What is claimed is:

1. A crystalline form of selpercatinib, which is characterized by at least one of:

(a) an x-ray powder diffraction (XRPD) pattern comprising a peak at 21.1° and one or more peaks at 17.1°, 17.7°, and 19.8° ± 0.2° 2θ as measured using an x-ray wavelength of 1.5418 Å; or

(b) a ^{13}C solid state NMR spectrum which comprises peaks referenced to the high field resonance of adamantane (δ = 29.5 ppm) at: 28.0, 48.0, 80.4, 106.8, 130.2, and 134.9 ppm (± 0.2 ppm, respectively).

2. The crystalline form of selpercatinib according to Claim 1, wherein the crystalline form is characterized by having an x-ray powder diffraction (XRPD) pattern comprising a peak at 21.1° and one or more peaks at 7.5°, 12.0°, 13.2°, 17.1°, 17.7°, and 19.8° ± 0.2° 2θ as measured using an x-ray wavelength of 1.5418 Å;

3. The crystalline form of selpercatinib according to Claim 1, wherein the crystalline form is characterized by having an x-ray powder diffraction (XRPD) pattern having characteristic peaks occurring at 7.5°, 10.9°, 12.0°, 13.2°, 17.1°, 17.7°, 18.2°, 19.8°, 21.1°, and 24.5° ± 0.2° 2θ.

4. The crystalline form of selpercatinib according to Claim 1, wherein the crystalline form is characterized by a ^{13}C solid state NMR spectrum which comprises peaks referenced to the high field resonance of adamantane (δ = 29.5 ppm) at: 26.4, 28.0, 42.0, 43.9, 48.0, 56.3, 69.5, 80.4, 102.3, 106.8, 115.2, 120.8, 130.2, 134.9, 140.6, 149.5, 152.5, and 163.5 ppm (± 0.2 ppm, respectively).

5. The crystalline form of selpercatinib according to Claim 1, wherein the crystalline form is characterized by a ^{13}C solid state NMR spectrum which comprises peaks referenced to the high field resonance of adamantane (δ = 29.5 ppm) at: 26.4, 27.4, 28.0, 42.0, 43.4, 43.9, 48.0, 53.9, 56.3, 58.3, 69.5, 77.9, 80.4, 102.3, 106.8, 113.6, 115.2, 118.2, 120.8, 125.2, 130.2, 134.9, 136.9, 140.6, 148.4, 149.5, 151.2, 152.5, 158.2, and 163.5 ppm (± 0.2 ppm, respectively).

6. A pharmaceutical composition comprising a crystalline form of selpercatinib according to any of Claims 1-5, and a pharmaceutically acceptable carrier, diluent, or excipient.

7. A pharmaceutical composition according to Claim 6, wherein the composition contains less than about 20% by wt. of other crystal forms of selpercatinib.

8. A pharmaceutical composition according to Claim 6, wherein the composition contains less than about 10% by wt. of other crystal forms of selpercatinib.

9. A pharmaceutical composition according to Claim 6, wherein the composition contains less than about 5% by wt. of other crystal forms of selpercatinib.

10. A method of treating cancer in a patient comprising administering to a patient in need of such treatment an effective amount of selpercatinib according to any of claims 1-9.

11. A pharmaceutical composition according to any of claims 6-9 for use in therapy.

12. A pharmaceutical composition according to any of claims 6-9 for use in the treatment of cancer.

13. The pharmaceutical composition for use according to claim 12, wherein the cancer is selected from the group consisting of: lung cancer, papillary thyroid cancer, medullary thyroid cancer, differentiated thyroid cancer, recurrent thyroid cancer, refractory differentiated thyroid cancer, multiple endocrine neoplasia type 2A or 2B (MEN2A or MEN2B, respectively), pheochromocytoma, parathyroid hyperplasia, breast cancer, colorectal cancer, papillary renal cell carcinoma, ganglioneuromatosis of the gastroenteric mucosa, and cervical cancer.

14. The pharmaceutical composition for use according to claim 13, wherein the cancer is medullary thyroid cancer.

15. The pharmaceutical composition for use according to claim 13, wherein the cancer is lung cancer and the lung cancer is small cell lung carcinoma, non-small cell lung cancer, bronchioles lung cell carcinoma, RET fusion lung cancer, or lung adenocarcinoma.

16. The pharmaceutical composition for use according to claim 15, wherein the cancer is RET fusion lung cancer.

17. A process for making the crystalline form of selpercatinib of claim 1, comprising the steps of:

(a) suspending selpercatinib in a solvent;

(b) heating the suspension to between 50 °C and 60 °C while stirring for 30 to 90 minutes;

(c) removing the heat and allowing the suspension to cool to room temperature to form solid crystals; and

(d) collecting the solid crystals.

18. The process of claim 17, wherein the solvent comprises methanol.

19. The process of claims 17 or 18, wherein the suspension is heated to 55 °C.

20. The process of any one of claims 17-19, wherein the suspension is stirred for 60 minutes.

21. The process of any one of claims 17-20, wherein the solid crystals are collected by vacuum filtration.

22. A method of converting selpercatinib Form A to selpercatinib Form B.

23. A method according to claim 22, the method comprising: combining selpercatinib Form A with a C_1-C_5 alcohol to generate a slurry; and isolating selpercatinib Form B from the slurry.

24. A method according to claims 22 or 23, wherein the C_1-C_5 alcohol is about 10 °C to about 30 °C.

25. A method according to any one of claims 22-24, wherein the C_1-C_5 alcohol is about 15-25 °C.

26. A method according to any one of claims 22-25, wherein the C_1-C_5 alcohol is about 20 °C.

27. A method according to claims 22 or 23, wherein the C_1-C_5 alcohol is about 10 °C to about 80 °C.

28. A method according to any one of claims 22-27, wherein the C_1-C_5 alcohol comprises methanol.

29. A method according to any one of claims 22-28, wherein C_1-C_5 alcohol comprises at least 90 wt% methanol.

30. A method according to any one of claims 22-29, wherein the slurry is stirred or otherwise agitated for at least about 10 minutes.

31. A method according to any one of claims 22-30, wherein isolating Form B comprises vacuum filtration.

32. A method according to any one of claims 22-31, wherein isolating Form B comprises centrifugal separation.

33. A method according to any one of claims 22-32, further comprising the drying of the selpercatinib Form B.

34. A method according to claim 22, the method comprising:

a. dissolving the selpercatinib Form A in a solvent comprising DMSO to form a solution;

b. adding water to the solution and thereby forming a slurry;

c. isolating the selpercatinib Form B.

35. A method according to claim 34, wherein the concentration of Form A dissolved in DMSO is about 10-15 mL/g.

36. A method according to claims 34 or 35, wherein the concentration of Form A dissolved in DMSO is about 12-13 mL/g.

37. A method according to any one of claims 34-36, wherein forming the solution of step a comprises heating the selpercatinib Form A and the solvent comprising DMSO to about 50 °C to about 70 °C.

38. A method according to any one of claims 34-37, wherein the solution is cooled to a temperature less than about 70 °C and greater than about 20 °C.

39. A method according to claim 37, wherein the solution is cooled to a temperature of about 50 °C.

40. A method according to any one of claims 34-39, wherein step b comprises adding about 0.1 to about 1 mL of water per gram of Form A to the solution.

41. A method according to any one of claims 34-40, wherein step b comprises adding about 0.3 mL of water per gram of Form A to the solution.

42. A method according to any one of claims 34-41, wherein step b further comprises adding about 1 to about 15 wt% of Form B seed crystals.

43. A method according to any one of claims 34-42, wherein step b further comprises adding about 1 to about 10 wt% of Form B seed crystals.

44. A method according to claim 42 or 43, wherein about 5 wt% of Form B seed crystals are added.

45. A method according to any one of claims 34-44, wherein the slurry is stirred for about 6 to about 72 hours, after the water is added in step b.

46. A method according to any one of claims 34-45, the slurry is stirred for at least 12 hours.

47. A method according to any one of claims 34-46, wherein step b further comprises adding a second tranche of water to the slurry.

48. A method according to claim 47, wherein about 0.5 to about 3 mL of water per gram of Form A is added to the slurry.

49. A method according to any one of claims 34-48, wherein the slurry of step b is cooled to about 20-30 °C.

50. A method according to any one of claims 34-49, wherein step c comprises filtration.

51. A method according to any one of claims 34-50, wherein the isolated selpercatinib Form B from step c is washed with a solvent comprising methanol, ACN, MTBE, or water.

52. A method according to claim 51, wherein the isolated selpercatinib Form B is washed with a solvent comprising methanol.

53. A method according to claim 52, wherein the isolated selpercatinib Form B is washed with methanol until the isolated selpercatinib Form B contains less than 0.5 wt % DMSO.

54. A method according to claim 22, the method comprising: combining selpercatinib Form A and methanol to form a slurry, and stirring the slurry until >99 wt% of the Form A is converted to Form B.

55. A method according to claim 54, wherein the slurry is stirred for about 18-24 hours.

56. A method according to claims 54 or 55, wherein the concentration of the selpercatinib Form A in the methanol is about 8 mL/g.

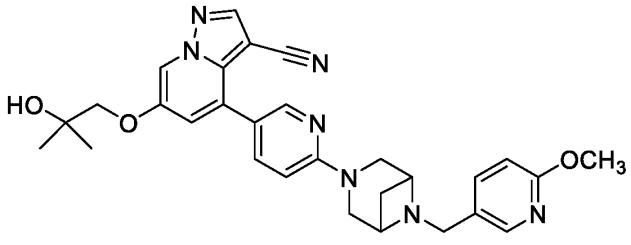
57. A method according to claim 22, the method comprising dissolving selpercatinib Form A in DMSO at about 60-80 °C to form a solution having a concentration of about 10-15 mL/g of DMSO per gram of Form A; cooling the solution to about 40-60 °C, adding water; optionally seeding the resulting mixture with Form B seed crystals; stirring the mixture; adding more water; heating the mixture to about 60-80 °C; cooling the mixture and isolating the Form B.

58. A method according to claim 57, wherein 5 wt% of Form B seed crystals are added to the mixture.

59. A method according to claim 57 or 58, wherein the first addition of water is about 0.1 mL/g of Form A to about 0.5 mL/g of Form A.

60. A method according to any one of claims 57-59, wherein the second addition of water is about 1.0-1.5 mL/g of Form A.

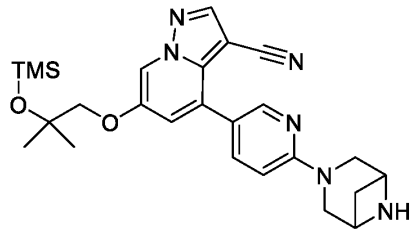
61. A process for preparing selpercatinib as polymorph Form B, of Formula I:



(Formula I)

or a pharmaceutically acceptable salt thereof,

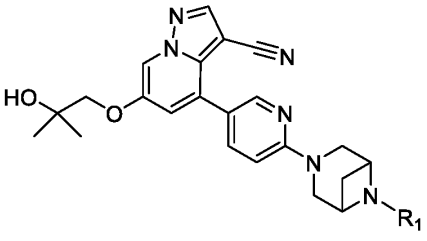
wherein the process comprises reacting a compound of the structure:



[3]

or a salt thereof, in a solvent with 6-methoxynicotinaldehyde in the presence of an acid and a reducing agent to prepare selpercatinib Form B or a pharmaceutically acceptable salt thereof.

62. The process of claim 61, further comprising preparing compound of structure **[3]**, or a salt thereof, the process comprising reacting a compound of the structure



[12]

or a salt thereof, wherein R_1 is an amine protecting group, with a deprotecting agent to form the compound of structure **[3]** or a salt thereof.

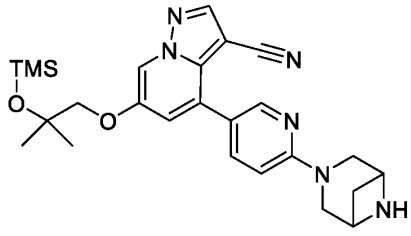
63. The process of any one of claims 61-62, wherein the deprotecting agent is selected from the group consisting of trifluoroacetic acid, hydrochloric acid, hydrobromic acid, hydriodic acid, phosphoric acid, sulfuric acid, methanesulfonic acid, p-toluene sulfonic acid, acetyl chloride, aluminum trichloride, and boron trifluoride.

64. The process of any one of claims 62-63, wherein the deprotecting agent is selected from the group consisting of sulfuric acid, p-toluene sulfonic acid, and acetyl chloride.

65. The process of any one of claims 61-64, wherein the reducing agent is selected from the group consisting of an alkali metal borohydride, a hydrazine

compound, citric acid, a citric acid salt, succinic acid, a succinic acid salt, ascorbic acid, and an ascorbic acid salt.

66. The process of any one of claims 61-65 wherein the reducing agent is selected from the group consisting of sodium triacetoxyborohydride (STAB), sodium borohydride, and sodium cyanoborohydride.
67. The process of any one of claims 61-66, wherein R_1 is selected from the group consisting of formyl, acetyl, trifluoroacetyl, benzyl, benzoyl, carbamate, benzyloxycarbonyl, p-methoxybenzyl carbonyl, tert-butyloxycarbonyl (Boc), trimethylsilyl, 2-trimethylsilyl-ethanesulfonyl, trityl and substituted trityl groups, allyloxycarbonyl, 9-fluorenylmethyloxycarbonyl, nitroveratryloxycarbonyl, p-methoxybenzyl, and tosyl.
68. The process of any one of claims 61-67, wherein R_1 is tert-butyloxycarbonyl (Boc).
69. The process of any one of claims 61-68, wherein the acid is selected from the group consisting of pivalic acid and acetic acid.
70. The process of any one of claims 61-69, wherein the reaction is performed in a solvent, and the solvent comprises anisole.
71. A compound that is 4-[6-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-3-pyridyl]-6-(2-methyl-2-trimethylsilyloxy-propoxy)pyrazolo[1,5-a]pyridine-3-carbonitrile, which has the structure **[3]**



[3]

or a pharmaceutically acceptable salt thereof.