CLAIMS

What is claimed is:

1. A crystalline form of {6-[(2-amino-3-chloropyridin-4-yl)sulfanyl]-3-[(3*S*,4*S*)-4-amino-3-methyl-2-oxa-8-azaspiro[4.5]decan-8-yl]-5-methylpyrazin-2-yl}methanol, or a pharmaceutically acceptable salt thereof, characterized as Compound 1 Form D.

2. The crystalline form of claim 1, wherein an X-ray powder diffraction pattern comprises 2θ values: about 18.48 and about 16.77.

3. The crystalline form of claim 2, wherein the X-ray powder diffraction pattern further comprises one or more 2θ values at about: 10.73, 11.03, 11.15, 12.58, 19.17, 19.54, 20.88, 22.47, and 25.59.

4. The crystalline form of claim 1, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 10A.

5. The crystalline form of any one of claims 1-4, wherein a differential scanning calorimetry (DSC) curve comprises an endotherm at about 51 °C, about 90 °C, or about 211 °C.

6. The crystalline form of any one of claims 1-4, wherein the DSC curve is substantially as shown in FIG. 13.

7. The crystalline form of any one of claims 1-6, having the unit cell dimensions: a = 14.0679(4) Å, b = 16.0057(4) Å, c = 19.1837(6) Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$; cell volume (V) of 4319.5(2) Å^3; and a space group of $P2_12_12$ space group.

8. A crystalline form of {6-[(2-amino-3-chloropyridin-4-yl)sulfanyl]-3-[(3*S*,4*S*)-4-amino-3-methyl-2-oxa-8-azaspiro[4.5]decan-8-yl]-5-methylpyrazin-2-yl}methanol, or a pharmaceutically acceptable salt thereof, characterized as Compound 1 Form B.

9. The crystalline form of claim 8, wherein an X-ray powder diffraction pattern comprises 2θ values: about 20.0 and about 17.9.

10. The crystalline form of claim 9, wherein the X-ray powder diffraction pattern further comprises one or more 2θ values at about: 7.8, 9.1, 9.4, 11.4, 12.8, 13.4, 15.7, 18.9, 20.9, 23.1, and 25.0.

11. The crystalline form of claim 8, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 3A.

12. The crystalline form of any one of claims 8-11, wherein a differential scanning calorimetry (DSC) curve comprises an endotherm at about 188 °C and/or about 211°C.

13. The crystalline form of any one of claims 8-11, wherein the DSC curve is substantially as shown in FIG. 6.

14. The crystalline form of any one of claims 8-11, having the unit cell dimensions: a = 9.65334(16) Å, b = 10.28825(18) Å, c = 11.62614(19) Å, α = 76.0621(15)°, β = 89.6714(13)°, γ = 76.4043(15)°; cell volume (V) of 1087.68(3) Å^3; and a space group of $P1$ space group.

15. A crystalline form of {6-[(2-amino-3-chloropyridin-4-yl)sulfanyl]-3-[(3*S*,4*S*)-4-amino-3-methyl-2-oxa-8-azaspiro[4.5]decan-8-yl]-5-methylpyrazin-2-yl}methanol, or a pharmaceutically acceptable salt thereof, characterized as Compound 1 Form C.

16. The crystalline form of claim 15, wherein an X-ray powder diffraction pattern comprises 2θ values: about 18.56 and about 16.62.

17. The crystalline form of claim 16, wherein the X-ray powder diffraction pattern further comprises one or more 2θ values at about: 10.78, 11.11, 12.29, 19.06, 19.57, 20.83, and 25.61.

18. The crystalline form of claim 15, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 8A.

19. The crystalline form of any one of claims 15-18, having the unit cell dimensions: a = 47.6458(8) Å, b = 14.4005(2) Å, c = 9.5460(2) Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$; cell volume (V) of 6549.8(2) Å^3; and a space group of $P2_12_12$.

20. A crystalline form of {6-[(2-amino-3-chloropyridin-4-yl)sulfanyl]-3-[(3*S*,4*S*)-4-amino-3-methyl-2-oxa-8-azaspiro[4.5]decan-8-yl]-5-methylpyrazin-2-yl}methanol, or a pharmaceutically acceptable salt thereof, characterized as Compound 1 Form A.

21. The crystalline form of claim 20, wherein an X-ray powder diffraction pattern comprises 2θ values: about 16.66 and about 18.50.

22. The crystalline form of claim 21, wherein the X-ray powder diffraction pattern further comprises one or more 2θ values at about: 10.76, 11.11, 12.35, 19.08, 19.52, 20.85, and 25.63.

23. The crystalline form of claim 20, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 1A.

24. The crystalline form of claim 20, having an onset melting temperature of about 213 °C.

25. A pharmaceutical composition comprising the crystalline form of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

26. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises Compound 1 Form D, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

27. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises Compound 1 Form C, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

28. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises Compound 1 Form B, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

29. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises Compound 1 Form A, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

30. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises at least two crystalline forms selected from
Compound 1 Form A, or a pharmaceutically acceptable salt thereof,
Compound 1 Form B, or a pharmaceutically acceptable salt thereof,
Compound 1 Form C, or a pharmaceutically acceptable salt thereof, and
Compound 1 Form D, or a pharmaceutically acceptable salt thereof,
and a pharmaceutically acceptable carrier.

31. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises Compound 1 Form D, or a pharmaceutically acceptable salt thereof, and Compound 1 Form A, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

32. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises Compound 1 Form D, or a pharmaceutically acceptable salt thereof, and Compound 1 Form B, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

33. A pharmaceutical composition of claim 25, wherein the pharmaceutical composition comprises Compound 1 Form D, or a pharmaceutically acceptable salt thereof, and Compound 1 Form C, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

34. A method of treating a disease associated with SHP2 modulation in a subject in need thereof, comprising administering to the subject an effective amount the crystalline form of any one of claims 1-24, or a pharmaceutically acceptable salt thereof.

35. The method of claim 34, wherein the disease is selected from Noonan Syndrome, Leopard Syndrome, juvenile myelomonocytic leukemias, neuroblastoma, melanoma, acute myeloid leukemia and cancers of the breast, lung and colon.

36. A crystalline form of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, for use as a medicament.

37. A crystalline form of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, for use in treating or preventing a disease associated with SHP2 modulation.

38. Use of a crystalline form of any one of claims 1-24, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a disease associated with SHP2 modulation.

39. A method of treating a disease associated with SHP2 modulation in a subject in need thereof, comprising administering to the subject an effective amount of a pharmaceutical composition of any one of claims 25-33.

40. The method of claim 39, wherein the disease is selected from Noonan Syndrome, Leopard Syndrome, juvenile myelomonocytic leukemias, neuroblastoma, melanoma, acute myeloid leukemia and cancers of the breast, lung and colon.

41. A pharmaceutical composition of any one of claims 25-33 for use as a medicament.

42. A pharmaceutical composition of any one of claims 25-33 for use in treating or preventing a disease associated with SHP2 modulation.

43. Use of a pharmaceutical composition of any one of claims 25-33 in the manufacture of a medicament for treating or preventing a disease associated with SHP2 modulation.