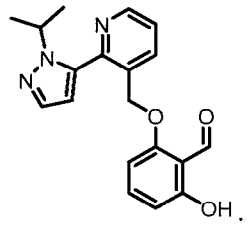
Claims

1. A crystalline ansolvate of Compound 1:



Compound 1

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

3. A composition comprising the crystalline ansolvate of claim 1.

4. The crystalline ansolvate of claim 1, wherein the crystalline ansolvate 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 Kα radiation) selected from 12.82°, 15.74°, 16.03°, 16.63°, 17.60°, 25.14°, 25.82° and 26.44° (each ±0.2 °2θ);

   Form II is characterized by at least one X-ray powder diffraction peak (Cu Kα radiation) selected from 13.37°, 14.37°, 19.95° and 23.92°2θ (each ±0.2 °2θ); and

   Material N is characterized by at least one X-ray powder diffraction peak (Cu Kα radiation) selected from 11.65°, 11.85°, 12.08°, 16.70°, 19.65° and 23.48 °2θ (each ±0.2 °2θ).

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

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

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

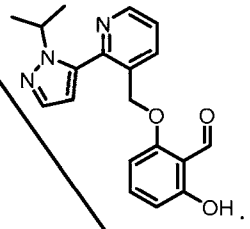
8. Use of a therapeutically effective amount of a crystalline ansolvate of claim 1 for increasing oxygen affinity of hemoglobin S.

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 ansolvate 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 ansolvated 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 Kα radiation) selected from 8.69, 11.73, 12.10, 15.26, 16.11, 17.45, 22.39, 22.55 and 23.70 ± 0.20;

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

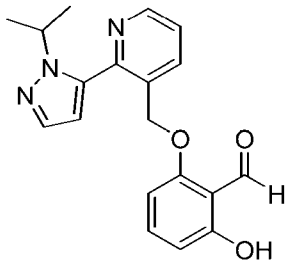
17. A method of preparing a crystalline solvate of claim 12 comprising contacting a free base ansolvate of Compound 1 with a solvent.

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.

CLAIMS

1. A crystalline ansolvate of Compound 1:



Compound 1

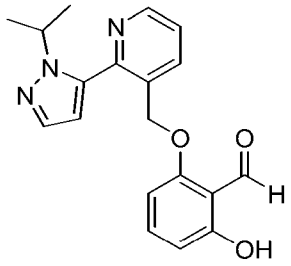
wherein the crystalline ansolvate comprises Form II, wherein Form II is characterized by at least one X-ray powder diffraction peak (Cu Kα radiation) selected from 13.37°, 14.37°, 19.95° and 23.92°2θ (each ±0.2 °2θ).

2. The crystalline ansolvate of claim 1, wherein Form II is characterized by at least two X-ray powder diffraction peaks (Cu Kα radiation) selected from 13.37°, 14.37°, 19.95° and 23.92°2θ (each ±0.2 °2θ).

3. The crystalline ansolvate of claim 1, wherein Form II is characterized by at least three X-ray powder diffraction peaks (Cu Kα radiation) selected from 13.37°, 14.37°, 19.95° and 23.92°2θ (each ±0.2 °2θ).

4. The crystalline ansolvate of claim 1, wherein Form II is characterized by X-ray powder diffraction peaks (Cu Kα radiation) at 13.37°, 14.37°, 19.95° and 23.92°2θ (each ±0.2 °2θ).

5. A crystalline ansolvate of Compound 1:



Compound 1

wherein the crystalline ansolvate comprises Form II,, wherein Form II is characterized by an X-ray powder diffraction pattern (Cu Kα radiation) substantially similar to that of FIG. 5.

6. The crystalline ansolvate of any one of the preceding claims, wherein the crystalline ansolvate comprises less than 25 mole % of crystalline Form I, crystalline Material N or amorphous forms of Compound 1;

wherein

Form I is characterized by X-ray powder diffraction peaks (Cu Kα radiation) at 12.82°, 15.74°, 16.03°, 16.63°, 17.60°, 25.14°, 25.82° and 26.44°2θ (each ±0.2 °2θ); and

Material N is characterized by X-ray powder diffraction peaks (Cu Kα radiation) at 11.65°, 11.85°, 12.08°, 16.70°, 19.65° and 23.48°2θ (each ±0.2 °2θ).

7. The crystalline ansolvate of claim 6, wherein the crystalline ansolvate comprises less than 10 mole % of crystalline Form I, crystalline Material N or amorphous forms of Compound 1.

8. The crystalline ansolvate of claim 6, wherein the crystalline ansolvate comprises less than 5 mole % of crystalline Form I, crystalline Material N or amorphous forms of Compound 1.

9. The crystalline ansolvate of claim 7, wherein the crystalline ansolvate comprises less than 5 mole % of crystalline Form I.

10. The crystalline ansolvate of any one of the preceding claims, wherein the crystalline ansolvate is substantially free of a solvated polymorph of Compound 1.

11. The crystalline ansolvate of any one of the preceding claims, wherein the crystalline ansolvate is substantially free of other ansolvate polymorphs of Compound 1.

12. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and the crystalline ansolvate of any one of claims 1-12.

13. The pharmaceutical composition of claim 12, wherein the crystalline ansolvate comprises less than 10 mole % of crystalline Form I, crystalline Material N or amorphous forms of Compound 1.

14. The pharmaceutical composition of claim 12, wherein the crystalline ansolvate comprises less than 5 mole % of crystalline Form I.

15. Use of a crystalline ansolvate of any one of claims 1-11 or a pharmaceutical composition of any one of claim 12 to 14 for use in the manufacture of a medicament forr increasing oxygen affinity of hemoglobin S in a subject.

16. Use of a crystalline ansolvate of any one of claims 1-11 or a pharmaceutical composition of any one of claim 12 to 14 for use in the manufacture of a medicament for treating sickle cell disease.

17. Use of a crystalline ansolvate of any one of claims 1-11 or a pharmaceutical composition of any one of claim 12 to 14 for use in the manufacture of a medicament for treating cancer, a pulmonary disorder, stroke, high altitude sickness, an ulcer, a pressure sore, Alzheimer's disease, acute respiratory disease syndrome, or a wound.

18. Use of a crystalline ansolvate of any one of claims 1-11 or a pharmaceutical composition of any one of claim 12 to 14 for use in the manufacture of a medicament for treating a pulmonary disorder.