

(I).

[0011] In one aspect, the disclosure relates to a cocrystal comprising the compound of formula (I) and citric acid.

[0011a] In an aspect, there is provided a cocrystal comprising a compound of formula (I) and citric acid, wherein the cocrystal is characterized by an X-ray powder diffraction pattern, acquired in reflection mode, comprising at least three peak positions, in degrees 2-theta ±0.2 degrees, selected from the group consisting of 5.7, 8.4, 11.4, 15.8, 18.1, 19.2, 21.1, 22.5, and 23.0.

[0012] In another aspect, the disclosure relates to a cocrystal comprising the compound of formula (I) and maleic acid.

[0013] In other aspects, the disclosure relates to crystalline forms of the free compound of formula (I).

[0014] In other aspects, the disclosure relates to a drug substance comprising a solid form of the compound of formula (I).

[0015] In other aspects, the disclosure relates to methods of preparing solid forms of the compound of formula (I).

[0016] In another aspect, the present application relates to a pharmaceutical composition comprising a solid form of the compound of formula (I) and one or more pharmaceutical excipients.

[0016a] In yet another aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of the cocrystal described herein and one or more pharmaceutical excipients.

[0017] In another aspect, the present application relates to a method of treating a cancer characterized by the presence of an IDH1 or IDH2 mutation in a patient in need

thereof, comprising administering a therapeutically effective amount of a solid form of the compound of formula (I), or a pharmaceutical composition thereof, to the patient.

[0017a] In yet another aspect, there is provided a use of a cocrystal described herein or a pharmaceutical composition described herein in the manufacture of a medicament for the treatment of a cancer characterized by the presence of an IDH1 or IDH2 mutation in a patient in need thereof.

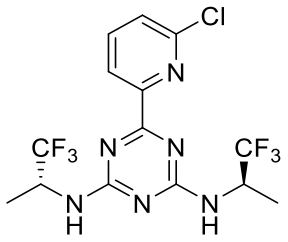
BRIEF DESCRIPTION OF THE DRAWINGS

[0018] Figure 1 depicts one-dimensional ^{1}H NMR spectra of Compound 1 in CD_3OD, taken over a range of temperatures from 25 °C to 85 °C.

[0019] Figure 2 depicts portions of one-dimensional ^{1}H NMR spectra of Compound 1 in CD_3OD, taken over a range of temperatures from 25 °C to 85 °C.

CLAIMS

1. A cocrystal comprising a compound of formula (I)



(I);

and citric acid, wherein the cocrystal is characterized by an X-ray powder diffraction pattern, acquired in reflection mode, comprising at least three peak positions, in degrees 2-theta ±0.2 degrees, selected from the group consisting of 5.7, 8.4, 11.4, 15.8, 18.1, 19.2, 21.1, 22.5, and 23.0.

2. The cocrystal of claim 1, wherein the cocrystal is characterized by an X-ray powder diffraction pattern, acquired in reflection mode, comprising:

(i) at least four peak positions, in degrees 2-theta (±0.2 degrees 2-theta), selected from the group consisting of 5.7, 8.4, 11.4, 15.8, 18.1, 19.2, 21.1, 22.5, and 23.0; or

(ii) peak positions, in degrees 2-theta (±0.2 degrees 2-theta), of 5.7 and 8.4, and at least three peak positions selected from the group consisting of 11.4, 15.8, 18.1, 19.2, 21.1, 22.5, and 23.0.

3. The cocrystal of claim 1 or 2, wherein the cocrystal is characterized by a differential scanning calorimetry thermogram comprising an endothermic peak having an onset temperature of 170.6 °C (±2.0 °C).

4. The cocrystal of any one of claims 1-3, further comprising water, optionally wherein the compound of formula (I), citric acid, and water are present in a molar ratio

of 2:1:1, and/or optionally wherein the cocrystal comprises four molecules of the compound of formula (I), two citric acid molecules, and two water molecules per unit cell.

5. A pharmaceutical composition comprising a therapeutically effective amount of the cocrystal of any one of claims 1-4 and one or more pharmaceutical excipients.

6. Use of a cocrystal of any one of claims 1-4 or a pharmaceutical composition of claim 5 in the manufacture of a medicament for the treatment of a cancer characterized by the presence of an IDH1 or IDH2 mutation in a patient in need thereof.

7. The use of claim 6, wherein the cancer is characterized by the presence of an IDH1 mutation, preferably an R132X mutation.

8. The use of claim 7, wherein the IDH1 mutation is an R132H or R132C mutation.

9. The use of claim 6, wherein the cancer is characterized by the presence of an IDH2 mutation, preferably an R140X mutation or an R172X mutation.

10. The use of claim 9, wherein the IDH2 mutation is an R140Q, R140W, or R140L mutation.

11. The use of claim 9, wherein the IDH2 mutation is an R172K or R172G mutation.

12. The use of any one of claims 7-11, wherein the IDH1 or IDH2 mutation results in accumulation of *R*(-)-2-hydroxyglutarate in the patient.

13. The use of any one of claims 6-12, wherein the cancer is glioma, acute myelogenous leukemia, sarcoma, melanoma, non-small cell lung cancer (NSCLC), cholangiocarcinomas, chondrosarcoma, myelodysplastic syndromes (MDS), myeloproliferative neoplasm (MPN), colon cancer, or angio-immunoblastic non-Hodgkin's lymphoma (NHL), preferably glioma.

14. The use of claim 13, wherein the glioma is a low grade glioma or a secondary high grade glioma, preferably a secondary high grade glioma that is glioblastoma.

15. The use of claim 14, wherein the glioma is a low grade glioma.

16. The use of any one of claims 6-15, wherein the cancer is refractory or relapsed.

17. The use of any one of claims 6-15, wherein the cancer is newly diagnosed or previously untreated.

18. The use of any one of claims 6-17, wherein the cocrystal or pharmaceutical composition is to be administered in an amount of about 10 mg, about 25 mg, about 50 mg, about 100 mg, about 200 mg, or about 300 mg per day, based on the amount of the compound of formula (I), preferably wherein the cocrystal or pharmaceutical composition is to be administered in an amount of about 10 mg or about 50 mg, once per day, based on the amount of the compound of formula (I).

19. The use of any one of claims 6-17, wherein the cocrystal or pharmaceutical composition is to be administered in an amount of about 10 to 50 mg/day, based on the amount of the compound of formula (I).

20. The use of any one of claims 6-17, wherein the cocrystal or pharmaceutical composition is to be administered in an amount of about 15 to 40 mg/day, based on the amount of the compound of formula (I).