Sorption Mass Plot of Compound 1 Form I;

[0051] Figure 34 shows the Dynamic Vapor Sorption Isotherm Plot of Compound 2 Form I;

[0052] Figure 35 shows the Dynamic Vapor Sorption Isotherm Plot of Compound 3 Form I;

[0053] Figure 36 shows the Dynamic Vapor Sorption Mass Plot of Compound 3 Form I.

DETAILED DESCRIPTION OF THE INVENTION

[0054] Provided herein are compositions comprising solid state forms of Compound 1, Compound 2, Compound 3, or any combinations thereof.

[0055] In some embodiments, Compound 1 was found to have a number of unexpected advantages. Of the Compound 1 crystalline forms, Compound 1 Form I was determined to be the more stable form with more favorable solid state properties. Compound 1 Form I was physically stable at stress conditions over a period of 7 days. Compound 1 Form I was the more stable form with favorable physicochemical properties and solubility/stability compared to Compound 3 Form I. Compound 3 Form I was non-hygroscopic and was physically and chemically stable at most stress conditions. Solubility of Compound 3 Form I showed pH dependency, and exhibited low solubility under less acidic conditions (e.g., pH > 5). Compound 2 Form I exhibited high crystallinity, high melting point, and generally high stability. Compound 2 Form I also demonstrated residual solvent issues. Solubility of Compound 2 Form I in water and many organic solvents was low.

Definitions

[0056] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in the art to which this invention belongs. All patents and publications referred to herein are incorporated by reference.

[0057] As used in the specification and claims, the singular form “a”, “an” and “the” includes plural references unless the context clearly dictates otherwise.

[0058] The term “hydrate” and “solvate” are meant to describe crystalline Compound 1 forms that include an amount of water or solvent, as supported by data derived from differential scanning calorimetry (DSC) experiments, thermogravimetric analysis (TGA) experiments, X-ray diffraction experiments, and/or the procedure for generating the solid crystalline form. In some embodiments,

a solvate crystalline form or hydrate crystalline form comprises at least 1.5%, 1.75%, 2.0%, 2.5%, 3.0%, 4.0%, 5.0%, 6.0%, 7.0%, 8.0%, 9.0%, 10.0%, 15.0%, or 20.0% of the total weight of the sample as water, solvent, or a combination thereof, as determined by TGA. In some embodiments, a solvate crystalline form or hydrate crystalline form exhibits at least one DSC endotherm onset before or within 30 °C of the boiling point of water or the solvent(s) used in the generation of the crystalline form. For example, a hydrate crystalline form may have a DSC endotherm onset at 108 °C, with the endotherm peak positioned at 124 °C.

[0059] Crystalline solid forms termed a "solvate," or "hydrate" are not meant to be limiting. For example, a solvate or hydrate can comprise a combination of water and solvent in the crystalline solid form.

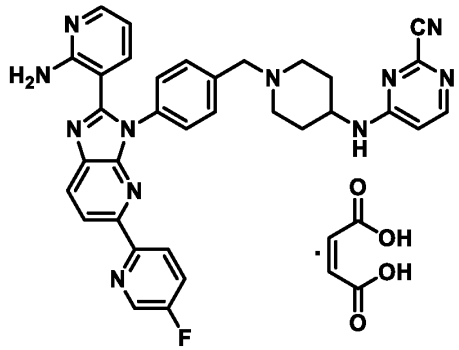
[0060] The term "type," "form," and "pattern" are meant to be used interchangeably and are meant to refer to a particular crystalline material with properties described herein. For example, "crystalline hydrate Type A," "crystalline hydrate Form A," and "XRPD Pattern A" refer to the same crystalline matter.

[0061] The term "about" when referring to a number or a numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and thus the number or numerical range, in some instances, will vary between 1% and 15% of the stated number or numerical range.

[0062] The term "substantially similar" as used herein means an analytical spectrum, such as XRPD pattern, DSC thermogram, or TGA thermogram, which resembles the reference spectrum to a great degree in both the peak locations and peak intensity.

Characterization of Compounds and Solid State Forms

[0063] One embodiment provides a solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate, depicted below as Compound 1,

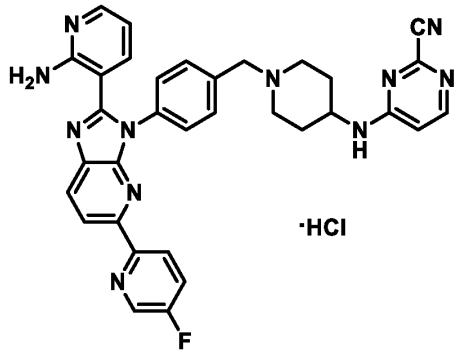


Compound 1

Wherein the solid form is crystalline. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 21.1° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.0° ± 0.3 and 24.0° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 4.9° ± 0.3, 19.2° ± 0.3, and 27.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.6° ± 0.3, 20.5° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, and 26.7° ± 0.3. In some embodiments, the solid form exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 1. In some embodiments, the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 234.6 °C ± 5.0. In some embodiments, the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 255.5 °C ± 5.0. In some embodiments, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 2. In some embodiments, the solid form does not exhibit a weight loss until a transition at 216.5 °C ± 10.0 as determined by thermogravimetric analysis. In some embodiments, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 2. In some embodiments, the amount of

other crystalline or amorphous forms is 10% (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5% (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1% (w/w) or less. In some embodiments, the solid form has a chemical purity of 97% or more. In some embodiments, the solid form has a chemical purity of 98% or more. In some embodiments, the solid form has a chemical purity of 99% or more. In some embodiments, the solid form has a chemical purity of 99.5% or more.

[0064] One embodiment provides a solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride, depicted below as Compound 2,

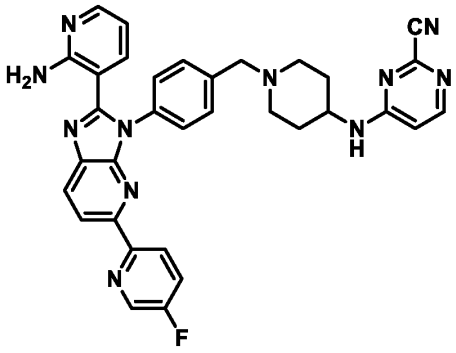


Compound 2

wherein the solid form is crystalline. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 22.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.3° ± 0.3 and 20.6° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 16.4° ± 0.3, 17.5° ± 0.3, and 18.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.3° ± 0.3, 25.6° ± 0.3, and 29.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.6° ± 0.3, 22.0° ± 0.3, 23.0° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.7° ± 0.3, 14.3° ± 0.3, 18.0° ± 0.3, 21.3° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected

from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 21. In some embodiments, the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 315.4 °C ± 5.0. In some embodiments, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 22. In some embodiments, the solid form exhibits a weight loss of 1.1% ± 0.5 weight loss up to 100.0 °C ± 10.0 as determined by thermogravimetric analysis. In some embodiments, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 22. In some embodiments, the amount of other crystalline or amorphous forms is 10% (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5% (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1% (w/w) or less. In some embodiments, the solid form has a chemical purity of 97% or more. In some embodiments, the solid form has a chemical purity of 98% or more. In some embodiments, the solid form has a chemical purity of 99% or more. In some embodiments, the solid form has a chemical purity of 99.5% or more.

[0065] One embodiment provides a solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile, depicted below as Compound 3,



Compound 3

wherein the solid form is crystalline. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 27.8 ° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.7° ± 0.3 and 24.1° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.4° ± 0.3, 14.9° ± 0.3, and 18.7° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.1° ± 0.3, 18.0° ± 0.3, and 22.0° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.8 ° ± 0.3, 19.4° ± 0.3, and 22.6° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.9° ± 0.3, 17.9° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ±

0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 27. In some embodiments, the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 270.7 °C ± 5.0. In some embodiments, the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 28. In some embodiments, the solid form exhibits a weight loss of 0.7% ± 0.5 weight loss up to 200.0 °C ± 10.0 as determined by thermogravimetric analysis. In some embodiments, the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 28. In some embodiments, the amount of other crystalline or amorphous forms is 10% (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5% (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1% (w/w) or less. In some embodiments, the solid form has a chemical purity of 97% or more. In some embodiments, the solid form has a chemical purity of 98% or more. In some embodiments, the solid form has a chemical purity of 99% or more. In some embodiments, the solid form has a chemical purity of 99.5% or more.

[0066] One embodiment provides a pharmaceutically acceptable salt of is 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile wherein the salt is selected from the group consisting of hydrochloride, maleate, citrate, sulfate, malate, mesylate, tosylate, besylate, fumarate, tartrate, phosphate, and succinate.

[0067] One embodiment provides a compound 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride.

[0068] One embodiment provides a compound 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate.

[0069] In one embodiment, the present invention provides solid state forms of Compound 1, Compound 2, and Compound 3. In one embodiment, the crystalline forms are characterized by the interlattice plane intervals determined by an X-ray powder diffraction (XRPD) diffractogram. The diffractogram is typically represented by a diagram plotting the intensity of the peaks versus the location of the peaks, i.e., diffraction angle 2Θ (two-theta) in degrees. The characteristic peaks of a given compound can be selected according to the peak locations and their relative intensity to

distinguish compounds and crystalline structures from others.Those skilled in the art recognize that the measurements of the XRD peak locations and/or intensity for a given crystalline form of the same compound will vary within a margin of error. The values of degree 2Θ allow appropriate error margins. Typically, the error margins are represented by "±". For example, the degree 2Θ of "8.716±0.3" denotes a range from 8.716+0.3, i.e., 9.016, to 8.716-0.3, i.e., 8.416. Depending on the sample preparation techniques, the calibration techniques applied to the instruments, human operational variation, and etc., those skilled in the art recognize that the margin of error for a XRD can be ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; ±0.05; or less. Additional details of the methods and equipment used for the XRD analysis are described in the Examples section.

[0070] In one embodiment, the crystalline forms are characterized by Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA). The DSC thermogram is typically expressed by a diagram plotting the normalized heat flow in units of Watts/gram ("W/g") versus the measured sample temperature in degree C. The DSC thermogram is generally evaluated for extrapolated onset and end (outset) temperatures, peak temperature, and heat of fusion. The single maximum value of a DSV thermogram is often used as the characteristic peak to distinguish one crystalline form from another crystalline form. The TGA thermogram is typically expressed by a diagram plotting the weight loss percentage (%) versus the measured sample temperature in degree C. In the figures disclosed herein, DSC and TGA thermograms have been plotted sharing an X axis (temperature), but have distinct Y axes of weight % and heat flow corresponding respectively to TGA and DSC measurements.

[0071] Those skilled in the art recognize that the measurements of the DSC and TGA thermograms for a given crystalline form of the same compound will vary within a margin of error. The values of a single maximum value, expressed in degree C, allow appropriate error margins. Typically, the error margins are represented by "±". For example, the single maximum value of "53.1 °C ±10.0" denotes a range from 53.1 °C + 10.0, i.e., 63.1 °C, to about 53.1 °C – 10.0, i.e., 43.1 °C. Depending on the sample preparation techniques, crystallization conditions, calibration techniques applied to the instruments, human operational variations, and etc., those skilled in the art recognize that the appropriate margin of error for a single maximum value can be ±10.0; ±7.5; ±5.0; ±2.5; ±2; ±1.5; ±1; ±0.5; or less for any of the powder diffraction reflections described herein.

[0072] Additional details of the methods and equipment used for the DSC and TGA thermogram analysis are described in the Examples section.

Compound 1

[0073] In some embodiments, the present invention provides a crystalline solid state of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-

yl)amino)pyrimidine-2-carbonitrile maleate, also known as Compound 1. In some embodiments, provided herein is crystalline Compound 1 Form I. In some embodiments, provided herein is crystalline Compound 1 Form II. In some embodiments, provided herein is crystalline Compound 1 Form III. In some embodiments, provided herein is crystalline Compound 1 Form IV. In some embodiments, provided herein is crystalline Compound 1 Form V. In some embodiments, provided herein is crystalline Compound 1 Form VI. In some embodiments, provided herein is crystalline Compound 1 Form VII. In some embodiments, provided herein is crystalline Compound 1 Form VIII. In some embodiments, provided herein is crystalline Compound 1 Form IX. In some embodiments, provided herein is crystalline Compound 1 Form X.

Compound 1 Form I

[0074] In some embodiments, the present invention provides crystalline solid state Compound 1 Form I. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 21.1° ± 0.3. In some embodiments, the solid form Compound 1 Form I exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.0° ± 0.3 and 24.0° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 4.9° ± 0.3, 19.2° ± 0.3, and 27.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.6° ± 0.3, 20.5° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, and 26.7° ± 0.3.

[0075] In some embodiments, the solid form Compound 1 Form I exhibits at least one X-ray powder diffraction reflection selected from 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3,

27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form I is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form I exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 1. In some embodiments, Compound 1 Form I exhibits at least one of the X-ray powder diffraction pattern reflections in Table 1.

Table 1. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form I.

2-Theta	d (Å)	Relative Intensity %
4.9	18.1	41.1
9.9	9.0	9.1
10.5	8.5	2.1
11.2	7.9	5.0
11.5	7.7	16.7
11.7	7.6	9.2
13.4	6.6	11.7
13.6	6.5	15.9
14.2	6.2	3.1
14.9	6.0	19.4
15.8	5.6	0.9
16.6	5.3	3.1
17.0	5.2	46.6
17.6	5.0	25.9
18.1	4.9	2.7
18.5	4.8	3.1
19.2	4.6	46.5
19.9	4.5	10.5
20.5	4.3	29.7
21.1	4.2	100.0
21.6	4.1	4.6
22.2	4.0	8.7
22.8	3.9	10.5
23.5	3.8	1.8
24.0	3.7	51.0
24.4	3.6	6.7
24.9	3.6	11.4
25.5	3.5	13.8
26.3	3.4	5.3
26.7	3.3	17.5

2-Theta	d (Å)	Relative Intensity %
27.4	3.3	41.8
27.9	3.2	5.0
28.2	3.2	7.8
28.7	3.1	2.2
29.3	3.0	1.0
29.7	3.0	11.7
30.1	3.0	7.6
30.6	2.9	7.6
31.4	2.9	21.2
32.1	2.8	1.9
33.9	2.6	4.6
34.9	2.6	2.1
35.6	2.5	2.2
36.1	2.5	4.6
36.5	2.5	2.1
37.7	2.4	3.0
38.3	2.3	1.3
39.3	2.3	2.0
39.7	2.3	1.6

[0076] In some embodiments, the crystalline solid state of Compound 1 Form I exhibits a DSC thermogram substantially similar to that shown in Figure 2. In some embodiments, the crystalline solid state of Compound 1 Form I exhibits a DSC endotherm at 234.6 °C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form I exhibits a DSC endotherm at 255.5 °C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 1 Form I are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[0077] In some embodiments, the crystalline solid state of Compound 1 Form I exhibits a TGA thermogram substantially similar to that shown in Figure 2. In some embodiments, the crystalline solid state of Compound 1 Form I does not exhibit TGA weight loss until a transition at 216.5°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form I is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[0078] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form I is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[0079] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form I has a chemical purity of 95% or more. In some embodiments, the

crystalline solid state form Compound 1 Form I has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form I has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form I has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form I has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form I has a chemical purity of 99.5% or more.

Compound 1 Form II

[0080] In some embodiments, the present invention provides crystalline solid state form of Compound 1 Form II. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 14.7° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.2° ± 0.3 and 23.6° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.9° ± 0.3, 13.2° ± 0.3, and 27.7° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.7° ± 0.3, 25.2° ± 0.3, and 25.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 18.5° ± 0.3 and 21.5° ± 0.3.

[0081] In some embodiments, the solid form Compound 1 Form II exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 8.9° ± 0.3, 9.7° ± 0.3, 11.2° ± 0.3, 13.2° ± 0.3, 14.7° ± 0.3, 18.5° ± 0.3, 21.5° ± 0.3, 23.6° ± 0.3, 25.2° ± 0.3, 25.9° ± 0.3, and 27.7° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 8.9° ± 0.3, 9.7° ± 0.3, 11.2° ± 0.3, 13.2° ± 0.3, 14.7° ± 0.3, 18.5° ± 0.3, 21.5° ± 0.3, 23.6° ± 0.3, 25.2° ± 0.3, 25.9° ± 0.3, and 27.7° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 8.9° ± 0.3, 9.7° ± 0.3, 11.2° ± 0.3, 13.2° ± 0.3, 14.7° ± 0.3, 18.5° ± 0.3, 21.5° ± 0.3, 23.6° ± 0.3, 25.2° ± 0.3, 25.9° ± 0.3, and 27.7° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 8.9° ± 0.3, 9.7° ± 0.3, 11.2° ± 0.3, 13.2° ± 0.3, 14.7° ± 0.3, 18.5° ± 0.3, 21.5° ± 0.3, 23.6° ± 0.3, 25.2° ± 0.3, 25.9° ± 0.3, and 27.7° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 8.9° ± 0.3, 9.7° ± 0.3, 11.2° ± 0.3, 13.2° ± 0.3, 14.7° ± 0.3, 18.5° ± 0.3, 21.5° ± 0.3, 23.6° ± 0.3, 25.2° ± 0.3, 25.9° ± 0.3, and 27.7° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 8.9° ± 0.3, 9.7° ± 0.3, 11.2° ± 0.3, 13.2° ± 0.3, 14.7° ± 0.3, 18.5° ± 0.3, 21.5° ± 0.3, 23.6° ± 0.3, 25.2° ± 0.3, 25.9° ± 0.3, and

27.7° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 8.9° ± 0.3, 9.7° ± 0.3, 11.2° ± 0.3, 13.2° ± 0.3, 14.7° ± 0.3, 18.5° ± 0.3, 21.5° ± 0.3, 23.6° ± 0.3, 25.2° ± 0.3, 25.9° ± 0.3, and 27.7° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form II is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form II exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 3. In some embodiments, Compound 1 Form II exhibits at least one of the X-ray powder diffraction pattern reflections in Table 2.

Table 2. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form II.

2-Theta	d (Å)	Relative Intensity %
3.0	29.4	0.0
5.9	15.1	3.9
8.9	10.0	64.3
9.7	9.1	18.2
11.2	7.9	70.6
11.7	7.6	57.0
13.2	6.7	28.5
13.6	6.5	17.9
14.7	6.0	100.0
15.6	5.7	12.7
16.7	5.3	4.8
17.6	5.0	75.4
18.5	4.8	17.2
19.5	4.6	7.0
20.1	4.4	13.9
20.2	4.4	13.7
20.6	4.3	14.7
21.5	4.1	17.4
23.6	3.8	65.8
25.2	3.5	18.5
25.9	3.4	18.5
26.8	3.3	16.8
27.6	3.2	18.0
27.7	3.2	21.5
28.3	3.2	8.5
30.0	3.0	4.8
30.7	2.9	5.9
32.8	2.7	7.4

[0082] In some embodiments, the crystalline solid state of Compound 1 Form II exhibits a DSC thermogram substantially similar to that shown in Figure 4. In some embodiments, the crystalline solid state of Compound 1 Form II exhibits a DSC endotherm at 52.4°C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form II exhibits a DSC endotherm at

145.9°C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form II exhibits a DSC endotherm at 183.1°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 1 Form II are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[0083] In some embodiments, the crystalline solid state of Compound 1 Form II exhibits a TGA thermogram substantially similar to that shown in Figure 4. In some embodiments, the crystalline solid state of Compound 1 Form II exhibits TGA weight loss of 2.7 % ± 0.5 at 100 °C ± 10.0. In some embodiments, the crystalline solid state of Compound 1 Form II exhibits TGA weight loss of 11.9 % ± 0.5 at 250 °C ± 10.0.In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form II is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[0084] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 1 Form II is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[0085] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form II has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form II has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form II has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form II has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form II has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form II has a chemical purity of 99.5% or more.

Compound 1 Form III

[0086] In some embodiments, the present invention provides crystalline solid state form of Compound 1 Form III. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.3° ± 0.3 and 18.7° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.5° ± 0.3 and 25.3° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.4° ± 0.3 and 22.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 4.6° ± 0.3, 18.4° ± 0.3, and 22.3° ± 0.3.

[0087] In some embodiments, the solid form Compound 1 Form III exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 4.6° ± 0.3, 9.3° ± 0.3, 10.4° ± 0.3, 17.9° ± 0.3, 18.4° ± 0.3, 18.7° ± 0.3, 19.5° ± 0.3, 22.3° ± 0.3, 22.9° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 4.6° ± 0.3, 9.3° ± 0.3, 10.4° ± 0.3, 17.9° ± 0.3, 18.4° ± 0.3, 18.7° ± 0.3, 19.5° ± 0.3, 22.3° ± 0.3, 22.9° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 4.6° ± 0.3, 9.3° ± 0.3, 10.4° ± 0.3, 17.9° ± 0.3, 18.4° ± 0.3, 18.7° ± 0.3, 19.5° ± 0.3, 22.3° ± 0.3, 22.9° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 4.6° ± 0.3, 9.3° ± 0.3, 10.4° ± 0.3, 17.9° ± 0.3, 18.4° ± 0.3, 18.7° ± 0.3, 19.5° ± 0.3, 22.3° ± 0.3, 22.9° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 4.6° ± 0.3, 9.3° ± 0.3, 10.4° ± 0.3, 17.9° ± 0.3, 18.4° ± 0.3, 18.7° ± 0.3, 19.5° ± 0.3, 22.3° ± 0.3, 22.9° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 4.6° ± 0.3, 9.3° ± 0.3, 10.4° ± 0.3, 17.9° ± 0.3, 18.4° ± 0.3, 18.7° ± 0.3, 19.5° ± 0.3, 22.3° ± 0.3, 22.9° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 4.6° ± 0.3, 9.3° ± 0.3, 10.4° ± 0.3, 17.9° ± 0.3, 18.4° ± 0.3, 18.7° ± 0.3, 19.5° ± 0.3, 22.3° ± 0.3, 22.9° ± 0.3, and 25.3° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form III is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form III exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 5. In some embodiments, Compound 1 Form III exhibits at least one of the X-ray powder diffraction pattern reflections in Table 3.

Table 3. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form III.

2-Theta	d (Å)	Relative Intensity %
4.6	19.2	17.2
9.3	9.5	58.6
10.4	8.5	23.0
10.8	8.2	7.7
11.5	7.7	10.0
12.0	7.4	6.1
13.4	6.6	4.5
13.6	6.5	20.4
14.3	6.2	1.2
15.0	5.9	44.4

2-Theta	d (Å)	Relative Intensity %
16.5	5.4	3.0
17.0	5.2	18.0
17.5	5.1	42.3
17.9	5.0	100.0
18.4	4.8	17.9
18.7	4.8	37.3
19.2	4.6	7.2
19.5	4.5	24.5
19.8	4.5	13.3
20.4	4.3	5.3
21.0	4.2	27.1
21.2	4.2	27.4
21.7	4.1	7.5
22.3	4.0	14.9
22.7	3.9	6.9
22.9	3.9	18.4
23.6	3.8	1.0
24.1	3.7	37.9
25.3	3.5	31.6
25.9	3.4	6.5
26.2	3.4	13.1
26.8	3.3	10.9
27.3	3.3	47.7
27.9	3.2	4.0
28.2	3.2	10.1
28.6	3.1	2.0
29.1	3.1	1.8
29.6	3.0	6.6
30.0	3.0	7.2
30.6	2.9	2.2
31.4	2.8	1.9
31.8	2.8	1.5
32.5	2.7	9.1
33.0	2.7	3.0
33.6	2.7	5.7
33.9	2.6	6.6
34.9	2.6	1.5
35.7	2.5	2.4
36.0	2.5	0.7
36.5	2.5	1.7
37.7	2.4	2.1
38.4	2.3	1.8
39.3	2.3	1.5

[0088] In some embodiments, the crystalline solid state of Compound 1 Form III exhibits a DSC thermogram substantially similar to that shown in Figure 6. In some embodiments, the crystalline solid state of Compound 1 Form III exhibits a DSC endotherm at 217.3°C ± 5.0. In certain

embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 1 Form III are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[0089] In some embodiments, the crystalline solid state of Compound 1 Form III exhibits a TGA thermogram substantially similar to that shown in Figure 6. In some embodiments, the crystalline solid state of Compound 1 Form III exhibits TGA weight loss of 0.2 % ± 0.5 at 89.9°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form III is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[0090] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 1 Form III is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[0091] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form III has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form III has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form III has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form III has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form III has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form III has a chemical purity of 99.5% or more.

Compound 1 Form IV

[0092] In some embodiments, the present invention provides crystalline solid state form of Compound 1 Form IV. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 27.8° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 14.2° ± 0.3 and 19.8° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 18.7° ± 0.3, 24.6° ± 0.3, and 25.1° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.2° ± 0.3, 18.0° ± 0.3, and 22.0° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.4° ± 0.3, 9.4° ± 0.3, and 22.6° ± 0.3.

[0093] In some embodiments, the solid form Compound 1 Form IV exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 7.4° ± 0.3, 9.4° ± 0.3, 14.2° ±

0.3, 15.2° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.8° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.6° ± 0.3, 25.1° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 9.4° ± 0.3, 14.2° ± 0.3, 15.2° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.8° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.6° ± 0.3, 25.1° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 9.4° ± 0.3, 14.2° ± 0.3, 15.2° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.8° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.6° ± 0.3, 25.1° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 9.4° ± 0.3, 14.2° ± 0.3, 15.2° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.8° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.6° ± 0.3, 25.1° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 9.4° ± 0.3, 14.2° ± 0.3, 15.2° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.8° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.6° ± 0.3, 25.1° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 9.4° ± 0.3, 14.2° ± 0.3, 15.2° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.8° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.6° ± 0.3, 25.1° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 9.4° ± 0.3, 14.2° ± 0.3, 15.2° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.8° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.6° ± 0.3, 25.1° ± 0.3, and 27.8° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form IV is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form IV exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 7. In some embodiments, Compound 1 Form IV exhibits at least one of the X-ray powder diffraction pattern reflections in Table 4.

Table 4. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form IV.

2-Theta	d (Å)	Relative Intensity %
4.7	18.9	4.7
5.1	17.3	5.6
7.4	11.9	26.1
8.9	10.0	11.7
9.4	9.4	25.8
10.3	8.6	19.1
11.9	7.5	15.3
12.2	7.2	8.6
13.0	6.8	3.1

2-Theta	d (Å)	Relative Intensity %
13.4	6.6	12.6
13.8	6.4	41.7
14.2	6.2	93.0
15.0	5.9	34.6
15.2	5.8	29.9
15.5	5.7	18.3
16.5	5.4	5.1
16.8	5.3	3.3
17.6	5.0	19.6
18.0	4.9	38.7
18.6	4.8	33.0
18.7	4.7	39.4
19.4	4.6	28.5
19.8	4.5	75.2
20.3	4.4	5.6
21.0	4.2	19.2
21.5	4.1	5.1
22.0	4.0	39.2
22.6	3.9	20.4
23.1	3.8	8.1
23.6	3.8	12.5
24.1	3.7	59.1
24.6	3.6	41.5
25.1	3.5	53.4
25.9	3.4	13.4
26.7	3.3	46.7
27.8	3.2	100.0
28.6	3.1	15.3
29.9	3.0	17.0
30.8	2.9	5.3
31.8	2.8	2.3
32.3	2.8	3.1
33.7	2.7	7.3
34.1	2.6	3.8
37.6	2.4	3.3
38.8	2.3	4.6

[0094] In some embodiments, the crystalline solid state of Compound 1 Form IV exhibits a DSC thermogram substantially similar to that shown in Figure 8. In some embodiments, the crystalline solid state of Compound 1 Form IV exhibits a DSC endotherm at 62.0°C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form IV exhibits a DSC endotherm at 181.7°C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form IV exhibits a DSC endotherm at 253.6°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 1 Form IV are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[0095] In some embodiments, the crystalline solid form Compound 1 Form IV exhibits a TGA thermogram substantially similar to that shown in Figure 8. In some embodiments, the crystalline solid state of Compound 1 Form IV exhibits TGA weight loss of 1.5 % ± 0.5 at 83.4°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form IV is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[0096] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form IV is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[0097] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form IV has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form IV has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form IV has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form IV has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form IV has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form IV has a chemical purity of 99.5% or more.

Compound 1 Form V

[0098] In some embodiments, the present invention provides crystalline solid state form of Compound 1 Form V. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 14.2° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 21.6° ± 0.3 and 27.8° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.8° ± 0.3, 18.9° ± 0.3, and 24.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.7° ± 0.3, 18.1° ± 0.3, and 22.2° ± 0.3. In some embodiments, 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 25.6° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.2° ± 0.3, 16.2° ± 0.3, and 16.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.3° ± 0.3, 13.2° ± 0.3, 21.9° ± 0.3, and 24.8° ± 0.3.

[0099] In some embodiments, the solid form Compound 1 Form V exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 7.3° ± 0.3, 10.2° ± 0.3, 10.8° ± 0.3, 13.2° ± 0.3, 14.2° ± 0.3, 15.7° ± 0.3, 16.2° ± 0.3, 16.9° ± 0.3, 18.1° ± 0.3, 18.6° ± 0.3, 18.9° ± 0.3, 21.6° ± 0.3, 21.9° ± 0.3, 22.2° ± 0.3, 23.0° ± 0.3, 24.4° ± 0.3, 24.8° ± 0.3, 25.6° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 7.3° ± 0.3, 10.2° ± 0.3, 10.8° ± 0.3, 13.2° ± 0.3, 14.2° ± 0.3, 15.7° ± 0.3, 16.2° ± 0.3, 16.9° ± 0.3, 18.1° ± 0.3, 18.6° ± 0.3, 18.9° ± 0.3, 21.6° ± 0.3, 21.9° ± 0.3, 22.2° ± 0.3, 23.0° ± 0.3, 24.4° ± 0.3, 24.8° ± 0.3, 25.6° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 7.3° ± 0.3, 10.2° ± 0.3, 10.8° ± 0.3, 13.2° ± 0.3, 14.2° ± 0.3, 15.7° ± 0.3, 16.2° ± 0.3, 16.9° ± 0.3, 18.1° ± 0.3, 18.6° ± 0.3, 18.9° ± 0.3, 21.6° ± 0.3, 21.9° ± 0.3, 22.2° ± 0.3, 23.0° ± 0.3, 24.4° ± 0.3, 24.8° ± 0.3, 25.6° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 7.3° ± 0.3, 10.2° ± 0.3, 10.8° ± 0.3, 13.2° ± 0.3, 14.2° ± 0.3, 15.7° ± 0.3, 16.2° ± 0.3, 16.9° ± 0.3, 18.1° ± 0.3, 18.6° ± 0.3, 18.9° ± 0.3, 21.6° ± 0.3, 21.9° ± 0.3, 22.2° ± 0.3, 23.0° ± 0.3, 24.4° ± 0.3, 24.8° ± 0.3, 25.6° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 7.3° ± 0.3, 10.2° ± 0.3, 10.8° ± 0.3, 13.2° ± 0.3, 14.2° ± 0.3, 15.7° ± 0.3, 16.2° ± 0.3, 16.9° ± 0.3, 18.1° ± 0.3, 18.6° ± 0.3, 18.9° ± 0.3, 21.6° ± 0.3, 21.9° ± 0.3, 22.2° ± 0.3, 23.0° ± 0.3, 24.4° ± 0.3, 24.8° ± 0.3, 25.6° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 7.3° ± 0.3, 10.2° ± 0.3, 10.8° ± 0.3, 13.2° ± 0.3, 14.2° ± 0.3, 15.7° ± 0.3, 16.2° ± 0.3, 16.9° ± 0.3, 18.1° ± 0.3, 18.6° ± 0.3, 18.9° ± 0.3, 21.6° ± 0.3, 21.9° ± 0.3, 22.2° ± 0.3, 23.0° ± 0.3, 24.4° ± 0.3, 24.8° ± 0.3, 25.6° ± 0.3, and 27.8° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 7.3° ± 0.3, 10.2° ± 0.3, 10.8° ± 0.3, 13.2° ± 0.3, 14.2° ± 0.3, 15.7° ± 0.3, 16.2° ± 0.3, 16.9° ± 0.3, 18.1° ± 0.3, 18.6° ± 0.3, 18.9° ± 0.3, 21.6° ± 0.3, 21.9° ± 0.3, 22.2° ± 0.3, 23.0° ± 0.3, 24.4° ± 0.3, 24.8° ± 0.3, 25.6° ± 0.3, and 27.8° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form V is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form V exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 9. In some embodiments, Compound 1 Form V exhibits at least one of the X-ray powder diffraction pattern reflections in Table 5.

Table 5. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form V.

2-Theta	d (Å)	Relative Intensity %
5.4	16.5	2.8
7.3	12.1	21.0
9.2	9.6	6.8
10.2	8.7	27.1
10.8	8.2	47.4
11.2	7.9	16.5
11.6	7.6	4.1
12.6	7.0	12.7
13.2	6.7	21.6
13.6	6.5	2.4
14.2	6.2	100.0
14.9	5.9	3.4
15.7	5.6	37.1
16.2	5.5	24.9
16.6	5.3	14.4
16.9	5.2	27.4
17.7	5.0	19.3
18.1	4.9	39.6
18.6	4.8	31.5
18.9	4.7	41.4
19.2	4.6	72.4
20.4	4.4	39.4
20.6	4.3	20.3
21.3	4.2	25.2
21.6	4.1	77.2
21.9	4.1	24.6
22.2	4.0	32.7
23.0	3.9	28.2
23.7	3.7	13.8
24.2	3.7	45.2
24.4	3.7	64.3
24.8	3.6	20.7
25.6	3.5	28.7
26.4	3.4	7.6
26.9	3.3	11.2
27.2	3.3	8.9
27.8	3.2	69.6
28.4	3.1	11.9
28.7	3.1	16.9
29.3	3.0	2.8
29.7	3.0	4.0
30.2	3.0	7.3
31.4	2.8	8.9
32.1	2.8	10.6
32.5	2.8	7.5
32.9	2.7	6.5
34.0	2.6	4.4

2-Theta	d (Å)	Relative Intensity %
34.8	2.6	4.2
35.4	2.5	6.3
36.2	2.5	3.2
36.7	2.4	2.7
37.7	2.4	1.3
38.3	2.4	4.1
39.0	2.3	2.7

[00100] In some embodiments, the crystalline solid state of Compound 1 Form V exhibits a DSC thermogram substantially similar to that shown in Figure 10. In some embodiments, the crystalline solid state of Compound 1 Form V exhibits a DSC endotherm at 62.0°C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form V exhibits a DSC endotherm at 48.4°C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form V exhibits a DSC endotherm at 163.4°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 1 Form V are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00101] In some embodiments, the crystalline solid state Compound 1 Form V exhibits a TGA thermogram substantially similar to that shown in Figure 10. In some embodiments, the crystalline solid state Compound 1 Form V exhibits TGA weight loss of 3.2 % ± 0.5 at 100°C ± 10.0. In some embodiments, the crystalline solid state Compound 1 Form V exhibits TGA weight loss of 17.1 % ± 0.5 at 230°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form V is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00102] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form V is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00103] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form V has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form V has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form V has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form V has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form V

has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form V has a chemical purity of 99.5% or more.

Compound 1 Form VI

[00104] In some embodiments, the present invention provides a crystalline solid state form of Compound 1 Form VI. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 26.1° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 25.1° ± 0.3 and 27.0° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.4° ± 0.3, and 23.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.8° ± 0.3 and 21.4° ± 0.3.

[00105] In some embodiments, the solid form Compound 1 Form VI exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 15.4° ± 0.3, 19.8° ± 0.3, 21.4° ± 0.3, 23.4° ± 0.3, 25.1° ± 0.3, 26.1° ± 0.3, and 27.0° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 15.4° ± 0.3, 19.8° ± 0.3, 21.4° ± 0.3, 23.4° ± 0.3, 25.1° ± 0.3, 26.1° ± 0.3, and 27.0° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 15.4° ± 0.3, 19.8° ± 0.3, 21.4° ± 0.3, 23.4° ± 0.3, 25.1° ± 0.3, 26.1° ± 0.3, and 27.0° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 15.4° ± 0.3, 19.8° ± 0.3, 21.4° ± 0.3, 23.4° ± 0.3, 25.1° ± 0.3, 26.1° ± 0.3, and 27.0° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 15.4° ± 0.3, 19.8° ± 0.3, 21.4° ± 0.3, 23.4° ± 0.3, 25.1° ± 0.3, 26.1° ± 0.3, and 27.0° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form VI is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form VI exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 11. In some embodiments, Compound 1 Form VI exhibits at least one of the X-ray powder diffraction pattern reflections in Table 6.

Table 6. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form VI.

2-Theta	d (Å)	Relative Intensity %
6.9	12.7	12.2
7.3	12.1	0.8
8.3	10.7	3.1
9.5	9.3	1.3
10.5	8.4	3.3

2-Theta	d (Å)	Relative Intensity %
11.3	7.8	1.9
12.2	7.2	11.4
13.0	6.8	2.7
13.4	6.6	16.2
13.9	6.4	5.4
14.3	6.2	5.1
15.4	5.8	17.5
15.6	5.7	4.8
16.6	5.3	2.0
16.9	5.2	4.7
17.2	5.1	1.9
17.5	5.1	2.9
18.2	4.9	9.8
18.6	4.8	2.7
19.1	4.7	22.1
19.8	4.5	12.2
21.4	4.2	14.5
21.6	4.1	10.0
22.1	4.0	8.8
22.6	3.9	4.0
23.0	3.9	6.9
23.4	3.8	17.8
24.0	3.7	28.0
25.1	3.5	21.3
26.1	3.4	100.0
27.0	3.3	31.3
27.5	3.2	1.5
28.2	3.2	6.1
28.5	3.1	3.2
28.9	3.1	2.1
29.5	3.0	3.5
30.6	2.9	1.9
31.6	2.8	1.3
32.2	2.8	0.9
32.9	2.7	0.7
33.6	2.7	3.3
34.5	2.6	1.8
35.4	2.5	1.2
36.3	2.5	2.0
37.3	2.4	1.2
38.0	2.4	1.1
39.3	2.3	1.3

[00106] In some embodiments, the crystalline solid state Compound 1 Form VI exhibits a DSC thermogram substantially similar to that shown in Figure 12. In some embodiments, the crystalline solid state of Compound 1 Form VI exhibits a DSC endotherm at 173.0°C ± 5.0. In some embodiments, the crystalline solid state of Compound 1 Form VI exhibits a DSC endotherm at

251.6°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 1 Form VI are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00107] In some embodiments, the crystalline solid state Compound 1 Form VI exhibits a TGA thermogram substantially similar to that shown in Figure 12. In some embodiments, the crystalline solid state of Compound 1 Form VI exhibits TGA weight loss of 14.5% ± 0.5 at 232.2°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form VI is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00108] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 1 Form VI is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00109] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form VI has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form VI has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form VI has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form VI has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form VI has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form VI has a chemical purity of 99.5% or more.

Compound 1 Form VII

[00110] In some embodiments, the present invention provides a crystalline solid state form of Compound 1 Form VII. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 14.4° ± 0.3 and 17.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 22.4° ± 0.3, 23.2° ± 0.3, and 25.5° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.9° ± 0.3, 22.7° ± 0.3, and 28.4° ± 0.3.

[00111] In some embodiments, the solid form Compound 1 Form VII exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 14.4° ± 0.3, 15.9° ± 0.3, 17.9° ± 0.3, 22.4° ± 0.3, 22.7° ± 0.3, 23.2° ± 0.3, 25.5° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected

from the group consisting of 14.4° ± 0.3, 15.9° ± 0.3, 17.9° ± 0.3, 22.4° ± 0.3, 22.7° ± 0.3, 23.2° ± 0.3, 25.5° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 14.4° ± 0.3, 15.9° ± 0.3, 17.9° ± 0.3, 22.4° ± 0.3, 22.7° ± 0.3, 23.2° ± 0.3, 25.5° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 14.4° ± 0.3, 15.9° ± 0.3, 17.9° ± 0.3, 22.4° ± 0.3, 22.7° ± 0.3, 23.2° ± 0.3, 25.5° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 14.4° ± 0.3, 15.9° ± 0.3, 17.9° ± 0.3, 22.4° ± 0.3, 22.7° ± 0.3, 23.2° ± 0.3, 25.5° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 14.4° ± 0.3, 15.9° ± 0.3, 17.9° ± 0.3, 22.4° ± 0.3, 22.7° ± 0.3, 23.2° ± 0.3, 25.5° ± 0.3, and 28.4° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form VII is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form VII exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 13. In some embodiments, Compound 1 Form VII exhibits at least one of the X-ray powder diffraction pattern reflections in Table 7.

Table 7. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form VII.

2-Theta	d (Å)	Relative Intensity %
7.3	12.0	14.6
9.2	9.6	6.7
10.1	8.7	14.8
10.7	8.3	18.3
11.3	7.8	16.6
12.7	7.0	4.8
13.3	6.6	18.0
14.4	6.2	49.3
15.9	5.6	25.3
16.4	5.4	13.1
16.9	5.2	35.6
17.4	5.1	7.0
17.9	4.9	53.1
18.5	4.8	15.2
19.3	4.6	59.9
20.4	4.3	49.3
21.2	4.2	82.0
21.6	4.1	13.3
22.4	4.0	41.5
22.7	3.9	24.0
23.2	3.8	33.2
23.8	3.7	53.5

2-Theta	d (Å)	Relative Intensity %
24.3	3.7	12.9
24.9	3.6	9.2
25.5	3.5	43.1
26.1	3.4	6.7
27.3	3.3	100.0
27.9	3.2	14.9
28.4	3.1	24.6
29.7	3.0	6.4
30.3	2.9	3.9
31.2	2.9	4.1
31.5	2.8	19.3
32.0	2.8	8.3
32.7	2.7	4.5
33.0	2.7	3.3
33.9	2.6	3.0
34.5	2.6	2.9
35.1	2.6	6.9
35.8	2.5	1.5
38.2	2.4	1.4

[00112] In some embodiments, the crystalline solid state Compound 1 Form VII exhibits a DSC thermogram substantially similar to that shown in Figure 14. In some embodiments, the crystalline solid state Compound 1 Form VII exhibits a DSC endotherm at 176.8°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state Compound 1 Form VII are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00113] In some embodiments, the crystalline solid state Compound 1 Form VII exhibits a TGA thermogram substantially similar to that shown in Figure 14. In some embodiments, the crystalline solid state of Compound 1 Form VII exhibits TGA weight loss of 5.9% ± 0.5 at 162.1°C ± 10.0. In some embodiments, the crystalline solid state of Compound 1 Form VII exhibits TGA weight loss of 13.0% ± 0.5 at 217.9°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form VII is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00114] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form VII is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00115] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form VII has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form VII has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form VII has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form VII has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form VII has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form VII has a chemical purity of 99.5% or more.

Compound 1 Form VIII

[00116] In some embodiments, the present invention provides a crystalline solid state form of Compound 1 Form VIII. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value 14.6° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.7° ± 0.3 and 21.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.1° ± 0.3 and 12.1° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value 9.7° ± 0.3 and 24.4° ± 0.3.

[00117] In some embodiments, the solid form Compound 1 Form VIII exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 8.7° ± 0.3, 9.7° ± 0.3, 10.1° ± 0.3, 12.1° ± 0.3, 14.6° ± 0.3, 21.9° ± 0.3, and 24.4° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 8.7° ± 0.3, 9.7° ± 0.3, 10.1° ± 0.3, 12.1° ± 0.3, 14.6° ± 0.3, 21.9° ± 0.3, and 24.4° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 8.7° ± 0.3, 9.7° ± 0.3, 10.1° ± 0.3, 12.1° ± 0.3, 14.6° ± 0.3, 21.9° ± 0.3, and 24.4° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 8.7° ± 0.3, 9.7° ± 0.3, 10.1° ± 0.3, 12.1° ± 0.3, 14.6° ± 0.3, 21.9° ± 0.3, and 24.4° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 8.7° ± 0.3, 9.7° ± 0.3, 10.1° ± 0.3, 12.1° ± 0.3, 14.6° ± 0.3, 21.9° ± 0.3, and 24.4° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form VIII is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form

VIII exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 15. In some embodiments, Compound 1 Form VIII exhibits at least one of the X-ray powder diffraction pattern reflections in Table 8.

Table 8. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form VIII.

2-Theta	d (Å)	Relative Intensity %
4.7	19.0	0.8
7.2	12.2	1.7
8.7	10.1	28.9
9.1	9.7	2.4
9.7	9.1	19.2
10.1	8.7	19.9
11.5	7.7	28.5
12.1	7.3	19.9
12.8	6.9	2.2
13.3	6.7	13.9
14.0	6.3	2.4
14.6	6.1	100.0
15.2	5.8	2.6
15.7	5.6	1.4
17.0	5.2	4.8
17.6	5.0	28.6
18.9	4.7	6.0
19.3	4.6	15.0
19.8	4.5	2.0
20.3	4.4	1.5
21.1	4.2	10.3
21.7	4.1	8.6
21.9	4.0	32.6
22.5	3.9	8.9
23.4	3.8	10.0
24.0	3.7	13.6
24.4	3.6	16.8
25.0	3.6	1.5
25.3	3.5	2.3
26.0	3.4	2.8
26.9	3.3	14.9
28.0	3.2	2.8
28.7	3.1	3.3
29.4	3.0	2.6
29.8	3.0	1.2
30.5	2.9	1.6
32.0	2.8	5.3
32.5	2.8	1.3
33.6	2.7	0.7
34.5	2.6	1.4
37.9	2.4	2.1

[00118] In some embodiments, the crystalline solid state Compound 1 Form VIII exhibits a DSC thermogram substantially similar to that shown in Figure 16. In some embodiments, the crystalline solid state Compound 1 Form VIII exhibits a DSC endotherm at 180.3°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state Compound 1 Form VIII are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00119] In some embodiments, the crystalline solid state Compound 1 Form VIII exhibits a TGA thermogram substantially similar to that shown in Figure 16. In some embodiments, the crystalline solid state Compound 1 Form VIII exhibits TGA weight loss of 12.6% ± 0.5 at 163.8°C ± 10.0. In some embodiments, the crystalline solid state Compound 1 Form VIII exhibits TGA weight loss of 11.7% ± 0.5 at 234.4°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state Compound 1 Form VIII is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00120] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 1 Form VIII is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00121] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form VIII has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form VIII has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form VIII has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form VIII has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form VIII has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form VIII has a chemical purity of 99.5% or more.

Compound 1 Form IX

[00122] In some embodiments, the present invention provides a crystalline solid state form of Compound 1 Form IX. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value 10.3° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.0° ± 0.3 and 23.0° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 20.0° ± 0.3 and 23.5° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder

diffraction reflection at a 2-theta value 14.0° ± 0.3, 18.5° ± 0.3, and 27.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value 14.6° ± 0.3, 27.0° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value 10.8° ± 0.3, 15.7° ± 0.3, and 26.3° ± 0.3.

[00123] In some embodiments, the solid form Compound 1 Form IX exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 10.3° ± 0.3, 10.8° ± 0.3, 12.0° ± 0.3, 14.0° ± 0.3, 14.6° ± 0.3, 15.7° ± 0.3, 18.5° ± 0.3, 20.0° ± 0.3, 23.0° ± 0.3, 23.5° ± 0.3, 26.3° ± 0.3, 27.0° ± 0.3, 27.9° ± 0.3, and 28.4° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form IX is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form IX exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 17. In some embodiments, Compound 1 Form IX exhibits at least one of the X-ray powder diffraction pattern reflections in Table 9.

Table 9. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form IX.

2-Theta	d (Å)	Relative Intensity %
7.7	11.5	100.0
9.2	9.7	14.5
10.0	8.9	11.0
10.3	8.5	51.4
10.8	8.2	15.4
12.0	7.4	51.4
13.4	6.6	12.1
14.0	6.3	24.6
14.6	6.0	21.5
15.3	5.8	5.4
15.7	5.6	15.1
16.1	5.5	11.6
16.4	5.4	13.6
17.0	5.2	9.0
17.4	5.1	15.5
17.6	5.0	11.1
18.0	4.9	5.8
18.5	4.8	32.3
18.7	4.7	12.0
19.4	4.6	10.1
20.0	4.4	44.2
20.6	4.3	53.8
21.2	4.2	5.2
21.6	4.1	6.4
22.1	4.0	4.3
23.0	3.9	51.4
23.5	3.8	34.2
23.8	3.7	83.3
24.1	3.7	19.0
24.9	3.6	10.0
25.3	3.5	7.7
25.7	3.5	9.4
26.3	3.4	18.4
27.0	3.3	18.9
27.9	3.2	27.9
28.4	3.1	19.7
28.7	3.1	11.1
29.6	3.0	7.0
30.3	2.9	10.1
31.6	2.8	4.0
32.2	2.8	2.5

[00124] In some embodiments, the crystalline solid state Compound 1 Form IX exhibits a DSC thermogram substantially similar to that shown in Figure 18. In some embodiments, the crystalline solid state Compound 1 Form IX exhibits a DSC endotherm at 83.8°C ± 5.0. In some

embodiments, the crystalline solid state Compound 1 Form IX exhibits a DSC endotherm at 154.7°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state Compound 1 Form IX are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00125] In some embodiments, the crystalline solid state Compound 1 Form IX exhibits a TGA thermogram substantially similar to that shown in Figure 18. In some embodiments, the crystalline solid state Compound 1 Form IX exhibits TGA weight loss of 0.6% ± 0.5 at 69.5°C ± 10.0. In some embodiments, the crystalline solid state Compound 1 Form IX exhibits TGA weight loss of 1.1% ± 0.5 at 109.3°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state Compound 1 Form IX is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00126] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form IX is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00127] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form IX has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form IX has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form IX has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form IX has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form IX has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form IX has a chemical purity of 99.5% or more.

Compound 1 Form X

[00128] In some embodiments, the present invention provides a crystalline solid state form of Compound 1 Form X. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.5° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 22.8° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.0° ± 0.3 and 22.1° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.7° ± 0.3 and 20.2° ± 0.3.

[00129] In some embodiments, the solid form Compound 1 Form X exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 10.0° ± 0.3, 10.7° ± 0.3, 12.5° ± 0.3, 20.2° ± 0.3, 22.1° ± 0.3, and 22.8° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 10.0° ± 0.3, 10.7° ± 0.3, 12.5° ± 0.3, 20.2° ± 0.3, 22.1° ± 0.3, and 22.8° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 10.0° ± 0.3, 10.7° ± 0.3, 12.5° ± 0.3, 20.2° ± 0.3, 22.1° ± 0.3, and 22.8° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 10.0° ± 0.3, 10.7° ± 0.3, 12.5° ± 0.3, 20.2° ± 0.3, 22.1° ± 0.3, and 22.8° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 1 Form X is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 1 Form X exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 19. In some embodiments, Compound 1 Form X exhibits at least one of the X-ray powder diffraction pattern reflections in Table 10.

Table 10. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 1 Form X.

2-Theta	d (Å)	Relative Intensity %
8.7	10.1	7.5
10.0	8.9	19.4
10.7	8.3	12.7
11.5	7.7	8.3
12.5	7.1	52.7
13.3	6.7	6.0
14.3	6.2	2.5
15.1	5.9	100.0
17.6	5.0	40.7
19.1	4.6	1.4
19.7	4.5	9.5
20.2	4.4	12.6
20.9	4.2	14.9
22.1	4.0	16.2
22.8	3.9	41.9
23.2	3.8	5.5
24.9	3.6	1.2
25.8	3.4	1.8
26.8	3.3	1.7
28.0	3.2	8.0
29.4	3.0	2.0
30.7	2.9	2.3
33.3	2.7	6.8
36.6	2.5	1.4
38.4	2.3	1.4

[00130] In some embodiments, the crystalline solid state of Compound 1 Form X exhibits a DSC thermogram substantially similar to that shown in Figure 20. In some embodiments, the crystalline solid state of Compound 1 Form X exhibits a DSC endotherm at 181.4°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 1 Form X are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00131] In some embodiments, the crystalline solid state of Compound 1 Form X exhibits a TGA thermogram substantially similar to that shown in Figure 20. In some embodiments, the crystalline solid state of Compound 1 FormX exhibits TGA weight loss of 0.7% ± 0.5 at 77.2°C ± 10.0. In some embodiments, the crystalline solid state of Compound 1 Form X exhibits TGA weight loss of 19.6% ± 0.5 at 241.2°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 1 Form X is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00132] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 1 Form X is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00133] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 1 Form X has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 1 Form X has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 1 Form X has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 1 Form X has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 1 Form X has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 1 Form X has a chemical purity of 99.5% or more.

Compound 2

[00134] In some embodiments, the present invention provides a crystalline solid state of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride, also known as Compound 2. In some embodiments, provided herein is crystalline Compound 2 Form I. In some embodiments, provided herein is crystalline Compound 2 Form II. In some embodiments, provided herein is crystalline Compound 2 Form III.

Compound 2 Form I

[00135] In some embodiments, the present invention provides crystalline solid state form of Compound 2 Form I. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 22.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.3° ± 0.3 and 20.6° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 16.4° ± 0.3, 17.5° ± 0.3, and 18.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.3° ± 0.3, 25.6° ± 0.3, and 29.4° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.6° ± 0.3, 22.0° ± 0.3, 23.0° ± 0.3, and 25.3° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.7° ± 0.3, 14.3° ± 0.3, 18.0° ± 0.3, 21.3° ± 0.3, and 32.3° ± 0.3.

[00136] In some embodiments, the solid form Compound 2 Form I exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 18.9° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 18.9° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 18.9° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 18.9° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 18.9° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 18.9° ± 0.3,

19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 18.9° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 2 Form I is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 2 Form I exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 21. In some embodiments, Compound 2 Form I exhibits at least one of the X-ray powder diffraction pattern reflections in Table 11.

Table 11. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 2 Form I.

2-Theta	d (Å)	Relative Intensity %
5.3	16.8	38.6
9.8	9.1	3.8
10.7	8.3	15.2
11.6	7.6	2.0
12.3	7.2	89.6
13.1	6.7	9.7
14.3	6.2	16.9
15.1	5.8	5.8
15.9	5.6	2.3
16.4	5.4	51.4
17.5	5.1	56.7
18.0	4.9	21.9
18.3	4.8	6.7
18.9	4.7	58.3
19.6	4.5	26.4
20.1	4.4	13.0
20.6	4.3	91.6
21.3	4.2	19.2
22.0	4.0	34.4
22.4	4.0	100.0
23.0	3.9	38.3
23.4	3.8	9.7
23.8	3.7	11.6
24.5	3.6	7.6
25.3	3.5	37.0
25.6	3.5	47.3
26.4	3.4	9.3
26.7	3.3	7.4
27.4	3.2	7.2
28.0	3.2	14.4
28.2	3.2	9.0
28.8	3.1	11.6

2-Theta	d (Å)	Relative Intensity %
29.1	3.1	9.9
29.4	3.0	39.3
30.1	3.0	11.4
31.0	2.9	10.6
31.3	2.9	6.3
32.0	2.8	5.5
32.3	2.8	15.2
33.1	2.7	3.8
33.4	2.7	1.4
33.7	2.7	9.9
34.0	2.6	6.2
34.4	2.6	9.2
34.9	2.6	5.4
35.4	2.5	10.8
35.6	2.5	4.5
36.1	2.5	4.0
37.0	2.4	2.6
37.2	2.4	1.2
37.8	2.4	0.9
38.4	2.3	2.7

[00137] In some embodiments, the crystalline solid state of Compound 2 Form I exhibits a DSC thermogram substantially similar to that shown in Figure 22. In some embodiments, the crystalline solid state of Compound 2 Form I exhibits a DSC endotherm at 315.4 °C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 2 Form I are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00138] In some embodiments, the crystalline solid state of Compound 2 Form I exhibits a TGA thermogram substantially similar to that shown in Figure 22. . In some embodiments, the crystalline solid state of Compound 2 Form I exhibits TGA weight loss of 1.1 % ± 0.5 at 100.0°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 2 Form I is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00139] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 2 Form I is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00140] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 2 Form I has a chemical purity of 95% or more. In some embodiments, the

crystalline solid state form Compound 2 Form I has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 2 Form I has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 2 Form I has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 2 Form I has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 2 Form I has a chemical purity of 99.5% or more.

Compound 2 Form II

[00141] In some embodiments, the present invention provides a crystalline solid state form of Compound 2 Form II. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 6.6° ± 0.3 and 18.5° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.9° ± 0.3 and 24.5° ± 0.3.

[00142] In some embodiments, the solid form Compound 2 Form II exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 6.6° ± 0.3, 9.9° ± 0.3, 18.5° ± 0.3, 19.9° ± 0.3, and 24.5° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 6.6° ± 0.3, 9.9° ± 0.3, 18.5° ± 0.3, 19.9° ± 0.3, and 24.5° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 6.6° ± 0.3, 9.9° ± 0.3, 18.5° ± 0.3, 19.9° ± 0.3, and 24.5° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 2 Form II is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 2 Form II exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 23. In some embodiments, Compound 2 Form II exhibits at least one of the X-ray powder diffraction pattern reflections in Table 12.

Table 12. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 2 Form II.

2-Theta	d (Å)	Relative Intensity %
4.7	19.0	1.1
5.8	15.1	0.8
6.6	13.4	17.8
8.3	10.7	2.0
9.4	9.4	7.7
9.9	8.9	77.8
12.2	7.3	13.9
13.7	6.5	1.3
14.1	6.3	28.8

2-Theta	d (Å)	Relative Intensity %
15.0	5.9	0.9
16.3	5.4	100.0
16.5	5.4	15.0
17.6	5.0	8.3
18.5	4.8	32.7
18.9	4.7	7.3
19.9	4.5	12.8
20.4	4.4	1.2
21.1	4.2	7.0
21.9	4.1	8.8
22.2	4.0	3.6
22.9	3.9	29.1
23.4	3.8	4.5
23.7	3.7	9.2
24.5	3.6	12.9
25.1	3.5	3.2
25.8	3.5	15.5
26.3	3.4	5.5
26.6	3.3	4.2
27.8	3.2	6.9
28.4	3.1	5.1
28.9	3.1	5.3
29.6	3.0	9.0
30.5	2.9	3.0
31.1	2.9	0.8
32.9	2.7	7.5
33.8	2.7	2.8
34.3	2.6	1.6
35.0	2.6	1.2
35.4	2.5	2.6
36.6	2.5	3.6
37.2	2.4	1.8
37.6	2.4	1.6
38.5	2.3	1.5

[00143] In some embodiments, the crystalline solid state of Compound 2 Form II exhibits a DSC thermogram substantially similar to that shown in Figure 24. In some embodiments, the crystalline solid state of Compound 2 Form II exhibits a DSC endotherm at 40.3°C ± 5.0. In some embodiments, the crystalline solid state of Compound 2 Form II exhibits a DSC endotherm at 201.0°C ± 5.0. In some embodiments, the crystalline solid state of Compound 2 Form II exhibits a DSC exotherm at 204.9°C ± 5.0. In some embodiments, the crystalline solid state of Compound 2 Form II exhibits a DSC endotherm at 303.3°C ± 5.0. In certain embodiments, the margin of error

for the endotherms of the crystalline solid state of Compound 2 Form II are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00144] In some embodiments, the crystalline solid state of Compound 2 Form II exhibits a TGA thermogram substantially similar to that shown in Figure 24. In some embodiments, the crystalline solid state of Compound 2 Form II exhibits TGA weight loss of 20.1 % ± 0.5 at 195.0°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 2 Form II is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00145] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 2 Form II is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00146] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 2 Form II has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 2 Form II has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 2 Form II has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 2 Form II has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 2 Form II has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 2 Form II has a chemical purity of 99.5% or more.

Compound 2 Form III

[00147] In some embodiments, the present invention provides a crystalline solid state form of Compound 2 Form III. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 9.5° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.8° ± 0.3 and 17.8° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 6.5° ± 0.3, 13.6° ± 0.3, and 13.9° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.9° ± 0.3, 16.1° ± 0.3, and 24.1° ± 0.3.

[00148] In some embodiments, the solid form Compound 2 Form III exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 6.5° ± 0.3, 9.5° ± 0.3, 11.9° ± 0.3, 13.6° ± 0.3, 13.9° ± 0.3, 15.8° ± 0.3, 16.1° ± 0.3, 17.8° ± 0.3, and 24.1° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected

from the group consisting of 6.5° ± 0.3, 9.5° ± 0.3, 11.9° ± 0.3, 13.6° ± 0.3, 13.9° ± 0.3, 15.8° ± 0.3, 16.1° ± 0.3, 17.8° ± 0.3, and 24.1° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 6.5° ± 0.3, 9.5° ± 0.3, 11.9° ± 0.3, 13.6° ± 0.3, 13.9° ± 0.3, 15.8° ± 0.3, 16.1° ± 0.3, 17.8° ± 0.3, and 24.1° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 6.5° ± 0.3, 9.5° ± 0.3, 11.9° ± 0.3, 13.6° ± 0.3, 13.9° ± 0.3, 15.8° ± 0.3, 16.1° ± 0.3, 17.8° ± 0.3, and 24.1° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 6.5° ± 0.3, 9.5° ± 0.3, 11.9° ± 0.3, 13.6° ± 0.3, 13.9° ± 0.3, 15.8° ± 0.3, 16.1° ± 0.3, 17.8° ± 0.3, and 24.1° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected the group consisting of 6.5° ± 0.3, 9.5° ± 0.3, 11.9° ± 0.3, 13.6° ± 0.3, 13.9° ± 0.3, 15.8° ± 0.3, 16.1° ± 0.3, 17.8° ± 0.3, and 24.1° ± 0.3. In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected the group consisting of 6.5° ± 0.3, 9.5° ± 0.3, 11.9° ± 0.3, 13.6° ± 0.3, 13.9° ± 0.3, 15.8° ± 0.3, 16.1° ± 0.3, 17.8° ± 0.3, and 24.1° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 2 Form III is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 2 Form III exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 25. In some embodiments, Compound 2 Form III exhibits at least one of the X-ray powder diffraction pattern reflections in Table 13.

Table 13. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 2 Form III.

2-Theta	d (Å)	Relative Intensity %
6.5	13.6	29.0
9.1	9.8	7.0
9.5	9.3	100.0
11.9	7.4	20.0
13.6	6.5	41.2
13.9	6.4	24.0
15.1	5.9	2.8
15.8	5.6	95.7
16.1	5.5	16.8
17.3	5.1	10.2
17.8	5.0	48.3
18.2	4.9	7.7
18.6	4.8	7.3
19.2	4.6	10.9
20.5	4.3	4.0
21.9	4.1	13.0
22.3	4.0	20.8

2-Theta	d (Å)	Relative Intensity %
22.9	3.9	4.3
23.2	3.8	3.9
24.1	3.7	16.2
25.0	3.6	4.1
25.4	3.5	39.1
26.2	3.4	10.7
26.7	3.3	4.3
27.2	3.3	14.4
27.5	3.2	8.6
28.1	3.2	6.4
28.3	3.2	5.8
29.0	3.1	6.7
30.1	3.0	2.0
30.4	2.9	2.0
32.0	2.8	4.2
32.5	2.8	1.8
35.5	2.5	1.6
36.1	2.5	1.1
37.2	2.4	1.4

[00149] In some embodiments, the crystalline solid state of Compound 2 Form III exhibits a DSC thermogram substantially similar to that shown in Figure 26. In some embodiments, the crystalline solid state of Compound 2 Form III exhibits a DSC endotherm at 79.5°C ± 5.0. In some embodiments, the crystalline solid state of Compound 2 Form III exhibits a DSC endotherm at 185.8°C ± 5.0. In some embodiments, the crystalline solid state of Compound 2 Form III exhibits a DSC endotherm at 308.5°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 2 Form III are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00150] In some embodiments, the crystalline solid state of Compound 2 Form III exhibits a TGA thermogram substantially similar to that shown in Figure 26. In some embodiments, the crystalline solid state of Compound 2 Form III exhibits TGA weight loss of 3.7 % ± 0.5 at 65.0°C ± 10.0. In some embodiments, the crystalline solid state of Compound 2 Form III exhibits TGA weight loss of 17.6 % ± 0.5 at 220.0°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 2 Form III is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00151] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 2 Form III is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In

some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00152] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 2 Form III has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 2 Form III has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 2 Form III has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 2 Form III has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 2 Form III has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 2 Form III has a chemical purity of 99.5% or more.

Compound 3

[00153] In some embodiments, the present invention provides a crystalline solid state of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile, also known as Compound 3. In some embodiments, provided herein is crystalline Compound 3 Form I.

Compound 3 Form I

[00154] In some embodiments, the present invention provides crystalline solid state form of Compound 3 Form I. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 27.8° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.7° ± 0.3 and 24.1° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.4° ± 0.3, 14.9° ± 0.3, and 18.7° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.1° ± 0.3, 18.0° ± 0.3, and 22.0° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.8° ± 0.3, 19.4° ± 0.3, and 22.6° ± 0.3. In some embodiments, the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.9° ± 0.3, 17.9° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

[00155] In some embodiments, the solid form Compound 3 Form I exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3,

and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In some embodiments, the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. . In some embodiments, the solid form exhibits at least seven X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3. In certain embodiments, the margin of error for any one of the reflections of Compound 3 Form I is selected from ±0.5; ±0.4; ±0.3; ±0.2; ±0.1; and ±0.05. In some embodiments, Compound 3 Form I exhibits the X-ray powder diffraction pattern substantially similar to that shown in Figure 27. In some embodiments, Compound 3 Form I exhibits at least one of the X-ray powder diffraction pattern reflections in Table 14.

Table 14. Peak listing for the X-ray powder diffractogram of the crystalline solid state form of Compound 3 Form I.

2-Theta	d (Å)	Relative Intensity %
7.4	11.9	47.8
8.8	10.0	27.1
9.3	9.5	14.5
11.2	7.9	1.2
11.9	7.5	16.4
13.4	6.6	11.3
14.5	6.1	10.0
14.9	5.9	43.2
15.1	5.9	35.5
16.5	5.4	6.7
16.8	5.3	1.9
17.4	5.1	2.8

2-Theta	d (Å)	Relative Intensity %
17.8	5.0	21.3
18.0	4.9	36.6
18.5	4.8	27.9
18.7	4.7	47.6
19.1	4.6	6.9
19.4	4.6	23.4
19.7	4.5	82.2
20.8	4.3	14.2
21.2	4.2	0.8
21.5	4.1	1.9
22.0	4.0	34.9
22.6	3.9	24.7
23.1	3.8	14.6
23.6	3.8	14.0
24.1	3.7	55.9
24.3	3.7	8.9
25.1	3.6	5.0
25.5	3.5	0.9
25.9	3.4	9.9
26.2	3.4	2.5
26.6	3.4	0.6
27.6	3.2	10.3
27.8	3.2	100.0
28.1	3.2	7.6
28.4	3.1	5.9
28.6	3.1	15.6
29.0	3.1	2.6
29.4	3.0	4.7
29.9	3.0	17.3
30.7	2.9	7.8
31.8	2.8	1.4
32.2	2.8	2.6
33.0	2.7	1.2
33.3	2.7	1.9
33.7	2.7	8.2
34.1	2.6	4.3
35.2	2.5	1.0
35.9	2.5	0.9
36.8	2.4	1.5
37.2	2.4	1.3
38.1	2.4	1.7
38.9	2.3	3.0
39.7	2.3	1.1
39.9	2.3	2.8

[00156] In some embodiments, the crystalline solid state of Compound 3 Form I exhibits a DSC thermogram substantially similar to that shown in Figure 28. In some embodiments, the

crystalline solid state of Compound 3 Form I exhibits a DSC endotherm at 270.7°C ± 5.0. In certain embodiments, the margin of error for the endotherms of the crystalline solid state of Compound 3 Form I are selected from ±15.0; ±10.0; ±5.0; and ±2.0.

[00157] In some embodiments, the crystalline solid state of Compound 3 Form I exhibits a TGA thermogram substantially similar to that shown in Figure 28. In some embodiments, the crystalline solid state of Compound 3 Form I exhibits TGA weight loss of 0.7 % ± 0.5 at 200.0°C ± 10.0. In certain embodiments, the margin of error for the TGA weight loss for the crystalline solid state of Compound 3 Form I is selected from ±5.0; ±2.0; ±1.0; ±0.5; and ±0.1.

[00158] In some embodiments, provided herein is a composition wherein the crystalline solid state form of Compound 3 Form I is substantially free of other crystalline or amorphous forms. In some embodiments, the amount of other crystalline or amorphous forms is 20 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 15 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 10 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 5 % (w/w) or less. In some embodiments, the amount of other crystalline or amorphous forms is 1 % (w/w) or less.

[00159] In some embodiments, provided herein is a composition wherein the crystalline solid state form Compound 3 Form I has a chemical purity of 95% or more. In some embodiments, the crystalline solid state form Compound 3 Form I has a chemical purity of 96% or more. In some embodiments, the crystalline solid state form Compound 3 Form I has a chemical purity of 97% or more. In some embodiments, the crystalline solid state form Compound 3 Form I has a chemical purity of 98% or more. In some embodiments, the crystalline solid state form Compound 3 Form I has a chemical purity of 99% or more. In some embodiments, the crystalline solid state form Compound 3 Form I has a chemical purity of 99.5% or more.

Pharmaceutical Compositions

[00160] In certain embodiments, Compound 1, Compound 2, or Compound 3 is administered as a pure chemical. In other embodiments, Compound 1, Compound 2, or Compound 3 is combined with a pharmaceutically suitable or acceptable carrier (also referred to herein as a pharmaceutically suitable (or acceptable) excipient, physiologically suitable (or acceptable) excipient, or physiologically suitable (or acceptable) carrier) selected on the basis of a chosen route of administration and standard pharmaceutical practice as described, for example, in *Remington: The Science and Practice of Pharmacy* (Gennaro, 21st Ed. Mack Pub. Co., Easton, PA (2005)).

[00161] One embodiment provides a pharmaceutical composition comprising a solid form of any one of the compounds provided herein and a pharmaceutically acceptable excipient.

[00162] One embodiment provides a method of preparing a pharmaceutical composition comprising mixing a solid form of a compound provided herein, and a pharmaceutically acceptable carrier.

[00163] Provided herein is a pharmaceutical composition comprising at least one of Compound 1, Compound 2, or Compound 3 together with one or more pharmaceutically acceptable carriers. The carrier(s) (or excipient(s)) is acceptable or suitable if the carrier is compatible with the other ingredients of the composition and not deleterious to the recipient (*i.e.,* the subject or the patient) of the composition.

[00164] One embodiment provides a pharmaceutical composition comprising a pharmaceutically acceptable excipient and Compound 1, Compound 2, or Compound 3.

[00165] One embodiment provides a method of preparing a pharmaceutical composition comprising mixing Compound 1, Compound 2, or Compound 3 and a pharmaceutically acceptable carrier.

[00166] In certain embodiments, Compound 1, Compound 2, or Compound 3 is substantially pure, in that it contains less than about 5%, or less than about 1%, or less than about 0.1%, of other organic small molecules, such as unreacted intermediates or synthesis by-products that are created, for example, in one or more of the steps of a synthesis method.

[00167] The dose of the composition comprising Compound 1, Compound 2, or Compound 3, differs depending upon the subject or patient's (e.g., human) condition. In some embodiments, such factors include general health status, age, and other factors.

[00168] Pharmaceutical compositions are administered in a manner appropriate to the disease to be treated (or prevented). An appropriate dose and a suitable duration and frequency of administration will be determined by such factors as the condition of the patient, the type and severity of the patient's disease, the particular form of the active ingredient, and the method of administration. In general, an appropriate dose and treatment regimen provides the composition(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit (e.g., an improved clinical outcome, such as more frequent complete or partial remissions, or longer disease-free and/or overall survival, or a lessening of symptom severity. Optimal doses are generally determined using experimental models and/or clinical trials. The optimal dose depends upon the body mass, weight, or blood volume of the patient.

[00169] Oral doses typically range from about 1.0 mg to about 1000 mg, one to four times, or more, per day.

Methods of Treatment

[00170] One embodiment provides Compound 1, Compound 2, or Compound 3, for use in a method of treatment of the human or animal body.

[00171] One embodiment provides Compound 1, Compound 2, or Compound 3, for use in a method of treatment of cancer or neoplastic disease.

[00172] One embodiment provides a use of Compound 1, Compound 2, or Compound 3, in the manufacture of a medicament for the treatment of cancer or neoplastic disease.

[00173] In some embodiments, described herein is a method of treating cancer in a patient in need thereof comprising administering to the patient Compound 1, Compound 2, or Compound 3. In some embodiments, described herein is a method of treating cancer in a patient in need thereof comprising administering to the patient a pharmaceutical composition comprising Compound 1, Compound 2, or Compound 3, and a pharmaceutically acceptable excipient.

[00174] Provided herein is the method wherein the pharmaceutical composition is administered orally.

[00175] One embodiment provides a solid form of a compound provided herein for use in a method of treatment of the human or animal body.

[00176] One embodiment provides a solid form of a compound provided herein for use in a method of treatment of cancer or neoplastic disease.

[00177] One embodiment provides use of a solid form of a compound provided herein in the manufacture of a medicament for the treatment of cancer or neoplastic disease.

[00178] One embodiment provides a method of treating a disease or disorder in a patient in need thereof, comprising administering to the patient a solid form of a compound provided herein. In some embodiments, the disease or disorder is cancer. In some embodiments, the disease or disorder is neoplastic disease.

[00179] One embodiment provides a method of treating a disease or disorder in a patient in need thereof, comprising administering to the patient a solid form of a compound provided herein and a pharmaceutically acceptable excipient. In some embodiments, the disease or disorder is cancer. In some embodiments, the disease or disorder is neoplastic disease.

[00180] Other embodiments and uses will be apparent to one skilled in the art in light of the present disclosures. The following examples are provided merely as illustrative of various embodiments and shall not be construed to limit the invention in any way.

EXAMPLES

[00181] The present disclosure is further illustrated by the following examples, which should not be construed as limiting in any way. The experimental procedures to generate the data shown are discussed in more detail below. The disclosure has been described in an illustrative manner, and

it is to be understood that the terminology used is intended to be in the nature of description rather than of limitation.

General Experimental, Instrument, and Methodology Details

[00182] A general synthesis for 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile is described in PCT/US2023/075058.

X-Ray Powder Diffraction (XRPD)

[00183] For XRPD analysis, a Bruker D8 Advance X-ray powder diffractometer was used equipped with a LynxEye XE-T detector. The XRPD parameters used are listed in Table 15.

Table 15. Parameters for XRPD experiments

Instrument	Bruker, D8 Advance
Radiation	Cu Kα (λ = 1.5418 Å)
Detector	LynxEye XE-T
Scan angle	3-40° (2θ)
Scan step	0.02° (2θ)
Scan speed	0.1 s/step
Tube voltage/current	40 KV/40 mA
Divergence slit	0.6 mm
Rotation	30 rpm
Sample holder	Zero-background sample pan

Differential Scanning Calorimetry (DSC)

[00184] DSC was performed using a Discovery DSC 250/ Q200 (TA Instruments, US). The sample was placed into an aluminum pan with pin hole and heated with the parameters in Table 16. The DSC parameters used are listed in Table 16.

Table 16. Parameters for DSC experiments

Instrument	TA, Discovery DSC 250/ Q200
Sample pan	Aluminum, pin-holed
Temperature range	25-300 °C
Heating rate	10 °C/min
Purge gas	N_2
Flow rate	50 mL/min

Thermo-Gravimetric Analysis (TGA)

[00185] TGA was carried out on a Discovery TGA 55/ Q500 (TA Instruments, US). The sample was loaded onto a pre-tared aluminum pan and heated with the parameters in Table 17. The

data was analyzed using TRIOS or TA Universal Analysis. The TGA parameters used are listed in Table 17.

Table 17. Parameters for TGA experiments

Instrument	TA, Discovery TGA 55/ Q500
Sample pan	Aluminum, open
Temperature range	RT-300 °C
Heating rate	10 °C/min
Purge gas	N_2
Flow rate for TGA55	Balance chamber: 40 mL/min
	Sample chamber: 25 mL/min
Flow rate for Q500	Balance chamber: 40 mL/min
	Sample chamber: 60 mL/min

Dynamic Vapor Sorption (DVS)

[00186] Moisture sorption/desorption data were collected on a DVS Intrinsic PLUS (SMS, UK). The sample was placed into a tared sample chamber and automatically weighed. Samples (e.g., anhydrate, hydrate) were analyzed with the setting parameters listed in Table 18.

Table 18. Parameters for DVS experiments

Instrument	SMS, DVS Intrinsic PLUS
dm/dt	0.002%/min
Drying/ Measurement temperature	40 °C/25 °C
Cycle	Full cycle
Minimum dm/dt stability duration	30 min
Maximum dm/dt equilibrium time	120 min
Save data rate	5 s
Gas and Total flow rate	N_2, 200 sccm
Post experiment total flow	200 sccm
RH step size	10% RH
Method	Adsorption: 0, 10, 20, 30, 40, 50, 60, 70, 80, 90
	Desorption: 80, 70, 60, 50, 40, 30, 20, 10, 0

Polarized Light Microscopy (PLM)

[00187] Light microscopy was performed using an ECLIPSE LV100POL (Nikon, JPN) microscope.

Proton Nuclear Magnetic Resonance (1H-NMR)

[00188] ^{1}H-NMR was performed using Bruker 400 MHz instrument. Samples were measured with the parameters in Table 19.

Table 19. Parameters for ^{1}H-NMR Analysis

Instrument	Bruker
Frequency	400 mHz
Scan times	4
Temperature	295 K
Relaxation delay	1 s

High Performance Liquid Chromatography (HPLC) Method

[00189] HPLC analysis was performed with an Agilent HPLC 1260 series instrument. HPLC method for solubility and stability testing is listed in Table 20.

Table 20. Parameters for HPLC experiments

Instrument	Agilent 1260 series		
Column	Poroshell 120 EC-C18, 1.7 µm, 4.6 x 100 mm		
Column temperature	40 ℃		
Mobile phase	A: 0.1%TFA in H2O B: 0.1%TFA in ACN		
Flow rate	1.0 mL/min		
Injection volume	4 µL		
Detector	DAD		
Wavelength	254 nm		
Run time	10.0 min		
Post time	3.0 min		
Diluent	ACN:water (v:v 1:1)		
Gradient	Time (min)	%A	%B
	0.0	90	10
	3.0	55	45
	6.0	55	45
	8.0	5	95
	10	5	95

Example 1: Summary of Salt Screen

[00190] A total of 12 acids were used for the salt screen and are presented in **Table 21** below.

Table 21. Acids Used for Salt Screen

No.	Acid
1	Hydrochloric acid (HCl)
2	Sulfuric acid (H_2SO_4)
3	p-Toluenesulfonic acid (TsOH)
4	Methanesulfonic acid (MsOH)
5	Phosphoric acid (H_3PO_4)
6	Maleic acid
7	L-Tartaric acid
8	Fumaric acid
9	Citric acid

10	L-Malic acid
11	Succinic acid
12	Benzenesulfonic acid

[00191] The solvents listed in **Table 22** below were used for the screen.

Table 22. Solvents used for Salt Screen

#	**Solvent**	#	**Solvent**
1	Methanol	10	Water
2	Ethanol	11	Toluene
3	2-Propanol	12	Ethyl acetate
4	Isobutanol	13	Isopropyl acetate
5	2-Butanone	14	*n*-Heptane
6	Tetrahydrofuran	15	Dioxane
7	Acetonitrile	16	Dimethyl sulfoxide
8	tert-Butyl methyl ether	17	Dichloromethane
9	Acetone	18	2-Me-THF

[00192] Salts were prepared on 25 mg scale. An appropriate amount of Compound 3 Form I was added in different solvents at RT or 50 °C, and then an acid was added to form the corresponding salt. If no precipitation occurred, various crystallization methods were attempted to prepare crystalline salts, including cooling crystallization, evaporation, and anti-solvent precipitation. Solids that were formed were collected by filtration, dried under vacuum and analyzed.

[00193] Of the 12 acids screened, 10 formed crystalline salts, and a total of 20 crystalline salt forms were obtained in the salt screen. Characterization data for samples of salts and Compound 3 Form I collected during the salt screen are summarized in **Table 23** below. B:A refers to Base: Acid. The counterion stoichiometry for some salts was not determined due to hygroscopicity or high solvents or polymorphism.

HCl Salt

[00194] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT, when the solid could not be dissolved completely. 1.1 eq. or 2.1 eq. of hydrochloric acid was added to the suspension and then the resulting mixture was kept stirring at RT overnight. Samples obtained with 2 eq. acid had different XRPD and NMR chemical shifts from the products which were prepared with 1 eq. acid. Thus, they were likely di-HCl salt and were assigned as di-HCl salt Pattern 1 and Pattern 2, respectively.

Sulfate Salt

[00195] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT and the solid could not be dissolved completely. 1.1 eq. or 2.1 eq. of sulfuric acid was added to the suspension and then the resulting mixture was kept stirring at RT or 50 °C.

[00196] XRPD patterns of the samples obtained with 2 eq acid had different XRPD and NMR chemical shifts from the products which were prepared with 1 eq acid, suggesting that mono- and di-sulfate salts were obtained during screening. Finally, two mono-sulfate and one di-sulfate were obtained.

Mesylate Salt

[00197] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT or 50 °C. 1.1 eq. or 2.1 eq. of MsOH acid was added to the mixture and then the mixture was kept stirring. If no solid was precipitated, then anti-solvent was added. One pattern of mono-mesylate and two patterns of di-mesylate were obtained. Among them, di-mesylate Pattern 2 had low crystallinity and was not characterized.

Tosylate Salt

[00198] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT or 50 °C whereupon the solid could not be dissolved completely. 1.1 eq. or 2.1 eq. of TsOH acid was added to the suspension and then the mixture was kept stirring. New patterns were obtained. NMR results indicated that Compound 3 Form I formed salts with both 1 eq. and 2 eq. of acids. According to NMR result, the ratio of base to acid in di-tosylate Pattern 2 was unreasonable (B:A = 1:0.4), therefore, it wasn't assigned as a form.

Besylate Salt

[00199] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT. 1.1 eq. or 2.1 eq. of Benzenesulfonic acid was added to the mixture and kept stirring. If no solid was obtained, anti-solvent was added. One pattern of mono-besylate and di-besylate were obtained. The crystallinity of di-besylate was low and not further characterized.

Maleate Salt

[00200] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT. The solid could not be dissolved completely. 1.1 eq of maleic acid was added to the suspension and then the mixture was kept stirring at RT overnight. If no solid precipitated, then anti-solvent was added. New patterns were obtained from different solvent systems. Among them, mono-maleate pattern 2 had low crystallinity.

Phosphate Salt

[00201] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT. The resulting solid could not be dissolved completely. 1.1 eq. of phosphoric acid was added to suspension and then the mixture was kept stirring at RT overnight. XRPD pattern of the samples obtained from MeOH and acetone were similar as Compound 3 Form I with extra peak, suggesting

they might not be salts. A new pattern was obtained from THF/water, which was a potential salt form, but crystallinity was low, therefore, it wasn't further characterized.

Fumarate Salt

[00202] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT. The resulting solid could not be dissolved completely. 1.1 eq. of fumaric acid was added to the suspension and then the mixture was kept stirring at RT overnight. Two new patterns were obtained, and both of them were similar as Compound 3 Form I with or without extra peaks. Pattern 1 was likely a pure form and further characterized.

Citrate Salt

[00203] About 25 mg of Compound 3 Form I was added in 0.5 mL of solvent at RT. The resulting solid could not be dissolved completely. 1.1 eq. of citric acid was added to the suspension and then the mixture was kept stirring at RT overnight. If no solid precipitated, then anti-solvent was added. A new pattern was obtained from THF/water, assigned as citrate Pattern 1. XRPD pattern was similar as the Compound 3 Form I but not exactly the same. The sample was further characterized.

Succinate Salt

[00204] About 25 mg of Compound 3 Form I was added in 0.5 mL of MeOH at RT. The solid could not be dissolved completely. 1.1 eq. of succinic acid was added to the suspension and then the mixture was kept stirring at RT overnight. If no solid precipitated, then anti-solvent was added. A new pattern was obtained from acetone, and was assigned succinate Pattern 1. XRPD pattern was similar as the Compound 3 Form I but not exactly the same. The sample was further characterized.

Tartrate Salt

[00205] About 25 mg of Compound 3 Form I was added in 0.5 mL of MeOH at RT, solid could not be dissolved completely. 1.1 eq. of L-tartaric acid was added to suspension and then the mixture was kept stirring at RT overnight. a new pattern with low crystallinity was obtained from THF/water, which was a potential tartrate crystalline sample. Due to low crystallinity, the sample was not further characterized.

Malate Salt

[00206] About 25 mg of Compound 3 Form I was added in 0.5 mL of MeOH at RT. The solid could not be dissolved completely. 1.1 eq. of L-malic acid was added to the suspension and then the mixture was kept stirring at RT overnight. If no solid precipitated, then anti-solvent was added. A new pattern was obtained from acetone and assigned as malate Pattern 1. XRPD pattern of the sample was similar as Compound 3 Form I but not exactly the same.

Table 23. Sample Salt Screen Data for Crystalline Salts Identified in Salt Screen

Salt B:A	Solvation	PLM Crystallinity	DSC, endo Onset/Pk °C, ΔH J/g	TGA Wt. loss%/T °C	DVS Wt. gain%	Comment
Compound 3 Form I	Anhydrate	Irregular High	270/271, 132	0.7/RT-200	0.13% at 80%RH 0.17% at 90%RH Reversible, form unchanged	Starting material, 1% DMF
Compound 2 Form I	Anhydrate	Irregular High	305/313, m/d	1.9/RT-100	0.30% at 80%RH 0.35% at 90%RH Reversible, form unchanged	Slightly hygroscopic, 0.3% MeOH
Di-HCl salt Form I	Hydrate	Irregular Moderate	34/74, 26 135/154, 44 216/226, 24	10.4/RT-171	/	~4 mol of water; no solvent
Compound 1 Form I 1:1	Anhydrate	Irregular High	226/230, 111 247/254, 12	0.8/RT-86	0.13% at 80%RH 0.18% at 90%RH Hysteresis, form unchanged	No solvent; more stable than Form III in solvent
Compound 1 Form II 1:1	Solvate/ hydrate	Irregular Moderate	30/52, 12 141/146, 1.8 173/183, 84 overlapped	2.7/RT-100 11.9/100-250	/	-0.75 mol of water; 0.8% acetone
Compound 1 Form III 1:1	Anhydrate	Irregular High	218/221, 129	11.3/170-250	/	No solvent
Compound 1 Form IV 1:1	Hydrate	Irregular Moderate	29/45, 14 176/183, 35 246/257, 45	4.2/RT-100	/	1.5 mol of water; 0.5% MeOH
Compound 1 Form V 1:1	Solvate	Irregular Moderate	28/45, 17 155/163, 88 overlapped	3.2/RT-100 17.1/100-230	/	10.1% THF, ~1 mol
Mono-Citrate Form I 1:1	Hydrate	Irregular Moderate	46/68, 62 94/105, 13 146/156, 9.9 167/192, 74	4.8/RT-65 2.9/65-135 1.9/135-155	/	4 mol of water; 0.6% THF and 0.1% MTBE

Salt B:A	Solvation	PLM Crystallinity	DSC, endo Onset/Pk °C, ΔH J/g	TGA Wt. loss%/T °C	DVS Wt. gain%	Comment
Mono-sulfate Form I	Solvate/ hydrate	Irregular Moderate	26/84, 228 232/247, 35 257/261, overlapped	1.9/RT-130	/	0.9% MeOH
Mono-sulfate Form II	Hydrate	Irregular High	50/91, 284 187/215, 88	11.6/RT-150	/	-4.5 mol of water; no solvent
Di-sulfate Form I	Solvate	Irregular Moderate	26/50, 59 275/283, endo/endo	0.3/RT-104	/	0.7% MeOH
Mono-malate Form I 1:1	Hydrate	High	29/72, 88 123/130, 12 174/198, 25 244/253, 36	3.3/RT-100	/	-1.5 mol of water; 0.1% acetone
Mono-mesylate Form I 1:1	Hydrate	Irregular High	41/76, 239 202/209, 51	3.9/RT-119 0.8/120-230	/	1.5 mol of water; 0.4% MTBE
Di-mesylate Form I 1:2	Hydrate	Irregular High	30/53, 19 85/112, 29 182/203, 29	5.1/RT-80 1.5/80-130	/	3 mol of water; no solvent
Mono-tosylate Form I 1:1	Solvate/ hydrate	Irregular High	101/126,41 163/174,14	3.2/RT-200	/	-1.25 mol of water; 0.8% THF
Di-tosylate Form I 1:1.8	Solvate/ hydrate	Irregular High	34/72, 69 152/163, 1.6 191/204, 37	3.2/RT-127	/	0.8% acetone
Mono-Besylate Form I 1:1	Hydrate	Irregular Moderate	106/139, 49 overlapped 225/235, 4.1	3.1/65-179	/	-1.2 mol of water; 0.3% THF and 0.05% MTBE
Mono-fumarate Form I 1:1	Hydrate	Moderate	25/68, 146 206/214, 36 221/253, 66	3.9/RT-100	/	1.5 mol of water
Mono-succinate Form I 1:1	Hydrate	Moderate	26/57, 101 181/185, 30	2.2/RT-100	/	-1 mol of water

Example 2: Polymorph Screen of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00207] A polymorph screen of Compound 1was performed to identify additional crystalline forms for further development. Form I was initially identified from MeOH by salt formation in the salt screen and obtained from most experiments in the polymorph screen. The list of solvents used for the polymorph screen of Compound 1 is provided in Table 24 below. In Table 24 below: methanol (MeOH), ethanol (EtOH), 2-Propanol (IPA), Isobutanol (IBA), butanone (MEK), tetrahydrofuran (THF), acetonitrile (ACN), tert-Butyl methyl ether (MTBE), ethyl acetate (EA), isopropyl acetate (IPAC), dimethyl sulfoxide (DMSO), N-methylpyrrolidone (NMP), 2-methyltetrahydrofuran (2-Me-THF), and N, N-Dimethylacetamide (DMA).

Table 24. List of Solvents used in Polymorph Screen of Compound 1

No.	Solvent	No.	Solvent
1	MeOH	12	EA
2	EtOH	13	IPAC
3	IPA	14	*n*-Heptane
4	IBA	15	DMSO
5	MEK	16	*n*-Hexane
6	THF	17	Cyclohexane
7	ACN	18	NMP
8	MTBE	19	Dioxane
9	Acetone	20	2-Me-THF
10	Water	21	DMA
11	Toluene		

Example 3: Synthesis of Crystalline Form I of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00208] Compound 1 Form I was initially identified from MeOH by salt formation in the salt screen and obtained from most experiments in the polymorph screen. Compound 1 Form I was irregular shaped crystals with small particle size and high crystallinity. TGA showed no weight loss prior to decomposition and DSC exhibited two endothermic peaks at 232 °C and 251°C (see Figure 2). No residual solvent was detected by ^{1}H-NMR and the molar ratio of the free base to acid was 1:1. Thus, Compound 1 Form I was assigned as an anhydrate.

[00209] DVS of Compound 1 Form I indicated that it was slightly hygroscopic with 0.18% water uptake at 90%RH as shown in Figure 32, and the crystal form remained unchanged after DVS testing.

[00210] In this study, to investigate the second endothermic peak in the DSC curve, Compound 1 Form I was heated to 242 °C at 10 °C/min by DSC, and then cooled to RT for analysis. A brown glassy sample was obtained and LCMS showed its purity was only 57% and an impurity was included with peak area% of 35% and $[M+H]^+$ of 706, suggesting it degraded at 242 °C and the second endothermic peak was caused by decomposition.

Example 4: Synthesis of Crystalline Form II of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00211] Compound 1 Form II was initially identified from acetone by salt formation in the salt screen. Compound 1 Form II was irregular shaped crystals with small particle size and moderate crystallinity. ^{1}H-NMR showed it contained 0.8% residual acetone and the ratio of the free base to acid was 1:1. TGA showed 2.8% weight loss from RT to 100 °C and 11.9% weight loss from 100 to 250 °C., as shown in Figure 4. DSC exhibited multiple endothermic peaks at 31, 141 and 173 °C (see Figure 4), might be due to desolvation/dehydration, melting or melting/decomposition. Therefore, Compound 1 Form II was a solvate/hydrate.

Example 5: Synthesis of Crystalline Form III of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00212] Compound 1 Form III was initially identified from THF/5% water/*n*-heptane/MTBE systems by salt forming reaction in the salt screen.

[00213] Additional Compound 1 Form III was prepared on a 50 mg scale for further testing. About 50 mg of Compound 3 was added into 20 V of THF/water (19/1) at 50 °C to obtain a suspension, and then 1.1 eq of maleic acid was added. A clear solution was obtained that was stirred at 50 °C for 30 min, cooled to RT and treated with 16 V of MTBE. An oil appeared at first when 4 V of *n*-heptane was added resulting in precipitation. The suspension was kept stirring at RT overnight and the resulting solids were collected by filtration, vacuum dried at 50 °C for 4 hours and characterized. Compound 1 Form III was irregular shaped crystals with small particle size. About 0.18% weight loss from 28 to 90 °C and onset of an endothermic peak at 213.2 °C due to melting/decomposition were observed by TGA and DSC (Figure 6), suggesting Compound 1 Form III was an anhydrate. ^{1}H-NMR showed that the ratio of the free base to acid was 1/1 and no residual

solvents were detected. This batch maleate Form III was used for the subsequent inter-conversion study.

Example 6: Synthesis of Crystalline Form IV of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00214] Compound 1 Form IV was initially identified initially identified from MeOH by salt forming reaction in the salt screen.

[00215] Additional Compound 1 Form III was prepared on a 50 mg scale for further testing. About 50 mg of Compound 3 was added into 1 mL of MeOH at RT to obtain a suspension, and then 1.1 eq of maleic acid was added. The resulting suspension was kept stirring at RT overnight. The solids were collected by filtration, vacuum dried at 50 °C for 4 hours and characterized. Compound 1 Form IV was irregular shaped crystals with small particle size and moderate crystallinity. ^{1}H-NMR showed the ratio of the free base to acid is 1/1 and no residual solvent was observed. TGA showed 1.5% weight loss from 27 to 83 °C due to loss of water (~0.6 mol water), as shown in Figure 8. DSC exhibited onset of three broad endothermic peaks at 41.1, 167.9 and 239.2 °C (see Figure 8), might be due to dehydration and melting/decomposition. Hence, Compound 1 Form IV was a hydrate.

Example 7: Synthesis of Crystalline Form V of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00216] Compound 1 Form V was initially generated from THF/water by salt forming reaction in the salt screen, and then identified from THF/5% water by slurry in the polymorph screen. Compound 1 Form V was irregular shaped crystals with small particle size and high crystallinity. About 10% THF was detected by ^{1}H-NMR and the molar ratio of the free base to acid was 1:1. TGA showed 3.2% weight loss from RT to 100 °C and 17.1% weight loss from 100 to 230 °C, as shown in Figure 10. DSC showed onset of broad endothermic peaks at 28.0 and 155.0 °C (See Figure 10). Thus, maleate Form V was a THF solvate (~1 mol THF).

Example 8: Synthesis of Crystalline Form VI of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00217] Compound 1 Form VI was identified from ACN by slurry method at RT. Compound 1 Form VI was small particle crystals with agglomeration and high crystallinity. About 6.9% residual ACN (~ 1 mol) was detected by ^{1}H-NMR. TGA showed 14.5% weight loss from 81 to 232

°C, as shown in Figure 12, which might be due to loss of water and solvent. DSC exhibited onset of two broad endothermic peaks at 165.7 and 228.9 °C (See Figure 12), due to desolvation/dehydration and decomposition, suggesting Compound 1 Form VI was a solvate/hydrate.

Example 9: Synthesis of Crystalline Form VII of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00218] Compound 1 Form VII was generated from 1,4-dioxane by slurry method at RT. Compound 1 Form VII was small particles with high crystallinity. TGA showed 18.9% weight loss from 111.6 to 217.9 °C in two steps due to loss of solvents (See Figure 14), and 19% residual 1,4-dioxane was detected by ^{1}H-NMR. DSC exhibited onset of two overlapped endothermic peaks at 168 and 177 °C due to desolvation, indicating Compound 1 Form VII was a di-dioxane solvate (~2 mol).

Example 10: Synthesis of Crystalline Form VIII of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00219] Compound 1 Form VIII was initially identified from DMA/acetone by heating-cooling cycle slurry, and then generated from NMP and DMA systems by anti-solvent precipitation. Compound 1 Form VIII was generated from NMP/MTBE and further characterized. Compound 1 Form VIII contained high level residual solvents (16% NMP) by ^{1}H-NMR. TGA showed multi-step weight losses due to loss of solvents and DSC exhibited a broad endothermic peak due to desolvation (See Figure 16), suggesting Compound 1 Form VIII was a solvate. Compound 1 Form VIII was likely an isostructural solvate.

Example 11: Synthesis of Crystalline Form IX of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00220] Compound 1 Form IX was identified from MeOH/water during water activity study. Equal amounts of Form I and IV converted to Form IX after slurring in MeOH/7% water at RT for 1 day. Form I was also converted to Form IX after stirring in MeOH/5% water and MeOH/7% water at RT and 50 °C for 1 day. Compound 1 Form IX was generated from MeOH/5% water at RT and further characterized.

[00221] Compound 1 Form IX was irregular shaped crystals with moderate crystallinity. The ^{1}H-NMR spectrum was consistent with that of Form I and no residual solvent was detected. TGA showed 1.7% weight loss from RT to 109 °C in two steps due to loss of water (~ 0.7 mol) and DSC

exhibited onset of two broad endothermic peaks at 57.4 and 147.3 °C due to dehydration, suggesting Compound 1 Form IX was a hydrate.

Example 12: Synthesis of Crystalline Form X of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00222] Compound 1 Form X was generated from DMSO/2-Me-THF/EtOH by reaction crystallization and further characterized. Compound 1 Form X was irregular shaped crystals with agglomeration and moderate crystallinity. TGA showed 0.7% weight loss from 24.0 to 77.2 °C and 19.6% weight loss from 77.2 to 241.2 °C (see Figure 20), while 9.5% residual DMSO (~ 1 mol) and 0.15% EtOH were detected by ^{1}H-NMR. DSC exhibited onset of a broad endothermic peak at 166.9 °C due to desolvation/decomposition, indicating Form X was a DMSO solvate.

Example 13: Characterization and Comparison of the Crystalline Forms of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00223] A summary of the characterization data for the solid forms of Compound 1 identified is shown below in Table 25.

Table 25. Summary of characterization data.

Form Solvation	PLM Crystallinity by XRPD	DSC, Onset/Peak Temperature (°C), ΔH (J/g)	TGA %wt. loss Temperature (°C)	Comment
Form I Anhydrate	Irregular High	232/235, 106 251/256, 9 (decomp.)	None/RT-200	DVS: 0.18% water uptake at 90% RH
Form II Solvate/Hydrate	Irregular Moderate	30/52, 12 141/146, 2 173/183, 84 (overlapped)	2.7/RT-100 11.9/100-250	0.8% acetone Only generated in the salt screen
Form III Anhydrate	Irregular High	213/217, 118	0.2/28-90	Repeat prepared as the product in the salt screen
Form IV Hydrate	Irregular Moderate	41/62, 24 168/182, 47 239/254, 44	1.5/27-83	~ 0.6 mol water Repeat prepared as the product in the salt screen
Form V THF Solvate	Irregular Moderate	28/48, 19 155/164, 90	3.2/RT-100 17.1/100-230	~ 1 mol THF

Form Solvation	PLM Crystallinity by XRPD	DSC, Onset/Peak Temperature (°C), ΔH (J/g)	TGA %wt. loss Temperature (°C)	Comment
		overlapped		
Form VI Solvate/hydrate	Irregular High	166/173, 148 229/252, 34	14.5/81-232	~ 1 mol ACN
Form VII 1,4-Dioxane solvate	Irregular High	168/177, 94 overlapped	5.9/112-162 13.0/162-218	~ 2 mol 1,4-dioxane
Form VIII NMP solvate	Irregular High	174/180, 180	12.6/48-164 11.7/164-234	~ 1.5 mol NMP; an isostructural solvate
Form IX Hydrate	Irregular High	57/84, 150 147/155, 19	0.6/34-70 1.1/70-109	~ 0.7 mol water
Form X DMSO solvate	Irregular High	167/181, 140	0.7/24-77 19.6-77-241	~ 1 mol DMSO Found from CPD study

Example 14: Inter-conversion Study of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00224] Inter-conversion study of Form I (anhydrate), III (anhydrate), IV (hydrate) was conducted in several non-aqueous solvents (MeOH, EtOH, acetone, EA, 2-Me-THF). As presented in **Table 26 below,** the mixture of Form I and IV completely converted to Form I in acetone and EA at RT and 50 °C. Moreover, the mixture of Form I and III completely or mainly converted to Form I at RT and 15 °C, while remained unchanged at 5 °C after slurring in EA and acetone for 6 days, suggesting Form I might reach equilibrium with Form III at 5 °C.

[00225] Overall, in non-aqueous solvents, Form I was more stable than Form IV at RT and 50 °C, also more stable than Form III at RT and 15 °C.

Table 26. Summary of inter-conversion study data.

Input	Solvent	Sample	Conc. (mg/mL	Temp.	Time	Output

Form I + IV (Equal amounts)	Acetone	A	40	RT	1 d	Form I
		B	40	50 °C	1 d	Form I
	EA	A	40	RT	1 d	Form I
		B	40	50 °C	1 d	Form I
Form I + III (Equal amounts)	MeOH	A	20	RT	1 d	Form I
	EA	B	20	RT	5 d	Mainly changed to Form I
	Acetone	C	40	5 °C	1, 3, 9 d	Form III + I
				15 °C	13 d	Form I
	EA	D	40	5 °C	1, 6, 14 d	Form III + I
				15 °C	7 d	Form I
	MeOH	E	40	5 °C	1 d	Form I

Example 15: Water Activity Study of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 1)

[00226] In addition, water activity study of Compound 1 Form I (anhydrate), Compound 1 Form IV (hydrate) and Compound 1 Form IX (hydrate) were performed in MeOH/water and EtOH/water systems, respectively. All results are summarized in **Table 27** and **Table 28** below. In MeOH with 3%, 5% and 7% water systems, pure Compound 1 Form I was used as the starting material first, and the results showed Compound 1 Form I remained unchanged in three systems at RT for 6 days, while dissociated to Compound 3 Form I at 50 °C for 1 day. Then, equal amounts of Compound 1 Form I and IV were used as the starting material to perform the competitive slurry in MeOH/7% water at RT. The mixture of Compound 1 Form I and IV converted to Form IX (hydrate) after 1 day. To investigate the reason, some repeat experiments were carried out. However, the output form was either Compound 1 Form I or Form IX, even in the same solvent system. Moreover, it also revealed that the crystallization behavior in MeOH is highly complex, perhaps due to solvent effect, hence MeOH is not suitable for water activity study.

[00227] Therefore, EtOH/water systems were selected for additional water activity study, as given in **Table 27**. All mixtures of Compound 1 (Form I and IV, Form I and IX) completely converted to Form I in EtOH with 3%, 5% and 7% water at RT for 1-2 days, and the pure Form I remained unchanged in three systems at RT for 1 day, suggesting Form I was more stable than Form IV and IX, and physically stable in EtOH/water with $a_w \leq 0.4$ at RT.

Table 27. Summary of Water Activity Study in MeOH/water

Input (compound 1)	Sample	Solvent	a_w	Temp.	Time	Output
Form I	A	MeOH/3% water	/	50 °C	1 d	Form I + trace Compound 3 Form I
					3 d	Form I + Compound 3 Form I
					6 d	Compound 3 Form I
	B	MeOH/3% water	0.098	RT	6 d	Form I
	C	MeOH/5% water	/	50 °C	1 d	Form I + Compound 3 Form I
					3 d	Compound 3 Form I
	D	MeOH/5% water	0.142	RT	6 d	Form I
	E	MeOH/7% water	/	50 °C	1 d	Form I + trace Compound 3 Form I
					2 d	Form I + Compound 3 Form I
					3 d	Compound 3 Form I
	F	MeOH/7% water	0.195	RT	6 d	Form I
Form I + IV (Equal amounts)	A	MeOH/7% water	/	RT	1 d	Form IX
	B	MeOH/3% water	/	RT	1 d	Form I
	C	MeOH/5% water	/	RT	1 d	Form I
	D	MeOH/7% water	/	RT	1 d	Form I
Form I	A	MeOH/5% water	0.142	RT	1 d	Form IX
	B	MeOH/5% water	0.143	RT	1 d	Form IX
	C	MeOH/7% water	0.195	RT	1 d	Form IX
	D	MeOH/7% water	0.192	RT	1 d	Form IX

Table 28. Summary of Water Activity Study in EtOH/water

Input	Sample	Solvent	a_w	Temp.	Time	Output
Form I + IV (Equal amounts)	A	EtOH	/	RT	1 d	Form I
	B	EtOH/3% water	0.216	RT	1 d	Form I
	C	EtOH/5% water	0.317	RT	1 d	Form I
	D	EtOH/7% water	0.406	RT	1 d	Form I
Form I	A	EtOH/3% water	0.216	RT	1 d	Form I
	B	EtOH/5% water	0.317	RT	1 d	Form I
	C	EtOH/7% water	0.406	RT	1 d	Form I
Form I and a few Form IX as seeds	A	EtOH/3% water	0.216	RT	2 d	Form I
	B	EtOH/5% water	0.317	RT	2 d	Form I
	C	EtOH/7% water	0.406	RT	2 d	Form I

Example 16: Solubility of Compound 1 Form I and Compound 3 Form I

[00228] Compound 1 Form I was determined to be the more stable form with more favorable solid-state properties. The solubility of Compound 1 Form I and Compound 3 Form I was measured

in water and bio-relevant media with the solid loading of 5 mg/mL (calculated as the free base) at 37 °C during the salt screen.

[00229] The solubility of Compound 3 Form I showed pH dependency, it was the highest in SGF, ~5 mg/mL, and the lowest in water, < 0.2 μg/mL. Compound 1 Form I had significant advantage over the free base in FeSSIF and water. Compound 3 Form I remained unchanged in water, Fasted State Simulated Intestinal Fluid (FaSSIF), and Fed State Simulated Intestinal Fluid (FeSSIF), while changed to a new pattern in Simulated Gastric Fluid (SGF). Compound 1 Form I also changed to this new pattern in SGF at 24 h, while partially dissociated to Compound 3 Form I in water, FaSSIF, and FeSSIF. Results are presented below in **Table 29** and **Table 30**. Limit of Quantification (LOQ) was set at 2 μg/mL.

Table 29. Solubility Data for Compound 1 Form I and Compound 3 Form I

Sample	Time	Water		SGF (pH1.2)		FaSSIF (pH6.5)		FeSSIF (pH5.0)	
		Solubility (mg/mL)	pH	Solubility (mg/mL)	pH	Solubility (mg/mL)	pH	Solubility (mg/mL)	pH
Compound 3 Form I	0.5 h	< LOQ	6.47	1.81	1.34	0.00017	6.49	0.0056	4.95
	2 h	< LOQ	6.84	2.04	1.35	0.0031	6.51	0.0066	4.95
	24 h	< LOQ	7.46	5.08	1.31	0.012	6.49	0.026	4.93
Compound 1 Form I	0.5 h	0.19	4.04	3.39	1.31	0.0024	6.36	0.27	4.96
	2 h	0.65	3.52	3.37	1.31	0.00068	5.64	0.46	4.96
	24 h	1.02	3.10	3.26	1.28	0.0040	5.43	0.43	4.91

Table 30. XRPD of Remaining Compound 3 Form I and Compound 1 Form I Solids

Sample	Time	Water	SGF (pH1.2)	FaSSIF (pH6.5)	FeSSIF (pH5.0)
Compound 3 Form I	0.5 h	/	Changed	/	/
	2 h	/	Changed	/	/
	24 h	Unchanged	Changed	Unchanged	Unchanged
Compound 1 Form I	0.5 h	Compound 1 Form I + Compound 3	Changed	Unchanged	/
	2 h	Compound 1 Form I + Compound 3	Compound 1 Form I	Compound 3 Form I	Unchanged
	24 h	Compound 1 Form I + Compound 3	Similar as Compound 3 Form I	Compound 3 Form I	Compound 1 Form I + Compound 3 Form I

Example 17: Solid Stability of Compound 1 Form I and Compound 3 Form I

[00230] Solid stability of Compound 1 Form I and Compound 3 Form I was evaluated at 60 °C (capped), 40 °C/75% RH (open) and RT/92.5% RH (open) conditions. Results are provided below in **Table 31**. Compound 1 Form I was chemically and physically stable at stress conditions, while the purity of Compound 3 Form I decreased by ~0.4% at 60 °C after 7 days.

Table 31. Solid Stability of Compound 1 Form I and Compound 3 Form I

Sample	T0		40 °C/75% RH-7 d		60 °C-7 d		92.5% RH-7 d	
	XRPD	Purity%	XRPD	Purity%	XRPD	Purity%	XRPD	Purity%
Compound 3 Form I	Unchanged	98.22	Unchanged	98.22	Unchanged	97.81	Unchanged	98.27
Compound 1 Form I	Unchanged	99.51	Unchanged	99.51	Unchanged	99.50	Unchanged	99.50

Example 18: Polymorph Screen of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride (Compound 2)

[00231] A polymorph screen of Compound 2 was performed to identify additional crystalline forms and to identify stable forms with favorable properties. A total of 20 solvents, provided in **Table 32** below were used for the solubility estimation. In the polymorph screen, a total of three crystal forms were identified for Compound 2, Form I was an anhydrate, while Form II and Form III were solvates or solvate/hydrates.

[00232] Polymorph screening was conducted using commonly used solvents by various crystallization methods, including slurry, thermal cycling, evaporation, cooling crystallization, anti-solvent precipitation and grinding. Forms II and III were obtained during screening and identified as solvate or hydrate/solvate. Based on thermal analysis and NMR results, residual solvent in Form I was hard to be removed.

Table 32. List of Solvents used in Polymorph Screen of Compound 2

No.	Solvent	No.	Solvent
1	MeOH	11	Toluene
2	EtOH	12	EA
3	IPA	13	IPAC
4	IBA	14	n-Heptane
5	2-Butanone	15	Dioxane
6	THF	16	DMSO
7	ACN	17	Dichloromethane
8	MTBE	18	2-Me-THF

9	Acetone	19	NMP
10	Water	20	DMA

Example 19: Synthesis of Crystalline Form I of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride (Compound 2)

[00233] Compound 2 Form I was identified during salt screening and was scaled up on 3 g at the beginning of the polymorph screening and could be obtained in most cases. Form I was the only identified anhydrate of Compound 2. The content of residual MeOH in Form I scaled sample was relatively high, and samples of Form I obtained during polymorph screen were analyzed by TGA and NMR to check the content of residual solvent. As shown in **Table 33** below, the residual MeOH was difficult to remove by slurry at 50 °C or other solvents were trapped into the samples. The results suggested that Form I had residual solvent.

Table 33. Content of Residual Solvent in Form I

Sample	Solvent	Method	TGA Wt. Loss%/T °C	^{1}H-NMR
A	EtOH	slurry at 50 °C	0.8%/RT-100	0.8% MeOH
B	IPA	slurry at 50 °C	0.7%/RT-100	0.7% MeOH
C	2-Butanone	slurry at 50 °C	0.9%/RT-100	0.7% MeOH
D	MTBE	slurry at 50 °C	0.7%/RT-100	0.6% MeOH, 0.1% MTBE
E	Acetone	slurry at 50 °C	0.7%/RT-100	0.4% MeOH, 0.2% Acetone
F	EA	slurry at 50 °C	0.8%/RT-100	0.6% MeOH, 0.1% EA
G	n-Heptane	slurry at 50 °C	0.9%/RT-100	0.5% MeOH, 0.2% heptane
H	2-Me-THF	slurry at 50 °C	0.6%/RT-100	0.6% MeOH
I	THF/H_2O (9/1)	slurry at 50 °C	0.5%/RT-100	0.3% MeOH
J	DMSO/EA (1/4)	slurry at 50 °C	0.5%/RT-100	0.4% MeOH, 0.1% EA, 0.1% DMSO
K	THF/H_2O (9/1)	thermal cycling	1.2%/RT-200	1.3% MeOH
L	DMSO/MEK (1/10)	Anti-solvent precipitation	2.0%/RT-200	1% DMSO, 1.0% MEK
M	NMP/EA (1/5)	Anti-solvent precipitation	2.7%/RT-200	2.1% NMP, 1.5% EA
N	DMA/MTBE (1/5)	Anti-solvent precipitation	2.7%/RT-200	2.1% DMA, 0.4% MTBE

Sample	Solvent	Method	TGA Wt. Loss%/T °C	^{1}H-NMR
O	DMA/EA (1/5)	Anti-solvent precipitation	1.6%/RT-200	0.6% DMA, 0.8% EA

[00234] Overall, Compound 2 Form I was the only anhydrous form with high melting point and high crystallinity, it was physically stable when a_w was not higher than 0.88. However, Compound 2 Form I had residual solvent issue.

Example 20: Synthesis of Crystalline Form II of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride (Compound 2)

[00235] Compound 2 Form II was obtained by precipitation in DMSO solvent systems. A sample of Compound 2 Form II was obtained from DMSO/EA and further characterized. The sample was irregular shaped crystalline with small particle size under PLM. Crystallinity of the sample was moderate. ^{1}H-NMR of the sample showed 20.0% residual DMSO. The sample was likely a solvate and contained 2 mol of DMSO. Chemical shift in NMR profile was the same as that of Form I, indicating Form II was still a mono-HCl salt.

Example 21: Synthesis of Crystalline Form III of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride (Compound 2)

[00236] Compound 2 Form III was obtained by precipitation in NMP solvent systems. A sample of Compound 2 Form II was obtained from NMP/2-Me-THF was further characterized. The sample was crystalline solid with aggregation under PLM. Crystallinity was moderate. NMR of this batch sample showed 17.3% residual NMP. The sample was likely a hydrate/solvate with 1.5 mol of water and 1.35 mol of NMP.

Example 22: Characterization and Comparison of the Crystalline Forms of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride (Compound 2)

[00237] A summary of the characterization data for the solid forms of Compound 2 identified is shown below in **Table 34**. DSC and TGA data for Compound 2 Form I can be found in Figure 22. DVS isotherm data for Compound 2 Form I can be found in Figure 34. DSC and TGA data for Compound 2 Form II can be found in Figure 24. DSC and TGA data for Compound 2 Form III can be found in Figure 26.

Table 34. Summary of characterization data.

Form Solvation	DSC, endo Onset/Peak Temperature (°C), ΔH (J/g)	TGA Wt. loss% at Temperature	DVS Wt. gain%	Comment
Compound 2 Form I Anhydrate	306/315, m/d	1.1/RT-100	0.30%, 80% RH 0.35%, 90% RH Reversible Form unchanged	Residual solvents, MeOH, etc.
Compound 2 Form II Solvate	26/40, 69 201/205, endo/exo 293/303, m/d	20.1/RT-195	/	2 mol DMSO
Compound 2 Form III Solvate/hydrate	26/79, 145 186/186, 23 299/309, m/d	3.7/RT-60 17.6/65-220	/	1.35 mol NMP 1.5 mol water

Example 23: Solubility of Compound 2 Form I

[00238] The solubilities of a sample of Compound 2 Form I was measured in water and bio-relevant media with the target concentration of 5 mg/mL (calculated as the free base) at 37 °C during salt screening. The results are summarized in **Table 35** and **Table 36** below. Solubility of the sample showed pH dependency, the highest solubility was obtained in SGF, ~5 mg/mL at 0.5 h, and lowest in FaSSIF, 0.00037 mg/mL at 0.5 h. Compound 2 Form I changed to a new pattern in SGF at 24 hours which was the same as that of free base. In water and FaSSIF, dissociation occurred and had tendency to convert to Compound 3 Form I. In FeSSIF, Compound 2 Form I remained unchanged after solubility test.

[00239] Solubility of Compound 2 Form I showed pH dependency. The highest solubility was obtained in SGF (pH 1.2), >5 mg/mL at 0.5 h, while lowest in FaSSIF, 0.0004 mg/mL. Dissociation and form changes were observed during solubility test.

Table 35. Solubility Data for Compound 2 Form I

Sample	Time	Water		SGF (pH1.2)		FaSSIF (pH6.5)		FeSSIF (pH5.0)	
		Solubility (mg/mL)	pH	Solubility (mg/mL)	pH	Solubility (mg/mL)	pH	Solubility (mg/mL)	pH
Compound 2 Form I	0.5h	0.059	5.86	>5, clear	1.29	0.00037	6.50	0.011	4.96
	2h	0.26	4.28	2.38	1.29	0.00093	6.48	0.011	4.96
	24h	0.57	3.29	3.16	1.26	0.0015	5.80	0.031	4.93

Table 36. XRPD of Remaining Solids in Media

Sample	Time	Water	SGF (pH1.2)	FaSSIF (pH6.5)	FeSSIF (pH5.0)
Compound 2 Form I	0.5h	Unchanged	/	/	/
	2h	Compound 2 Form I + Compound 3 Form I	/	Unchanged	/
	24h	Compound 2 Form I + Compound 3 Form I	Changed, similar as Compound 3 Form I in SGF	Compound 3 Form I	Unchanged

Example 24: Solid Stability of Compound 2 Form I

[00240] Solid state stability of a sample of Compound 2 Form I was evaluated at 60 °C (in capped vial), 40 °C/75%RH (open) and RT/92.5%RH (open) conditions during salt screening. The results are summarized in **Table 37** below. Compound 2 Form I was chemically and physically stable at stress conditions for 7 days.

Table 37. Solid Stability of Compound 2 Form I

Sample	T0		40°C/75%RH 7 days		60°C 7 days		92.5%RH 7 days	
	XRPD	Purity (%)	XRPD	Purity (%)	XRPD	Purity (%)	XRPD	Purity (%)
Compound 2 Form I	unchanged	99.22	unchanged	99.16	unchanged	99.17	unchanged	99.16

Example 25: Polymorph Screen of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 3)

[00241] A polymorph screen of Compound 3 was performed to identify crystalline forms for further development. The solvents used for the polymorph screen of Compound 3 are provided in **Table 38** below. In Table 38 below: methanol (MeOH), ethanol (EtOH), 2-propanol (IPA),), Isobutanol (IBA), butanone (MEK), tetrahydrofuran (THF), acetonitrile (ACN), tert-Butyl methyl ether (MTBE), ethyl acetate (EA), isopropyl acetate (IPAC), dimethyl sulfoxide (DMSO), dichloromethane (DCM), and 2-methyltetrahydrofuran (2-Me-THF).

[00242] Compound 3 Form I was used as the starting material for the polymorph screen by various methods including slurry, cooling crystallization, anti-solvent precipitation, thermal cycling and evaporation method. Considering Compound 3 Form I showed low solubility in most tested solvents, an

amorphous material of Compound 3 was prepared and used to conduct polymorph screen by slurry and anti-solvent precipitation. Compound 3 Form I was obtained in most cases, and no new form was found. According to the NMR and TGA results, Compound 3 Form I obtained by various methods during screening had high content residual solvent.

Table 38. List of Solvents used in Polymorph Screen of Compound 3

#	Solvent	#	Solvent
1	MeOH	10	Water
2	EtOH	11	Toluene
3	IPA	12	EA
4	IBA	13	IPAC
5	MEK	14	n-Heptane
6	THF	15	Dioxane
7	ACN	16	DMSO
8	MTBE	17	DCM
9	Acetone	18	2-Me-THF

Example 26: Crystalline Form I of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate (Compound 3) and Characterization Data

[00243] Compound 3 Form I was characterized by small irregular shaped crystals as observed under PLM. TGA showed 0.7% gradual weight loss from RT to 200 °C and DSC exhibited a sharp endothermic peak at 270 °C which was attributed to melting/decomposition, as shown in Figure 28. NMR showed the presence of about 1.2% residual DMF.

[00244] Based on these results, Compound 3 Form I was determined to be an anhydrate. DVS result indicated that Form I was non-hygroscopic with 0.13% and 0.17% water uptake at 80%RH and 90%RH, respectively, as shown in Figure 35, and the XRPD pattern of the solid remained unchanged after DVS testing. Solid state stability results showed that Compound 3 Form I was physically and chemically stable at all stress conditions except at 60 °C for 7 days where the purity decreased by 0.4%

[00245] Solubility of free base Form I showed pH dependency, it was the highest in SGF, ~5 mg/mL, and reduced to <0.03 mg/mL when pH raised to ~5. A summary of characterization data can be found in **Table 39** below.

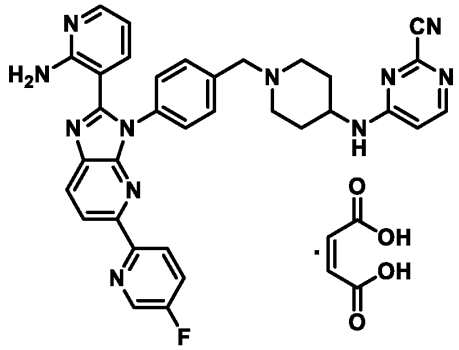
Table 39. Summary of Characterization Data for Compound 3 Form I

Compound		Compound 3 Form I
Sample		A
Purity		98.22%
Solvation		None - Anhydrate
PLM		Irregular
XRPD		High crystallinity
DSC **Onset/Peak, ΔH**		270/271°C, 132 J/g melt/decomposition
TGA **Wt. loss @T**		0.7% between RT and 200°C
DVS **Wt. gain**		0.13% at 80%RH 0.17% at 90%RH Reversible and form remained unchanged
^{1}H-NMR		1.2% DMF
Solubility (mg/mL) 0.5/2/24h	**Water**	<0.0002 during testing
	FaSSIF	0.0002 / 0.003 / 0.012
	FeSSIF	0.006 / 0.007 / 0.026
	SGF	1.81 / 2.04 / 5.08
Solid form in solubility testing		Changed to a new pattern in SGF, while unchanged in other media
Solid stability for 7 d	**40 °C/75%RH**	98.22%, form unchanged
	60 °C	97.81%, form unchanged
	RT/92.5%RH	98.27%, form unchanged
Comment		Residual solvent issue, chemically unstable at 60°C, and low solubility in water

[00246] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

1. A solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate, depicted below as Compound 1,



Compound 1

wherein the solid form is crystalline.

2. The solid form of claim 1, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 21.1° ± 0.3.

3. The solid form of claim 2, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.0° ± 0.3 and 24.0° ± 0.3.

4. The solid form of claim 2 or 3, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 4.9° ± 0.3, 19.2° ± 0.3, and 27.4° ± 0.3.

5. The solid form of any one of claims 2 to 4, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 17.6° ± 0.3, 20.5° ± 0.3, and 31.4° ± 0.3.

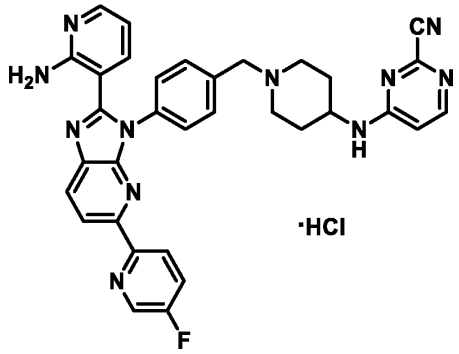
6. The solid form of any one of claims 2 to 5, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, and 26.7° ± 0.3.

7. The solid form of claim 1, wherein the solid form exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3.

8. The solid form of claim 1, wherein the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3.

9. The solid form of claim 1, wherein the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3.
10. The solid form of claim 1, wherein the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3.
11. The solid form of claim 1, wherein the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3.
12. The solid form of claim 1, wherein the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3.
13. The solid form of claim 1, wherein the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 1.
14. The solid form of any one of claims 1 to 13, wherein the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 234.6 °C ± 5.0.
15. The solid form of any one of claims 1 to 13, wherein the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 255.5 °C ± 5.0.
16. The solid form of any one of claims 1 to 13, wherein the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 2.
17. The solid form of any one of claims 1 to 13, wherein the solid form does not exhibit a weight loss until a transition at 216.5 °C ± 10.0 as determined by thermogravimetric analysis.
18. The solid form of any one of claims 1 to 13, wherein the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 2.
19. The solid form of any one of claims 1 to 13, wherein the amount of other crystalline or amorphous forms is 10% (w/w) or less.
20. The solid form of any one of claims 1 to 13, wherein the amount of other crystalline or amorphous forms is 5% (w/w) or less.

21. The solid form of any one of claims 1 to 13, wherein the amount of other crystalline or amorphous forms is 1% (w/w) or less.
22. The solid form of any one of claims 1 to 13, wherein the solid form has a chemical purity of 97% or more.
23. The solid form of any one of claims 1 to 13, wherein the solid form has a chemical purity of 98% or more.
24. The solid form of any one of claims 1 to 13, wherein the solid form has a chemical purity of 99% or more.
25. The solid form of any one of claims 1 to 13, wherein the solid form has a chemical purity of 99.5% or more.
26. A solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride, depicted below as Compound 2,



Compound 2

wherein the solid form is crystalline.

27. The solid form of claim 26, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 22.4° ± 0.3.
28. The solid form of claim 27, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 12.3° ± 0.3 and 20.6° ± 0.3.
29. The solid form of claim 27 or 28, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 16.4° ± 0.3, 17.5° ± 0.3, and 18.9° ± 0.3.
30. The solid form of any one of claims 27 to 29, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 5.3° ± 0.3, 25.6° ± 0.3, and 29.4° ± 0.3.
31. The solid form of any one of claims 27 to 30, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.6° ± 0.3, 22.0° ± 0.3, 23.0° ± 0.3, and 25.3° ± 0.3.

32. The solid form of any one of claims 27 to 31, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 10.7° ± 0.3, 14.3° ± 0.3, 18.0° ± 0.3, 21.3° ± 0.3, and 32.3° ± 0.3.

33. The solid form of claim 26, wherein the solid form exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 4.9° ± 0.3, 11.5° ± 0.3, 13.6° ± 0.3, 14.9° ± 0.3, 17.0° ± 0.3, 17.6° ± 0.3, 19.2° ± 0.3, 20.5° ± 0.3, 21.1° ± 0.3, 24.0° ± 0.3, 26.7° ± 0.3, 27.4° ± 0.3, and 31.4° ± 0.3.

34. The solid form of claim 26, wherein the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3.

35. The solid form of claim 26, wherein the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3.

36. The solid form of claim 26, wherein the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3.

37. The solid form of claim 26, wherein the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3.

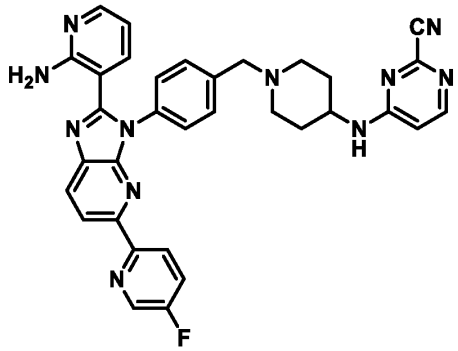
38. The solid form of claim 26, wherein the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 5.3° ± 0.3, 10.7° ± 0.3, 12.3° ± 0.3, 14.3° ± 0.3, 16.4° ± 0.3, 17.5° ± 0.3, 18.0° ± 0.3, 19.6° ± 0.3, 20.6° ± 0.3, 21.3° ± 0.3, 22.0° ± 0.3, 22.4° ± 0.3, 23.0° ± 0.3, 25.3° ± 0.3, 25.6° ± 0.3, 29.4° ± 0.3, and 32.3° ± 0.3.

39. The solid form of claim 26, wherein the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 21.

40. The solid form of any one of claims 26 to 39, wherein the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 315.4 °C ± 5.0.

41. The solid form of any one of claims 26 to 39, wherein the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 22.

42. The solid form of any one of claims 26 to 39, wherein the solid form exhibits a weight loss of 1.1% ± 0.5 weight loss up to 100.0 °C ± 10.0 as determined by thermogravimetric analysis.
43. The solid form of any one of claims 26 to 39, wherein the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 22.
44. The solid form of any one of claims 26 to 39, wherein the amount of other crystalline or amorphous forms is 10% (w/w) or less.
45. The solid form of any one of claims 26 to 39, wherein the amount of other crystalline or amorphous forms is 5% (w/w) or less.
46. The solid form of any one of claims 26 to 39, wherein the amount of other crystalline or amorphous forms is 1% (w/w) or less.
47. The solid form of any one of claims 26 to 39, wherein the solid form has a chemical purity of 97% or more.
48. The solid form of any one of claims 26 to 39, wherein the solid form has a chemical purity of 98% or more.
49. The solid form of any one of claims 26 to 39, wherein the solid form has a chemical purity of 99% or more.
50. The solid form of any one of claims 26 to 39, wherein the solid form has a chemical purity of 99.5% or more.
51. A solid form of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile, depicted below as Compound 3,



Compound 3

wherein the solid form is crystalline.
52. The solid form of claim 51, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 27.8 ° ± 0.3.

53. The solid form of claim 52, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 19.7° ± 0.3 and 24.1° ± 0.3.

54. The solid form of claim 52 or 53, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 7.4° ± 0.3, 14.9° ± 0.3, and 18.7° ± 0.3.

55. The solid form of any one of claims 52 to 54, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 15.1° ± 0.3, 18.0° ± 0.3, and 22.0° ± 0.3.

56. The solid form of any one of claims 52 to 55, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 8.8 ° ± 0.3, 19.4° ± 0.3, and 22.6° ± 0.3.

57. The solid form of any one of claims 52 to 56, wherein the solid form exhibits an X-ray powder diffraction reflection at a 2-theta value of 11.9° ± 0.3, 17.9° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

58. The solid form of claim 51, wherein the solid form exhibits at least one X-ray powder diffraction reflection selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

59. The solid form of claim 51, wherein the solid form exhibits at least two X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

60. The solid form of claim 51, wherein the solid form exhibits at least three X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

61. The solid form of claim 51, wherein the solid form exhibits at least four X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

62. The solid form of claim 51, wherein the solid form exhibits at least five X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ± 0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

63. The solid form of claim 51, wherein the solid form exhibits at least six X-ray powder diffraction reflections selected from the group consisting of 7.4° ± 0.3, 8.8° ± 0.3, 11.9° ±

0.3, 14.9° ± 0.3, 15.1° ± 0.3, 17.8° ± 0.3, 18.0° ± 0.3, 18.7° ± 0.3, 19.4° ± 0.3, 19.7° ± 0.3, 22.0° ± 0.3, 22.6° ± 0.3, 24.1° ± 0.3, 27.8° ± 0.3, 28.6° ± 0.3, and 29.9° ± 0.3.

64. The solid form of claim 51, wherein the solid form exhibits the X-ray powder diffraction pattern as shown in Figure 27.

65. The solid form of any one of claims 51 to 64, wherein the solid form exhibits a differential scanning calorimetry thermogram comprising an endothermic peak at 270.7 °C ± 5.0.

66. The solid form of any one of claims 51 to 64, wherein the solid form exhibits the differential scanning calorimetry thermogram as shown in Figure 28.

67. The solid form of any one of claims 51 to 64, wherein the solid form exhibits a weight loss of 0.7% ± 0.5 weight loss up to 200.0 °C ± 10.0 as determined by thermogravimetric analysis.

68. The solid form of any one of claims 51 to 64, wherein the solid form exhibits the thermogravimetric analysis thermogram as shown in Figure 28.

69. The solid form of any one of claims 51 to 64, wherein the amount of other crystalline or amorphous forms is 10% (w/w) or less.

70. The solid form of any one of claims 51 to 64, wherein the amount of other crystalline or amorphous forms is 5% (w/w) or less.

71. The solid form of any one of claims 51 to 64, wherein the amount of other crystalline or amorphous forms is 1% (w/w) or less.

72. The solid form of any one of claims 51 to 64, wherein the solid form has a chemical purity of 97% or more.

73. The solid form of any one of claims 51 to 64, wherein the solid form has a chemical purity of 98% or more.

74. The solid form of any one of claims 51 to 64, wherein the solid form has a chemical purity of 99% or more.

75. The solid form of any one of claims 51 to 64, wherein the solid form has a chemical purity of 99.5% or more.

76. A pharmaceutically acceptable salt of 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile wherein the salt is selected from the group consisting of hydrochloride, maleate, citrate, sulfate, malate, mesylate, tosylate, besylate, fumarate, tartrate, phosphate, and succinate.

77. A compound 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile hydrochloride.

78. A compound 4-((1-(4-(2-(2-aminopyridin-3-yl)-5-(5-fluoropyridin-2-yl)-3H-imidazo[4,5-b]pyridin-3-yl)benzyl)piperidin-4-yl)amino)pyrimidine-2-carbonitrile maleate.
79. A pharmaceutical composition comprising the solid form of any one of claims 1-78 and a pharmaceutically acceptable excipient.
80. A method of preparing a pharmaceutical composition comprising mixing a solid form of any one of claims 1-78, and a pharmaceutically acceptable carrier.
81. A solid form of any one of claims 1-78 for use in a method of treatment of the human or animal body.
82. A solid form of any one of claims 1-78 for use in a method of treatment of cancer or neoplastic disease.
83. Use of a solid form of any one of claims 1-78, in the manufacture of a medicament for the treatment of cancer or neoplastic disease.
84. A method of treating a disease or disorder in a patient in need thereof, comprising administering to the patient a solid form as described in any one of claims 1-78.
85. The method of claim 84, wherein the disease or disorder is cancer.
86. The method of claim 84, wherein the disease or disorder is neoplastic disease.
87. A method of treating a disease or disorder in a patient in need thereof, comprising administering to the patient a solid form as described in any one of claims 1-78 and a pharmaceutically acceptable excipient.
88. The method of claim 87, wherein the disease or disorder is cancer.
89. The method of claim 87, wherein the disease or disorder is neoplastic disease.