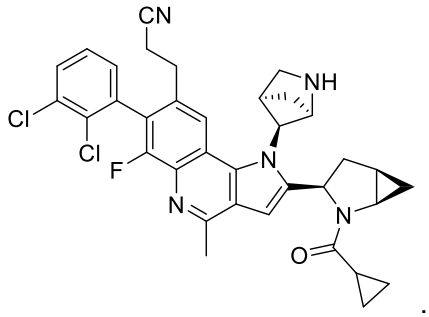
mutant KRAS is required for early tumor onset and maintenance in animal models (A. D. Cox, *et al. Nat. Rev. Drug. Discov.*, **2014**, *13(11)*, 828-51).

Taken together, these findings indicate that KRAS mutations play a critical role in human cancers. Development of inhibitors targeting KRAS, including mutant KRAS, will therefore be useful in the clinical treatment of diseases that are characterized by involvement of KRAS, including diseases characterized by the involvement or presence of a KRAS mutation.

SUMMARY

Provided herein are crystalline forms, salts, and crystalline salt forms, of 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile having the following structure:



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This compound, referred to herein as “Compound 1,” is a KRAS inhibitor, particularly of KRAS having a G12D mutation, that can be used for the treatment of various cancers and other diseases.

In one aspect, provided herein is a compound that is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile, or a pharmaceutically acceptable salt thereof, wherein the compound is crystalline.

In another aspect, provided herein is a pharmaceutical composition comprising:

a) the compound or pharmaceutically acceptable salt thereof as described herein;

b) a disintegrant;

c) a binder;

d) an anti-caking agent; and

e) a lubricant.

In another aspect, provided herein is a pharmaceutical composition comprising:

a) the compound or pharmaceutically acceptable salt thereof as described herein;

b) sodium starch glycolate;

c) MCC PH102;

d) colloidal silicon dioxide;

e) sodium stearyl fumarate; and

f) magnesium stearate.

In another aspect, provided herein is a dosage form comprising the compound or pharmaceutically acceptable salt thereof as described herein or the pharmaceutical composition as described herein.

In another aspect, provided herein is use of the compound or pharmaceutically acceptable salt thereof as described herein, the pharmaceutical composition as described herein, or the dosage form of as described herein, in the manufacture of a medicament for treating cancer.

In another aspect, provided herein is use of the compound or pharmaceutically acceptable salt thereof as described herein, the pharmaceutical composition as described herein, or the dosage form of as described herein, in the manufacture of a medicament for treating cancer, wherein the use comprises identifying that a subject is in need of treatment of a cancer and that abnormally proliferating cells of the cancer comprise KRAS having a G12D mutation.

In another aspect, provided herein is the compound or pharmaceutically acceptable salt thereof as described herein, the pharmaceutical composition as described herein, or the dosage form of as described herein, for use in therapy.

In another aspect, provided herein is a process for preparing 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate comprising reacting 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile with aqueous hydrochloric acid.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows the XRPD diffractogram of Compound 1 hydrochloride dihydrate (Form I).

Figure 2 shows the DSC thermogram of Compound 1 hydrochloride dihydrate (Form I).

Figure 3 shows the TGA thermogram of Compound 1 hydrochloride dihydrate (Form I).

Figure 4 shows the XRPD diffractogram of Compound 1 dihydrochloride.

Figure 5 shows the DSC thermogram of Compound 1 dihydrochloride.

Figure 6 shows the TGA thermogram of Compound 1 dihydrochloride.

Figure 7 shows the XRPD diffractogram of Compound 1 fumarate.

Figure 8 shows the DSC thermogram of Compound 1 fumarate.

Figure 9 shows the TGA thermogram of Compound 1 fumarate.

Figure 10 shows the XRPD diffractogram of Compound 1 L-tartrate.

CLAIMS

What is claimed is:

1. A compound that is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile, or a pharmaceutically acceptable salt thereof, wherein the compound is crystalline.

2. The compound or pharmaceutically acceptable salt thereof of claim 1, which is a pharmaceutically acceptable salt.

3. The compound or pharmaceutically acceptable salt thereof of claim 2, wherein the pharmaceutically acceptable salt is selected from the group consisting of hydrochloride, di-hydrochloride, fumarate, L-tartrate, adipate, and phosphate salts.

4. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, which is a solvate.

5. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, which is a hydrate.

6. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride.

7. The compound or pharmaceutically acceptable salt thereof claim 6, which is a solvate.

8. The compound or pharmaceutically acceptable salt thereof of claim 6 or 7, which is a hydrate.

9. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 8, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate.

10. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form I.

11. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 10, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.8, 13.5, 17.2, 19.2, 20.5, 22.8, 23.1, 23.5, and 26.0.

12. The compound or pharmaceutically acceptable salt thereof of claim 10, which is characterized by an XRPD diffractogram having at least three (or at least four, five, six, seven, eight, nine, or all) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.8, 13.5, 17.2, 19.2, 20.5, 22.8, 23.1, 23.5, and 26.0.

13. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 10, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.8, and 13.5.

13. The compound or pharmaceutically acceptable salt thereof of any one of claims any one of claims 6 to 10, which is characterized by an XRPD diffractogram having at least six of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 55.7, 7.8, 13.5, 17.2, 19.2, 20.5, 22.8, 23.1, 23.5, and 26.0.

14. The compound or pharmaceutically acceptable salt thereof of claim 10, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.8, 13.5, 17.2, 19.2, and 23.1.

15. The compound or pharmaceutically acceptable salt thereof of any one of claims any one of claims 6 to 10, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.8, 13.5, 17.2, 19.2, 20.5, 22.8, 23.1, 23.5, and 26.0.

16. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 15, which is characterized by an XRPD diffractogram substantially as depicted in Figure 1.

17. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 16, which has a DSC thermogram characterized by an exotherm having a peak at about 271 °C.

18. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 17, which has a DSC thermogram characterized by an exotherm having an onset at about 265 °C.

19. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 18, which has a DSC thermogram substantially as depicted in Figure 2.

20 The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 19, which has a TGA thermogram substantially as depicted in Figure 3.

21. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, comprising crystals that are monoclinic.

22. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9 and 21, comprising crystals wherein the space group is $P2_1$.

23. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9 and 21, comprising crystals having cell parameters of substantially a = 13.8490(4) Å, b = 8.0204(2) Å, c = 15.5461(4) Å, α = 90°, β = 100.617(3)°, γ = 90°, and/or V = 1697.21(8) Å^3.

24. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9 and 21, comprising crystals having cell parameters substantially as shown in Table A.

25. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form II.

26. The compound or pharmaceutically acceptable salt thereof of claim 25, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.8, 7.6, 11.4, 12.5, 14.4, 17.9, and 25.3.

27. The compound or pharmaceutically acceptable salt thereof of claim 25, which is characterized by an XRPD diffractogram having at least three (or at least four, five, six, or all) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.8, 7.6, 11.4, 12.5, 14.4, 17.9, and 25.3.

28. The compound or pharmaceutically acceptable salt thereof of claim 27, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 7.6, 12.5, and 17.9.

29. The compound or pharmaceutically acceptable salt thereof of claim 25, which is characterized by an XRPD diffractogram having at least six of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 55.8, 7.6, 11.4, 12.5, 14.4, 17.9, and 25.3.

30. The compound or pharmaceutically acceptable salt thereof of claim 29, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.8, 7.6, 11.4, 12.5, 14.4, 17.9, and 25.3.

31. The compound or pharmaceutically acceptable salt thereof of any one of claims 25 to 30, which is characterized by an XRPD diffractogram substantially as depicted in Figure 22.

32. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form III.

33. The compound or pharmaceutically acceptable salt thereof of claim 32, which is characterized by an XRPD diffractogram substantially as depicted in Figure 23.

34. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form IV.

35. The compound or pharmaceutically acceptable salt thereof of claim 34, which is characterized by an XRPD diffractogram substantially as depicted in Figure 24.

36. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form V.

37. The compound or pharmaceutically acceptable salt thereof of claim 36, which is characterized by an XRPD diffractogram substantially as depicted in Figure 25.

38. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form VI.

39. The compound or pharmaceutically acceptable salt thereof of claim 38, which is characterized by an XRPD diffractogram substantially as depicted in Figure 26.

40. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form VII.

41. The compound or pharmaceutically acceptable salt thereof of claim 40, which is characterized by an XRPD diffractogram substantially as depicted in Figure 27.

42. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form VIII.

43. The compound or pharmaceutically acceptable salt thereof of claim 42, which is characterized by an XRPD diffractogram substantially as depicted in Figure 28.

44. The compound or pharmaceutically acceptable salt thereof of any one of claims 6 to 9, which is Form IX.

45. The compound or pharmaceutically acceptable salt thereof of claim 44, which is characterized by an XRPD diffractogram substantially as depicted in Figure 29.

46. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile dihydrochloride.

47. The compound or pharmaceutically acceptable salt thereof of claim 46, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.6, 5.9, 10.7, 12.0, 12.8, 13.2, 15.6, 15.9, 18.5, 20.1, 22.1, and 23.9.

48. The compound or pharmaceutically acceptable salt thereof of claim 46, which is characterized by an XRPD diffractogram having at least three (or four, five, six, seven, eight, nine, ten, eleven, or all) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.6, 5.9, 10.7, 12.0, 12.8, 13.2, 15.6, 15.9, 18.5, 20.1, 22.1, and 23.9.

49. The compound or pharmaceutically acceptable salt thereof of claim 48, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.6, 5.9, and 22.1.

50. The compound or pharmaceutically acceptable salt thereof of claim 46, which is characterized by an XRPD diffractogram having at least seven peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.6, 5.9, 10.7, 12.0, 12.8, 13.2, 15.6, 15.9, 18.5, 20.1, 22.1, and 23.9.

51. The compound or pharmaceutically acceptable salt thereof of claim 50, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.6, 5.9, 10.7, 13.2, 18.5, 22.1, and 23.9.

52. The compound or pharmaceutically acceptable salt thereof of claim 48, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at

angles (± 0.2 degrees) of 5.6, 5.9, 10.7, 12.0, 12.8, 13.2, 15.6, 15.9, 18.5, 20.1, 22.1, and 23.9.

53. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 46 to 52, which is characterized by an XRPD diffractogram substantially as depicted in Figure 4.

54. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 46 to 53, which has a DSC thermogram characterized by an exotherm having a peak at about 267 °C.

55. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 46 to 54, which has a DSC thermogram characterized by an exotherm having an onset at about 256 °C.

56. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 46 to 55, which has a DSC thermogram substantially as depicted in Figure 5.

57. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 46 to 56, which has a TGA thermogram substantially as depicted in Figure 6.

58. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile fumarate.

59. The compound or pharmaceutically acceptable salt thereof of claim 58, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 12.9, 15.1, 17.3, 17.7, 19.8, 20.0, 20.8, 22.0, and 23.7.

60. The compound or pharmaceutically acceptable salt thereof of claim 58, which is characterized by an XRPD diffractogram having at least three (or four, five, six, seven, eight, or all) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 12.9, 15.1, 17.3, 17.7, 19.8, 20.0, 20.8, 22.0, and 23.7.

61. The compound or pharmaceutically acceptable salt thereof of claim 60, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 12.9, 17.7, and 23.7.

62. The compound or pharmaceutically acceptable salt thereof of claim 58, which is characterized by an XRPD diffractogram having at least six peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 12.9, 15.1, 17.3, 17.7, 19.8, 20.0, 20.8, 22.0, and 23.7.

63. The compound or pharmaceutically acceptable salt thereof of claim 62, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 12.9, 15.1, 17.7, 20.0, 22.0, and 23.7.

64. The compound or pharmaceutically acceptable salt thereof of claim 58, which is characterized by an XRPD diffractogram having at least nine peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 12.9, 15.1, 17.3, 17.7, 19.8, 20.0, 20.8, 22.0, and 23.7.

65. The compound or pharmaceutically acceptable salt thereof of claim 64, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 12.9, 15.1, 17.3, 17.7, 19.8, 20.0, 20.8, 22.0, and 23.7.

66. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 58 to 65, which is characterized by an XRPD diffractogram substantially as depicted in Figure 7.

67. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 58 to 66, which has a DSC thermogram characterized by an exotherm having a peak at about 200 °C.

68. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 58 to 67, which has a DSC thermogram characterized by an exotherm having an onset at about 199 °C.

69. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 58 to 68, which has a DSC thermogram characterized by an endotherm substantially as depicted in Figure 8.

70. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 58 to 69, which has a TGA thermogram substantially as depicted in Figure 9.

71. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile L-tartrate.

72. The compound or pharmaceutically acceptable salt thereof of claim 71, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 9.3, 16.7, 18.6, 19.1, 19.4, 19.6, 22.3, 22.6, and 24.6.

73. The compound or pharmaceutically acceptable salt thereof of claim 71, which is characterized by an XRPD diffractogram having at least three (or four, five, six, seven, eight, or all) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 9.3, 16.7, 18.6, 19.1, 19.4, 19.6, 22.3, 22.6, and 24.6.

74. The compound or pharmaceutically acceptable salt thereof of claim 73, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 9.3, 18.6, and 24.6.

75. The compound or pharmaceutically acceptable salt thereof of claim 71, which is characterized by an XRPD diffractogram having at least six peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 9.3, 16.7, 18.6, 19.1, 19.4, 19.6, 22.3, 22.6, and 24.6.

76. The compound or pharmaceutically acceptable salt thereof of claim 75, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 9.3, 16.7, 18.6, 19.6, 22.3, and 24.6.

77. The compound or pharmaceutically acceptable salt thereof of claim 71, which is characterized by an XRPD diffractogram having at least nine peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 9.3, 16.7, 18.6, 19.1, 19.4, 19.6, 22.3, 22.6, and 24.6.

78. The compound or pharmaceutically acceptable salt thereof of claim 77, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 9.3, 16.7, 18.6, 19.1, 19.4, 19.6, 22.3, 22.6, and 24.6.

79. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 71 to 78, which is characterized by an XRPD diffractogram substantially as depicted in Figure 10.

80. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 71 to 79, which has a DSC thermogram characterized by an endotherm having a peak at about 208 °C.

81. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 71 to 79, which has a DSC thermogram characterized by an endotherm having an onset at about 181 °C.

82. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 71 to 80, which has a DSC thermogram characterized by an endotherm substantially as depicted in Figure 11.

83. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 71 to 82, which has a TGA thermogram substantially as depicted in Figure 12.

84. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile adipate.

85. The compound or pharmaceutically acceptable salt thereof of claim 84, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 6.3, 9.1, 10.1, 18.2, 19.2, 24.3, 34.1, and 49.8.

86. The compound or pharmaceutically acceptable salt thereof of claim 84, which is characterized by an XRPD diffractogram having at least three (or four, five, six, seven, or all) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 6.3, 9.1, 10.1, 18.2, 19.2, 24.3, 34.1, and 49.8.

87. The compound or pharmaceutically acceptable salt thereof of claim 86, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 6.3, 9.1, and 24.3.

88. The compound or pharmaceutically acceptable salt thereof of claim 84, which is characterized by an XRPD diffractogram having at least six peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 6.3, 9.1, 10.1, 18.2, 19.2, 24.3, 34.1, and 49.8.

89. The compound or pharmaceutically acceptable salt thereof of claim 88, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 6.3, 9.1, 18.2, 19.2, 34.1, and 49.8.

90. The compound or pharmaceutically acceptable salt thereof of claim 84, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 6.3, 9.1, 10.1, 18.2, 19.2, 24.3, 34.1, and 49.8.

91. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 84 to 90, which is characterized by an XRPD diffractogram substantially as depicted in Figure 13.

92. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 84 to 91, which has a DSC thermogram characterized by an endotherm having at least one peak at about 154°C, 189°C, or 199ºC.

93. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 84 to 92, which has a DSC thermogram characterized by an endotherm having an onset at about 26 °C.

94. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 84 to 93, which has a DSC thermogram characterized by an endotherm substantially as depicted in Figure 14.

95. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 84 to 94, which has a TGA thermogram substantially as depicted in Figure 15.

96. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile phosphate.

97. The compound or pharmaceutically acceptable salt thereof of claim 96, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 4.5, 13.5, 13.7, 16.5, 16.9, 18.1, 21.5, 23.5, and 24.4.

98. The compound or pharmaceutically acceptable salt thereof of claim 96, which is characterized by an XRPD diffractogram having at least three (or four, five, six, seven, eight, or all) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 4.5, 13.5, 13.7, 16.5, 16.9, 18.1, 21.5, 23.5, and 24.4.

99. The compound or pharmaceutically acceptable salt thereof of claim 98, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 4.5, 13.5, and 13.7.

100. The compound or pharmaceutically acceptable salt thereof of claim 96, which is characterized by an XRPD diffractogram having at least six peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 4.5, 13.5, 13.7, 16.5, 16.9, 18.1, 21.5, 23.5, and 24.4.

101. The compound or pharmaceutically acceptable salt thereof of claim 100, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 4.5, 13.5, 13.7, 16.5, 21.5, and 24.4.

102. The compound or pharmaceutically acceptable salt thereof of claim 96, which is characterized by an XRPD diffractogram having at least nine peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 4.5, 13.5, 13.7, 16.5, 16.9, 18.1, 21.5, 23.5, and 24.4.

103. The compound or pharmaceutically acceptable salt thereof of claim 102, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 4.5, 13.5, 13.7, 16.5, 16.9, 18.1, 21.5, 23.5, and 24.4.

104. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 96 to 103, which is characterized by an XRPD diffractogram substantially as depicted in Figure 16.

105. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 96 to 104, which has a DSC thermogram characterized by an exotherm having a peak at about 227 °C.

106. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 96 to 105, which has a DSC thermogram characterized by an exotherm having an onset at about 218 °C.

107. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 96 to 106, which has a DSC thermogram characterized by an endotherm substantially as depicted in Figure 17.

108. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 96 to 107, which has a TGA thermogram substantially as depicted in Figure 18.

109. The compound or pharmaceutically acceptable salt thereof of claim 1, which is 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile.

110. The compound or pharmaceutically acceptable salt thereof of claim 109, which is characterized by an XRPD diffractogram having at least one (or two) of the following peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.1, 8.3, 13.0, 13.5, 14.3, 15.5, 18.7, 20.8, and 22.7.

111. The compound or pharmaceutically acceptable salt thereof of claim 109, which is characterized by an XRPD diffractogram having at least three (or four, five, six, seven, eight, nine, or all) of the following peaks in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.1, 8.3, 13.0, 13.5, 14.3, 15.5, 18.7, 20.8, and 22.7.

112. The compound or pharmaceutically acceptable salt thereof of claim 111, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.1, and 8.3.

113. The compound or pharmaceutically acceptable salt thereof of claim 109, which is characterized by an XRPD diffractogram having at least six peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.1, 8.3, 13.0, 13.5, 14.3, 15.5, 18.7, 20.8, and 22.7.

114. The compound or pharmaceutically acceptable salt thereof of claim 113, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.1, 8.3, 13.0, 15.5, and 18.7.

115. The compound or pharmaceutically acceptable salt thereof of claim 109, which is characterized by an XRPD diffractogram having at least nine peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.1, 8.3, 13.0, 13.5, 14.3, 15.5, 18.7, 20.8, and 22.7.

116. The compound or pharmaceutically acceptable salt thereof of claim 115, which is characterized by an XRPD diffractogram having peaks expressed in degrees-2-theta at angles (± 0.2 degrees) of 5.7, 7.1, 8.3, 13.0, 13.5, 14.3, 15.5, 18.7, 20.8, and 22.7.

117. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 109 to 116, which is characterized by an XRPD diffractogram substantially as depicted in Figure 19.

118. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 109 to 117, which has a DSC thermogram characterized by an endotherm having a peak at about 195 °C.

119. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 109 to 118, which has a DSC thermogram characterized by an endotherm having an onset at about 176 °C.

120. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 109 to 119, which has a DSC thermogram characterized by an endotherm substantially as depicted in Figure 20.

121. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 5 and 109 to 120, which has a TGA thermogram substantially as depicted in Figure 21.

122. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 121, wherein the 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile is 3-((R_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile.

123. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 121, wherein the 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile is 3-((S_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile.

124. A pharmaceutical composition comprising:

a) the compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 123;

b) a disintegrant;

c) a binder;

d) an anti-caking agent; and

e) a lubricant.

125. The pharmaceutical composition of claim 124, wherein the composition further comprises

f) an additive or a second lubricant.

126. The pharmaceutical composition of claim 124 or 125, wherein disintegrant b) is sodium starch glycolate.

127. The pharmaceutical composition of any one of claims 124 to 126, wherein binder c) is HPMC (Methocel E5 Premium LV Hydroxypropyl Methylcellulose) or MCC PH102.

128. The pharmaceutical composition of any one of claims 124 to 127, wherein anti-caking agent d) is colloidal silicon dioxide.

129. The pharmaceutical composition of any one of claims 124 to 128, wherein lubricant e) is sodium stearyl fumarate.

130. The pharmaceutical composition of any one of claims 124 to 129, wherein second lubricant or additive f) is magnesium stearate.

131. A pharmaceutical composition comprising:

a) the compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 123;

b) sodium starch glycolate;

c) MCC PH102;

d) colloidal silicon dioxide;

e) sodium stearyl fumarate; and

f) magnesium stearate.

132. A dosage form comprising the compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 123 or the pharmaceutical composition of any one of claims 124 to 131.

133. The dosage form of claim 132, wherein the dosage form is in the form of a tablet.

134. The dosage form of claim 132 or 133, wherein the compound or pharmaceutically acceptable salt thereof is present in an amount that provides a dose of from about 25 mg to about 200 mg of 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile per dosage form.

135. The dosage form of any one of claims 132 to 134, wherein the compound or pharmaceutically acceptable salt thereof is present in an amount that provides a dose of about 25 mg of 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile per dosage form.

136. The dosage form of any one of claims 132 to 134, wherein the compound or pharmaceutically acceptable salt thereof a) is present in an amount that provides a dose of about 100 mg of 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile per dosage form.

137. The dosage form of any one of claims 132 to 136, wherein the compound or pharmaceutically acceptable salt thereof a) is present in an amount that provides a dose of about 200 mg of 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile per dosage form.

138. Use of the compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 123, the pharmaceutical composition of any one of claims 124 to 131, or the dosage form of any one of claims 132 to 136, in the manufacture of a medicament for treating cancer.

139. The use of claim 138, wherein the cancer is associated with expression or activity of a KRAS protein.

140. The use of claim 138 or 139, wherein the cancer is associated with expression or activity of a KRAS protein having a G12D mutation.

141. Use of the compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 123, the pharmaceutical composition of any one of claims 124 to 131, or the dosage form of any one of claims 132 to 136, in the manufacture of a medicament for treating cancer, wherein the use comprises identifying that a subject is in need of treatment of a cancer and that abnormally proliferating cells of the cancer comprise KRAS having a G12D mutation.

142. The use of claim 141, wherein the cancer is colorectal cancer.

143. The use of claim 141, wherein the cancer is pancreatic cancer.

144. The use of claim 141, wherein the cancer is pancreatic ductal cancer.

145. The use of claim 141, wherein the cancer is lung cancer.

146. The use of claim 141, wherein the cancer is non-small cell lung cancer (NCSLC).

147. The use of any one of claims 138 to 146, wherein the cancer is metastatic.

148. The use of any one of claims 138 to 147, wherein abnormally proliferating cells of the cancer comprise KRAS having a G12D mutation.

149. The compound or pharmaceutically acceptable salt thereof of any one of claims 1 to 123, the pharmaceutical composition of any one of claims 124 to 131, or the dosage form of any one of claims 132 to 136, for use in therapy.

150. A process for preparing 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile hydrochloride dihydrate comprising reacting 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile with aqueous hydrochloric acid.

151. The process of claim 150, wherein the reacting is performed in a solvent comprising an alcohol.

152. The process of claim 151, wherein the reacting is performed in a solvent comprising a dialkyl ether.

153. The process of claim 150, wherein the reacting is performed in a solvent comprising an alkanoic acid ester.

154. The process of claim 150, wherein the reacting is performed in a solvent comprising an alcohol, a dialkyl ether and an alkanoic acid alkyl ester.

155. The process of claim 150 or 151, wherein the alcohol is methanol.

156. The process of claim 152 or 154, wherein the dialkyl ether is methyl tert-butyl ether.

157. The process of claim 153 or 154, wherein the alkanoic acid alkyl ester is ethyl acetate.

158. The process of any one of claims 150 to 157, wherein the 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile and hydrochloric acid are reacted in a molar ratio of substantially 1:1.

159. The process of any one of claims 150 to 158, wherein the 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile is 3-((R_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile.

160. The process of any one of claims 150 to 158, wherein the 3-(1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile is 3-((S_a)-1-((1*R*,4*R*,5*S*)-2-azabicyclo[2.1.1]hexan-5-yl)-2-((1*R*,3*R*,5*R*)-2-(cyclopropanecarbonyl)-2-azabicyclo[3.1.0]hexan-3-yl)-7-(2,3-dichlorophenyl)-6-fluoro-4-methyl-1*H*-pyrrolo[3,2-*c*]quinolin-8-yl)propanenitrile.