CLAIMS

1. A pharmaceutical formulation for oral administration 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.
2. The pharmaceutical formulation of claim 1, wherein 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.
3. The pharmaceutical formulation of claim 2, wherein the diluent is microcrystalline cellulose.
4. The pharmaceutical formulation of claim 1, wherein 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, and a gum.
5. The pharmaceutical formulation of claim 4, wherein the disintegrating agent is croscarmellose sodium.
6. The pharmaceutical formulation of claim 1, wherein 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.
7. The pharmaceutical formulation of claim 6, wherein the surfactant is sodium lauryl sulfate.
8. The pharmaceutical formulation of claim 1, wherein 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.
9. The pharmaceutical formulation of claim 8, wherein the lubricant is magnesium stearate.
10. The pharmaceutical formulation of claim 1 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.

11. The pharmaceutical formulation of claim 10, wherein the dosage form is a hard gelatin capsule.

12. 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 at least one of the following properties:

(a) an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in **Fig. 1**;

(b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.7±0.1° 2-Theta, 13.6±0.1° 2-Theta, 16.1±0.1° 2-Theta, 18.9±0.1° 2-Theta, 21.3±0.1° 2-Theta, and 21.6±0.1° 2-Theta;

(c) substantially the same X-ray powder diffraction (XRPD) pattern post storage at 40°C and 75% relative humidity (RH) for at least a week;

(d) substantially the same X-ray powder diffraction (XRPD) pattern post storage at 25°C and 97% relative humidity (RH) for at least a week;

(e) Infrared (IR) spectrum substantially similar to the one set forth in **Fig. 2**;

(f) Infrared (IR) spectrum weak peaks at about 1584 cm^{-1}, about 1240 cm^{-1}, about 1147 cm^{-1}, about 1134 cm^{-1}, about 1099 cm^{-1}, and about 1067cm^{-1};

(g) a differential scanning calorimetry (DSC) thermogram substantially similar to the one set forth in **Fig. 3**;

(h) a thermo-gravimetric analysis (TGA) thermogram substantially similar to the one set forth in **Fig. 4**;

(i) a DSC thermogram with an endotherm having an onset at about 154°C and a peak at about 157°C and an exotherm at about 159°C;

(j) non-hygroscopicity;

(k) an observed aqueous solubility of about 0.013 mg/mL at about pH 8;

or

(l) combinations thereof.

13. The crystalline form of claim 12, wherein the crystalline form has an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in **Fig. 1**.

14. The crystalline form of claim 12, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.7±0.1° 2-Theta, 13.6±0.1° 2-Theta, 16.1±0.1° 2-Theta, 18.9±0.1° 2-Theta, 21.3±0.1° 2-Theta, and 21.6±0.1° 2-Theta.

15. The crystalline form of claim 12, wherein the crystalline form has substantially the same X-ray powder diffraction (XRPD) pattern post storage at 40°C and 75% relative humidity (RH) for at least a week.

16. The crystalline form of claim 12, wherein the crystalline form has substantially the same X-ray powder diffraction (XRPD) pattern post storage at 25°C and 97% relative humidity (RH) for at least a week.

17. The crystalline form of claim 12, wherein the crystalline form has a differential scanning calorimetry (DSC) thermogram substantially similar to the one set forth in **Fig. 3**.

18. The crystalline form of claim 12, wherein the crystalline form is unsolvated.

19. The crystalline form of claim 12, wherein the crystalline form is anhydrous.

20. The pharmaceutical formulation of claim 12, wherein 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one is crystalline Form A.

21. A pharmaceutical formulation for oral administration comprising:

(a) 140 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) 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.

CLAIMS

WHAT IS CLAIMED IS:

1. A pharmaceutical formulation for oral administration 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.
2. The pharmaceutical formulation of claim 1, wherein 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.
3. The pharmaceutical formulation of claim 2, wherein the diluent is microcrystalline cellulose.
4. The pharmaceutical formulation of claim 1, wherein 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.
5. The pharmaceutical formulation of claim 4, wherein the disintegrating agent is croscarmellose sodium.
6. The pharmaceutical formulation of claim 1, wherein 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.
7. The pharmaceutical formulation of claim 6, wherein the surfactant is sodium lauryl sulfate.
8. The pharmaceutical formulation of claim 1, wherein 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.
9. The pharmaceutical formulation of claim 8, wherein the lubricant is magnesium stearate.
10. The pharmaceutical formulation of claim 1 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.

11. The pharmaceutical formulation of any one of claims 1-10, wherein the dosage form is a hard gelatin capsule.

12. 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.

13. The package of claim 12 wherein each unit dosage comprises:

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; and

d) 4.2 wt% of sodium lauryl sulfate; and e) 0.5 wt% of magnesium stearate.

14. 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 at least one of the following properties:

(a) an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in **Fig. 1**;

(b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.7±0.1° 2-Theta, 13.6±0.1° 2-Theta, 16.1±0.1° 2-Theta, 18.9±0.1° 2-Theta, 21.3±0.1° 2-Theta, and 21.6±0.1° 2-Theta;

(c) substantially the same X-ray powder diffraction (XRPD) pattern post storage at 40°C and 75% RH for at least a week;

(d) substantially the same X-ray powder diffraction (XRPD) pattern post storage at 25°C and 97% RH for at least a week;

(e) Infrared (IR) spectrum substantially similar to the one set forth in **Fig. 2**;

(f) Infrared (IR) spectrum weak peaks at about 1584 cm^{-1}, about 1240 cm^{-1}, about 1147 cm^{-1}, about 1134 cm^{-1}, about 1099 cm^{-1}, and about 1067cm^{-1};

(g) a DSC thermogram substantially similar to the one set forth in **Fig. 3**;

(h) a thermo-gravimetric analysis (TGA) thermogram substantially similar to the one set forth in **Fig. 4**;

(i) a DSC thermogram with an endotherm having an onset at about 154°C and a peak at about 157°C and an exotherm at about 159°C;

(j) non-hygroscopicity;

(k) an observed aqueous solubility of about 0.013 mg/mL at about pH 8;

or

(l) combinations thereof.

15. The crystalline form of claim 14, wherein the crystalline form has an X-Ray powder diffraction (XRPD) pattern substantially the same as shown in **Fig. 1**.

16. The crystalline form of claim 14, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.7±0.1° 2-Theta, 13.6±0.1° 2-Theta, 16.1±0.1° 2-Theta, 18.9±0.1° 2-Theta, 21.3±0.1° 2-Theta, and 21.6±0.1° 2-Theta.

17. The crystalline form of claim 14, wherein the crystalline form has substantially the same X-ray powder diffraction (XRPD) pattern post storage at 40°C and 75% RH for at least a week.

18. The crystalline form of claim 14, wherein the crystalline form has substantially the same X-ray powder diffraction (XRPD) pattern post storage at 25°C and 97% RH for at least a week.

19. The crystalline form of claim 14, wherein the crystalline form has an Infrared (IR) spectrum substantially similar to the one set forth in **Fig. 2**.

20. The crystalline form of claim 14, wherein the crystalline form has an Infrared (IR) spectrum weak peaks at about 1584 cm^{-1}, about 1240 cm^{-1}, about 1147 cm^{-1}, about 1134 cm^{-1}, about 1099 cm^{-1}, and about 1067cm^{-1}.

21. The crystalline form of claim 14, wherein the crystalline form has a melting temperature of about 155-156°C.

22. The crystalline form of claim 14, wherein the crystalline form has a DSC thermogram substantially similar to the one set forth in **Fig. 3**.

23. The crystalline form of claim 14, wherein the crystalline form has a thermo-gravimetric analysis (TGA) thermogram substantially similar to the one set forth in **Fig. 4**.

24. The crystalline form of claim 14, wherein the crystalline form has a DSC thermogram with an endotherm having an onset at about 154°C and a peak at about 157°C and an exotherm at about 159°C.
25. The crystalline form of claim 14, wherein the crystalline form is non-hygroscopic.
26. The crystalline form of claim 14, wherein the crystalline form has an observed aqueous solubility of about 0.013 mg/mL at about pH 8.
27. The crystalline form of claim 14, wherein the crystalline form that is characterized as having properties (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), and (k).
28. The crystalline form of any one of claims 14-27, wherein the crystalline form was obtained from ethyl acetate, isopropyl acetate, tetrahydrofuran, methyl isobutyl ketone (MIBK), methyl ethyl ketone (MEK), nitromethane, methanol, ethanol, acetonitrile, dioxane, methyl tert-butyl ether (MTBE), anisole, acetone, heptanes, a methanol/water or an acetone/heptane mixture.
29. The crystalline form of any one of claims 14-28, wherein the crystalline form is unsolvated.
30. The crystalline form of any one of claims 14-29, wherein the crystalline form is anhydrous.
31. The pharmaceutical formulation of any one of claims 1-11, wherein 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one is crystalline Form A.
32. A pharmaceutical formulation for oral administration comprising:
(a) 140 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) 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. The package of claim 12 or claim 13, wherein 1-((R)-3-(4-amino-3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)piperidin-1-yl)prop-2-en-1-one is crystalline Form A.
34. A method of treating cancer in a mammal comprising administering to the mammal a pharmaceutical formulation according to any one of claims 1-11, 31 or 32.
35. The method of claim 34, wherein the cancer is a B cell malignancy.
36. The method of claim 34, wherein the cancer is a B cell malignancy selected from chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL), mantle cell lymphoma (MCL), diffuse large B Cell lymphoma (DLBCL), and multiple myeloma.

37. The method of claim 34, wherein the cancer is a lymphoma, leukemia or a solid tumor.

38. The method of claim 34, wherein the cancer is diffuse large B cell lymphoma, follicular lymphoma, chronic lymphocytic lymphoma, chronic lymphocytic leukemia, B-cell prolymphocytic leukemia, lymphoplasmacytic lymphoma/Waldenström macroglobulinemia, splenic marginal zone lymphoma, plasma cell myeloma, plasmacytoma, extranodal marginal zone B cell lymphoma, nodal marginal zone B cell lymphoma, mantle cell lymphoma, mediastinal (thymic) large B cell lymphoma, intravascular large B cell lymphoma, primary effusion lymphoma, burkitt lymphoma/leukemia, or lymphomatoid granulomatosis. In some embodiments, where the subject is suffering from a cancer, an anti-cancer agent is administered to the subject in addition to one of the above-mentioned compounds. In one embodiment, the anti-cancer agent is an inhibitor of mitogen-activated protein kinase signaling