applicant has now found that inhalation compositions are suitable dosage form for compound (I), specifically dry powder inhaler composition.

The applicant has now found that inhalable composition comprising compound (I) and pharmaceutically acceptable salts thereof that is suitable for pulmonary administration.

SUMMARY ~~OF THE INVENTION~~

The present ~~invention~~ disclosure relates to a~~n~~ pharmaceutical composition comprising compound (I) or a pharmaceutically acceptable salt thereof.

~~One embodiment~~ There is provided ~~is~~ an inhalable composition comprising compound (I) or a pharmaceutically acceptable salt thereof.

One aspect is an inhalable composition comprising: 2-{4-[(2S)-1,1-difluoro-2-hydroxypropyl]phenyl}-N-{4-[3-(2-ethylphenyl)pyrazine-2-yl] phenyl}acetamide (compound (I)) or a pharmaceutically acceptable salt thereof.

There is also provided ~~Another embodiment is~~ an inhalable composition comprising a therapeutically effective amount of compound (I) or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipient(s).

Another aspect is an inhalable composition comprising 2-{4-[(2S)-1,1-difluoro-2-hydroxypropyl]phenyl}-N-{4-[3-(2-ethylphenyl)pyrazine-2-yl] phenyl}acetamide (compound (I)) or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.

Another example ~~embodiment~~ is an inhalable dry powder composition comprising compound (I) or a pharmaceutically acceptable salt thereof.

Another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof.

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof for preventing, inhibiting, suppressing, and/or treating at least one pulmonary disease.

In some examples~~embodiments~~, the pulmonary disease is selected from asthma, COPD, bronchitis, chronic or acute bronchoconstriction, adult respiratory distress syndrome, acute lung injury, and bronchiectasis.

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof for preventing, inhibiting, suppressing, and/or treating COPD.

The inhalable dry powder composition may comprise a therapeutically effective amount of compound (I) or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipient(s).

Another example ~~embodiment~~ is a composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof.

In one example~~embodiment~~, the composition is a capsule dosage form.

One example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof, in the range of from about 0.1 mg to about 20 mg and one or more pharmaceutically acceptable excipient(s).

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof, in the range of from about 0.1 mg to about 20 mg and a diluent.

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising: a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof, in the range of from about 0.1 mg to about 20 mg and a lactose component.

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof, in the range of from about 0.1 mg to about 20 mg and a lactose component having a d_{90} particle size less than about 60 microns.

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof, in the range of from about 0.1 mg to about 20 mg and a lactose component having a d_{90} particle size less than about 200 microns.

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof, in the range of from about 0.1 mg to about 20 mg and a lactose component, wherein the lactose component comprises i) lactose particles having a d_{90} particle size less than about 60 microns and ii) lactose particles having a d_{90} particle size less than about 200 microns.

Yet another example ~~embodiment~~ is an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof, in the range of from about 0.1 mg to about 20 mg and a lactose component, wherein the lactose component has an average particle size of from about 1 microns to about 200 microns.

In some examples~~embodiments~~, the inhalable dry powder composition is physically and chemically stable.

In an example~~embodiment~~, the present ~~invention~~ disclosure relates to a method of preventing, inhibiting, suppressing, and/or treating at least one pulmonary disease(s) characterized by airflow obstruction or limitation, or a symptom occurring in pulmonary region, including but not limited to asthma, emphysema, bronchitis, COPD, sinusitis, respiratory

depression, reactive airways dysfunction syndrome (RADS), acute respiratory distress syndrome (ARDS), irritant induced asthma, occupational asthma, symptoms of pulmonary infection(s), sensory hyper-reactivity, airway (or pulmonary) inflammation, multiple chemical sensitivity, aid in smoking cessation therapy, pneumonia, bronchitis, influenza, Severe Acute Respiratory Syndrome (SARS), SARS-CoV-2 (COVID-19), tuberculosis, and whooping cough (pertussis), and the like in a subject in need thereof.

Yet another example ~~embodiment~~ is a method of preventing, inhibiting, suppressing, and/or treating at least one pulmonary disease in a subject in need thereof comprising administering a therapeutically dosage effective amount of compound (I) or a pharmaceutically acceptable salt thereof to the subject via inhalation.

Yet another example ~~embodiment~~ is a method of treating symptom(s) of pulmonary infection(s) in a subject in the need thereof, comprising administering a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof to the subject via inhalation.

In some examples~~embodiments~~, the pulmonary infection(s) includes viral, bacterial, or fungal infection. The symptoms of pulmonary infection(s) is mild to severe breathing problem, dry or productive cough, chest pain, whooping cough and/or sore throat.Yet another embodiment is a method of preventing, inhibiting, suppressing, and/or treating at least one pulmonary disease in a subject in need thereof comprising administering an inhalable dry powder composition comprising compound (I) or a pharmaceutically acceptable salt thereof to the subject via inhalation.

Yet another example ~~embodiment~~ is a method of preventing, inhibiting, suppressing, and/or treating at least one pulmonary disease in a subject in need thereof comprising administering an inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof to the subject via inhalation.

In one example~~embodiment~~, the pulmonary disease is one or more condition(s) selected from asthma, emphysema, bronchitis, COPD, sinusitis, respiratory depression, reactive airways dysfunction syndrome (RADS), acute respiratory distress syndrome (ARDS), irritant induced asthma, occupational asthma, symptoms of pulmonary infection(s), sensory hyper-reactivity, airway (or pulmonary) inflammation, multiple chemical sensitivity, aid in smoking cessation therapy, pneumonia, bronchitis, influenza, SARS, SARS-CoV-2 (COVID-19), tuberculosis, and whooping cough (pertussis).

Yet another example ~~embodiment~~ is a method of preventing, inhibiting, suppressing, and/or treating COPD comprising administering a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof to the subject via inhalation.

Yet another example ~~embodiment~~ is a method of preventing, inhibiting, suppressing, and/or treating COPD comprising administering an inhalation powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof to the subject via inhalation.

Yet another example ~~embodiment~~ is a method of administering, comprising administering compound (I) or a pharmaceutically acceptable salt thereof to the subject via inhalation.

In one example~~embodiment~~, the method of administration comprises administering a therapeutically effective amount of compound (I) or a pharmaceutically acceptable salt thereof with an inhalation device.

Yet another example ~~embodiment~~ is a method of administering inhalable dry powder composition comprising a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof to the subject; wherein the method

comprises administration of a unit dosage rapidly with one or two, small volume breaths as needed.

Another aspect is use of the inhalable composition as defined herein in the manufacture of a medicament for preventing, inhibiting, suppressing, and/or treating a pulmonary disease, wherein the composition includes a therapeutically effective dosage amount of the compound (I) or a pharmaceutically acceptable salt thereof in the range of from about 0.1 mg to about 20 mg.

~~Yet another embodiment~~ There is also provided ~~is~~ a process for preparing an inhalable dry composition comprising compound (I) or a pharmaceutically acceptable salt thereof comprising: i) mixing a therapeutically effective dosage amount of compound (I) or a pharmaceutically acceptable salt thereof with one or more pharmaceutically acceptable excipient(s), and ii) filling the blend in a capsule/blister/sachet dosage form meant for unit dose dry powder inhaler.

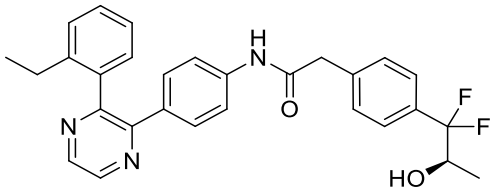
Another aspect is a process for preparing an inhalable composition of claim 3 comprising the steps of: (i) blending compound (I) or a pharmaceutically acceptable salt thereof with a part or full quantity of one or more excipient(s) or co-milling of compound (I) with one or more excipient(s); (ii) optionally blending the mixture obtained in step (i) with the remaining part of excipient(s); (iii) optionally conditioning the blend from step (i) or (ii); and (iv) filling the final blend of step (i) or step (ii) or step (iii) in a capsule or a blister.

DETAILED DESCRIPTION

The terms used herein are defined as follows. If a definition set forth in the present application and a definition set forth later in a non-provisional application claiming priority from the present provisional application are in conflict, the definition in the non-provisional application shall control the meaning of the terms.

The term singular forms "a," "an" and "the" include plural references unless the context clearly dictates otherwise. Thus, for example, reference to "an excipient" includes a single excipient as well as two or more different excipients, and the like.

The chemical compound referred herein as compound (I) in the context of the present invention has the following chemical structure:



Compound (I)