

CLAIMS

1. A tablet for oral administration comprising:

- a. —Compound 1, Compound 1 Form I, Compound 1 Form II, and/or Compound 1 HCl Salt Form A;
- b. —a filler;
- c. —a disintegrant;
- d. —a surfactant;
- e. —a lubricant; and
- f. —at least one of a binder or a glidant.

2. The tablet of claim 1, wherein Compound 1, Compound 1 Form I, Compound 1 Form II, and/or Compound 1 HCl Salt Form A is present in the tablet in an amount ranging from about 25 mg to about 500 mg.

3. The tablet of claim 1, wherein the amount of Compound 1, Compound 1 Form I, Compound 1 Form II, and/or Compound 1 HCl Salt Form A in the tablet ranges from about 15 wt% to about 75 wt% by weight of the tablet.

4. The tablet of claim 1, wherein the amount of Compound 1, Compound 1 Form I, Compound 1 Form II, and/or Compound 1 HCl Salt Form A in the tablet ranges from about 40 wt% to about 70 wt% by weight of the tablet.

5. The tablet of claim 1 having the following formulation:

Roller Compaction Granule Blend	(%w/w)
Compound 1	20-40
Microcrystalline cellulose	30-50
Mannitol	10-30
Croscarmellose Sodium	1-5
Sodium Lauryl Sulfate	0.1-2

Colloidal Silica	(%)
Magnesium Stearate	
Tablet Composition	(%)
Roller Compaction Granule Blend	99
Magnesium Stearate	(%)

6. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	(%)
Compound 1	(%)
Microcrystalline cellulose	

Polyvinylpyrrolidone	6
Sodium Lauryl Sulfate	6
Tablet Composition	(%)
High Shear Granule Blend	7
Microcrystalline cellulose	4
Croscarmellose Sodium	6
Magnesium Stearate	6
Film-Coated Tablet	(%)
Core Tablet Composition	5

9. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	(%w/w)
Compound 1 Form I	40-80
Microcrystalline cellulose	20-40
Mannitol	10-15
Croscarmellose Sodium	1-5
Polyvinylpyrrolidone	1-10
Sodium Lauryl Sulfate	0.1-2
Tablet Composition	(%w/w)
High Shear Granule Blend	95-99
Croscarmellose Sodium	1-4
Magnesium Stearate	0.1-1

10. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	(%w/w)
Compound 1 Form I	50
Microcrystalline cellulose	30
Mannitol	13
Croscarmellose Sodium	2
Polyvinylpyrrolidone	4
Sodium Lauryl Sulfate	1
Tablet Composition	(%w/w)
High Shear Granule Blend	97.5

Croscarmellose Sodium	2.0
Magnesium Stearate	0.5

11. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	(%w/w)
Compound 1 Form I	60
Microcrystalline cellulose	20
Mannitol	13
Croscarmellose Sodium	2
Polyvinylpyrrolidone	4
Sodium Lauryl Sulfate	1
Tablet Composition	(%w/w)
High Shear Granule Blend	97.5
Croscarmellose Sodium	2.0
Magnesium Stearate	0.5

12. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	(%w/w)
Compound 1 Form I	60
Microcrystalline cellulose	20
Mannitol	13
Croscarmellose Sodium	2
Polyvinylpyrrolidone	4
Sodium Lauryl Sulfate	1

Tablet Composition	(%)
High-Shear-Granule-Blend	
Microcrystalline-cellulose	
Croscarmellose-Sodium	
Magnesium-Stearate	

13. The tablet of claim 1 having the following formulation:

Twin-Screw-Granule-Blend	(%)
Compound 1 Form 1	
Microcrystalline-cellulose	

Croscarmellose Sodium	
Polyvinylpyrrolidone	
Sodium Lauryl Sulfate	
Tablet Composition (%)	
Twin-Screw Granule Blend	
Microcrystalline cellulose	
Croscarmellose Sodium	
Magnesium Stearate	

Film Coat	3
Wax	Trace

16. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	mg
Compound 1 Form I	200
Microcrystalline cellulose	66
Mannitol	43
Croscarmellose Sodium	7
Polyvinylpyrrolidone	13
Sodium Lauryl Sulfate	3
Core Tablet Composition (200 mg dose)	mg
High Shear Granule Blend	332
Microcrystalline cellulose	56
Croscarmellose Sodium	8
Magnesium Stearate	4
Film Coated Tablet (200 mg dose)	mg
Core Tablet Composition	400
Film Coat	12
Wax	trace

17. The tablet of claim 1 having the following formulation:

Twin Serew Granule Blend	
Compound I Form I	
Microcrystalline cellulose	
Mannitol	
Croscarmellose Sodium	
Polyvinylpyrrolidone	
Sodium Lauryl Sulfate	
Core Tablet Composition (200-mg dose)	
Twin Serew Granule Blend	

High-Shear Granule Blend	
Microcrystalline cellulose	
Croscarmellose Sodium	
Magnesium Stearate	
Film-Coated Tablet (200 mg dose)	
Core Tablet Composition	
Film-Coat	
Wax	

Film Coated Tablet (300 mg dose)	
Core Tablet Composition	
Film Coat	
Wax	

20. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	
Compound 1 Form 1	
Microcrystalline cellulose	

Wax	
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21. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	(%)
Compound 1 Form I	
Microcrystalline cellulose	
Mannitol	
Croscarmellose Sodium	
Polyvinylpyrrolidone	

High Shear Granule Blend	
Microcrystalline cellulose	
Croscarmellose Sodium	
Magnesium Stearate	

23. The tablet of claim 1 having the following formulation:

High Shear Granule Blend	
Compound 1 Form I or Form II	
Microcrystalline cellulose	
Magnesium Stearate	

	Croscarmellose Sodium	
	Polyvinylpyrrolidone	
	Sodium Lauryl Sulfate	
	Core Tablet Composition (200 mg dose)	
2	Twin Screw Granule Blend Microcrystalline cellulose Croscarmellose Sodium Magnesium Stearate	

26. The tablet of claim 1 having the following formulation:

Twin Screw Granule Blend	
Compound 1 Form 1	
Microcrystalline cellulose	
Croscarmellose Sodium	
Polyvinylpyrrolidone	
Sodium Lauryl Sulfate	
Core Tablet Composition (200 mg dose)	
Twin Screw Granule Blend	

	Polyvinylpyrrolidone	
	Sodium Lauryl Sulfate	
	Core Tablet Composition (400 mg dose)	
2	Twin Screw Granule Blend	
	Microcrystalline-cellulose	
	Croscarmellose-Sodium	
	Magnesium-Stearate	
	Film Coated Tablet	
	(400 mg dose, 620 mg total)	

~~34. The tablet of claim 1, wherein Compound 1 is in Form I characterized by a diffraction pattern substantially similar to that of Figure 1.~~

~~35. The tablet of claim 1, wherein Compound 1 is in Form I characterized by a diffraction pattern substantially similar to that of Figure 2.~~

36]. A method of treating or lessening the severity of a disease in a patient comprising administering to the patient ~~the tablet of claim 1~~ a tablet for oral administration comprising:

a. Compound 1, Compound 1 Form I, Compound 1 Form II, and/or Compound 1 HCl Salt Form A;

b. a filler;

c. a disintegrant;

d. a surfactant;

e. a lubricant; and

f. at least one of a binder or a glidant,

wherein the disease is selected from cystic fibrosis, asthma, smoke induced COPD, chronic bronchitis, rhinosinusitis, constipation, pancreatitis, pancreatic insufficiency, male infertility, mild pulmonary disease, idiopathic pancreatitis, allergic bronchopulmonary aspergillosis (ABPA), liver disease, hereditary emphysema, hereditary hemochromatosis, coagulation-fibrinolysis deficiencies, protein C deficiency, Type 1 hereditary angioedema, lipid processing deficiencies, familial hypercholesterolemia, Type 1 chylomicronemia, abetalipoproteinemia, lysosomal storage diseases, I-cell disease/pseudo-Hurler, mucopolysaccharidoses, Sandhof/Tay-Sachs, Crigler-Najjar type II, polyendocrinopathy/hyperinsulemia, Diabetes mellitus, Laron dwarfism, myeloperoxidase deficiency, primary hypoparathyroidism, melanoma, glycanosis CDG type 1, congenital hyperthyroidism, osteogenesis imperfecta, hereditary hypofibrinogenemia, ACT deficiency, Diabetes insipidus (DI), neurophyseal DI, neprogenic DI, Charcot-Marie Tooth syndrome, Perlizaeus-Merzbacher disease, neurodegenerative diseases, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, progressive supranuclear palsy, Pick's disease, several polyglutamine neurological disorders, Huntington's, spinocerebellar ataxia type I, spinal and bulbar muscular atrophy, dentatorubal pallidoluyian, myotonic dystrophy, spongiform

encephalopathies, hereditary Creutzfeldt-Jakob disease, Fabry disease, Straussler-Scheinker syndrome, COPD, dry-eye disease, Sjogren's disease, Osteoporosis, Osteopenia, Gorham's Syndrome, chloride channelopathies, myotonia congenita, Bartter's syndrome type III, Dent's disease, hyperekplexia, epilepsy, hyperekplexia, lysosomal storage disease, Angelman syndrome, Primary Ciliary Dyskinesia (PCD), inherited disorders of the structure and/or function of cilia, PCD with situs inversus, PCD without situs inversus, or ciliary aplasia.

372. The method of claim 361, wherein the disease is cystic fibrosis, emphysema, COPD, or dry-eye disease.

383. The method of claim 361, wherein the disease is cystic fibrosis wherein the patient has a *F508del* CFTR mutation.

394. The method of claim 383, wherein the patient is homozygous for *F508del*.

405. The method of claim 383, wherein the patient is heterozygous for *F508del*.

416. The method of claim 361, wherein the method comprises administering an additional therapeutic agent.

427. The method of claim 416, wherein the therapeutic agent is selected from a mucolytic agent, bronchodilator, an anti-biotic, an anti-infective agent, an anti-inflammatory agent, a CFTR potentiator, or a nutritional agent.

438. The method of claim 416, wherein the additional therapeutic agent is N-(5-hydroxy-2,4-ditert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide.

~~44. A kit comprising the tablet of claim 1, and a separate therapeutic agent or pharmaceutical composition thereof.~~

~~45. The kit of claim 44, wherein the Compound 1 is in Form I.~~

~~46. The kit of claim 44, wherein the therapeutic agent is a cystic fibrosis corrector other than Compound 1.~~

~~47. The kit of claim 44, wherein the therapeutic agent is a cystic fibrosis potentiator.~~

~~48. The kit of claim 44, wherein the therapeutic agent is N-(5-hydroxy-2,4-ditert-butyl-phenyl)-4-oxo-1H-quinoline-3-carboxamide.~~

- ~~49. The kit of claim 44, wherein the tablet of claim 1 and the therapeutic agent are in separate containers.~~
- ~~50. The kit of claim 49, wherein the separate containers are bottles.~~
- ~~51. The kit of claim 49, wherein the separate containers are vials.~~
- ~~52. The kit of claim 49, wherein the separate containers are blister packs.~~
- ~~53. A continuous process for preparing a tablet comprising Compound 1 comprising the steps of:~~
- ~~a) — mixing Compound 1, 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;~~
 - ~~f) — compressing the blend from step d) into a tablet; and~~
 - ~~g) — coating the tablet from step e).~~
- ~~54. The process of claim 53, wherein Compound 1 is in Form I.~~