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

[0031] In one example, 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] In a further example 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.

[0032a] In one aspect, provided herein is a pharmaceutical formulation for oral administration comprising:

(a) ~~about~~ 40 mg to 200 mg ~~140 mg~~ 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) 40 wt % to 50 wt % of one or more diluents;

(c) 2 wt % to 7 wt % of one or more surfactants; and

(d) 0.2 to 1.0 wt % of one or more lubricants.

[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.

[0039a] In another aspect, provided herein is a pharmaceutical formulation for oral administration comprising:

(a) 40 mg to 200 mg 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) 40 wt% to 50 wt% of microcrystalline cellulose;

(c) 3 wt% to 10 wt% croscarmellose sodium;

(d) 2 wt% to 7 wt% of sodium lauryl sulfate; and

(e) 0.2 wt% to 1.0 wt% of magnesium stearate.

[0040] In some examples, provided herein is a pharmaceutical formulation for oral administration comprising:

[0041] (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;

[0042] (b) about 40 wt% to about 50 wt% of microcrystalline cellulose;

[0043] (c) about 3 wt% to about 10 wt% of croscarmellose sodium;

[0044] (d) about 2 wt% to about 7 wt% of sodium lauryl sulfate; and

[0045] (e) about 0.2 wt% to about 1.0 wt% of magnesium stearate.

[0045a] In another aspect, provided herein is a pharmaceutical composition comprising:

(a) 40 mg 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 in a crystalline form;

(b) 57.4 wt% of microcrystalline cellulose;

(c) 10.0 wt% of croscarmellose sodium; and

(d) 3.0 wt% of sodium lauryl sulfate.

[0045b] In another aspect, provided herein is a pharmaceutical composition comprising:

(a) 40 mg 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) 77.5 mg of microcrystalline cellulose;

(c) 13.5 mg croscarmellose sodium; and

(d) 4.0 mg sodium lauryl sulfate.

[0045c] In another aspect, provided herein is a pharmaceutical composition comprising:

(a) 140 mg 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) 23 wt% of microcrystalline cellulose;

(c) 10 wt% of croscarmellose sodium; and

(d) 6.1 wt% of sodium lauryl sulfate.

[0045d] In another aspect, provided herein is a pharmaceutical composition comprising:

(a) 140 mg 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) 53 mg of microcrystalline cellulose;

(c) 23 mg croscarmellose sodium; and

(d) 14 mg sodium lauryl sulfate.

[0045e] In another aspect, provided herein is a pharmaceutical composition comprising:

(a) 140 mg 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.

[0045f] In another aspect, provided herein is a pharmaceutical composition comprising:

(a) 140 mg 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) 151.4 mg of microcrystalline cellulose;

(c) 23.0 mg sodic croscarmellose;

(d) 14.0 mg sodium lauryl sulfate; and

(e) 1.6 mg magnesium stearate.

[0045g] In another aspect, provided herein is a pharmaceutical composition comprising:

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

(b) 8.5 wt% of microcrystalline cellulose;

(c) 10 wt% of croscarmellose sodium; and

(d) 7.4 wt% of sodium lauryl sulfate.

[0045h] In another aspect, provided herein is a pharmaceutical composition comprising:

(a) 200 mg 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) 23 mg of microcrystalline cellulose;

(c) 27 mg croscarmellose sodium; and

(d) 20 mg sodium lauryl sulfate.

[0046] In some examples, provided herein is a pharmaceutical formulation for oral administration comprising:

[0047] (a) about 40 wt% to about 50 wt% 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;

[0048] (b) about 40 wt% to about 50 wt% of microcrystalline cellulose;

[0049] (c) about 3 wt% to about 10 wt% of croscarmellose sodium;

[0050] (d) about 2 wt% to about 7 wt% of sodium lauryl sulfate; and

[0051] (e) about 0.2 wt% to about 1.0 wt% of magnesium stearate.

[0052] In some examples, provided herein is a pharmaceutical formulation for oral administration comprising:

[0053] (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;

[0054] (b) 45.9 wt% of microcrystalline cellulose;

[0055] (c) 7.0 wt% of croscarmellose sodium;

[0056] (d) 4.2 wt% of sodium lauryl sulfate; and

[0057] (e) 0.5 wt% of magnesium stearate.

CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical formulation for oral administration comprising:

(a) ~~about~~ 40 mg to 200 mg ~~140 mg~~ 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) 40 wt % to 50 wt % of one or more diluents;

(c) 2 wt % to 7 wt % of one or more surfactants; and

(d) 0.2 to 1.0 wt % of one or more lubricants.

~~2. The pharmaceutical formulation of claim 1, comprising about 20 wt % to about 70 wt % of one or more diluents.~~

~~3. The pharmaceutical formulation of claim 1, comprising about 2 wt % to about 7wt % of one or more surfactants.~~

~~4. The pharmaceutical formulation of claim 1, comprising:~~

~~(a) about 140 mg 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 20 wt % to about 70 wt % of one or more diluents;~~

~~(c) about 2 wt % to about 7 wt % of one or more surfactants; and~~

~~(d) one or more lubricants.~~

~~5.~~2. The pharmaceutical formulation of claim ~~4~~1, wherein the formulation is in the form of a hard gelatin capsule.

~~6.~~3. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more diluents are 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.

~~7.~~4. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more diluents are selected from the group consisting of lactose, sucrose, dextrose, mannitol, xylitol, sorbitol, calcium phosphate, starches, modified starches, microcrystalline cellulose, and microcellulose.

~~8.~~5. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more diluents are selected from the group consisting of lactose, sucrose, mannitol, calcium phosphate, starches, modified starches, and microcrystalline cellulose.

~~9.~~6. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more diluents is microcrystalline cellulose.

~~10.~~7. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more surfactants are selected from the group consisting of sodium lauryl sulfate, polyoxyethylene sorbitan

monooleate, polysorbates, poloxamers, and copolymers of ethylene oxide and propylene oxide.

~~11.~~8. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more surfactants are selected from the group consisting of sodium lauryl sulfate, poloxamers, and copolymers of ethylene oxide and propylene oxide.

~~12.~~9. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more surfactants are selected from the group consisting of sodium lauryl sulfate, sorbitan monooleate, polyoxyethylene sorbitan monooleate, polysorbates, poloxamers, bile salts, glyceryl monostearate, and copolymers of ethylene oxide and propylene oxide.

~~13.~~10. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more surfactants is sodium lauryl sulfate.

~~14.~~11. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more lubricants are selected from the group consisting of stearic acid, talc, sodium stearyl fumarate, magnesium stearate, and zinc stearate.

~~15.~~12. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more lubricants are selected from the group consisting of stearic acid, talc, sodium stearyl fumarate, and magnesium stearate.

~~16.~~13. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more lubricants are selected from the group consisting of stearic acid, calcium hydroxide, talc, corn starch, sodium stearyl fumarate, sodium stearates, magnesium stearate, zinc stearate, and waxes.

~~17.~~14. The pharmaceutical formulation of claim ~~4~~1, wherein the one or more lubricants is magnesium stearate.

~~18.~~15. The pharmaceutical formulation of claim ~~4~~1, wherein the formulation further comprises one or more disintegrating agents.

~~19.~~16. The pharmaceutical formulation of claim ~~18~~15, wherein the one or more disintegrating agents are 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, cross-linked polymer, cross-linked polyvinylpyrrolidone, sodium alginate, a clay, and a gum.

~~20.~~17. The pharmaceutical formulation of claim ~~18~~15, wherein the one or more disintegrating agents are selected from the group consisting of natural starch, a pregelatinized starch, a sodium starch, methylcrystalline cellulose, methylcellulose, croscarmellose, croscarmellose sodium, sodium starch glycolate, crospovidone, sodium alginate, a clay, and a gum.

~~21.~~18. The pharmaceutical formulation of claim ~~18~~15, wherein the one or more disintegrating agents are selected from the group consisting of natural starch, a pregelatinized starch, a sodium starch, methylcrystalline cellulose, croscarmellose, croscarmellose sodium, sodium starch glycolate, and crospovidone.

~~22.~~19. The pharmaceutical formulation of claim ~~18~~15, wherein the one or more disintegrating agents is croscarmellose sodium.

~~23.~~20. The pharmaceutical formulation of claim ~~4~~1, wherein:

a) the one or more diluents are 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;

b) the one or more surfactants are selected from the group consisting of sodium lauryl sulfate, polyoxyethylene sorbitan monooleate, polysorbates, poloxamers, and copolymers of ethylene oxide and propylene oxide; and

c) the one or more lubricants are selected from the group consisting of stearic acid, talc, sodium stearyl fumarate, magnesium stearate, and zinc stearate.

~~24.~~21. The pharmaceutical formulation of claim ~~4~~1, wherein:

a) the one or more diluents are selected from the group consisting of lactose, sucrose, dextrose, mannitol, xylitol, sorbitol, calcium phosphate, starches, modified starches, microcrystalline cellulose, and microcellulose;

b) the one or more surfactants are selected from the group consisting of sodium lauryl sulfate, poloxamers, and copolymers of ethylene oxide and propylene oxide; and

c) the one or more lubricants are selected from the group consisting of stearic acid, calcium hydroxide, talc, corn starch, sodium stearyl fumarate, sodium stearates, magnesium stearate, zinc stearate, and waxes.

~~25.~~22. The pharmaceutical formulation of claim ~~4~~1, wherein:

a) the one or more diluents is microcrystalline cellulose; and

b) the one or more lubricants is magnesium stearate.

~~26.~~23. The pharmaceutical formulation of claim ~~18~~15, wherein:

a) the one or more diluents are 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;

b) the one or more surfactants are selected from the group consisting of sodium lauryl sulfate, polyoxyethylene sorbitan monooleate, polysorbates, poloxamers, and copolymers of ethylene oxide and propylene oxide;

c) the one or more lubricants are selected from the group consisting of stearic acid, talc, sodium stearyl fumarate, magnesium stearate, and zinc stearate; and

d) the one or more disintegrating agents are 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, cross-linked polymer, cross-linked polyvinylpyrrolidone, sodium alginate, a clay, and a gum.

~~27.~~24. The pharmaceutical formulation of claim ~~18~~15, wherein:

a) the one or more diluents are selected from the group consisting of lactose, sucrose, dextrose, mannitol, xylitol, sorbitol, calcium phosphate, starches, modified starches, microcrystalline cellulose, and microcellulose;

b) the one or more surfactants are is selected from the group consisting of sodium lauryl sulfate, poloxamers, and copolymers of ethylene oxide and propylene oxide;

c) the one or more lubricants are selected from the group consisting of stearic acid, calcium hydroxide, talc, corn starch, sodium stearyl fumarate, sodium stearates, magnesium stearate, zinc stearate, and waxes; and

d) the one or more disintegrating agents are selected from the group consisting of natural starch, a pregelatinized starch, a sodium starch, methylcrystalline cellulose, methylcellulose, croscarmellose, croscarmellose sodium, sodium starch glycolate, crospovidone, sodium alginate, a clay, and a gum.

~~28.~~25. The pharmaceutical formulation of claim ~~18~~15, wherein:

a) the one or more diluents are microcrystalline cellulose;

b) the one or more surfactants is sodium lauryl sulfate;

c) the one or more lubricants is magnesium stearate; and

d) the one or more disintegrating agents is croscarmellose sodium.

26. The pharmaceutical formulation of claim 1 for oral administration comprising:

(a) 40 mg to 200 mg 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) 40 wt% to 50 wt% of the diluent;

(c) 3 wt% to 10 wt% of a disintegrating agent;

(d) 2 wt% to 7 wt% of the surfactant; and

(e) 0.2 wt% to 1.0 wt% of the lubricant.

27. A pharmaceutical formulation for oral administration comprising:

(a) 40 mg to 200 mg 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) 40 wt% to 50 wt% of microcrystalline cellulose;

(c) 3 wt% to 10 wt% croscarmellose sodium;

(d) 2 wt% to 7 wt% of sodium lauryl sulfate; and

(e) 0.2 wt% to 1.0 wt% of magnesium stearate.

28. A pharmaceutical composition comprising:

(a) 40 mg 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 in a crystalline form;

(b) 57.4 wt% of microcrystalline cellulose;

(c) 10.0 wt% of croscarmellose sodium; and

(d) 3.0 wt% of sodium lauryl sulfate.

29. A pharmaceutical composition comprising:

(a) 40 mg 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) 77.5 mg of microcrystalline cellulose;

(c) 13.5 mg croscarmellose sodium; and

(d) 4.0 mg sodium lauryl sulfate.

30. A pharmaceutical composition comprising:

(a) 140 mg 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) 23 wt% of microcrystalline cellulose;

(c) 10 wt% of croscarmellose sodium; and

(d) 6.1 wt% of sodium lauryl sulfate.

31. A pharmaceutical composition comprising:

(a) 140 mg 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) 53 mg of microcrystalline cellulose;

(c) 23 mg croscarmellose sodium; and

(d) 14 mg sodium lauryl sulfate.

32. A pharmaceutical composition comprising:

(a) 140 mg 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.

33. A pharmaceutical composition comprising:

(a) 140 mg 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) 151.4 mg of microcrystalline cellulose;

(c) 23.0 mg sodic croscarmellose;

(d) 14.0 mg sodium lauryl sulfate; and

(e) 1.6 mg magnesium stearate.

34. A pharmaceutical composition comprising:

(a) 200 mg 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) 8.5 wt% of microcrystalline cellulose;

(c) 10 wt% of croscarmellose sodium; and

(d) 7.4 wt% of sodium lauryl sulfate.

35. A pharmaceutical composition comprising:

(a) 200 mg 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) 23 mg of microcrystalline cellulose;

(c) 27 mg croscarmellose sodium; and

(d) 20 mg sodium lauryl sulfate.