[0030] In some examples, crystalline Form F is solvated. In some examples, crystalline Form F is solvated with methanol.

[0030a] In one aspect, there is provided a crystalline form of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that is:
(a) a crystalline Form A that has an X-ray powder diffraction (XRPD) pattern comprising 2-Theta peaks at 16.1±0.1°, 18.9±0.1°, and 21.6±0.1°;
(b) a crystalline Form B that has an X-ray powder diffraction (XRPD) pattern comprising 2-Theta peaks at 5.2±0.1°, 10.2±0.1°, and 20.8±0.1°; or
(c) a crystalline Form C that has an X-ray powder diffraction (XRPD) pattern comprising 2-Theta peaks at 7.0±0.1°, 14.0±0.1°, and 18.2±0.1°.

[0030b] In another aspect, there is provided a crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has an XRPD pattern comprising 2-Theta peaks at 16.1±0.1°, 18.9±0.1°, and 21.6±0.1°.

[0030c] In another aspect, there is provided a crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 5.7±0.1°, 13.6±0.1°, 16.1±0.1°, 18.9±0.1°, 21.3±0.1°, and 21.6±0.1°.

[0030d] In another aspect, there is provided a crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one having an XRPD pattern comprising 2-Theta peaks at 5.7±0.1°, 18.9±0.1°, and 21.3±0.1°.

[0030e] In another aspect, there is provided a crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 5.2±0.1°, 10.2±0.1°, and 20.8±0.1°.

[0030f] In another aspect, there is provided a crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 5.2±0.1°, 10.2±0.1°, 16.5±0.1°, 18.5±0.1°, and 20.8±0.1°.

[0030g] In another aspect, there is provided a crystalline Form C of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 7.0±0.1°, 14.0±0.1°, and 18.2±0.1°.

[0030h] In another aspect, there is provided a crystalline Form C of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 7.0±0.1°, 14.0±0.1°, 15.7±0.1°, 18.2±0.1°, 19.1±0.1°, 19.5±0.1°, 20.3±0.1°, 22.1±0.1°, and 22.9±0.1°.

[0030i] In another aspect, there is provided a crystalline form of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that is:
(a) a crystalline Form A that has an infrared (IR) spectrum with peaks at 1584 cm^{-1}, 1240 cm^{-1}, 1147 cm^{-1}, 1134 cm^{-1}, 1099 cm^{-1}, and 1067 cm^{-1}; or
(b) a crystalline Form B that has an IR spectrum with peaks at 1586 cm^{-1}, 1573 cm^{-1}, 1562 cm^{-1}, 1229 cm^{-1}, 1141 cm^{-1}, 1103 cm^{-1}, 1056 cm^{-1}, and 1033 cm^{-1}.

[0030j] In another aspect, there is provided a crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has an IR spectrum with peaks at 1584 cm^{-1}, 1240 cm^{-1}, 1147 cm^{-1}, 1134 cm^{-1}, 1099 cm^{-1}, and 1067 cm^{-1}.

[0030k] In another aspect, there is provided a crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has an IR spectrum with peaks at 1586 cm^{-1}, 1573 cm^{-1}, 1562 cm^{-1}, 1229 cm^{-1}, 1141 cm^{-1}, 1103 cm^{-1}, 1056 cm^{-1}, and 1033 cm^{-1}.

[0030l] In another aspect, there is provided an unsolvated crystalline form of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that is:
(a) a crystalline Form A that has a differential scanning calorimetry (DSC) thermogram having an endotherm with a peak at 157 °C;
(b) a crystalline Form B that has a DSC thermogram having an endotherm with a peak at 115 °C to 118 °C; or
(c) a crystalline Form C that has a DSC thermogram having an endotherm with a peak at 137 °C to 139 °C.

[0030m] In another aspect, there is provided an unsolvated crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has a DSC thermogram having an endotherm with a peak at 157 °C.

[0030n] In another aspect, there is provided an unsolvated crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has a DSC thermogram having an endotherm with a peak at 115 °C to 118 °C.

[0030o] In another aspect, there is provided an unsolvated crystalline Form C of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has a DSC thermogram having an endotherm with a peak at 137 °C to 139 °C.

[0031] Described herein is a pharmaceutically acceptable salt of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one, wherein the pharmaceutically acceptable salt is an acid addition salt. In some examples, the pharmaceutically acceptable salt is amorphous. In some examples, the pharmaceutically acceptable salt is crystalline.

[0032] There are provided pharmaceutical compositions, which include 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one as described herein, and at least one additional ingredient selected from pharmaceutically acceptable carriers, diluents and excipients. In some examples, the pharmaceutical composition comprises Form A. In some examples, the pharmaceutical composition comprises Form B. In some examples, the pharmaceutical composition comprises Form C. In some examples, the pharmaceutical composition comprises Form D. In some examples, the pharmaceutical composition comprises Form E. In some examples, the pharmaceutical composition comprises Form F. In some examples, the pharmaceutical composition is in a form suitable for oral administration to a mammal. In some examples, the pharmaceutical composition is an oral solid dosage form. In some examples, the pharmaceutical composition comprises about 0.5mg to about 1000mg of crystalline 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one.

[0033] In another example, provided herein is a pharmaceutical formulation for oral administration comprising:

[0034] (a) about 40 mgs to about 200 mgs of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one;

[0035] (b) about 40 wt% to about 50 wt% of a diluent;

[0036] (c) about 3 wt% to about 10 wt% of a disintegrating agent;

[0037] (d) about 2 wt% to about 7 wt% of a surfactant; and

[0038] (e) about 0.2 wt% to about 1.0 wt% of a lubricant.

[0039] In some examples, the diluent is selected from the group consisting of lactose, sucrose, dextrose, dextrates, maltodextrin, mannitol, xylitol, sorbitol, cyclodextrins, calcium phosphate, calcium sulfate, starches, modified starches, microcrystalline cellulose, microcellulose, and talc. In some examples the diluent is microcrystalline cellulose. In some examples, the disintegrating agent is selected from the group consisting of natural starch, a pregelatinized starch, a sodium starch, methylcrystalline cellulose, methylcellulose, croscarmellose, croscarmellose sodium, cross-linked sodium carboxymethylcellulose, cross-

linked carboxymethylcellulose, cross-linked croscarmellose, cross-linked starch such as sodium starch glycolate, cross-linked polymer such as crospovidone, cross-linked polyvinylpyrrolidone, sodium alginate, a clay, or a gum. In some examples, the disintegrating agent is croscarmellose sodium. In some examples, the surfactant is selected from the group consisting of sodium lauryl sulfate, sorbitan monooleate, polyoxyethylene sorbitan monooleate, polysorbates, polaxomers, bile salts, glyceryl monostearate, copolymers of ethylene oxide and propylene oxide. In some examples, the surfactant is sodium lauryl sulfate. In some examples, the lubricant is selected from the group consisting of stearic acid, calcium hydroxide, talc, corn starch, sodium stearyl fumerate, stearic acid, sodium stearates, magnesium stearate, zinc stearate, and waxes. In some examples, the lubricant is magnesium stearate.

[00123] (b) 151.4 mgs of microcrystalline cellulose;

[00124] (c) 23.0 mgs of croscarmellose sodium;

[00125] (d) 14.0 mgs of sodium lauryl sulfate; and

(e) 1.6 mgs of magnesium stearate.

[00126] In another example, provided herein is a pharmaceutical formulation comprising: a) about 40 mgs to about 200 mgs of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one; b) about 40 wt% to about 50 wt% of a diluent; c) about 3 wt% to about 10 wt% of a disintegrating agent; d) about 2 wt% to about 7 wt% of a surfactant; and e) about 0.2 wt% to about 1.0 wt% of a lubricant; wherein the formulation is in a unit dosage form in a blister pack, and said blister pack comprises metal or plastic foil. In some examples, is a pharmaceutical formulation comprising: a) 140 mgs of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one; b) 45.9 wt% of microcrystalline cellulose; c) 7.0 wt% of croscarmellose sodium; d) 4.2 wt% of sodium lauryl sulfate; and e) 0.5 wt% of magnesium stearate wherein the formulation is in a unit dosage form in a blister pack, and said blister pack comprises metal or plastic foil.

[00127] There is provided a package comprising one or more discrete blister pockets, wherein each blister pocket comprises a unit dosage form comprising:

a) about 40 mgs to about 200 mgs of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one;

b) about 40 wt% to about 50 wt% of a diluent; c) about 3 wt% to about 10 wt% of a disintegrating agent; d) about 2 wt% to about 7 wt% of a surfactant; and

e) about 0.2 wt% to about 1.0 wt% of a lubricant;

wherein each blister pocket comprises metal or plastic foil.

[00128] In another example, provided herein is a pharmaceutical formulation comprising: a) about 40 mgs to about 200 mgs of crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one; b) about 40 wt% to about 50 wt% of a diluent; c) about 3 wt% to about 10 wt% of a disintegrating agent; d) about 2 wt% to about 7 wt% of a surfactant; and e) about 0.2 wt% to about 1.0 wt% of a

CLAIMS

WHAT IS CLAIMED IS:

1. A crystalline form of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that is:

(a) a crystalline Form A that has an X-ray powder diffraction (XRPD) pattern comprising 2-Theta peaks at 16.1±0.1°, 18.9±0.1°, and 21.6±0.1°;

(b) a crystalline Form B that has an X-ray powder diffraction (XRPD) pattern comprising 2-Theta peaks at 5.2±0.1°, 10.2±0.1°, and 20.8±0.1°; or

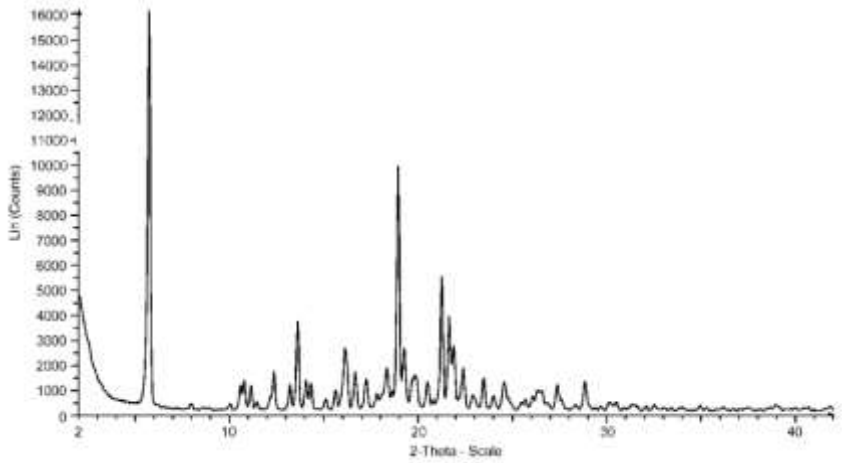
(c) a crystalline Form C that has an X-ray powder diffraction (XRPD) pattern comprising 2-Theta peaks at 7.0±0.1°, 14.0±0.1°, and 18.2±0.1°.

2. A crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has an XRPD pattern comprising 2-Theta peaks at 16.1±0.1°, 18.9±0.1°, and 21.6±0.1°.

3. A crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 5.7±0.1°, 13.6±0.1°, 16.1±0.1°, 18.9±0.1°, 21.3±0.1°, and 21.6±0.1°.

4. A crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one having an XRPD pattern comprising 2-Theta peaks at 5.7±0.1°, 18.9±0.1°, and 21.3±0.1°.

5. The crystalline Form A of any one of claims 2-4, wherein the crystalline form has an XRPD pattern as shown below.



6. The crystalline Form A of any one of claims 2-4, wherein one or more of the following applies:

(a) the crystalline form has the same XRPD pattern post storage at 40°C and 75% relative humidity (RH) for at least a week;

(b) the crystalline form has the same XRPD pattern post storage at 25°C and 97% relative humidity (RH) for at least a week; or

(c) the crystalline form is non-hygroscopic.

7. A crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 5.2±0.1°, 10.2±0.1°, and 20.8±0.1°.

8. A crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 5.2±0.1°, 10.2±0.1°, 16.5±0.1°, 18.5±0.1°, and 20.8±0.1°.

9. The crystalline Form B of claim 7 or 8, wherein one or more of the following applies:

(a) the crystalline form has the same XRPD pattern post storage at 40°C and 75% relative humidity (RH) for at least a week; or

(b) the crystalline form has the same XRPD pattern post storage at 25°C and 97% relative humidity (RH) for at least a week.

10. A crystalline Form C of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 7.0±0.1°, 14.0±0.1°, and 18.2±0.1°.

11. A crystalline Form C of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-l-one having an XRPD pattern comprising 2-Theta peaks at 7.0±0.1°, 14.0±0.1°, 15.7±0.1°, 18.2±0.1°, 19.1±0.1°, 19.5±0.1°, 20.3±0.1°, 22.1±0.1°, and 22.9±0.1°.

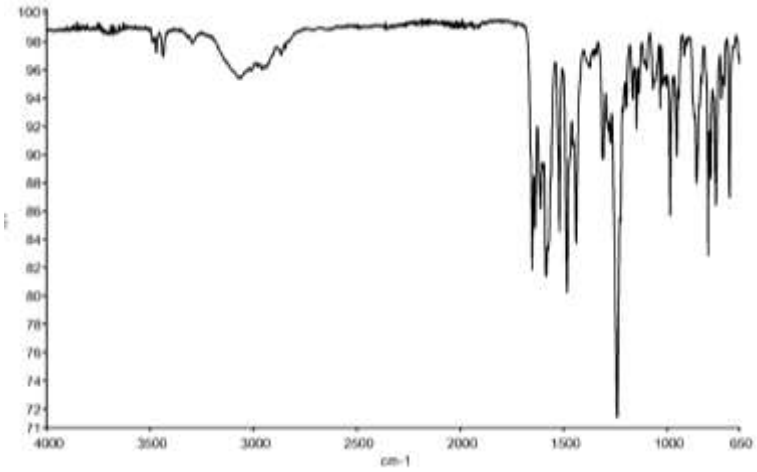
12. A crystalline form of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that is:

(a) a crystalline Form A that has an infrared (IR) spectrum with peaks at 1584 cm^{-1}, 1240 cm^{-1}, 1147 cm^{-1}, 1134 cm^{-1}, 1099 cm^{-1}, and 1067 cm^{-1}; or

(b) a crystalline Form B that has an IR spectrum with peaks at 1586 cm^{-1}, 1573 cm^{-1}, 1562 cm^{-1}, 1229 cm^{-1}, 1141 cm^{-1}, 1103 cm^{-1}, 1056 cm^{-1}, and 1033 cm^{-1}.

13. A crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has an IR spectrum with peaks at 1584 cm^{-1}, 1240 cm^{-1}, 1147 cm^{-1}, 1134 cm^{-1}, 1099 cm^{-1}, and 1067 cm^{-1}.

14. The crystalline Form A of claim 13, wherein the IR spectrum is as the one set forth below.



15. A crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has an IR spectrum with peaks at 1586 cm^{-1}, 1573 cm^{-1}, 1562 cm^{-1}, 1229 cm^{-1}, 1141 cm^{-1}, 1103 cm^{-1}, 1056 cm^{-1}, and 1033 cm^{-1}.

16. An unsolvated crystalline form of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that is:

(a) a crystalline Form A that has a differential scanning calorimetry (DSC) thermogram having an endotherm with a peak at 157 °C;

(b) a crystalline Form B that has a DSC thermogram having an endotherm with a peak at 115 °C to 118 °C; or

(c) a crystalline Form C that has a DSC thermogram having an endotherm with a peak at 137 °C to 139 °C.

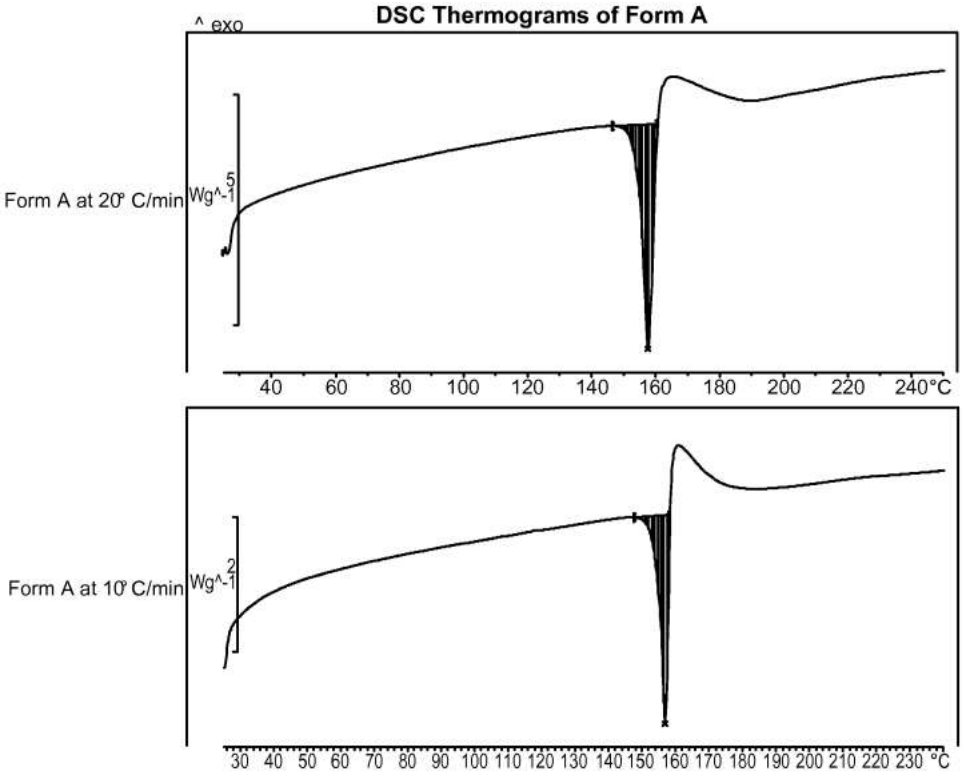
17. An unsolvated crystalline Form A of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has a DSC thermogram having an endotherm with a peak at 157 °C.

18. The crystalline Form A of claim 17, wherein the DSC thermogram has an endotherm having an onset at 154 °C.

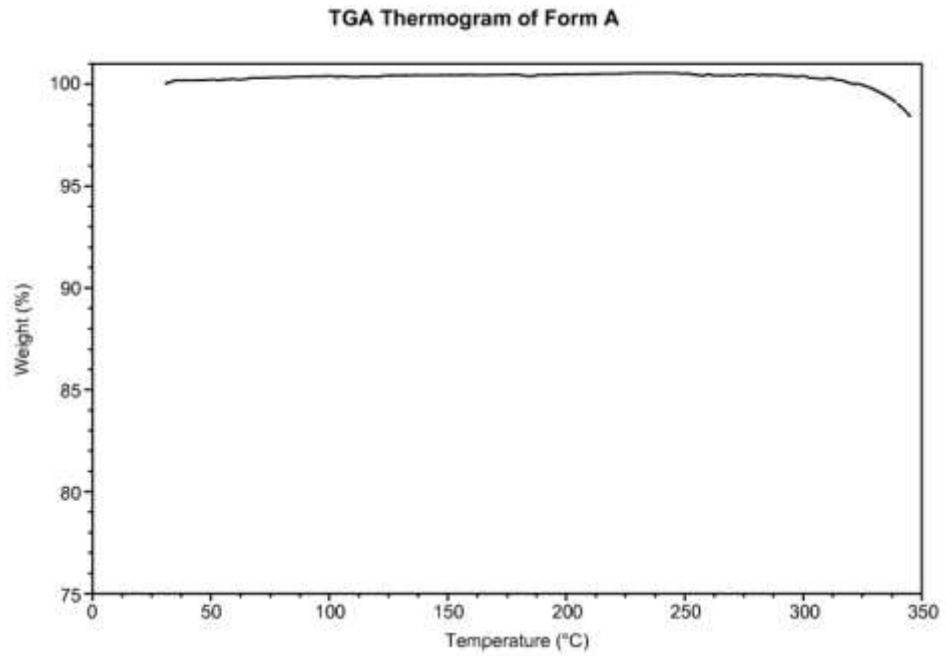
19. The crystalline Form A of claim 17, wherein the DSC thermogram has an exotherm at 159 °C.

20. The crystalline Form A of claim 17, wherein the DSC thermogram was generated by heating the crystalline form at a rate of 10°C/min.

21. The crystalline Form A of claim 17, wherein the crystalline form has a DSC thermogram as the one set forth below.



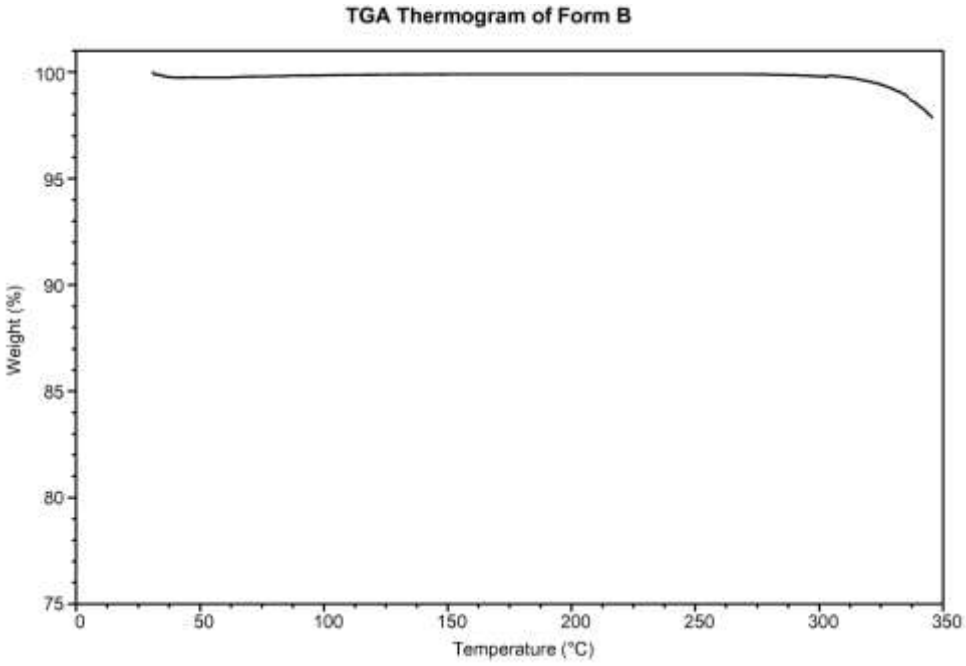
22. The crystalline Form A of claim 17, wherein the crystalline form has a thermogravimetric analysis (TGA) thermogram as the one set forth below.



23. An unsolvated crystalline Form B of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has a DSC thermogram having an endotherm with a peak at 115 °C to 118 °C.

24. The crystalline Form B of claim 23, wherein the DSC thermogram has an endotherm having an onset at 99 °C to 106 °C.

25. The crystalline Form B of claim 24, wherein the crystalline form has a thermogravimetric analysis (TGA) thermogram as the one set forth below.



26. An unsolvated crystalline Form C of 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one that has a DSC thermogram having an endotherm with a peak at 137 °C to 139 °C.

27. The crystalline Form C of claim 26, wherein the DSC thermogram has an endotherm having an onset at 134 °C to 135 °C.

28. The crystalline Form C of claim 26, wherein the crystalline form has a thermogravimetric analysis (TGA) thermogram as the one set forth below.

