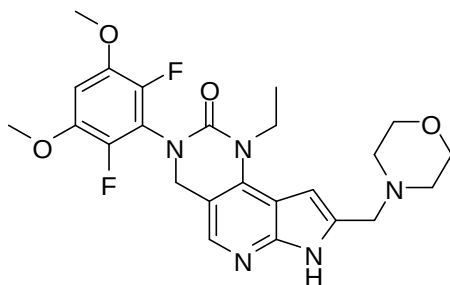


WHAT IS CLAIMED IS:

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



Compound 1

~~in the manufacture of a medicament for the treatment of cholangiocarcinoma, and wherein the medicament is to be administered to a patient a daily dose of about 5 mg to about 20 mg. wherein the solid form has crystalline Form I.~~

2. ~~The solid form of claim 1, having one or more characteristic X-ray powder diffraction ("XRPD") peaks selected from about 6.8, about 12.9, about 25.4, about 25.8, about 26.2 and about 27.5 degrees 2-theta.~~

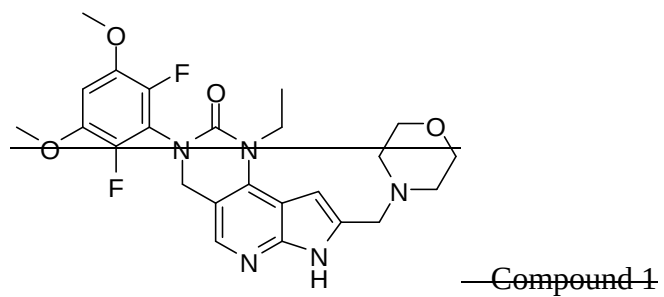
3. ~~The solid form of claim 1 or 2, having an XRPD pattern with characteristic peaks as substantially shown in Figure 1.~~

4. ~~The solid form of any one of claims 1-3, having at least one endothermic peak at a temperature of about 276 °C in a differential scanning calorimetry ("DSC") thermogram.~~

5. ~~The solid form of any one of claims 1-3, having a DSC thermogram substantially as depicted in Figure 2.~~

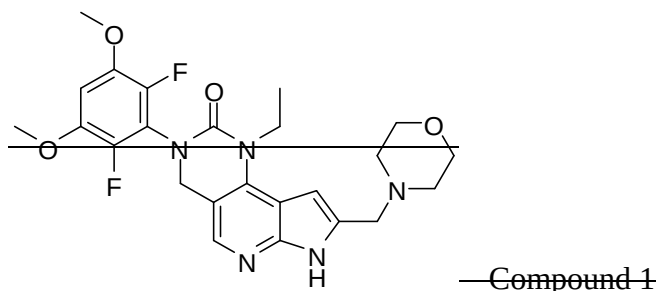
6. ~~The solid form of any one of claims 1-3, having a thermogravimetric analysis ("TGA") thermogram substantially as depicted in Figure 3.~~

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



wherein the solid form has crystalline ~~Form II, Form III, Form IV, Form V, Form VI, Form VII, Form VIII, Form IX, Form X, Form XI, Form XII, Form XIII, Form XIV, Form XV, Form XVI, Form XVII, Form XVIII, Form XIX, Form XX, Form XXI, Form XXII, Form XXIII, Form XXIV, Form XXV or Form XXVI.~~

8. — ~~A solid form of Compound 1 having the formula:~~



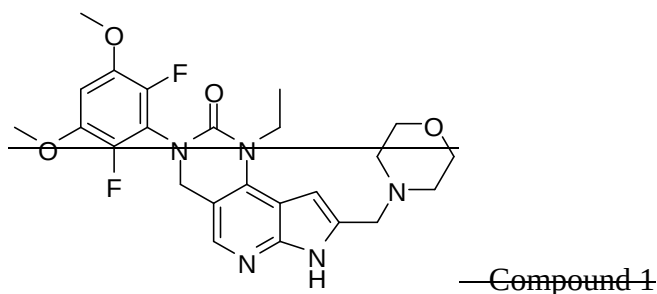
wherein the solid form is amorphous.

9. — ~~A pharmaceutical composition comprising a solid form of any one of claims 1-8, and a pharmaceutically acceptable carrier or excipient.~~

10. — ~~A method of inhibiting an FGFR enzyme comprising contacting the enzyme with a solid form of any one of claims 1-8, or a composition of claim 9.~~

11. — ~~A method of treating cancer in a patient comprising the patient in need thereof, a therapeutically effective amount of a solid form of any one of claims 1-8, or a composition of claim 9.~~

12. — ~~A process for preparing Form I of Compound 1, having the formula~~



comprising crystallizing Compound 1 from a solvent.

13. — The process of claim 12, wherein the solvent is a mixture of dichloromethane and methyl t-butyl ether.

14. — The process of claim 12, wherein the crystallizing comprises a) heating a solution of Compound 1 in the solvent to an elevated temperature for a first period of time and b) cooling to a reduced temperature for a second period of time.

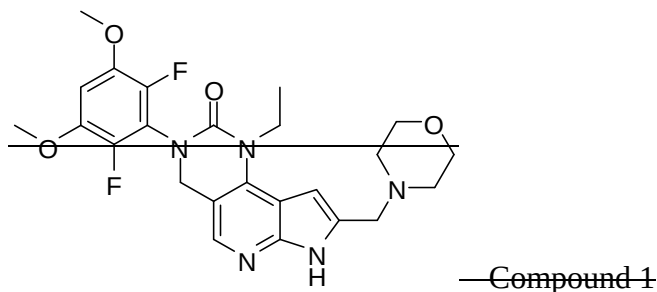
15. — The process of claim 14, wherein the elevated temperature is $\geq 35^{\circ}\text{C}$.

16. — The process of claim 14, wherein the first period of time is greater than 5 h.

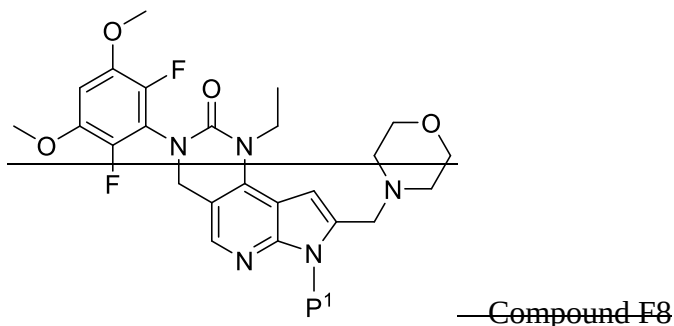
17. — The process of claim 14, wherein the reduced temperature is about 23°C .

18. — The process of claim 14, wherein the second period of time is greater than 10 h.

19. — A process for preparing Compound 1 having the formula



comprising: a) deprotecting compound F8 having the formula:



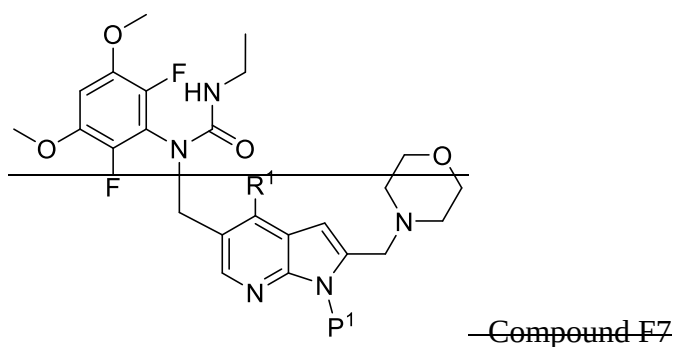
with a base to afford Compound 1, wherein P¹ is an amino protecting group.

20. The process of claim 19, wherein P¹ of Compound F8 is phenylsulphonyl.

21. ~~The process of claim 19 or 20, wherein the base in step a) is aqueous NaOH.~~

22. ~~The process of any one of claims 19-21, wherein the deprotecting in step a) is carried out in a solvent comprising 1,4-dioxane.~~

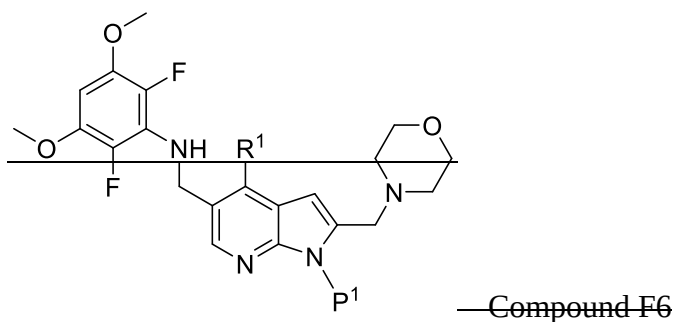
23. ~~The process of any one of claims 19-22, wherein Compound F8 is produced by a process comprising b) reacting Compound F7 having the formula:~~



~~with a base, wherein P¹ is an amino protecting group and R¹ is Cl, Br or I.~~

24. ~~The process of claim 23, wherein the base in step b) is lithium hexamethyldisilazide.~~

25. ~~The process of claim 23 or 24, wherein compound F7 is produced by a process comprising c) reacting Compound F6 having the formula:~~



~~wherein P¹ is an amino protecting group and R¹ is Cl, Br or I;~~

~~with ethyl isocyanate.~~

26. ~~The process of claim 25, wherein the reacting in step c) is carried out in the presence of an acid.~~

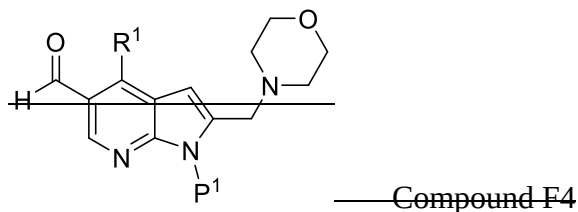
27. ~~The process of claim 26, wherein the acid in step c) is methanesulfonic acid.~~

28. — The process of any of claims 25-27, further comprising purifying Compound F7.

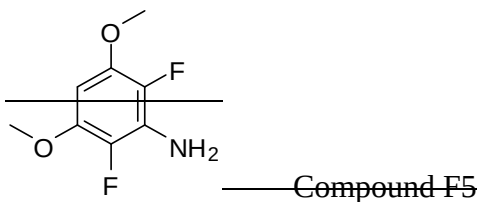
29. — The process of claim 28, wherein the purifying comprises mixing compound F7 with a first organic solvent at an elevated temperature to produce a first mixture; filtering the first mixture to produce a first solid; mixing the first solid with water to produce a second mixture; filtering the second mixture to produce a second solid; and mixing the second solid with a second organic solvent.

30. — The process of claim 29, wherein the first organic solvent comprises acetonitrile and the second organic solvent comprises heptane.

31. — The process of any one of claims 25-30, wherein compound F6 is produced by a process comprising d) reacting compound F4 having the formula:



with compound F5 having the formula:

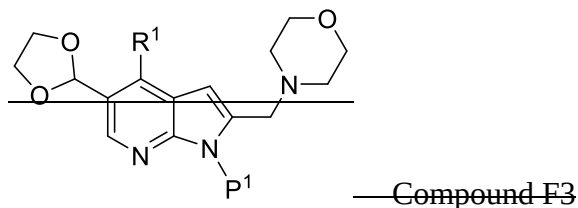


in the presence of a Lewis acid and a reducing agent, wherein P¹ is an amino protecting group and R² is Cl, Br or I.

32. — The process of claim 31, wherein the Lewis acid in step d) is chlorotrimethylsilane.

33. — The process of claim 31, wherein the reducing agent in step d) is BH₃-THF.

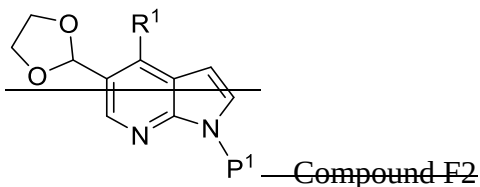
34. — The process of any one of claims 31–33, wherein compound F4 is produced by a process comprising e) reacting compound F3 having the formula:



with an acid, wherein P¹ is an amino protecting group.

35. — The process of claim 34, wherein the acid in step e) is HCl.

36. — The process of claim 34 or 35, wherein compound F3 is prepared by a process comprising f) reacting compound F2 having the formula:



with N-formylmorpholine in the presence of base to form a mixture; and contacting the mixture with morpholine and an acid in the presence of a reducing agent.

37. — The process of claim 36, wherein the base in step f) is lithium diisopropylamide.

38. — The process of claim 36 or 37, wherein the acid in step f) is acetic acid.

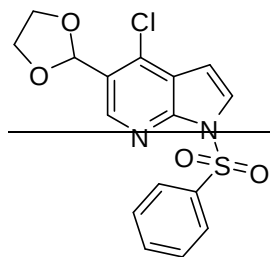
39. — The process of any one of claims 36–38, wherein the reducing agent in step f) is sodium triacetoxyborohydride.

40. — The process of any one of claims 19–39, wherein P¹ of Compound F2 is benzenesulfonyl.

41. — The process of any one of claims 19–40, wherein R¹ is Cl.

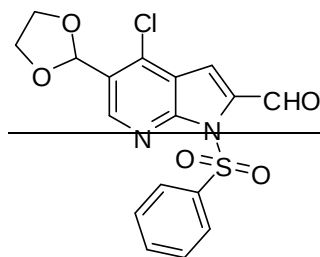
42. A process for preparing Compound 1 comprising:

a) contacting Compound 2 having the formula:



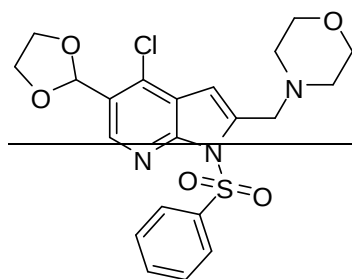
Compound 2

with N-formylmorpholine in the presence of a base to form Compound 2a having the formula:



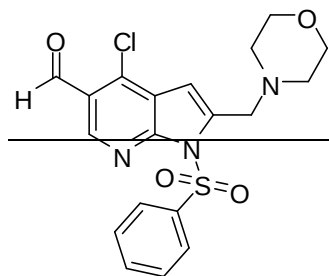
Compound 2a;

b) reacting Compound 2a with morpholine in the presence of an acid and a reducing agent to form Compound 3 having the formula:



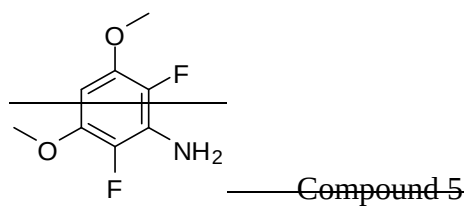
Compound 3;

c) converting Compound 3 to Compound 4 having the formula:

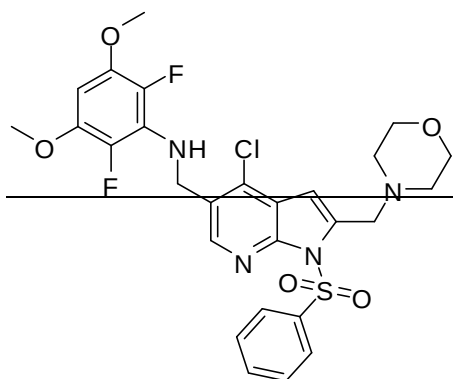


Compound 4;

d) reacting Compound 4 with Compound 5 having the formula:

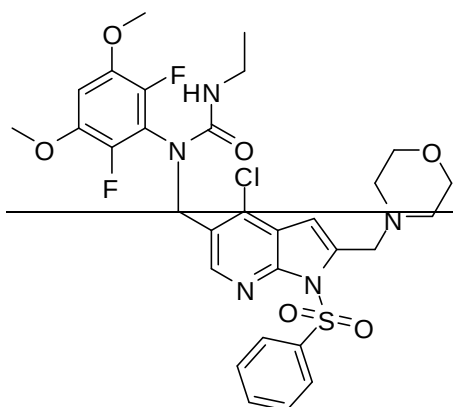


in the presence of a Lewis acid and a reducing agent to form Compound 6 having the formula:



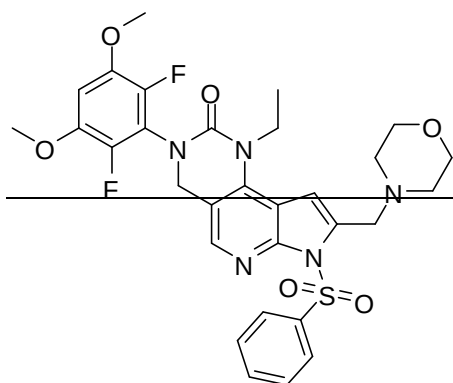
—Compound 6;

—e) reacting Compound 6 with ethyl isocyanate to form Compound 7 having the formula:



—Compound 7

—f) contacting Compound 7 with a base to form Compound 8 having the formula:



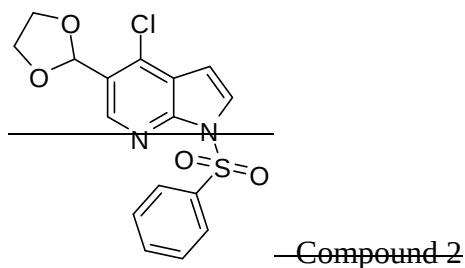
—Compound 8

and,

—g) contacting Compound 8 with a base.

43. —The process of claim 42, further comprising recrystallizing Compound 1 in a solvent to produce Form I of Compound 1.

44. — The process of claim 42 or 43, wherein the base in step a) is lithium diisopropylamide.
45. — The process of any one of claims 42-44, wherein the acid in step b) is acetic acid and the reducing agent is sodium triacetoxyborohydride.
46. — The process of any one of claims 42-45, wherein the converting in step c) is carried out in the presence of aqueous hydrochloric acid.
47. — The process of any one of claims 42-46, wherein in step d) the Lewis acid is chlorotrimethylsilane and the reducing agent is $\text{BH}_3\text{-THF}$.
48. — The process of any one of claims 42-47, wherein the reacting in step e) further comprises purifying Compound 7.
49. — The process of any one of claims 42-48, wherein the base in step f) is lithium hexamethyldisilazide.
50. — The process of any one of claims 42-49, wherein the base in step g) is NaOH .
51. — A process for preparing Compound 2 having the formula:



comprising:

- a) — contacting 1H-pyrrolo[2,3-b]pyridine with an oxidizing agent to form 1H-pyrrolo[2,3-b]pyridine 7-oxide;
- b) reacting 1H-pyrrolo[2,3-b]pyridine 7-oxide with a chlorination agent to form 4-chloro-1H-pyrrolo[2,3-b]pyridine;

- e) reacting 4-chloro-1H-pyrrolo[2,3-b]pyridine with triisopropylsilyl chloride to form 4-chloro-1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridine;
- d) reacting 4-chloro-1-(triisopropylsilyl)-1H-pyrrolo[2,3-b]pyridine with N,N-dimethylformamide in the presence of a base to form 4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carbaldehyde;
- e) reacting 4-chloro-1H-pyrrolo[2,3-b]pyridine-5-carbaldehyde with benzenesulfonyl chloride in the presence of a base to form 4-chloro-1-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine-5-carbaldehyde; and
- f) reacting 4-chloro-1-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine-5-carbaldehyde with ethylene glycol in the presence of an acid to produce Compound 2.

52. — The process of claim 51, wherein the oxidizing agent in step a) is m-chloroperoxybenzoic acid.

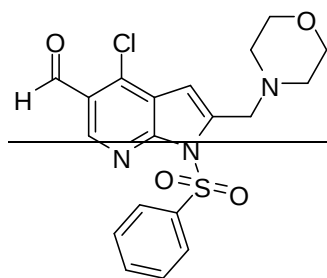
53. — The process of claim 51 or 52, wherein the chlorination agent in step b) is methanesulfonyl chloride.

54. — The process of any one of claims 51-53, wherein the base in step d) is s-BuLi.

55. — The process of any one of claim 51-54, wherein the base in step e) is cesium carbonate.

56. — The process of any one of claims 51-55, wherein the acid in step f) is p-toluenesulfonic acid.

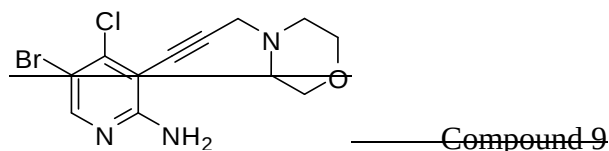
57. — A process for preparing Compound 4 having the formula:



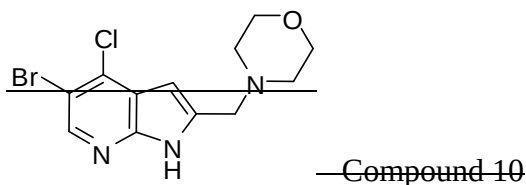
— Compound 4

comprising:

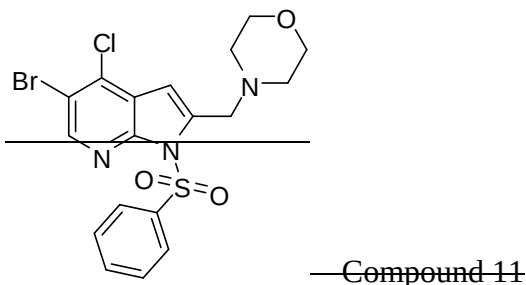
- a) ~~contacting 2-amino-4-chloropyridine with a bromination agent to form 5-bromo-4-chloropyridin-2-amine;~~
- b) ~~contacting 5-bromo-4-chloropyridin-2-amine with an iodination agent to form 5-bromo-4-chloro-3-iodopyridin-2-amine;~~
- c) ~~reacting 5-bromo-4-chloro-3-iodopyridin-2-amine with 4-(prop-2-ynyl)morpholine in the presence of a catalyst to form Compound 9 having the formula:~~



- d) ~~reacting Compound 9 with a base to form Compound 10 having the formula:~~



- e) ~~reacting compound 10 with benzenesulfonyl chloride in the presence of a base to form compound 11 having the formula:~~



- f) ~~contacting compound 11 with an alkyl-magnesium halide agent to form a mixture and adding N,N-dimethylformamide to the mixture to produce Compound 4.~~

58. ~~The process of claim 57, wherein the bromination agent in step a) is N-bromosuccinimide.~~

59. ~~The process of claim 57 or 58, wherein the iodination agent in step b) is iodine.~~

60. ~~The process of any one of claims 57-59, wherein step b) is carried out in the presence of sulfuric acid and periodic acid.~~

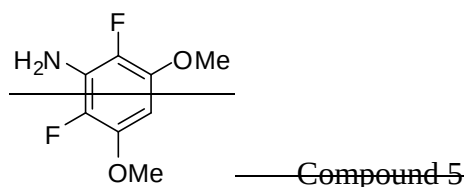
61. — The process of any one of claims 57-60, wherein the catalyst in step c) is a combination of CuI and Pd(PPh₃)₄.

62. — The process of any one of claims 57-61, wherein the base in step d) is KOtBu.

63. — The process of any one of claims 57-62, wherein the base in step e) is NaH.

64. — The process of any one of claims 57-63, wherein the alkyl magnesium halide agent in step f) is isopropylmagnesium chloride.

65. — A process for preparing Compound 5 having the formula:

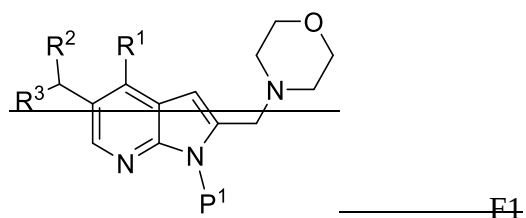


comprising:

- a) contacting pentafluorobenzoic acid with an alkyl alcohol in the presence of an acid to form methyl pentafluorobenzoate;
- b) reacting pentafluorobenzoate with benzylamine in the presence of base to form methyl 4-(benzylamino)-2,3,5,6-tetrafluorobenzoate;
- c) contacting methyl 4-(benzylamino)-2,3,5,6-tetrafluorobenzoate with sodium methoxide to form a mixture; adding water to the mixture to generate 4-(benzylamino)-3,5-difluoro-2,6-dimethoxybenzoic acid;
- d) heating 4-(benzylamino)-3,5-difluoro-2,6-dimethoxybenzoic acid to generate N-benzyl-2,6-difluoro-3,5-dimethoxyaniline; and
- e) reacting N-benzyl-2,6-difluoro-3,5-dimethoxyaniline with ammonium formate in the presence of palladium on carbon to form Compound 5.

66. — The process of claim 65, wherein the alkyl alcohol in step a) is methanol, and the base in step b) is N,N-diisopropylamine.

67. — A compound of Formula F1:



or a salt thereof, wherein:

P^1 is an amino-protecting group;

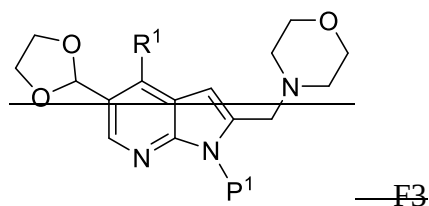
R^1 is Cl, Br or I;

R^2 and R^3 are each independently C_{1-6} -alkoxy; or

R^2 and R^3 taken together with the carbon atom to which they are attached form 1,3-dioxolan-2-yl or 1,3-dioxan-2-yl; or

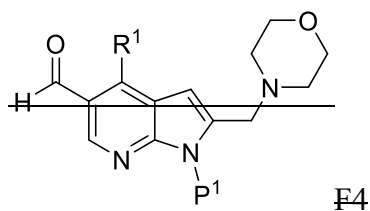
R^2 and R^3 taken together form oxo.

68. — The compound of claim 67, having Formula F3:



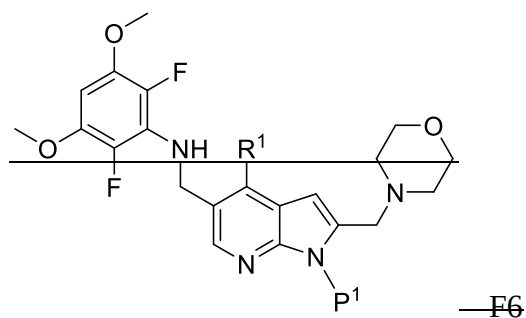
or a salt thereof.

69. — The compound of claim 67, having Formula F4:



or a salt thereof.

70. — A compound having Formula F6:

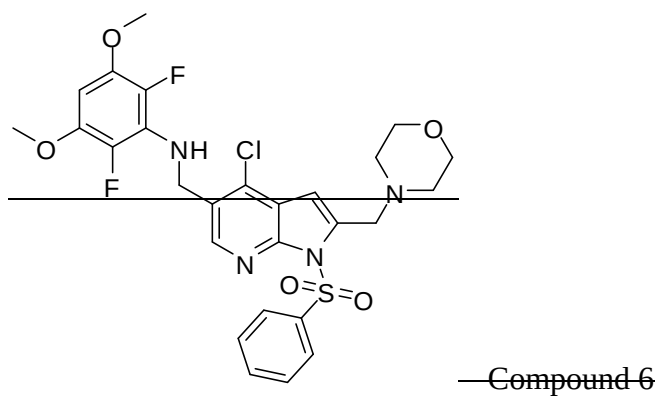


or a salt thereof, wherein:

P^1 is an amino protecting group;

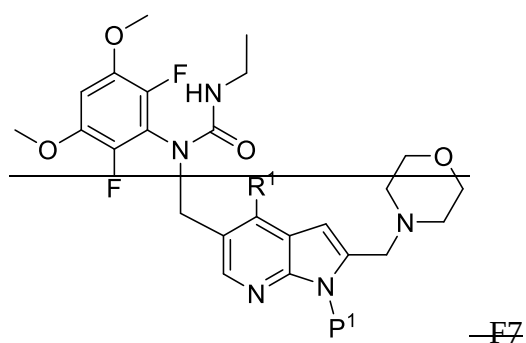
R^1 is Cl, Br or I.

71. — The compound of claim 70, having the formula:



or a salt thereof.

72. — A compound having Formula F7:

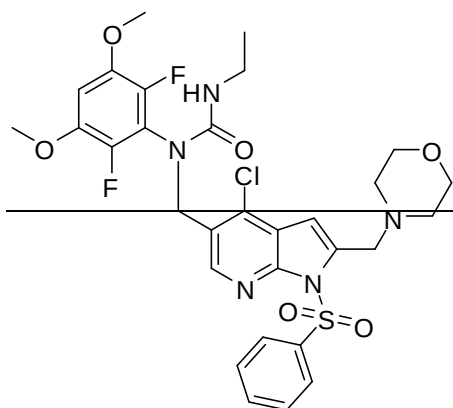


or a salt thereof, wherein:

P^1 is an amino protecting group;

R^1 is Cl, Br or I.

73. — The compound of claim 72, having the formula:

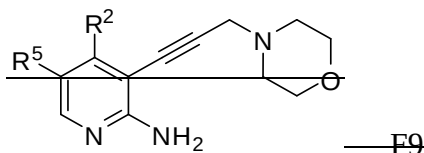


—Compound 7

or a salt thereof.

74. — The compound of any one of claims 67-70 and 72, or a salt thereof, wherein R^1 is Cl.

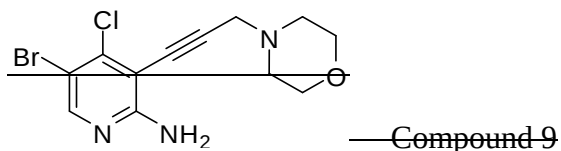
75. — A compound of Formula F9:



—F9

or a salt thereof, wherein R^2 and R^5 are each independently Br, Cl or I.

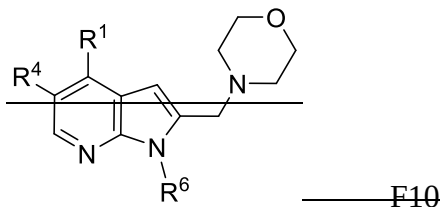
76. — The compound of claim 75, having the formula:



—Compound 9

or a salt thereof.

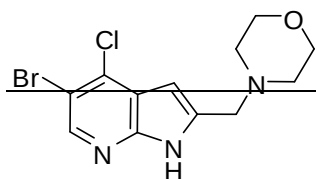
77. — A compound of Formula F10:



—F10

or a salt thereof, wherein R^1 and R^4 are each independently Br, Cl or I; and R^6 is H or benzenesulfonyl.

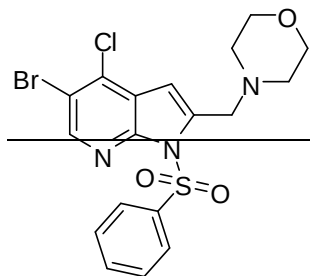
78. ~~The compound of claim 77, having the formula:~~



~~Compound 10~~

or a salt thereof.

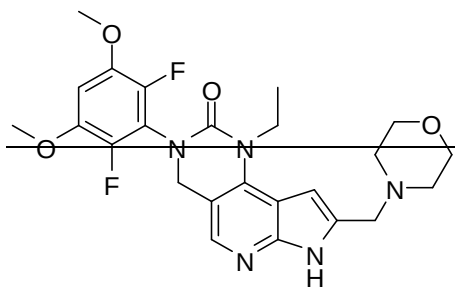
79. ~~The compound of claim 77, having the formula:~~



~~Compound 11~~

or a salt thereof.

80. ~~A method of treating cholangiocarcinoma in a patient in need thereof comprising administering to the patient a therapeutically effective amount of Compound 1 having the formula:~~



~~Compound 1.~~

812. ~~The method use~~ of claim 801, wherein the cholangiocarcinoma is advanced or metastatic cholangiocarcinoma.

823. ~~The method use~~ of claim 801, wherein the cholangiocarcinoma is surgically unresectable.

834. ~~The method use~~ of claim 801, wherein the cholangiocarcinoma is intrahepatic.

845. ~~The method~~use of claim 801, wherein the cholangiocarcinoma is extrahepatic.

856. ~~The method use~~ of claim 801, wherein the cholangiocarcinoma is hilar or perihilar.

867. ~~The method use~~ of claim 801, wherein the cholangiocarcinoma is distal extrahepatic.

878. ~~The method use of any one of claims claim~~ 801-86, wherein the cholangiocarcinoma is characterized by FGF/FGFR genetically altered tumors.

889. ~~The method use~~ of claim 878, wherein the tumor exhibits FGFR2 translocations.

8910. ~~The method use~~ of claim 889, wherein the FGFR2 translocation is selected from the group consisting of FGFR2-BICC1, FGFR2-AHCYL1, FGFR2-MACF1, and FGFR2 intron 17 rearrangement.

9011. ~~The method use~~ of claim 878, wherein the tumor exhibits FGF/FGFR alterations other than FGFR2 translocations.

9112.— ~~The method use of any one of claims claim~~ 801-86, wherein the cholangiocarcinoma does not exhibit FGF/FGFR genetically altered tumors.

9213. ~~The method use of any one of claims claim~~ 801-91, wherein the patient has failed at least one previous treatment.

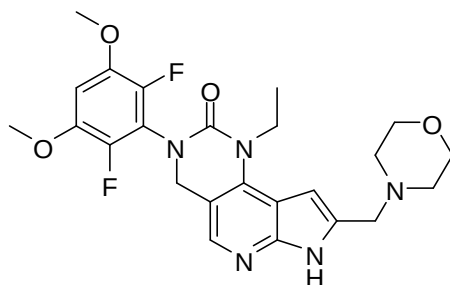
93.—14. ~~The method use~~ of claim 9213, wherein the previous treatment is surgery or radiation therapy.

94.—15. ~~The method use of any one of claims claim~~ 801-93, wherein the patient has a history of hepatitis.

95.—16. ~~The method use~~ of claim 9415, wherein the hepatitis is chronic hepatitis B or hepatitis C.

96. ~~The method of any one of claims 80-95, wherein Compound 1 is administered orally.~~

97. ~~The method of any one of claims 80-96,~~ 21. Use of Compound 1 having the formula:



Compound 1.

in the manufacture of a medicament for the treatment of cholangiocarcinoma, wherein the medicament is to be ~~wherein Compound 1 is administered once daily~~ as a tablet, and wherein the tablet comprises about 0.5 to about 10 mg of Compound 1.

98.—~~The method of any one of claims 80-96, wherein Compound 1 is administered in a daily dose of about 5 mg to about 20 mg.~~

99.—~~The method of any one of claims 80-96~~¹²⁵¹⁷. ~~The method~~ use of claim 801, wherein ~~Compound 1~~ the medicament is to be administered in a daily dose of about 10 mg to about 15 mg.

100.—~~18. The method use of any one of claims~~^{claim 801}-96, wherein the medicament ~~Compound 1~~ is to be administered in a daily dose of about 13.5 mg.

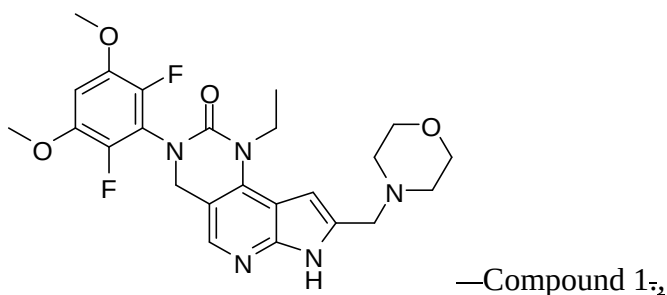
101.—~~19. The method use of any one of claims~~^{claim 801}-100, wherein the medicament ~~Compound 1~~ is to be administered as a tablet.

102.—~~The method of claim 101, wherein the tablet comprises about 1 mg to about 10 mg of Compound 1.~~

103.—~~The method of claim 101, wherein the tablet comprises about 1 mg to about 5 mg of Compound 1.~~

104.—~~The method of claim 101, wherein the tablet comprises about 2 mg or about 4.5 mg of Compound 1.~~

105.—~~38. Use A method of treating myeloid/lymphoid neoplasms in a patient in need thereof comprising administering to the patient a therapeutically effective amount of Compound 1 having the formula:~~



106.in the manufacture of a medicament for the treatment of cholangiocarcinoma, wherein the medicament is to be administered to a patient in a 21-day dosing regimen, wherein the 21-day dosing regimen comprises:

- (a) a first period wherein the medicament is to be administered once daily for 14 days;
- and
- (b) a second period wherein the medicament is not to be administered for 7 days.

20. The method-use of claim 1051, wherein the myeloid-lymphoid neoplasm the medicament is 8p11 myeloproliferative syndrome to be administered in a daily dose of about 9 mg.

107. The method of claim 105, wherein the myeloid/lymphoid neoplasm is associated with eosinophilia.

108. 22. The method-use of claim 10521, wherein the myeloid/lymphoid neoplasm tablet comprises about 0.5 mg to about 5 mg of Compound 1.

23. The use of claim 21, wherein the tablet comprises about 9 mg of Compound 1.

24. The use of claim 21, wherein the tablet comprises about 4.5 mg of Compound 1.

25. The use of claim 21, wherein the cholangiocarcinoma is advanced or metastatic cholangiocarcinoma.

26. The use of claim 21, wherein the cholangiocarcinoma is surgically unresectable.

27. The use of claim 21, wherein the cholangiocarcinoma is intrahepatic.

28. The use of claim 21, wherein the cholangiocarcinoma is extrahepatic.

29. The use of claim 21, wherein the cholangiocarcinoma is hilar or perihilar.

30. The use of claim 21, wherein the cholangiocarcinoma is distal extrahepatic.

31. The use of claim 21, wherein the cholangiocarcinoma is characterized by FGF/FGFR genetically altered tumors.

32. The use of claim 31, wherein the tumor exhibits an 8p11-FGFR2 translocations.

33. The use of claim 32, wherein the FGFR2 translocation is selected from the group consisting of FGFR2-BICC1, FGFR2-AHCYL1, FGFR2-MACF1, and FGFR2 intron 17 rearrangement.

10934. The method use of claim 10831, wherein the 8p11 translocation is associated with activation of FGFR1. tumor exhibits FGF/FGFR alterations other than FGFR2 translocations.

11035. The method use of any one of claims 105-109 claim 21, wherein Compound 1 is administered orally. the cholangiocarcinoma does not exhibit FGF/FGFR genetically altered tumors.

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36. The method use of any one of claims 105-110 claim 21, wherein Compound 1 is administered once daily. the patient has failed at least one previous treatment.

11237. The method use of any one claim 36, wherein the previous treatment is surgery or radiation therapy.

39. The use of claims 105-111 claim 38, wherein the medicament Compound 1 is to be administered in a daily dose of about 5 mg to about 20 mg during the first period.

113. 40. The method use of any one of claims 105-111 claim 38, wherein Compound 1 the medicament is to be administered in a daily dose of about 10 mg to about 15 mg. during the first period.

114. 41. The method use of any one of claims 105-111 claim 38, wherein Compound 1 the medicament is to be administered in a daily dose of about 13.5 mg during the first period.

115. 42. The method used of any one claim 38, wherein the medicament is to be administered in a daily dose of claims 105-114 about 9 mg during the first period.

~~150~~43. The use of claim 38, wherein ~~Compound 1~~the medicament is to be administered as a tablet during the first period.

~~116.~~—44. The ~~method~~use of claim ~~115~~43, wherein the tablet comprises about ~~10.5~~ mg to about 10 mg of Compound 1.

~~117.~~—45. The ~~method~~use of claim ~~115~~43, wherein the tablet comprises about ~~10.5~~ mg to about 5 mg of Compound 1.

~~118.~~—46. The ~~method~~use of claim ~~115~~43, wherein the tablet comprises about ~~29~~ mg ~~or of~~ Compound 1.

47. The use of claim 43, wherein the tablet comprises about 4.5 mg of Compound 1.

~~119. A method of increasing survival~~
48. The use of claim 38, wherein the cholangiocarcinoma is advanced or metastatic cholangiocarcinoma.

49. The use of claim 38, wherein the cholangiocarcinoma is surgically unresectable.

50. The use of claim 38, wherein the cholangiocarcinoma is intrahepatic.

51. The use of claim 38, wherein the cholangiocarcinoma is extrahepatic.

52. The use of claim 38, wherein the cholangiocarcinoma is hilar or ~~progression-free survival in a patient that has~~perihilar.

53. The use of claim 38, wherein the cholangiocarcinoma is distal extrahepatic.

54. The use of claim 38, wherein the cholangiocarcinoma is characterized by ~~an~~FGF/FGFR genetically altered tumors.

55. The use of claim 54, wherein the tumor exhibits FGFR2 fusion, ~~comprising administering Compound 1 to the patient.~~translocations.

56. The use of claim 55, wherein the FGFR2 translocation is selected from the group consisting of FGFR2-BICC1, FGFR2-AHCYL1, FGFR2-MACF1, and FGFR2 intron 17 rearrangement.

57. The use of claim ~~161~~54, wherein the tumor exhibits FGF/FGFR alterations other than FGFR2 translocations.

58. The use of claim ~~128~~38, wherein the cholangiocarcinoma does not exhibit FGF/FGFR genetically altered tumors.

59. The use of claim 42838, wherein the patient has failed at least one previous treatment.

60. The use of claim 46659, wherein the previous treatment is surgery or radiation therapy.