dehydration, acidosis, impaired growth and death. Acute and chronic diarrheas represent a major medical problem in many areas of the world. Diarrhea is both a significant factor in malnutrition and the leading cause of death (5,000,000 deaths/year) in children less than five years old.

[00019] Secretory diarrheas are also a dangerous condition in patients with acquired immunodeficiency syndrome (AIDS) and chronic inflammatory bowel disease (IBD). Sixteen million travelers to developing countries from industrialized nations every year develop diarrhea, with the severity and number of cases of diarrhea varying depending on the country and area of travel.

[00020] Accordingly, there is a need for potent and selective CFTR potentiators of wild-type and mutant forms of human CFTR. These mutant CFTR forms include, but are not limited to, ΔF508del, G551D, R117H, 2789+5G->A.

[00021] There is also a need for modulators of CFTR activity, and compositions thereof, which can be used to modulate the activity of the CFTR in the cell membrane of a mammal.

[00022] There is a need for methods of treating diseases caused by mutation in CFTR using such modulators of CFTR activity.

[00023] There is a need for methods of modulating CFTR activity in an *ex vivo* cell membrane of a mammal.

[00024] In addition, there is a need for stable solid forms of said compound that can be used readily in pharmaceutical compositions suitable for use as therapeutics.

SUMMARY ~~OF THE INVENTION~~

[00024a] In a first aspect of the present disclosure, there is provided N-(4-(7-azabicyclo[2.2.1]heptan-7-yl)-2-(trifluoromethyl)phenyl)-4-oxo-5-(trifluoromethyl)-1,4-dihydroquinoline-3-carboxamide characterized as Form A-HCl, wherein the Form A-HCl is characterized by one or more peaks in an X-ray powder diffraction pattern selected from the group consisting of a peak at about 7.1 degrees, a peak at about 21.2 degrees, a peak from about 6.9 to about 7.3 degrees, a peak from about 8.0 to about 8.4 degrees, a peak from about 13.9 to about 14.3 degrees, a peak from about 21.0 to about 21.4 degrees, a peak from about 14.5 to about 14.9 degrees, a peak from about 16.2 to about 16.6 degrees, a peak from about 18.5 to about 18.9 degrees, and a peak from about 22.6 to about 23.0 degrees; or wherein the Form A-HCl is characterized by a single crystal which is determined to possess a monoclinic crystal system; a $P2_1/c$ space group; and the following unit cell dimensions:

a = 13.6175(4) Å;

b = 21.614(3) Å;

c = 8.3941(4) Å;

$\alpha = 90°$;

$\beta = 112.303°$; and

$\gamma = 90°$.

[00024b] In a second aspect of the present disclosure, there is provided a pharmaceutical composition comprising Form A-HCl as defined herein, and a pharmaceutically acceptable adjuvant or carrier.

[00024c] In a third aspect of the present disclosure, there is provided N-(4-(7-azabicyclo[2.2.1]heptan-7-yl)-2-(trifluoromethyl)phenyl)-4-oxo-5-(trifluoromethyl)-1,4-dihydroquinoline-3-carboxamide characterized as Form B, wherein the Form B is characterized by one or more peaks in an X-ray powder diffraction pattern selected from the group consisting of a peak from about 6.5 to about 6.9 degrees, a peak from about 9.2 to about 9.6 degrees, a peak from about 11.0 to about 11.4 degrees, a peak from about 13.2 to about 13.6 degrees, a peak from about 15.0 to about 15.4 degrees, a peak from about 17.0 to about 17.4 degrees, a peak from about 17.6 to about 18.0 degrees, a peak from about 17.9 to about 18.3 degrees, a peak from about 19.1 to about 19.5 degrees, a peak from about 19.9 to about 20.3 degrees, a peak from about 21.0 to about 21.5 degrees, a peak from about 21.8 to 22.2 degrees, a peak from about 23.8 to about 24.2 degrees, a peak from about 26.0 to about 26.4 degrees, a peak from about 27.1 to about 27.5 degrees, a peak from about 27.5 to about 27.9 degrees, and a peak from about 28.7 to about 29.1 degrees; or wherein Form B is characterized by a peak from about 6.5 to about 6.9 degrees; a peak from about 9.8 to about 10.2 degrees; a peak from about 11.0 to about 11.4 degrees; a peak from about 13.2 to about 13.6 degrees; and a peak from about 23.8 to about 24.2 degrees in an X-ray powder diffraction; or wherein the Form B is characterized by a single crystal determined to possess a monoclinic crystal system, a $P2_1/c$ space group, and the following unit cell dimensions:

a = 13.5429(4) Å;

b = 13.4557(4) Å;

c = 12.0592(4) Å;

$\alpha = 90°$;

$\beta = 101.193°$; and

$\gamma = 90°$.

[00024d] In a fourth aspect of the present disclosure, there is provided a pharmaceutical composition comprising Form B as defined herein, and a pharmaceutically acceptable adjuvant or carrier.

[00024e] In a fifth aspect of the present disclosure, there is provided N-(4-(7-azabicyclo[2.2.1]heptan-7-yl)-2-(trifluoromethyl)phenyl)-4-oxo-5-(trifluoromethyl)-1,4-dihydroquinoline-3-carboxamide characterized as Form B-HCl, wherein the Form B-HCl is characterized by one or more of the following: a peak from about 8.1 to about 8.5 degrees, a peak from about 14.6 to about 15.1 degrees, a peak from about 16.5 to about 16.9 degrees, 3 peaks from about 17.6 to about 18.4 degrees, 2 peaks from about 21.4 to about 22.1 degrees, 2 peaks from about 22.8 to about 23.8 degrees, 2 peaks from about 24.7 to about 25.4 degrees, a peak from about 26.1 to about 27.3 degrees, a peak from about 30.9 to about 31.3 degrees, and a peak from about 38.2 to about 38.7 degrees in an X-ray powder diffraction pattern; or wherein the Form B-HCl is characterized by a peak from about 8.1 to about 8.5 degrees; a peak from about 8.8 to about 9.2 degrees; a peak from about 12.8 to about 13.2 degrees; a peak from about 17.8 to about 18.2 degrees; and a peak from about 22.8 to about 23.2 degrees in an X-ray powder diffraction; or wherein the Form B-HCl is characterized by a single crystal determined to possess a monoclinic crystal system, a $P2_1/a$ space group, and the following unit cell dimensions:

$a = 12.57334(5)$ Å;

$b = 19.68634(5)$ Å;

$c = 8.39399(5)$ Å;

$\alpha = 90°$;

$\beta = 90.0554°$; and

$\gamma = 90°$.

[00024f] In a sixth aspect of the present disclosure, there is provided a pharmaceutical composition comprising Form B-HCl as defined herein, and a pharmaceutically acceptable adjuvant or carrier.

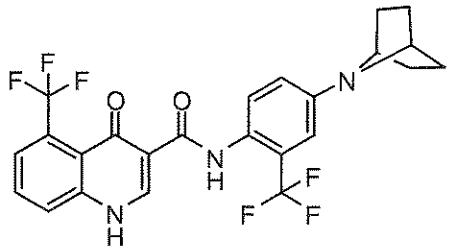
[00024g] In a seventh aspect of the present disclosure, there is provided the use of Form A-HCl, Form B, Form B-HCl as defined herein, or any combination of these forms in the manufacture of medicament for treating or lessening the severity of a disease in a patient, wherein said disease is selected from cystic fibrosis, asthma, smoke induced COPD, chronic bronchitis, rhinosinusitis, constipation, pancreatitis, pancreatic insufficiency, male infertility caused by congenital bilateral absence of the vas deferens (CBAVD), mild pulmonary disease, idiopathic pancreatitis, allergic bronchopulmonary aspergillosis (ABPA), liver disease, hereditary emphysema, hereditary hemochromatosis, coagulation-fibrinolysis deficiencies, including protein C deficiency, Type 1 hereditary angioedema, lipid processing deficiencies, including familial hypercholesterolemia, Type 1 chylomicronemia, abetalipoproteinemia, lysosomal storage diseases, including I-cell disease/pseudo-Hurler, mucopolysaccharidoses, Sandhof/Tay-Sachs, Crigler-Najjar type II, polyendocrinopathy/ hyperinsulinemia, Diabetes mellitus, Laron dwarfism, myeloperoxidase deficiency, primary hypoparathyroidism, melanoma, glycanosis CDG type 1, congenital hyperthyroidism, osteogenesis imperfecta, hereditary hypofibrinogenemia, ACT deficiency, Diabetes insipidus (DI), neurohypophyseal DI, nephrogenic DI, Charcot-Marie Tooth syndrome, Pelizaeus-Merzbacher disease, neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, progressive supranuclear palsy, Pick's disease, several polyglutamine neurological disorders including Huntington's, spinocerebellar ataxia type I, spinal and bulbar muscular atrophy, dentatorubral pallidoluysian atrophy, and myotonic dystrophy, as well as spongiform encephalopathies, including hereditary Creutzfeldt-Jakob disease (due to prion protein processing defect), Fabry disease, Gerstmann-Sträussler-Scheinker syndrome, COPD, dry-eye disease, or Sjogren's disease, Osteoporosis, Osteopenia, bone healing and bone growth (including bone repair, bone regeneration, reducing bone resorption and increasing bone deposition), Gorham's Syndrome, chloride channelopathies such as myotonia congenita (Thomson and Becker forms), Bartter's syndrome type III, Dent's disease, epilepsy, hyperekplexia, lysosomal storage disease, Angelman syndrome, and Primary Ciliary Dyskinesia (PCD), a term for inherited disorders of the structure and/or function of cilia, including PCD with situs inversus (also known as Kartagener syndrome), PCD without situs inversus and ciliary aplasia.

[00024h] In an eighth aspect of the present disclosure, there is provided the use of Form A-HCl, Form B, Form B-HCl as defined herein, or any combination of these forms in the manufacture of medicament for treating or lessening the severity of a disease in a patient, wherein said disease is associated with reduced CFTR function due to mutations in the gene encoding CFTR or environmental factors, and wherein said disease is cystic fibrosis, chronic bronchitis, recurrent bronchitis, acute bronchitis, male infertility caused by congenital bilateral absence of the vas deferens (CBAVD), female infertility caused by congenital absence of the uterus and vagina (CAUV), idiopathic chronic pancreatitis (ICP), idiopathic recurrent pancreatitis, idiopathic acute pancreatitis, chronic rhinosinusitis, primary sclerosing cholangitis, allergic bronchopulmonary aspergillosis, diabetes, dry eye, constipation, allergic bronchopulmonary aspergillosis (ABPA), bone diseases, and asthma.

[00024i] In a ninth aspect of the present disclosure, there is provided the use of Form A-HCl, Form B, Form B-HCl as defined herein, or any combination of these forms in the manufacture of medicament for treating or lessening the severity of a disease in a patient, wherein said disease is associated with normal CFTR function.

[00024j] In a tenth aspect of the present disclosure, there is provided an in vitro method of modulating CFTR activity in a biological sample, said method comprising the step of contacting said CFTR with Form A-HCl, Form B, Form B-HCl as defined herein, or any combination of these forms.

[00025] The present disclosure~~invention~~ relates to solid forms of N-(4-(7-azabicyclo[2.2.1]heptan-7-yl)-2-(trifluoromethyl)phenyl)-4-oxo-5-(trifluoromethyl)-1,4-dihydroquinoline-3-carboxamide (hereinafter "Compound I") which has the structure below:



Compound I.

[00026] Compound I and pharmaceutically acceptable compositions thereof are useful for treating or lessening the severity of a variety of diseases, disorders, or conditions, including, but not limited to, cystic fibrosis, asthma, smoke induced COPD, chronic bronchitis, rhinosinusitis, constipation, pancreatitis, pancreatic insufficiency, male infertility caused by

congenital bilateral absence of the vas deferens (CBAVD), mild pulmonary disease, idiopathic pancreatitis, allergic bronchopulmonary aspergillosis (ABPA), liver disease, hereditary emphysema, hereditary hemochromatosis, coagulation-fibrinolysis deficiencies, such as protein C deficiency, Type 1 hereditary angioedema, lipid processing deficiencies, such as familial hypercholesterolemia, Type 1 chylomicronemia, abetalipoproteinemia, lysosomal storage diseases, such as I-cell disease/pseudo-Hurler, mucopolysaccharidoses, Sandhof/Tay-Sachs, Crigler-Najjar type II, polyendocrinopathy/hyperinsulemia, Diabetes mellitus, Laron dwarfism, myleoperoxidase 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 such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, progressive supranuclear plasy, Pick's disease, several polyglutamine neurological disorders such as Huntington's, spinocerebullar ataxia type I, spinal and bulbar muscular atrophy, dentatorubal pallidoluysian, and myotonic dystrophy, as well as spongiform encephalopathies, such as hereditary Creutzfeldt-Jakob disease (due to prion protein processing defect), Fabry disease, Straussler-Scheinker syndrome, COPD, dry-eye disease, or Sjogren's disease, Osteoporosis, Osteopenia, bone healing and bone growth (including bone repair, bone regeneration, reducing bone resorption and increasing bone deposition), Gorham's Syndrome, chloride channelopathies such as myotonia congenita (Thomson and Becker forms), Bartter's syndrome type III, Dent's disease, hyperekplexia, epilepsy, hyperekplexia, lysosomal storage disease, Angelman syndrome, and Primary Ciliary Dyskinesia (PCD), a term for inherited disorders of the structure and/or function of cilia, including PCD with situs inversus (also known as Kartagener syndrome), PCD without situs inversus and ciliary aplasia.

[00027] In one embodimentaspect, Compound I is in a substantially crystalline form referred to as Form B, Form A-HCl, or Form B-HCl, as described and characterized herein.

[00028] In another embodimentaspect, Compound I is in a hydrochloride salt form referred to as Form A-HCl or Form B-HCl as described and characterized herein.

[00029] In another embodimentaspect, Compound I is in a hydrochloride salt form referred to as Form B-HCl as described and characterized herein.

[00030] Processes described herein can be used to prepare the compositions of this invention comprising Form B, Form A-HCl, Form B-HCl, or any combination of these forms.