CLAIMS

1. A pharmaceutical composition comprising a fixed dosage amount of 3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl) cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid (Compound 1) Form I and a solid dispersion comprising substantially amorphous N-(5-hydroxy-2,4-ditert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide (Compound 2).

2. The pharmaceutical composition of claim 1 further comprising:

a. a filler;

b. a disintegrant;

c. a surfactant; and

d. a binder;

referred to as **PC-I**.

3. The pharmaceutical composition of claim 1, comprising 30 to 55 percent by weight Compound 1 Form I, and 10 to 45 percent by weight solid dispersion comprising substantially amorphous Compound 2.

4. The pharmaceutical composition of claim 2 having the following formulation:

	% by wgt.
Compound 1 Form I	35-50
Solid dispersion comprising substantially amorphous Compound 2	25-40
Microcrystalline cellulose	10-20
Croscarmellose sodium	1-3
Sodium lauryl sulfate	0.5-2
Polyvinylpyrrolidone	0-5

referred to as **PC-II**.

5. A pharmaceutical composition comprising:

a. Compound 1 Form I;

b. a solid dispersion comprising substantially amorphous Compound 2;

c. a filler;

d. a disintegrant;

e. a surfactant;

f. a binder; and

g. a lubricant;

referred to as **PC-III**.

6. The pharmaceutical composition of claim 5, comprising about 100 to 250 mg of Compound 1 Form I, and about 80 to 150 mg of substantially amorphous Compound 2.

7. The pharmaceutical composition of claim 5, comprising about 200 mg of Compound 1 Form I, and about 125 mg of substantially amorphous Compound 2.

8. The pharmaceutical composition of claim 5, comprising about 200 mg of Compound 1 Form I, and about 83 mg of substantially amorphous Compound 2.

9. The pharmaceutical composition of claim 5, comprising about 150 mg of Compound 1 Form I, and about 125 mg of substantially amorphous Compound 2.

10. The pharmaceutical composition of claim 5, comprising 25 to 50 percent by weight Compound 1 Form I, and 15 to 35 percent by weight a solid dispersion comprising substantially amorphous Compound 2.

11. The pharmaceutical composition of claim 5 having the following formulation:

	% by wgt.
Compound 1 Form I	25-50
A solid dispersion comprising substantially amorphous Compound 2	15-35
Microcrystalline cellulose	20-30
Croscarmellose sodium	3-10

Sodium lauryl sulfate	0.5-2
Polyvinylpyrrolidone	0-5
Magnesium stearate	0.5-2

referred to as **PC-IV**.

12. The pharmaceutical composition of claim 5, further comprising a colorant and a wax.

13. The pharmaceutical composition of claim 2, wherein the pharmaceutical composition is a solid oral pharmaceutical composition.

14. The pharmaceutical composition claim 13, wherein the solid oral pharmaceutical composition is a granule.

15. The granule of claim 14 having the following formulation:

	% by wgt.
Compound 1 Form I	43
Solid dispersion comprising substantially amorphous Compound 2	34
Microcrystalline cellulose	17
Croscarmellose sodium	2
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3

referred to as **PC-V**.

16. The granule of claim 14 having the following formulation:

	% by wgt.
Compound 1 Form I	38
Solid dispersion comprising substantially amorphous Compound 2	40

Microcrystalline cellulose	16
Croscarmellose sodium	2
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3

referred to as **PC-VI**.

17. The granule of claim 14 having the following formulation:

	% by wgt.
Compound 1 Form I	51
Solid dispersion comprising substantially amorphous Compound 2	27
Microcrystalline cellulose	16
Croscarmellose sodium	2
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3

referred to as **PC-VII**.

18. The pharmaceutical composition of claim 5, wherein the pharmaceutical composition is a solid oral pharmaceutical composition.

19. The pharmaceutical composition claim 18, wherein the solid oral pharmaceutical composition is a tablet.

20. The tablet claim 19 having the following formulation:

	% by wgt.
Compound 1 Form I	35
Solid dispersion comprising substantially amorphous Compound 2	28

~~Microcrystalline cellulose~~	~~26~~
~~Croscarmellose sodium~~	~~6~~
~~Sodium lauryl sulfate~~	~~1~~
~~Polyvinylpyrrolidone~~	~~3~~
~~Magnesium stearate~~	~~1~~

~~referred to as **PC-VIII**.~~

~~21. The tablet of claim 19 having the following formulation:~~

	~~% by wgt.~~
~~Compound 1 Form I~~	~~31~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~32~~
~~Microcrystalline cellulose~~	~~26~~
~~Croscarmellose sodium~~	~~6~~
~~Sodium lauryl sulfate~~	~~1~~
~~Polyvinylpyrrolidone~~	~~3~~
~~Magnesium stearate~~	~~1~~

~~referred to as **PC-IX**.~~

~~22. The tablet of claim 19 having the following formulation:~~

	~~% by wgt.~~
~~Compound 1 Form I~~	~~41~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~22~~
~~Microcrystalline cellulose~~	~~26~~
~~Croscarmellose sodium~~	~~6~~
~~Sodium lauryl sulfate~~	~~1~~

~~Polyvinylpyrrolidone~~	~~3~~
~~Magnesium stearate~~	~~1~~

~~referred to as **PC-X**.~~

~~23. The tablet of claim 19 having the following formulation:~~

	~~mg~~
~~Compound 1 Form I~~	~~200~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~156~~
~~Microcrystalline cellulose~~	~~150~~
~~Croscarmellose sodium~~	~~34~~
~~Sodium lauryl sulfate~~	~~4~~
~~Polyvinylpyrrolidone~~	~~15~~
~~Magnesium stearate~~	~~6~~

~~referred to as **PC-XI**.~~

~~24. The tablet of claim 19 having the following formulation:~~

	~~mg~~
~~Compound 1 Form I~~	~~150~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~156~~
~~Microcrystalline cellulose~~	~~129~~
~~Croscarmellose sodium~~	~~30~~
~~Sodium lauryl sulfate~~	~~4~~
~~Polyvinylpyrrolidone~~	~~13~~
~~Magnesium stearate~~	~~5~~

~~referred to as **PC-XII**.~~

~~25. The tablet of claim 19 having the following formulation:~~

	~~mg~~
~~Compound 1 Form I~~	~~200~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~104~~
~~Microcrystalline cellulose~~	~~128~~
~~Croscarmellose sodium~~	~~29~~
~~Sodium lauryl sulfate~~	~~4~~
~~Polyvinylpyrrolidone~~	~~13~~
~~Magnesium stearate~~	~~5~~

~~referred to as **PC-XIII**.~~

~~26. The tablet of claim 19 having the following formulation:~~

	~~% by wgt.~~
~~Compound 1 Form I~~	~~34~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~27~~
~~Microcrystalline cellulose~~	~~25~~
~~Croscarmellose sodium~~	~~6~~
~~Sodium lauryl sulfate~~	~~1~~
~~Polyvinylpyrrolidone~~	~~3~~
~~Magnesium stearate~~	~~1~~
~~Colorant~~	~~3~~

~~referred to as **PC-XIV**.~~

~~27. The tablet of claim 19 having the following formulation:~~

	% by wgt.
Compound 1 Form I	30
Solid dispersion comprising substantially amorphous Compound 2	31
Microcrystalline cellulose	25
Croscarmellose sodium	6
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3
Magnesium stearate	1
Colorant	3

referred to as **PC-XV**.

28. The tablet of claim 19 having the following formulation:

	% by wgt.
Compound 1 Form I	40
Solid dispersion comprising substantially amorphous Compound 2	21
Microcrystalline cellulose	25
Croscarmellose sodium	6
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3
Magnesium stearate	1
Colorant	3

referred to as **PC-XVI**.

29. The tablet claim 19 having the following formulation:

	mg

~~Compound 1 Form I~~	~~200~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~156~~
~~Microcrystalline cellulose~~	~~150~~
~~Croscarmellose sodium~~	~~34~~
~~Sodium lauryl sulfate~~	~~4~~
~~Polyvinylpyrrolidone~~	~~15~~
~~Magnesium stearate~~	~~6~~
~~Colorant~~	~~17~~

~~referred to as **PC-XVII**.~~

~~30. The tablet of claim 19 having the following formulation:~~

	~~mg~~
~~Compound 1 Form I~~	~~200~~
~~Substantially amorphous Compound 2~~	~~125~~
~~Microcrystalline cellulose~~	~~150~~
~~Croscarmellose sodium~~	~~34~~
~~Sodium lauryl sulfate~~	~~4~~
~~Polyvinylpyrrolidone~~	~~15~~
~~Magnesium stearate~~	~~6~~
~~Colorant~~	~~17~~

~~referred to as **PC-XVIII**.~~

~~31. The tablet of claim 19 having the following formulation:~~

	~~mg~~
~~Compound 1 Form I~~	~~150~~
~~Solid dispersion comprising~~	~~156~~

substantially amorphous Compound 2	
Microcrystalline cellulose	129
Croscarmellose sodium	29
Sodium lauryl sulfate	4
Polyvinylpyrrolidone	13
Magnesium stearate	5
Colorant	15

referred to as **PC-XIX**.

32. The tablet of claim 19 having the following formulation:

	mg
Compound 1 Form I	200
Solid dispersion comprising substantially amorphous Compound 2	104
Microcrystalline cellulose	128
Croscarmellose sodium	29
Sodium lauryl sulfate	4
Polyvinylpyrrolidone	13
Magnesium stearate	5
Colorant	14

referred to as **PC-XX**.

33. The tablet of claim 19 having the following formulation:

	mg
Compound 1 Form I	200
Solid dispersion comprising substantially amorphous	83

~~Compound 2~~	
~~Microcrystalline cellulose~~	~~128~~
~~Croscarmellose sodium~~	~~29~~
~~Sodium lauryl sulfate~~	~~4~~
~~Polyvinylpyrrolidone~~	~~13~~
~~Magnesium stearate~~	~~5~~
~~Colorant~~	~~14~~

~~referred to as **PC-XXI**.~~

~~34. The tablet of claim 19 having the following formulation:~~

~~Component~~	~~% by wgt.~~
~~Compound 1 Form I~~	~~20-40~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~30-40~~
~~Microcrystalline cellulose~~	~~20-30~~
~~Croscarmellose sodium~~	~~1-10~~
~~Polyvinylpyrrolidone~~	~~1-5~~
~~Sodium lauryl sulfate~~	~~0.1-1~~
~~Magnesium stearate~~	~~0.5-1.5~~

~~referred to as **PC-XXII**.~~

~~35. The tablet of claim 19 having the following formulation:~~

~~Component~~	~~mg/Tablet~~
~~Compound 1 Form I~~	~~100~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~156~~
~~Microcrystalline cellulose~~	~~55~~
~~Croscarmellose sodium~~	~~7~~
~~Polyvinylpyrrolidone~~	~~11~~
~~Sodium lauryl sulfate~~	~~3~~
~~Total Granules~~	~~332~~
~~Croscarmellose sodium~~	~~18~~
~~Microcrystalline cellulose~~	~~53~~
~~Magnesium stearate~~	~~4~~

~~Total Tablet~~	~~407~~

~~referred to as **PC-XXIII**.~~

~~36. The tablet of claim 19 having the following formulation:~~

~~Component~~	~~mg/Tablet~~
~~Compound 1 Form I~~	~~150~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~156~~
~~Microcrystalline cellulose~~	~~65~~
~~Croscarmellose sodium~~	~~8~~
~~Polyvinylpyrrolidone~~	~~13~~
~~Sodium lauryl sulfate~~	~~4~~
~~Total Granules~~	~~396~~
~~Croscarmellose sodium~~	~~22~~
~~Microcrystalline cellulose~~	~~64~~
~~Magnesium stearate~~	~~5~~
~~Total Tablet~~	~~487~~

~~referred to as **PC-XXIV**.~~

~~37. The tablet of claim 19 having the following formulation:~~

~~Component~~	~~mg/Tablet~~
~~Compound 1 Form I~~	~~75~~
~~Solid dispersion comprising substantially amorphous Compound 2~~	~~156~~
~~Microcrystalline cellulose~~	~~49~~
~~Croscarmellose sodium~~	~~6~~
~~Polyvinylpyrrolidone~~	~~10~~
~~Sodium lauryl sulfate~~	~~3~~
~~Total Granules~~	~~299~~
~~Croscarmellose sodium~~	~~17~~
~~Microcrystalline cellulose~~	~~48~~

Magnesium stearate	4
Core Tablet	368
Pink Opadry	11
Total Tablet	379

referred to as **PC-XXV**.

38. A method of treating, lessening the severity of, or symptomatically treating cystic fibrosis in a patient comprising administering to the patient an effective amount of the pharmaceutical composition of claim 1.

39. The method of claim 38, wherein the pharmaceutical composition has the formulation of any one of **PC-I** to **PC-XXV**.

40. The method of claim 38, wherein the patient has a ΔF508 CFTR mutation.

41. The method of claim 40, wherein the patient is homozygous in ΔF508.

42. The method of claim 40, wherein the patient is heterozygous in ΔF508.

43. A method of preparing a granule comprising wet granulating the following components:

a. Compound 1 Form I;

b. a solid dispersion comprising substantially amorphous Compound 2;

c. a filler;

d. a disintegrant;

e. a surfactant; and

f. a binder.

44. A method of preparing a tablet comprising compressing:

i) a plurality of granular pharmaceutical compositions comprising the following components:

a. Compound 1 Form I;

b. a solid dispersion comprising substantially amorphous Compound 2;

c. a filler;

d. a disintegrant;

~~e. a surfactant; and~~

~~f. a binder;~~

~~ii) a disintegrant;~~

~~iii) a filler; and~~

~~iv) a lubricant.~~

~~45. A continuous process for preparing a tablet comprising Compound 1 Form I and a solid dispersion comprising substantially amorphous Compound 2 comprising the steps of:~~

~~a) mixing Compound 1 Form I, a solid dispersion comprising substantially amorphous Compound 2, a filler, and a disintegrant in a blender to form a blend;~~

~~b) preparing a granulation solution with water, a binder, and a surfactant;~~

~~c) feeding the blend from step a) into a continuous twin screw granulator while adding the granulation solution from step b) to produce granules;~~

~~d) drying the granules from step c) and milling them;~~

~~e) blending the milled granules from step d) with a filler, disintegrant, and lubricant to form a blend; and~~

~~f) compressing the blend from step e) into a tablet.~~

~~46. A kit comprising the pharmaceutical composition of claim 1 and a separate therapeutic agent.~~

~~47. The kit of claim 46, wherein the pharmaceutical composition and the therapeutic agent are in separate containers.~~

~~48. The kit of claim 47, wherein the containers are bottles, vials, or blister packs, or combination thereof.~~

1. A solid oral pharmaceutical composition comprising:

200 mg of 3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl) cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid (Compound 1) Form I and

a solid dispersion comprising substantially amorphous N-(5-hydroxy-2,4-ditert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide (Compound 2) and a polymer,

wherein the substantially amorphous Compound 2 is present in the solid oral pharmaceutical composition in an amount of 125 mg,

wherein Compound 1 Form I is characterized by one or more peaks at 15.4, 16.3, and 14.5 degrees in an X-ray powder diffraction pattern,

wherein substantially amorphous Compound 2 has less than 15% crystallinity, and

wherein the solid oral pharmaceutical composition is a tablet comprising 25 to 50 percent by weight Compound 1 Form I, and 15 to 35 percent weight of a solid dispersion comprising Compound 2.

2. The solid oral pharmaceutical composition of claim 1 further comprising:

a. a filler;

b. a disintegrant;

c. a surfactant; and

d. a binder;

referred to as **PC-I**.

3. The solid oral pharmaceutical composition of claim 2, further comprising:

e. a lubricant

referred to as **PC-III**.

4. The solid oral pharmaceutical composition of claim 1, wherein the solid oral pharmaceutical composition further comprises:

a filler which is microcystalline cellulose in an amount from 20 to 30 percent by weight,

a disintegrant which is croscarmelose sodium in an amount from 3 to 10 percent by weight,

a surfactant which is sodium lauryl sulfate in an amount from 0.5 to 2 percent by weight,

a binder which is polyvinylpyrrolidone in an amount from 0 to 5 percent by weight, and

a lubricant which is magnesium stearate, in an amount from 0.5 to 2 percent by weight.

5. The solid oral pharmaceutical composition of claim 1, comprising 30 to 50 percent by weight Compound 1 Form I.

6. The solid oral pharmaceutical composition of any of claims 1-4 having the following formulation:

	% by wgt.
Compound 1 Form I	25-50
A solid dispersion comprising substantially amorphous Compound 2	15-35
Microcrystalline cellulose	20-30
Croscarmellose sodium	3-10
Sodium lauryl sulfate	0.5-2
Polyvinylpyrrolidone	0-5
Magnesium stearate	0.5-2

referred to as **PC-IV**.

7. The solid oral pharmaceutical composition of any of claims 1-6, further comprising a colorant and a wax.

8. The tablet of any of claims 1-7 having the following formulation:

	% by wgt.
Compound 1 Form I	35

Solid dispersion comprising substantially amorphous Compound 2	28
Microcrystalline cellulose	26
Croscarmellose sodium	6
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3
Magnesium stearate	1

referred to as **PC-VIII**, or:

	% by wgt.
Compound 1 Form I	31
Solid dispersion comprising substantially amorphous Compound 2	32
Microcrystalline cellulose	26
Croscarmellose sodium	6
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3
Magnesium stearate	1

referred to as **PC-IX**,

or:

	mg
Compound 1 Form I	200
Solid dispersion comprising substantially amorphous Compound 2	156

Microcrystalline cellulose	150
Croscarmellose sodium	34
Sodium lauryl sulfate	4
Polyvinylpyrrolidone	15
Magnesium stearate	6

referred to as **PC-XI**, or:

	% by wgt.
Compound 1 Form I	34
Solid dispersion comprising substantially amorphous Compound 2	27
Microcrystalline cellulose	25
Croscarmellose sodium	6
Sodium lauryl sulfate	1
Polyvinylpyrrolidone	3
Magnesium stearate	1
Colorant	3

referred to as **PC-XIV**, or:

	% by wgt.
Compound 1 Form I	30
Solid dispersion comprising substantially amorphous Compound 2	31
Microcrystalline cellulose	25
Croscarmellose sodium	6
Sodium lauryl sulfate	1

Polyvinylpyrrolidone	3
Magnesium stearate	1
Colorant	3

referred to as **PC-XV**, or:

	mg
Compound 1 Form I	200
Solid dispersion comprising substantially amorphous Compound 2	156
Microcrystalline cellulose	150
Croscarmellose sodium	34
Sodium lauryl sulfate	4
Polyvinylpyrrolidone	15
Magnesium stearate	6
Colorant	17

referred to as **PC-XVII**.

9. A solid oral pharmaceutical composition comprising:

100 mg of 3-(6-(1-(2,2-difluorobenzo[d][1,3]dioxol-5-yl) cyclopropanecarboxamido)-3-methylpyridin-2-yl)benzoic acid (Compound 1) Form I and

a solid dispersion comprising substantially amorphous N-(5-hydroxy-2,4-ditert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide (Compound 2) and a polymer,

wherein the substantially amorphous Compound 2 is present in the solid oral pharmaceutical composition in an amount of 125 mg,

wherein Compound 1 Form I is characterized by one or more peaks at 15.4, 16.3, and 14.5 degrees in an X-ray powder diffraction pattern,

wherein substantially amorphous Compound 2 has less than 15% crystallinity,

and wherein the solid oral pharmaceutical composition is a tablet having the following formulation:

Component	mg/Tablet
Compound 1 Form I	100
Solid dispersion comprising substantially amorphous Compound 2	156
Microcrystalline cellulose	55
Croscarmellose sodium	7
Polyvinylpyrrolidone	11
Sodium lauryl sulfate	3
Total Granules	332
Croscarmellose sodium	18
Microcrystalline cellulose	53
Magnesium stearate	4
Total Tablet	407

referred to as **PC-XXIII**.

10. The tablet of any of claims 1-7 having the following formulation:

	mg
Compound 1 Form I	200
Substantially amorphous Compound 2	125
Microcrystalline cellulose	150
Croscarmellose sodium	34
Sodium lauryl sulfate	4
Polyvinylpyrrolidone	15

Magnesium stearate	6
Colorant	17

referred to as **PC-XVIII**.

11. A method of preparing a tablet according to any one of claims 1-9, wherein the method comprises:

a) wet granulating the following components to produce a granule:

a. Compound 1 Form I;

b. a solid dispersion comprising substantially amorphous Compound 2;

c. a filler;

d. a disintegrant;

e. a surfactant; and

f. a binder;

and

b) compressing the following components to produce a tablet:

i. a plurality of granules from step a);

ii) a disintegrant;

iii) a filler; and

iv) a lubricant,

wherein Compound 1 Form I is characterized by one or more peaks at 15.4, 16.3, and 14.5 degrees in an X-ray powder diffraction pattern, and

wherein substantially amorphous Compound 2 has less than 15% crystallinity.

12. A kit comprising the solid oral pharmaceutical composition of claim 1 and a separate therapeutic agent.

13. The kit of claim 12, wherein the solid oral pharmaceutical composition and the therapeutic agent are in separate containers.

14. The kit of claim 13, wherein the containers are bottles, vials, or blister packs, or combination thereof.