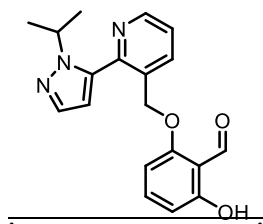


Claims

1. ~~A crystalline anhydrate of Compound 1:~~



Compound 1

2. ~~The crystalline anhydrate of claim 1, which is substantially free of a solvated polymorph of Compound 1.~~

3. ~~A composition comprising the crystalline anhydrate of claim 1.~~

4. ~~The crystalline anhydrate of claim 1, wherein the crystalline anhydrate comprises one or more of Form I, Form II or Material N, wherein~~

~~Form I is characterized by at least one X-ray powder diffraction peak (Cu K α radiation) selected from 12.82°, 15.74°, 16.03°, 16.63°, 17.60°, 25.14°, 25.82° and 26.44° (each $\pm 0.2^\circ 2\theta$);~~

~~Form II is characterized by at least one X-ray powder diffraction peak (Cu K α radiation) selected from 13.37°, 14.37°, 19.95° and 23.92° 2θ (each $\pm 0.2^\circ 2\theta$);~~
~~and~~

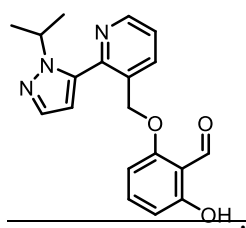
~~Material N is characterized by at least one X-ray powder diffraction peak (Cu K α radiation) selected from 11.65°, 11.85°, 12.08°, 16.70°, 19.65° and 23.48° 2θ (each $\pm 0.2^\circ 2\theta$).~~

5. ~~The crystalline anhydrate of claim 4, wherein the crystalline anhydrate comprises Form II.~~

6. ~~The crystalline anhydrate of claim 4, wherein the crystalline anhydrate comprises Material N.~~

7. ~~A method of preparing a crystalline anhydrate of claim 1 comprising slurrying a salt of Compound 1 in a solvent and disproportionating the Compound 1 salt to form the crystalline anhydrate.~~

8. — ~~Use of a therapeutically effective amount of a crystalline anhydrate of claim 1 for increasing oxygen affinity of hemoglobin S.~~
9. — ~~Use of a therapeutically effective amount of a composition of claim 3 for increasing oxygen affinity of hemoglobin S.~~
10. — ~~Use of a therapeutically effective amount of a crystalline anhydrate of claim 1 for treatment of oxygen deficiency associated with sickle cell anemia.~~
11. — ~~Use of a therapeutically effective amount of a composition of claim 3 for treatment of oxygen deficiency associated with sickle cell anemia, the method comprising administering to a subject in need thereof.~~
12. — A crystalline solvate of Compound 1:



Compound 1

13. — ~~The crystalline solvate of claim 12, which is substantially free of an unsolvated polymorph of Compound 1.~~
14. — ~~A composition comprising the crystalline solvate of claim 12 or claim 13.~~
15. — ~~The crystalline solvate of claim 12, comprising one or more of Material E, Material F, Material G, Material H, Material J, Material K, Material L, Material M, Material O or Material P.~~
16. — ~~The crystalline solvate of claim 15, wherein:~~

~~Material E is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 8.69, 11.73, 12.10, 15.26, 16.11, 17.45, 22.39, 22.55 and 23.70 $\pm$ 0.20;~~

Material F is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 8.47, 8.81, 12.75, 13.17, 14.92, 15.63, 17.01 23.73, and 24.07 ± 0.20 ;

Material G is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 8.47, 11.45, 12.62, 14.66, 15.69, 17.01, 18.47, 20.32, 22.61, 23.08, 23.43 and 23.70 ± 0.20 ;

Material H is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 8.61, 11.67, 15.33, 16.28, 17.28, 22.58, 23.51 and 25.77 ± 0.20 ;

Material J is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 8.52, 8.88, 12.79, 15.04, 15.61, 17.11, 22.81, 23.87, 24.17, 24.62 and 26.44 ± 0.20 ;

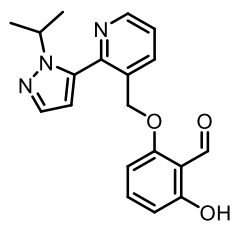
Material K is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 8.52; 8.83, 11.35, 15.04, 15.74, 17.11, 23.46, 23.58, 24.08 and 25.99 ± 0.20 ;

Material L is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 8.61, 8.78, 11.67, 14.94, 15.28, 16.14, 17.30, 22.75, 23.71 and 26.05 ± 0.20 ; and

Material M is characterized by at least one, two, or three X-ray powder diffraction peak (Cu K α radiation) selected from 7.74, 10.05, 12.82, 15.33, 16.80, 20.82, 21.14, 25.80 and 26.97 ± 0.20 .

17. — A method of preparing a crystalline solvate of claim 12 comprising contacting a free base an solvate of Compound 1 with a solvent.
18. — Use of a therapeutically effective amount of a crystalline solvate of claim 12 for increasing oxygen affinity of hemoglobin S.
19. — Use of a therapeutically effective amount of a crystalline solvate of claim 12 for treatment of oxygen deficiency associated with sickle cell anemia.

1. A crystalline form of Compound 1:



Compound 1

characterized by at least three X-ray powder diffraction peaks (Cu K α radiation) selected from 11.65°, 11.85°, 12.08°, 16.70°, 19.65°, and 23.48°2 θ , each $\pm$ 0.2°2 θ .

2. The crystalline form of claim 1, characterized by an X-ray powder diffraction pattern (Cu K α radiation) substantially similar to FIG 7.

3. The crystalline form of claim 1, characterized by an endothermic peak at 95 $\pm$ 2 °C as measured by differential scanning calorimetry.

4. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and a crystalline form of any one of claims 1-3.

5. A crystalline form of any one of claims 1-3 for use in treating sickle cell disease.

6. A pharmaceutical composition of claim 4 for use in treating sickle cell disease.

7. Use of a crystalline form of any one of claims 1-3 in the manufacture of a medicament for treating sickle cell disease.