CLAIMS

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 having an X-ray powder diffraction pattern comprising peaks having 2θ values of 18.48 and 16.77, each peak between ± 0.2 degrees 2θ.

2. The crystalline form of claim 1, wherein the crystalline form is {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.

3. The crystalline form of claim ~~1, or a pharmaceutically acceptable salt thereof, wherein an X-ray powder diffraction pattern comprises 2θ values: about 18.48 and about 16.77.~~

~~4. The crystalline form of claim~~ 2, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern further comprises one or more peaks having 2θ values selected from the group consisting of about 10.73, about 11.03, about 11.15, about 12.58, about 19.17, about 19.54, about 20.88, about 22.47, and about 25.59, each peak between ± 0.2 degrees 2θ.

~~5~~4. The crystalline form of claim 1, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 10A.

~~6~~5. The crystalline form of claim 1, or a pharmaceutically acceptable salt thereof, wherein a differential scanning calorimetry (DSC) curve comprises an endotherm at about 51 °C, about 90 °C, or about 211 °C.

~~7~~6. The crystalline form of claim 1, or a pharmaceutically acceptable salt thereof, wherein the DSC curve is substantially as shown in FIG. 13.

~~8~~7. 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 having an X-ray powder diffraction pattern comprising peaks having 2θ values of 20.0 and 17.9, each peak between ± 0.2 degrees 2θ.

~~9~~8. The crystalline form of claim ~~8, or a pharmaceutically acceptable salt thereof, wherein an X-ray powder diffraction pattern comprises 2θ values: about 20.0 and about 17.9.~~

~~10. The crystalline form of claim 9~~7, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern further comprises one or more peaks having 2θ values selected from the group consisting of about 7.8, about 9.1, about 9.4, about 11.4, about 12.8, about 13.4, about 15.7, about 18.9, about 20.9, about 23.1, and about 25.0, each peak between ± 0.2 degrees 2θ.

~~11~~9. The crystalline form of claim ~~8~~7, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 3A.

~~12~~10. The crystalline form of claim ~~8~~7, or a pharmaceutically acceptable salt thereof, wherein the DSC curve is substantially as shown in FIG. 6.

~~13~~11. 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 having an X-ray powder diffraction pattern comprising peaks having 2θ values of 18.56 and 16.62, each peak between ± 0.2 degrees 2θ.

~~14~~12. The crystalline form of claim ~~13, or a pharmaceutically acceptable salt thereof, wherein an X-ray powder diffraction pattern comprises 2θ values: about 18.56 and about 16.62.~~

~~15. The crystalline form of claim 14~~11, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern further comprises one or more peaks having 2θ values selected from the group consisting of about 10.78, about 11.11, about 12.29, about 19.06, about 19.57, about 20.83, and about 25.61, each peak between ± 0.2 degrees 2θ.

~~16~~13. The crystalline form of claim ~~13~~11, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 8A.

~~17~~14. 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 having an X-ray powder diffraction pattern comprising peaks having 2θ values of 16.66 and 18.5, each peak between ± 0.2 degrees 2θ.

~~18~~15. The crystalline form of claim ~~17, or a pharmaceutically acceptable salt thereof, wherein an X-ray powder diffraction pattern comprises 2θ values: about 16.66 and about 18.50.~~

~~19. The crystalline form of claim 18~~14, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern further comprises one or more peaks having 2θ values selected from the group consisting of about 10.76, about 11.11, about 12.35, about 19.08, about 19.52, about 20.85, and about 25.63, each peak between ± 0.2 degrees 2θ.

~~20~~16. The crystalline form of claim ~~17~~14, or a pharmaceutically acceptable salt thereof, wherein the X-ray powder diffraction pattern is substantially in accordance with that shown in FIG. 1A.

~~21~~17 A pharmaceutical composition comprising the crystalline form of claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~22~~18. A pharmaceutical composition comprising the crystalline form of claim ~~8~~7, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~23~~19. A pharmaceutical composition comprising the crystalline form of claim ~~13~~11, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~24~~20. A pharmaceutical composition comprising a crystalline form of claim ~~17~~14, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

~~25~~21. A pharmaceutical composition of claim ~~21~~16, wherein the pharmaceutical composition further comprises one or more crystalline forms selected from the group consisting of
Compound 1 Form A, or a pharmaceutically acceptable salt thereof,
Compound 1 Form B, or a pharmaceutically acceptable salt thereof, and
Compound 1 Form C, or a pharmaceutically acceptable salt thereof;
and a pharmaceutically acceptable carrier.

~~26~~22. Use of an effective amount of the crystalline form of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, 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.

~~27~~23. Use of an effective amount of the crystalline form of claim ~~8~~7, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, 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.

~~28~~24. Use of an effective amount of the crystalline form of claim ~~13~~11, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, 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.

~~29~~25. Use of an effective amount of the crystalline form of claim ~~17~~14, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, 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.

~~30~~26. Use of an effective amount of the crystalline form of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, wherein the disease is selected from esophageal cancer, gastric carcinoma, anaplastic large-cell lymphoma, and glioblastoma.

~~31~~27. Use of an effective amount of the crystalline form of claim ~~8~~7, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, wherein the disease is selected from esophageal cancer, gastric carcinoma, anaplastic large-cell lymphoma, and glioblastoma.

~~32~~28. Use of an effective amount of the crystalline form of claim ~~13~~11, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, wherein the disease is selected from esophageal cancer, gastric carcinoma, anaplastic large-cell lymphoma, and glioblastoma.

~~33~~29. Use of an effective amount of the crystalline form of claim ~~17~~14, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease associated with SHP2 modulation in a subject in need thereof, wherein the disease is selected from esophageal cancer, gastric carcinoma, anaplastic large-cell lymphoma, and glioblastoma.