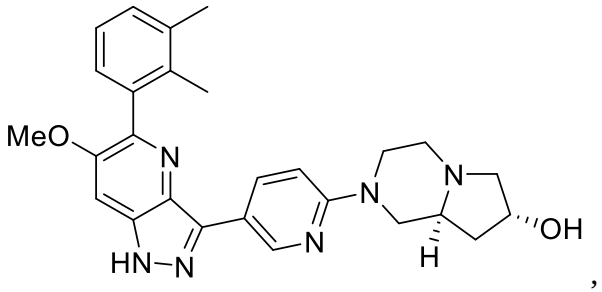
What is claimed is:

1. A solid form of Compound 1 having the formula:



,

wherein the solid form is crystalline.

2. The solid form of claim 1, wherein the solid form is Compound 1 Form I.

3. The solid form of claim 2, having at least one characteristic X-ray powder diffraction (XRPD) peak selected from about 4.9, about 9.3, about 12.3, about 14.7, and about 16.3 degrees 2-theta.

4. The solid form of claim 2, having at least one characteristic XRPD peak selected from about 4.9, about 9.3, about 12.3, about 14.7, about 16.3, about 17.8, about 19.4, about 20.5, about 21.9, about 24.4, and about 25.1 degrees 2-theta.

5. The solid form of claim 2, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 1.

6. The solid form of any one of claims 2-5, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 70 ºC and about 190 ºC.

7. The solid form of any one of claims 2-5, having a DSC thermogram substantially as depicted in FIG. 2.

8. The solid form of any one of claims 2-7, having a TGA thermogram substantially as depicted in FIG. 3.

9. The solid form of claim 1, wherein the solid form is a methanol solvate.

10. The solid form of claim 9, wherein the solid form is Compound 1 Form II.

11. The solid form of claim 9 or 10, having at least one characteristic XRPD peak selected from about 7.4, about 12.7, about 13.6, about 20.8, and about 23.2 degrees 2-theta.

12. The solid form of claim 9 or 10, having at least one characteristic XRPD peak selected from about 7.4, about 12.5, about 12.7, about 13.6, about 14.5, about 15.7, about 16.9, about 20.8, about 23.2, and about 25.9 degrees 2-theta.

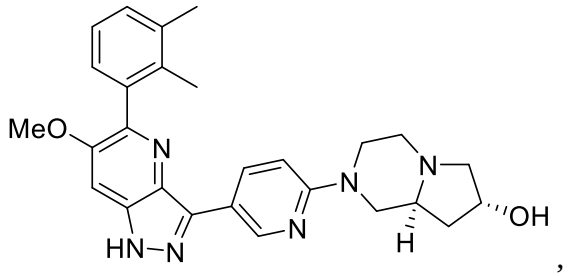
13. The solid form of claim 9 or 10, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 4.

14. The solid form of any one of claims 9-13, which exhibits a DSC thermogram having an endotherm peak at a temperature of about 162 ºC.

15. The solid form of any one of claims 9-13, having a DSC thermogram substantially as depicted in FIG. 5.

16. The solid form of any one of claims 9-15, having a TGA thermogram substantially as depicted in FIG. 6.

17. A salt which is an acid addition salt of Compound 1, having the structure:



,

wherein the acid is phosphoric acid, hydrochloric acid, *L*-tartaric acid, malonic acid, methanesulfonic acid, adipic acid, fumaric acid, maleic acid, malic acid, or succinic acid.

18. The salt of claim 17, wherein the acid is phosphoric acid.

19. The salt of claim 18, wherein the salt is crystalline.

20. The salt of claim 19, wherein the salt is Compound 1 Phosphate Form I.

21. The salt of claim 20, having at least one characteristic XRPD peak selected from about 8.2, about 9.6, about 13.8, about 15.0 and about 22.6 degrees 2-theta.

22. The salt of claim 20, having at least one characteristic XRPD peak selected from about 8.2, about 9.6, about 13.8, about 15.0, about 16.1, about 16.6, about 18.4, about 19.3, about 20.1, and about 22.6 degrees 2-theta.

23. The salt of claim 20, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 9.

24. The salt of any one of claims 20-23, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 63 ºC and about 246 ºC.

25. The salt of any one of claims 20-23, having a DSC thermogram substantially as depicted in FIG. 10.

26. The salt of any one of claims 20-25, having a TGA thermogram substantially as depicted in FIG. 11.

27. The salt of claim 19, wherein the salt is Compound 1 Phosphate Form II.

28. The salt of claim 27, having at least one characteristic XRPD peak selected from about 3.9, about 6.9, about 12.9, about 18.3, and about 23.5 degrees 2-theta.

29. The salt of claim 27, having at least one characteristic XRPD peak selected from about 3.9, about 6.9, about 11.6, about 12.9, about 15.6, about 16.9, about 18.3, about 23.5 and about 26.8 degrees 2-theta.

30. The salt of claim 27, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 12.

31. The salt of any one of claims 27-30, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 151 ºC and about 250 ºC.

32. The salt of any one of claims 27-30, having a DSC thermogram substantially as depicted in FIG. 13.

33. The salt of any one of claims 27-32, having a TGA thermogram substantially as depicted in FIG. 14.

34. The salt of claim 19, wherein the salt is an acetonitrile solvate.

35. The salt of claim 19 or 34, wherein the salt is Compound 1 Phosphate Form III.

36. The salt of claim 35, having at least one characteristic XRPD peak selected from about 3.9, about 5.0, about 16.2, and about 22.5 degrees 2-theta.

37. The salt of claim 35, having at least one characteristic XRPD peak selected from about 3.9, about 5.0, about 5.7, about 8.1, about 12.4, about 14.0, about 16.2, about 17.0, about 20.3 and about 22.5 degrees 2-theta.

38. The salt of claim 35, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 15.

39. The salt of any one of claims 35-38, which exhibits a DSC thermogram having an endotherm peak at a temperature of about 203 ºC.

40. The salt of any one of claims 35-38, having a DSC thermogram substantially as depicted in FIG. 16.

41. The salt of any one of claims 35-40, having a TGA thermogram substantially as depicted in FIG. 17.

42. The salt of claim 17, wherein the acid is hydrochloric acid.

43. The salt of claim 42, wherein the salt is crystalline.

44. The salt of claim 43, wherein the salt is of Compound 1 Hydrochloride Form I.

45. The salt of claim 44, having at least one characteristic XRPD peak selected from about 5.0, about 6.4, about 7.8, about 10.1, about 15.1, and about 24.0 degrees 2-theta.

46. The salt of claim 44, having at least one characteristic XRPD peak selected from about 5.0, about 6.4, about 7.8, about 10.1, about 15.1, about 15.7, about 19.8, about 21.0, about 24.0, about 25.2, about 26.2, and about 26.4 degrees 2-theta.

47. The salt of claim 44, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 18.

48. The salt of any one of claims 44-47, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 124 ºC and about 204 ºC.

49. The salt of any one of claims 44-47, having a DSC thermogram substantially as depicted in FIG. 19.

50. The salt of any one of claims 44-49, having a TGA thermogram substantially as depicted in FIG. 20.

51. The salt of claim 43, wherein the salt is of Compound 1 Hydrochloride Form II.

52. The salt of claim 51, having at least one characteristic XRPD peak selected from about 4.4, about 6.6, about 7.0, about 9.0, about 11.1, and about 13.8 degrees 2-theta.

53. The salt of claim 51, having at least one characteristic XRPD peak selected from about 4.4, about 6.6, about 7.0, about 9.0, about 11.1, about 13.8, about 14.8, about 15.3, about 18.1, about 23.7, about 24.8, about 25.7, and about 26.2 degrees 2-theta.

54. The salt of claim 51, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 21.

55. The salt of any one of claims 51-54, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 137 ºC and about 230 ºC.

56. The salt of any one of claims 51-54, having a DSC thermogram substantially as depicted in FIG. 22.

57. The salt of any one of claims 51-56, having a TGA thermogram substantially as depicted in FIG. 23.

58. The salt of claim 17, wherein the acid is an *L*-tartaric acid.

59. The salt of claim 58, wherein the salt is crystalline.

60. The salt of claim 59, having at least one characteristic XRPD peak selected from about 11.7, about 13.9, about 15.2, about 21.8, and about 23.8 degrees 2-theta.

61. The salt of claim 59, having at least one characteristic XRPD peak selected from about 11.7, about 12.6, about 13.9, about 15.2, about 15.6, about 17.0, about 18.5, about 21.8, and about 23.8 degrees 2-theta.

62. The salt of claim 59, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 24.

63. The salt of any one of claims 59-62, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 70 ºC and about 129 ºC.

64. The salt of any one of claims 59-62, having a DSC thermogram substantially as depicted in FIG. 25.

65. The salt of any one of claims 59-64, having a TGA thermogram substantially as depicted in FIG. 26.

66. The salt of claim 17, wherein the acid is a malonic acid.

67. The salt of claim 66, wherein the salt is crystalline.

68. The salt of claim 67, having at least one characteristic XRPD peak selected from about 4.0, about 9.0, about 13.9, about 17.1, about 17.9, about 18.8, and about 22.7 degrees 2-theta.

69. The salt of claim 67, having at least one characteristic XRPD peak selected from about 4.0, about 9.0, about 13.1, about 13.9, about 14.0, about 17.1, about 17.9, about 18.8, about 20.7, and about 22.7 degrees 2-theta.

70. The salt of claim 67, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 27.

71. The salt of any one of claims 67-70, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 57 ºC and about 173 ºC.

72. The salt of any one of claims 67-70, having a DSC thermogram substantially as depicted in FIG. 28.

73. The salt of any one of claims 67-72, having a TGA thermogram substantially as depicted in FIG. 29.

74. The salt of claim 17, wherein the acid is a methanesulfonic acid.

75. The salt of claim 74, wherein the salt is crystalline.

76. The salt of claim 75, having at least one characteristic XRPD peak selected from about 4.9, about 5.7, about 8.0, about 9.9, and about 22.2 degrees 2-theta.

77. The salt of claim 75, having at least one characteristic XRPD peak selected from about 4.9, about 5.7, about 8.0, about 9.9, about 11.8, about 19.6, about 20.0, about 20.6, and about 22.2 degrees 2-theta.

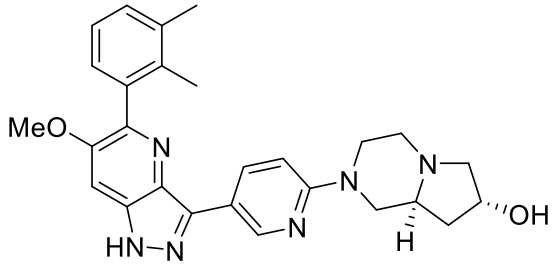
78. The salt of claim 75, having an XRPD pattern with characteristic peaks as substantially shown in FIG. 30.

79. The salt of any one of claims 75-78, which exhibits a DSC thermogram having endotherm peaks at temperatures of about 93 ºC and about 178 ºC.

80. The salt of any one of claims 75-78, having a DSC thermogram substantially as depicted in FIG. 31.

81. The salt of any one of claims 75-80, having a TGA thermogram substantially as depicted in FIG. 32.

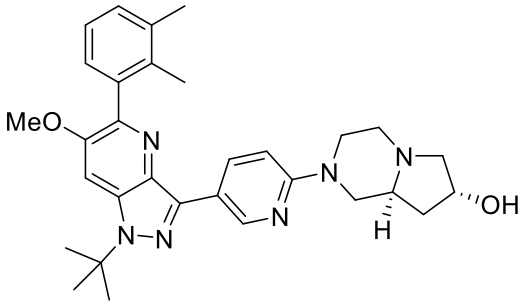
82. A process for preparing Compound 1 having the formula:



Compound 1,

or a salt thereof, comprising:

deprotecting Compound 2 having the formula:



Compound 2,

or a salt thereof, with A1, wherein A1 is an acid.

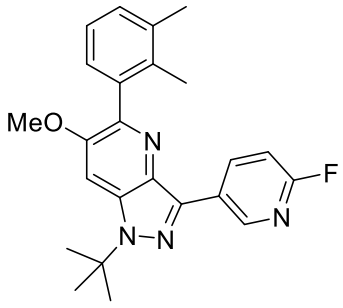
83. The process of claim 82, wherein A1 is an inorganic acid.

84. The process of claim 82 or 83, wherein A1 is sulfuric acid.

85. The process of any one of claims 82-84, wherein the deprotecting is performed in the presence of S1, wherein S1 is a protic solvent.

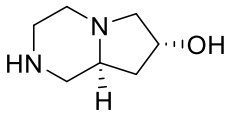
86. The process of claim 85, wherein S1 is water.

87. The process of any one of claims 82-86, wherein Compound 2 or a salt thereof is prepared by a process comprising: contacting Compound 3 having the formula:



Compound 3,

or a salt thereof, with Compound 4 having the formula:



Compound 4,

or a salt thereof, in the presence of B1, wherein B1 is a base.

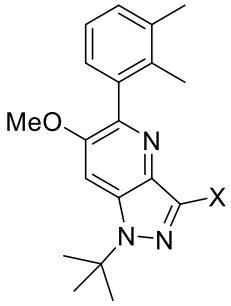
88. The process of claim 87, wherein B1 is an organolithium base.

89. The process of claim 87, wherein B1 is n-butyllithium.

90. The process of any one of claims 87-89, wherein the contacting is performed in the presence of S2, wherein S2 is a polar aprotic solvent.

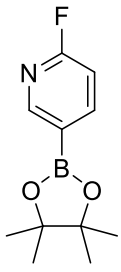
91. The process of claim 90, wherein S2 is tetrahydrofuran.

92. The process of any one of claims 87-91, wherein Compound 3 or a salt thereof is prepared by a process comprising: coupling Compound 5 having the formula:



Compound 5,

or a salt thereof, wherein X is halo, with Compound 6 having the formula:



Compound 6,

or a salt thereof, in the presence of CA1 and B2, wherein CA1 is a catalyst and B2 is a base.

93. The process of claim 92, wherein CA1 is a palladium catalyst.

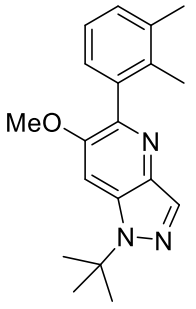
94. The process of claim 92 or 93, wherein CA1 is bis(di-tert-butyl(4-dimethylaminophenyl)phosphine)dichloropalladium (II) (Pd-132).

95. The process of any one of claims 92-94, wherein B2 is an inorganic base.

96. The process of any one of claims 92-95, wherein B2 is potassium phosphate tribasic monohydrate.

97. The process of any one of claims 92-96, wherein X is Br.

98. The process of any one of claims 92-97, wherein Compound 5 or a salt thereof is prepared by a process comprising: halogenating Compound 7 having the formula:



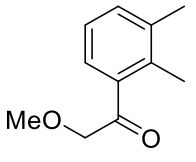
Compound 7,

or a salt thereof, in the presence of H1, wherein H1 is a halogenating agent.

99. The process of claim 98, wherein H1 is a brominating reagent.

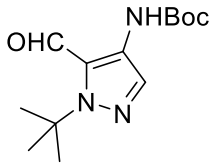
100. The process of claim 98, wherein H1 is N-bromosuccinimide.

101. The process of any one of claims 98-100, wherein Compound 7 or a salt thereof is prepared by a process comprising: contacting Compound 8 having the formula:



Compound 8,

or a salt thereof, with Compound 9 having the formula:



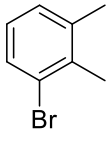
Compound 9,

or a salt thereof, in the presence of A2, wherein A2 is an acid.

102. The process of claim 101, wherein A2 is a sulfonic acid.

103. The process of claim 101 or 102, wherein A2 is methanesulfonic acid.

104. The process of any one of claims 101-103, wherein Compound 8 or a salt thereof is prepared by a process comprising: treating Compound 10 having the formula:

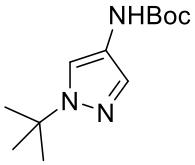


Compound 10,

or a salt thereof, with magnesium in the presence of 2-methoxyacetonitrile.

105. The process of claim 104 wherein the treating of Compound 10 with magnesium is performed in presence of iodine.

106. The process of any one of claims 101-105, wherein Compound 9 or a salt thereof is prepared by a process comprising: reacting Compound 11 having the formula:



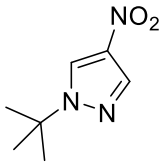
Compound 11,

or a salt thereof, with B3 followed by N,N-dimethylformamide, wherein B3 is a base.

107. The process of claim 106, wherein B3 is an organolithium base.

108. The process of claim 106 or 107, wherein B3 is n-butyllithium.

109. The process of any one of claims 106-108, wherein Compound 11 or a salt thereof is prepared by a process comprising: reducing Compound 12 having the formula:



Compound 12,

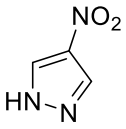
or a salt thereof, in the presence of di-tert-butyl dicarbonate and CA2, wherein CA2 is a catalyst.

110. The process of claim 109, wherein the reducing of Compound 12 is performed under a hydrogen atmosphere.

111. The process of claim 109 or 110, wherein CA2 is a hydrogenation catalyst.

112. The process of any one of claims 109-111, wherein CA2 is 10% palladium on carbon.

113. The process of any one of claims 109-112, wherein Compound 12 or a salt thereof is prepared by a process comprising: treating Compound 13 having the formula:



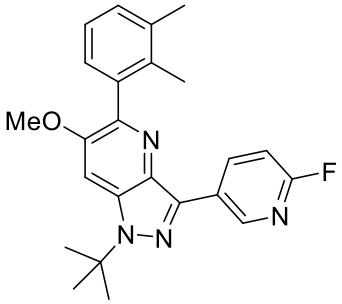
Compound 13

or a salt thereof, with tert-butyl acetate in the presence of A3, wherein A3 is an acid.

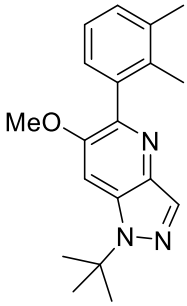
114. The process of claim 113, wherein A3 is an inorganic acid.

115. The process of claim 113 or 114, wherein A3 is sulfuric acid.

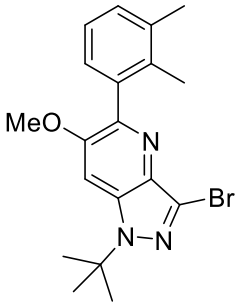
116. A compound selected from the following:



,



, and



,

or a salt of any of the aforementioned.

117. A pharmaceutical composition comprising a solid form of any one of claims 1-16 or a salt of any one of claims 17-81, and a pharmaceutically acceptable carrier or excipient.

118. A method of inhibiting an FGFR3 enzyme, said method comprising contacting *in vitro* a solid form of any one of claims 1-16 or a salt of any one of claims 17-81 with said enzyme.

119. Use of a solid form of any one of claims 1-16 or a salt of any one of claims 17-81 in the manufacture of a medicament for the treatment of a cancer in a patient.

120. The use of claim 119, wherein the cancer is selected from adenocarcinoma, bladder cancer, breast cancer, cervical cancer, cholangiocarcinoma, endometrial cancer, gastric cancer, glioma, head and neck cancer, lung cancer, ovarian cancer, leukemia, and multiple myeloma.