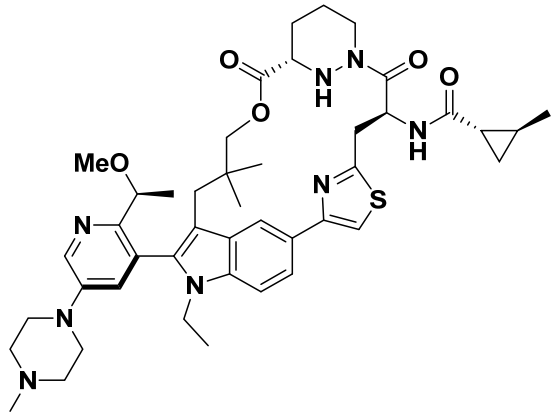
Claims:

1. A crystalline solid form of Compound A:



Compound A

2. The crystalline solid form of claim 1, wherein the solid form is:
   Form 1;
   Form 2;
   Form 3;
   Form 4;
   Form 5;
   Form 6;
   Form 7; or
   Form 8.

3. The crystalline solid form of claim 1, wherein the solid form is Form 1 having peaks at diffraction angles 2θ (°) of 5.2 ± 0.5, 8.4 ± 0.5, and 10.0 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

4. The crystalline solid form of claim 1, wherein the solid form is Form 1 having peaks at diffraction angles 2θ (°) of 10.7 ± 0.5, 14.4 ± 0.5, and 16.7 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

5. The crystalline solid form of claim 1, wherein the solid form is Form 1 having peaks at diffraction angles 2θ (°) of 5.2 ± 0.5, 8.4 ± 0.5, 10.0 ± 0.5, 10.7 ± 0.5, 14.4 ± 0.5, and 16.7 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

6. The crystalline solid form of claim 1, wherein the solid form is Form 1 having peaks at diffraction angles 2θ (°) of 17.0 ± 0.5, 18.4 ± 0.5, and 20.5 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

7. The crystalline solid form of claim 1, wherein the solid form is Form 1 having peaks at diffraction angles 2θ (°) of 5.2 ± 0.5, 8.4 ± 0.5, 10.0 ± 0.5, 10.7 ± 0.5, 14.4 ± 0.5, 16.7 ± 0.5, 17.0 ± 0.5, 18.4 ± 0.5, and 20.5 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

8. The crystalline solid form of any one of claims 1 to 7, wherein the solid form is Form 1 having a differential scanning calorimetry (DSC) profile with endothermic onsets at 66.8°C ± 0.5 and 95.8°C ± 0.5.

9. The crystalline solid form of any one of claims 1 to 8, wherein the solid form is Form 1 having a thermogravimetric analysis (TGA) profile that exhibits a weight loss of 6.0% ± 0.5 (w/w) between ambient and 100.0°C ± 0.5.

10. A pharmaceutical composition comprising the crystalline solid form of any one of claims 3 to 9, and a pharmaceutically acceptable carrier or excipient.

11. A method of making the solid form of any one of claims 3 to 9, comprising preparing a slurry of Compound A in a suitable solvent or buffer to precipitate crystalline solids of Form 1, isolating the solids from the slurry, and drying the solids.

12. The method of claim 11, wherein the slurry is prepared in a suitable solvent, and the solvent is a mixture of methanol and water.

13. The crystalline solid form of claim 1, wherein the solid form is Form 5 having a DSC profile with endothermic onsets at 32.1°C ± 0.5 and 81.2°C ± 0.5.

14. The crystalline solid form of claim 13, wherein the solid form is Form 5 having a TGA profile that exhibits a weight loss of 4.8% ± 0.5 (w/w) between ambient and 150.0°C ± 0.5.

15. The crystalline solid form of claim 13 or 14, wherein the solid form is Form 5 having an X-ray powder diffractogram as shown in FIG. 18.

16. The crystalline solid form of claim 1, wherein the solid form is Form 2 having peaks at diffraction angles 2θ (°) of 5.9 ± 0.5 and 14.7 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

17. The crystalline solid form of claim 16, wherein the solid form is Form 2 having a DSC profile with endothermic onsets at about 43.5 ºC and 131.5 ºC; or having a TGA profile that exhibits a weight loss of about 5.1% (w/w) from ambient to 80°C and about 2.3% (w/w) from 80°C to 160°C.

18. The crystalline solid form of claim 1, wherein the solid form is Form 3 having peaks at diffraction angles 2θ (°) 4.9 ± 0.5 and 7.4 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

19. The crystalline solid form of claim 1, wherein the solid form is Form 4 having peaks at diffraction angles 2θ (°) of 5.2 ± 0.5, 5.9 ± 0.5, 12.1 ± 0.5, 14.5 ± 0.5, 16.4 ± 0.5, 17.9 ± 0.5, and 19.4 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

20. The crystalline solid form of claim 19, wherein the solid form is Form 4 having a DSC profile with an endothermic onset at about 30.9°C; or having a TGA profile that exhibits weight loss of about 4.6% (w/w) between ambient and 80°C and 2.5% (w/w) from 80°C to 160°C.

21. The crystalline solid form of claim 1, wherein the solid form is Form 6 having peaks at diffraction angles 2θ (°) of 4.7 ± 0.5, 7.5 ± 0.5, 7.9 ± 0.5, 10.3 ± 0.5, 11.2 ± 0.5, 13.1 ± 0.5, 17.4 ± 0.5, 17.7 ± 0.5, 19.1 ± 0.5, 19.8 ± 0.5, 20.6 ± 0.5, 21.7 ± 0.5, 22.4 ± 0.5, 23.1 ± 0.5, 24.1 ± 0.5, 25.2 ± 0.5, and 26.2 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

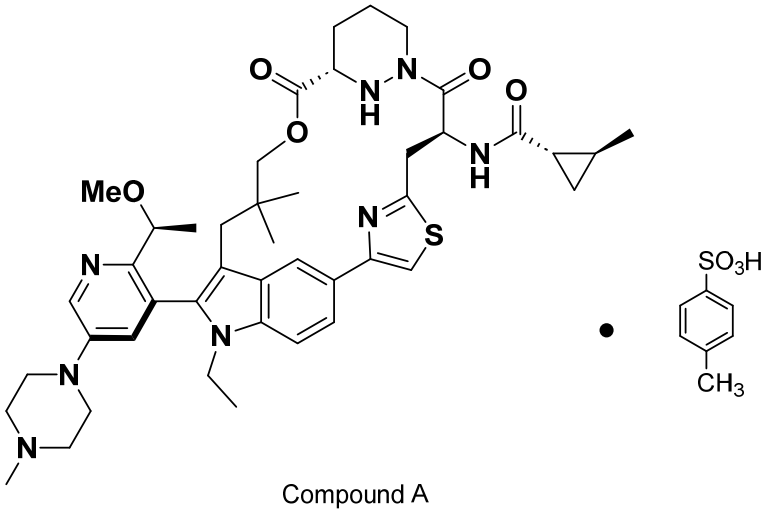
22. The crystalline solid form of claim 21, wherein the solid form is Form 6 having a DSC profile with endothermic onsets at about 53.3°C and 166.4°C; or having a TGA profile exhibiting a weight loss of about 6.7% (w/w) at 150°C.

23. The crystalline solid form of claim 1, wherein the solid form is Form 7 having peaks at diffraction angle 2θ (°) of 5.4 ± 0.5, 8.4 ± 0.5, 8.4 ± 0.5, 10.7 ± 0.5, 11.1 ± 0.5, 11.5 ± 0.5, 11.8 ± 0.5, 12.8 ± 0.5, 13.2 ± 0.5, 14.0 ± 0.5, 15.2 ± 0.5, 15.8 ± 0.5, 16.9 ± 0.5, 17.3 ± 0.5, 19.3 ± 0.5, 20.2 ± 0.5, 21.2 ± 0.5, 21.8 ± 0.5, 22.7 ± 0.5, 23.1 ± 0.5, 23.4 ± 0.5, 24.9 ± 0.5, 26.7 ± 0.5, 27.4 ± 0.5, 31.7 ± 0.5, and 39.2 ±

0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

24. The crystalline solid form of claim 1, wherein the solid form is Form 8 having peaks at diffraction angle 2θ (°) of 5.4 ± 0.5, 6.6 ± 0.5, 8.0 ± 0.5, 8.5 ± 0.5, 9.1 ± 0.5, 10.1 ± 0.5, 10.9 ± 0.5, 11.3 ± 0.5, 12.3 ± 0.5, 13.6 ± 0.5, 16.0 ± 0.5, and 17.5 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

25. A crystalline solid form of a tosylate salt of Compound A:



Compound A

26. The crystalline solid form of claim 25, having peaks at diffraction angles 2θ (°) of 5.9 ± 0.5, 9.4 ± 0.5, and 9.8 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

27. The crystalline solid form of claim 25 or 26, having peaks at diffraction angles 2θ (°) of 10.2 ± 0.5, 10.6 ± 0.5, 11.0 ± 0.5, and 16.1 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X rays or calculated from X-ray diffractometry.

28. The crystalline solid form of claim 25 or 26, having peaks at diffraction angle 2θ (°) of 12.6 ± 0.5, 12.8 ± 0.5, 14.2 ± 0.5, and 17.2 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

29. The crystalline solid form of claim 25, having peaks at diffraction angle 2θ (°) of 5.9 ± 0.5, 9.4 ± 0.5, 9.8 ± 0.5, 10.2 ± 0.5, 10.6 ± 0.5, 11.0 ± 0.5, 12.6 ± 0.5, 12.8 ± 0.5, 14.2 ± 0.5, 16.1 ± 0.5, and 17.2 ± 0.5 as measured by X-ray diffractometry by irradiation with Cu Kα X-rays or calculated from X-ray diffractometry.

30. The crystalline solid form of claim 25 or 29, having a DSC profile having endothermic onsets at 99.5°C ± 0.5, 230.7°C ± 0.5, and 262.4°C ± 0.5; or having a TGA profile exhibiting a weight loss of 2.7% ± 0.5 (w/w) between ambient and 50.0°C ± 0.5, or weight loss of 3.2% ± 0.5 (w/w) between ambient and 200.0°C ± 0.5.

31. Use of a therapeutically effective amount of the solid form of any one of claims 1 to 30, or the pharmaceutical composition of claim 10, in the manufacture of a medicament for treating cancer in a subject in need thereof.

32. Use of a therapeutically effective amount of the solid form of any one of claims 1 to 30, or the pharmaceutical composition of claim 10, in the manufacture of a medicament for treating a Ras protein-related disorder in a subject in need thereof.

33. Use of a therapeutically effective amount of the solid form of any one of claims 1 to 30, or the pharmaceutical composition of claim 10, in the manufacture of a medicament for inhibiting a Ras protein in a cell.