computational prediction of pharmaceutical crystal structures and polymorphism," *Advanced Drug Delivery Reviews 56*:301-319 ("Price"); and Bernstein, 2004, "Crystal Structure Prediction and Polymorphism," *ACA Transactions 39*:14-23 (a great deal still needs to be learned and done before one can state with any degree of confidence the ability to predict a crystal structure, much less polymorphic forms)). The preparation of solid forms is of great importance in the development of a safe, effective, stable, and marketable pharmaceutical compound.

[0010] Citation or identification of any references in this disclosure is not to be construed as an admission that the references are prior art to this disclosure.

3. SUMMARY

[0011] Provided herein are compositions of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one, or a pharmaceutically acceptable salt, isotopologue, metabolite or solid form thereof. In one embodiment, the solid form is crystalline.

[0011a] In one aspect, there is provided a pharmaceutical composition comprising an effective amount of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one, or a pharmaceutically acceptable salt, isotopologue, O-desmethyl-metabolite or solid form thereof, stearic acid and lactose monohydrate.

In another embodiment, the solid form is a single-component crystalline form of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one. In yet another embodiment, the solid form is crystalline Form A of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one.

[0012] In yet another embodiment, the solid form is a hydrate. In yet another embodiment, the solid form is hydrate Form B of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one.

[0013] In yet another embodiment, the solid form is anhydrous. In yet another embodiment, the solid form is anhydrous Form C of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one.

[0014] In yet another embodiment, the solid form is a solvate. In yet another embodiment, the solid form is methanol solvate Form D of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one.

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising an effective amount of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one, or a pharmaceutically acceptable salt, isotopologue, O-desmethyl-metabolite or solid form thereof, stearic acid and lactose monohydrate.

2. The pharmaceutical composition of claim 1, comprising about 0.1-5% by weight of stearic acid.

3. The pharmaceutical composition of claim 2, comprising about 0.4% by weight of stearic acid.

4. The pharmaceutical composition according to any one of claims 1 to 3, comprising about 40-60% by weight of lactose monohydrate.

5. The pharmaceutical composition of claim 4, comprising about 49.2% by weight of lactose monohydrate.

6. The pharmaceutical composition according to any one of claims 1 to 5, further comprising microcrystalline cellulose.

7. The pharmaceutical composition of claim 6, wherein the microcrystalline cellulose is AVICEL PH 102®.

8. The pharmaceutical composition of claim 7, comprising about 20-40% by weight of AVICEL PH 102®.

9. The pharmaceutical composition of claim 8, comprising about 31% by weight of AVICEL PH 102®.

10. The pharmaceutical composition according to any one of claims 1 to 9, further comprising a disintegrant.

11. The pharmaceutical composition of claim 10, wherein the disintegrant is croscarmellose sodium.

12. The pharmaceutical composition of claim 10, wherein the disintegrant is AC-DI-SOL®.

13. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition comprises from about 1-5% by weight of AC-DI-SOL®.

14. The pharmaceutical composition according to any one of claims 1 to 13, wherein the pharmaceutical composition comprises about 40-60% by weight of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one, or a pharmaceutically acceptable salt, isotopologue, or solid form thereof.

15. The pharmaceutical composition of claim 14, wherein the pharmaceutical composition comprises about 15% by weight of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one or a pharmaceutically acceptable salt, isotopologue, or solid form thereof.

16. The pharmaceutical composition of claim 15, wherein the pharmaceutical composition comprises Form A of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((*trans*)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-*b*]pyrazin-2(1*H*)-one.

17. The pharmaceutical composition according to any one of claims 1 to 16, further comprising magnesium stearate.

18. The pharmaceutical composition of claim 17, wherein the pharmaceutical composition comprises from about 0.5-3% by weight of magnesium stearate.

19. The pharmaceutical composition of claim 18, wherein the pharmaceutical composition comprises from about 1% by weight of magnesium stearate.

20. The pharmaceutical composition according to any one of ~~any~~ claims 1 to 19, wherein the pharmaceutical composition is formulated as a tablet.

21. The pharmaceutical composition of claim 20, wherein the tablet is film coated.

22. The pharmaceutical composition of claim 21, wherein the film coating is about 4% by weight of the tablet.

~~23. A method for treating or preventing cancer, an inflammatory condition, an immunological condition, a neurodegenerative disease, diabete, obesity, a neurological disorder, an age-related disease, a cardiovascular condition, or a conditions treatable or preventable by inhibition of a kinase pathway, comprising administering an effective amount of a pharmaceutical composition of claim 1 to a subject in need thereof.~~

~~24. The method of claim 23, wherein the kinase pathway is the TOR kinase pathway.~~

~~25. A method for achieving a Response Evaluation Criteria in Solid Tumors (RECIST 1.1) of complete response, partial response or stable disease in a subject comprising~~

~~administering an effective amount of a pharmaceutical composition of claim 1 to a subject having a solid tumor.~~

~~26. A method for improving International Workshop Criteria (IWC) for NHL, International Uniform Response Criteria for Multiple Myeloma (IURC), Eastern Cooperative Oncology Group Performance Status (ECOG) or Response Assessment for Neuro-Oncology (RANO) Working Group for GBM, comprising administering an effective amount of a pharmaceutical composition of claim 1 to a subject in need thereof.~~

~~27.~~23. The pharmaceutical composition according to claim 1, comprising a s~~S~~olid Form A of 7-(6-(2-hydroxypropan-2-yl)pyridin-3-yl)-1-((trans)-4-methoxycyclohexyl)-3,4-dihydropyrazino[2,3-b]pyrazin-2(1H)-one.

~~28.~~24. The pharmaceutical composition of claim 23, wherein t~~T~~he solid Form A ~~of claim 27, having~~has an X-ray powder diffraction pattern with one or more peaks expressed in two-theta at approximately 8.3, 13.2, 18.2 or 21.7 degrees.

~~29.~~25. The pharmaceutical composition of claim 24, wherein t~~T~~he solid Form A ~~of claim 28, having~~ has a DSC thermogram with an endotherm at a peak temperature of about 199 °C.

~~30.~~26. The pharmaceutical composition of claim 25, wherein t~~T~~he solid Form A ~~of claim 29, having~~ has less than about 0.1% weight loss between about 25 °C to about 100 °C in a thermogravimetric thermogram.

~~31.~~27. The pharmaceutical composition of claim 26, wherein t~~T~~he solid Form A ~~of claim 30, wherein Form A~~ is anhydrous.

~~32.~~28. The pharmaceutical composition of claim 27, wherein t~~T~~he solid Form A ~~of claim 31, wherein Form A~~ is substantially pure.