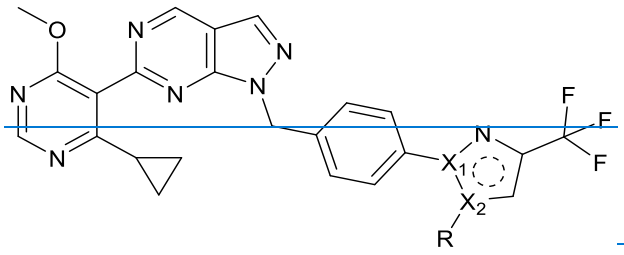
CLAIMS

~~1. A solid state form of a compound of Formula (I):~~



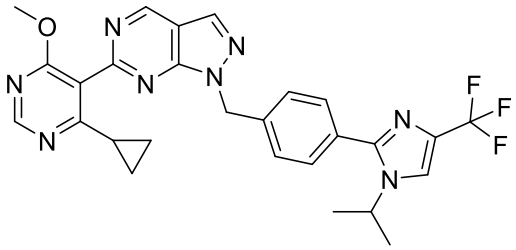
~~(I),~~

~~or a pharmaceutically acceptable salt thereof,~~

~~wherein R is C_{1-3} alkyl; and~~

~~X_1 and X_2 are independently selected from the group consisting of N and C.~~

~~2.~~1. ~~The solid state form of claim 1, which is a~~A solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II):



(II),

or a pharmaceutically acceptable salt thereof;

wherein the solid state form is a pharmaceutically acceptable co-crystal formed between 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II) and a pharmaceutically acceptable acid.

~~3. The solid state form of claim 2, wherein the solid state form is a pharmaceutically acceptable co-crystal of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II) and a second pharmaceutically acceptable compound.~~

~~4. The solid state form of claim 3, wherein the pharmaceutically acceptable co-crystal is formed between 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-~~

~~(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II) and a pharmaceutically acceptable acid.~~

~~5.~~2. The solid state form of claim ~~4~~1, wherein the pharmaceutically acceptable acid is gentisic acid.

~~6.~~3. The solid state form of claim ~~5~~2, wherein the gentisic acid co-crystal is crystalline Form 2 characterized by an XRPD pattern having peaks at 16.6 ± 0.2, 18.7 ± 0.2, and 22.5 ± 0.2 degrees two theta.

~~7. The solid state form of claim 5, characterized by an XRPD pattern as shown in FIG. 9.~~

~~8.~~4. The solid state form of claim ~~5~~2, characterized by an endothermic peak at about 186.0 °C, as determined by DSC.

~~9. The solid state form of claim 5, characterized by a DSC profile as shown in FIG. 10.~~

~~10.~~5. The solid state form of claim ~~5~~2, characterized by an about 3.17 wt% loss between room temperature and about 170 °C, as determined by TGA.

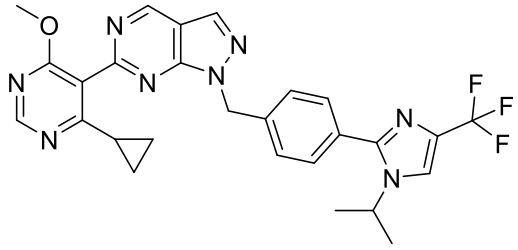
~~11. The solid state form of claim 5, characterized by a TGA profile as shown in FIG. 10.~~

~~12.~~6. The solid state form of claim ~~5~~2, characterized by at least two of the following:

a) an XRPD pattern as shown in FIG. 9;
b) a DSC profile as shown in FIG. 10; or
c) a TGA profile as shown in FIG. 10.

~~13.~~7. A mixture comprising the solid state form of any one of claims ~~5-12~~2-6 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).

~~14.~~8. ~~The~~ A solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II) ~~of claim 1 or 2~~



(II),

or a pharmaceutically acceptable salt thereof;

selected from the group consisting of:

a) crystalline Form A, wherein Form A is characterized by an XRPD pattern having peaks at 14.3 ± 0.2, 21.5 ± 0.2, and 21.8 ± 0.2 degrees two theta;

b) crystalline Form C, wherein Form C is characterized by an XRPD pattern having peaks at 14.2 ± 0.2, 17.0 ± 0.2, and 19.1 ± 0.2 degrees two theta;

c) crystalline Form D, wherein Form D is characterized by an XRPD pattern having peaks at 13.9 ± 0.2, 15.2 ± 0.2, and 19.3 ± 0.2 degrees two theta;

d) crystalline Form E, wherein Form E is characterized by an XRPD pattern having peaks at 10.6 ± 0.2, 18.7 ± 0.2, and 20.9 ± 0.2 degrees two theta; and

e) crystalline Form F, wherein Form F is characterized by an XRPD pattern having peaks at 10.7 ± 0.2, 14.3 ± 0.2, and 21.8 ± 0.2 degrees two theta;

or combinations thereof.

~~15.~~9. The solid state form of claim ~~14~~8, wherein the solid state form is crystalline Form A, and wherein the solid state form is characterized by at least one of the following:

a) an XRPD pattern as shown in FIG. 1;

b) an endothermic peak at about 165 °C, as determined by DSC;

c) a DSC profile as shown in FIG. 2;

d) an about 0.93 wt% loss between room temperature and about 150 °C, as determined by TGA; or

e) a TGA profile as shown in FIG. 2.

~~16. The solid state form of claim 15, characterized by at least one of the following:~~

~~a) an XRPD pattern as shown in FIG. 1;~~

~~b) an endothermic peak at about 165 °C, as determined by DSC;~~

~~c) a DSC profile as shown in FIG. 2;~~

~~d) an about 0.93 wt% loss between room temperature and about 150 °C, as determined by TGA; or~~

~~e) a TGA profile as shown in FIG. 2.~~

~~17. A mixture comprising the solid state form claim 15 or 16 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).~~

~~18.~~10. The solid state form of claim ~~14~~8, wherein the solid state form is crystalline Form C, and wherein the solid state form is characterized by an XRPD pattern as shown in FIG. 3.

~~19. The solid state form of claim 18, characterized by an XRPD pattern as shown in FIG. 3.~~

~~20. A mixture comprising the solid state form of claim 18 or 19 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).~~

~~21.~~11. The solid state form of claim ~~14~~8, wherein the solid state form is crystalline Form D, and wherein the solid state form is characterized by an XRPD pattern as shown in FIG. 4.

~~22. The solid state form of claim 21, characterized by an XRPD pattern as shown in FIG. 4.~~

~~23. A mixture comprising the solid state form of claim 21 or 22 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).~~

~~24.~~12. The solid state form of claim ~~14~~8, wherein the solid state form is crystalline Form E, and wherein the solid state form is characterized by at least one of the following:

a) an XRPD pattern as shown in FIG. 5;

b) an endothermic peak at about 107 °C, as determined by DSC;

c) a DSC profile as shown in FIG. 6;

d) an about 13.5 wt% loss between room temperature and about 200 °C, as determined by TGA; or

e) a TGA profile as shown in FIG. 6.

~~25. The solid state form of claim 24, characterized by at least one of the following:~~

~~a) an XRPD pattern as shown in FIG. 5.~~

~~b) an endothermic peak at about 107 °C, as determined by DSC.~~

~~c) a DSC profile as shown in FIG. 6.~~

~~d) an about 13.5 wt% loss between room temperature and about 200 °C, as determined by TGA.~~

~~e) a TGA profile as shown in FIG. 6.~~

~~26. A mixture comprising the solid state form of claim 24 or 25 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).~~

~~27.~~13. The solid state form of claim ~~14~~8, wherein the solid state form is crystalline Form F, and wherein the solid state form is characterized by one of the following:

a) an XRPD pattern as shown in FIG. 25;

b) an endothermic peak at about 157 ˚C, as determined by DSC; or

c) a DSC profile as shown in FIG. 26.

~~28. The solid state form of claim 37, characterized by one of the following:~~

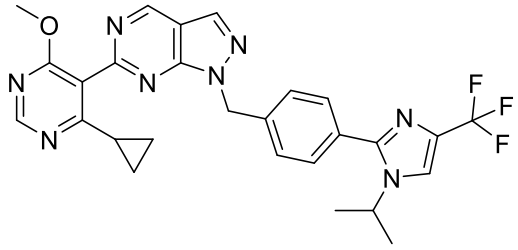
~~a) an XRPD pattern as shown in FIG. 25.~~

~~b) an endothermic peak at about 157˚C, as determined by DSC.~~

~~c) a DSC profile as shown in FIG. 26.~~

~~29. A mixture comprising the solid state form of claim 27 or 28 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).~~

~~30.~~14. ~~The solid state form of claim 2,~~A solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II):



(II),

or a pharmaceutically acceptable salt thereof;

wherein the solid state form is a pharmaceutically acceptable salt formed between~~of~~ 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II) and a pharmaceutically acceptable acid.

~~31. The solid state form of claim 30, wherein the pharmaceutically acceptable salt is formed between 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II) and a pharmaceutically acceptable acid.~~

~~32.~~15. The solid state form of claim ~~30~~14, wherein the pharmaceutically acceptable salt is a hydrochloric acid salt; and wherein the hydrochloric acid salt is crystalline Form 1 characterized by an XRPD pattern having peaks at 12.5 ± 0.2, 22.4 ± 0.2, and 23.9 ± 0.2 degrees two theta.

~~33. The solid state form of claim 32, wherein the hydrochloric acid salt is crystalline Form 1 characterized by an XRPD pattern having peaks at 12.5 ± 0.2, 22.4 ± 0.2, and 23.9 ± 0.2 degrees two theta.~~

~~34. The solid state form of claim 32, characterized by at least one of the following:~~

~~a) an XRPD pattern as shown in FIG. 7;~~

~~b) an endothermic peak at about 142.1 °C, as determined by DSC;~~

~~c) a DSC profile as shown in FIG. 8;~~

d) an about 4.04 wt% loss between about 30 °C and about 100 °C, as determined by TGA; or

e) a TGA profile as shown in FIG. 8.

35. A mixture comprising the solid state form of claim 33 or 34 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).

36.16. The solid state form of claim 41, wherein the pharmaceutically acceptable acid is benzoic acid, and wherein the benzoic acid co-crystal is crystalline Form 8 characterized by an XRPD pattern having peaks at 12.1 ± 0.2, 14.2 ± 0.2, and 16.5 ± 0.2 degrees two theta.

37. The solid state form of claim 36, wherein the benzoic acid co-crystal is crystalline Form 8 characterized by an XRPD pattern having peaks at 12.1 ± 0.2, 14.2 ± 0.2, and 16.5 ± 0.2 degrees two theta.

38. The solid state form of claim 36, characterized by at least two of the following:

a) an XRPD pattern as shown in FIG. 29;

b) a DSC profile as shown in FIG. 30; or

c) a TG-FTIR profile as shown in FIG. 31.

39. A mixture comprising the solid state form of claim 37 or 38 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).

40.17. The solid state form of claim 41, wherein the pharmaceutically acceptable acid is salicylic acid, and wherein the salicylic acid co-crystal is crystalline Form 9 characterized by an XRPD pattern having peaks at 11.0 ± 0.2, 16.5 ± 0.2, 17.3 ± 0.2 and 25.3 ± 0.2 degrees two theta.

41. The solid state form of claim 40, wherein the salicylic acid co-crystal is crystalline Form 9 characterized by an XRPD pattern having peaks at 11.0 ± 0.2, 16.5 ± 0.2, 17.3 ± 0.2 and 25.3 ± 0.2 degrees two theta.

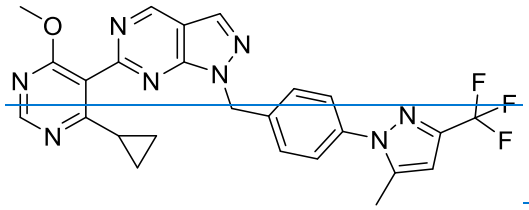
42. The solid state form of claim 40, characterized by at least one of the following:

a) an XRPD pattern as shown in FIG. 33; or

b) a ^{1}HNMR profile as shown in FIG. 34

43. A mixture comprising the solid state form of claim 41 or 42 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (II).

44. The solid state form of claim 1, which is a solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (III):



(III),

or a pharmaceutically acceptable salt thereof.

45. The solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (III) of claim 44 selected from the group consisting of:

a) crystalline Form A1, wherein Form A1 is characterized by an XRPD pattern having peaks at 16.1 ± 0.2, 16.7 ± 0.2, and 24.8 ± 0.2 degrees two theta;

b) crystalline Form B1, wherein Form B1 is characterized by an XRPD pattern having peaks at 12.9 ± 0.2, 14.5 ± 0.2, and 22.6 ± 0.2 degrees two theta;

or combinations thereof.

46. The solid state form of claim 45, wherein the solid state form is crystalline Form A1.

47. The solid state form of claim 46, characterized by at least one of the following:

a) an XRPD pattern as shown in FIG. 11;

b) an endothermic peak at about 150.5 °C, as determined by DSC;

c) a DSC profile as shown in FIG. 12;

d) an about 0.95 wt% loss between room temperature and about 120 °C, as determined by TGA; or

e) a TGA profile as shown in FIG. 12.

48. A mixture comprising the solid state form of claim 46 or 47 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (III).

49. The solid state form of claim 45, wherein the solid state form is crystalline Form B1.

50. The solid state form of claim 107, characterized by at least one of the following:

a) an XRPD pattern as shown in FIG. 13;

b) an endothermic peak at about 161.2 °C, as determined by DSC;

c) a DSC profile as shown in FIG. 14;

d) an about 1.58 wt% loss between room temperature and about 120 °C, as determined by TGA; or

e) a TGA profile as shown in FIG. 14.

51. A mixture comprising the solid state form of claim 49 or 50 and a second solid state form of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (III).

52. The solid state form of claim 44, wherein the solid state form is a pharmaceutically acceptable salt or co-crystal of 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (III).

53. The solid state form of claim 52, wherein the pharmaceutically acceptable salt or co-crystal is formed between 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine of Formula (III) and a pharmaceutically acceptable acid.

~~54. The solid state form of claim 15, wherein crystalline Form A has a unit cell that indexes as monoclinic.~~

~~55. The solid state form of claim 15, wherein crystalline Form A has a unit cell with an *a* value of about 12.054 Å, a *b* value of about 8.775 Å, and a *c* value of about 24.837 Å.~~

~~56. The solid state form of claim 15, wherein crystalline Form A has a unit cell with a volume of about 2603.68 Å^3.~~

~~57. The solid state form of claim 6, wherein crystalline Form 2 has a unit cell that indexes as monoclinic.~~

~~58. The solid state form of claim 6, wherein crystalline Form 2 has a unit cell with an *a* value of about 11.113 Å, a *b* value of about 12.356 Å, and a *c* value of about 24.048 Å.~~

~~59. The solid state form of claim 6, wherein crystalline Form 2 has a unit cell with a volume of about 3223.93 Å^3.~~

~~60. The solid state form of claim 46, wherein crystalline Form A1 has a unit cell that indexes as monoclinic.~~

~~61. The solid state form of claim 46, wherein crystalline Form A1 has a unit cell with an *a* value of about 12.545 Å, a *b* value of about 8.640 Å, and a *c* value of about 21.660 Å.~~

~~62. The solid state form of claim 47, wherein crystalline Form A1 has a unit cell with a volume of about 2336.13 Å^3.~~

~~63. The solid state form or mixture of any preceding claim, wherein the solid state form is substantially free of other polymorphic forms.~~

~~64. The solid state form or mixture of any preceding claim, wherein the pharmaceutically acceptable co-crystal is a hydrate, anhydrate, or solvate thereof.~~

~~65. The solid state form or mixture of any preceding claim, wherein the solid state form is a crystalline form.~~

~~66. The solid state form or mixture of any preceding claim, wherein the pharmaceutically acceptable salt is a hydrate, anhydrate, or solvate thereof.~~

~~67. The solid state form or mixture of claim 64 or 66, wherein the solvate is a dichloromethane solvate.~~

~~68. The solid state form or mixture of any preceding claim, wherein the pharmaceutically acceptable salt is a hydrochloric acid salt.~~

~~69. The solid state form or mixture of any preceding claim, wherein the solid state form is an amorphous form.~~

~~70. The solid state form or mixture of any preceding claim, wherein the pharmaceutically acceptable acid is selected from the group consisting of 1-hydroxy-2-naphthoic acid, 4-aminosalicylic acid, ascorbic acid, adipic acid, L-aspartic acid, benzene sulfonic acid, benzoic acid, trans-cinnamic acid, citric acid, ethanedisulfonic acid, fumaric acid, galactaric acid, gentisic acid, gluconic acid, D-glucuronic acid, glutamic acid, glutaric acid, glycolic acid, hexanoic acid, hippuric acid, hydrobromic acid, hydrochloric acid, lactic acid, maleic acid, L-malic acid, malonic acid, R-mandelic acid, methanesulfonic acid, mucic acid, naphthalene sulfonic acid, nicotinic acid, oxalic acid, palmitic acid, p-toluene sulfonic acid, phosphoric acid, propionic acid, saccharin, salicylic acid, stearic acid, succinic acid, sulfuric acid, L-tartaric acid, vanillic acid, vanillin, ethyl maltol, gallic acid, gallic acid ethyl ester, 4-hydroxybenzoic acid, 4-hydroxybenzoic acid methyl ester, 3,4,5- trihydroxybenzoic acid, nicotinamide, L-proline, and D-sorbitol.~~

~~71. The solid state form or mixture of any preceding claim, wherein the pharmaceutically acceptable acid is selected from the group consisting of hydrochloric acid, hydrobromic acid, ethanedisulfonic acid, methanesulfonic acid, gentisic acid, benzoic acid, salicylic acid, and gallic acid.~~

~~72. The solid state form or mixture of any preceding claim, wherein the pharmaceutically acceptable acid is gentisic acid.~~

~~73.~~18. A pharmaceutical composition comprising ~~one or more of~~ the solid state form~~s~~ or mixture~~s of claims 1-72~~ of any one of claims 1-17, and one or more pharmaceutically acceptable carriers or diluents.

~~74. A solid dosage form comprising one or more of the solid state forms or mixtures of claims 1-72.~~

~~75.~~19. ~~A method for treating cancer comprising administering one or more of t~~The solid state form~~s~~ or mixture~~s of claims 1-72~~ of any one of claims 1-17~~,~~ or the pharmaceutical composition of claim ~~73~~18~~,~~ ~~or the solid dosage form of claim 74, to a patient in need thereof~~ for use as a cancer treating agent.

~~76.~~20. Use of ~~one or more of~~ the solid state form~~s~~ or mixture~~s of claims 1-72, the pharmaceutical composition claim 73, or the solid dosage form of claim 74~~ of any one of claims 1-17, or the pharmaceutical composition of claim 18, for the manufacture of a medicament for treating cancer.

~~77.~~21. ~~The~~ Use of the solid state form~~s~~ or mixture~~s of claims 1-72, the pharmaceutical composition claim 73, or the solid dosage form of claim 74~~ of any one of claims 1-17, or the pharmaceutical composition of claim 18, for ~~use in a method for treating~~the treatment of cancer.