Certain patient groups are particularly susceptible to COPD exacerbations. This includes patients suffering from additional respiratory conditions such as asthma and patients suffering from allergic conditions. Patients susceptible to COPD exacerbations have typically experienced COPD exacerbations previously.

COPD exacerbations can be severe and can limit the quality of life of COPD patients. Not all drugs which are disclosed for use in treating COPD are equally effective in reducing the severity and/or frequency of COPD exacerbations or time to first COPD exacerbation. It would therefore be advantageous for a COPD drug to be used which is particularly effective in reducing the severity and/or frequency of COPD exacerbations when there is a specific clinical need to address such exacerbations.

SUMMARY

It is a surprising finding of the present disclosure that ensifentrine is highly effective in reducing the frequency and/or severity of COPD exacerbations in COPD patients. In particular, ensifentrine has been found to lead to a more pronounced reduction in COPD exacerbations compared to many known treatments for COPD.

In an aspect, there is provided the use of a compound in the manufacture of a medicament for decreasing the frequency and/or severity of chronic obstructive pulmonary disease (COPD) exacerbations in a patient suffering from COPD, wherein the compound is ensifentrine or a pharmaceutically acceptable salt thereof.

In another aspect, there is provided the use of a compound in the manufacture of a medicament for treating chronic obstructive pulmonary disease (COPD) in a patient, wherein:

the compound is ensifentrine or a pharmaceutically acceptable salt thereof; and

the patient is susceptible to COPD exacerbations.

In another aspect, there is provided a suspension formulation having the composition:

Constituent	**Concentration (mg/mL)**
Ensifentrine particles (RPL554)	1.2
Polysorbate 20 (Tween 20)	0.50
Sorbitan Monolaurate (Span 20)	0.05
Sodium Dihydrogen Phosphate Dihydrate	0.744
Disodium Hydrogen Phosphate Dihydrate	0.853
Sodium Chloride	8.60
Water	q.s. to 1 mL

The disclosure accordingly provides a compound for use in a method for decreasing the frequency and/or severity of chronic obstructive pulmonary disease (COPD) exacerbations in a patient suffering from COPD, wherein the compound is ensifentrine or a pharmaceutically acceptable salt thereof. The disclosure also provides a compound for use in a method for increasing the time to first COPD exacerbation in a patient suffering from COPD, wherein the compound is ensifentrine or a pharmaceutically acceptable salt thereof.

Also provided by the disclosure is a compound for use in a method for treating chronic obstructive pulmonary disease (COPD) in a patient, wherein: the compound is ensifentrine or a pharmaceutically acceptable salt thereof; and the patient is susceptible to COPD exacerbations.

The disclosure also provides a method for decreasing the frequency and/or severity of chronic obstructive pulmonary disease (COPD) exacerbations in a patient suffering from COPD, the method comprising administering a therapeutically effective amount

of a compound to the patient, which compound is ensifentrine or a pharmaceutically acceptable salt thereof.

The disclosure further provides a method of treating COPD in a patient, which method comprises administering a therapeutically effective amount of a compound which is ensifentrine or a pharmaceutically acceptable salt thereof to the patient, wherein the patient is susceptible to COPD exacerbations.

Further provided by the disclosure is use of a compound in the manufacture of a medicament for use in a method for decreasing the frequency and/or severity of chronic obstructive pulmonary disease (COPD) exacerbations in a patient suffering from COPD, wherein the compound is ensifentrine or a pharmaceutically acceptable salt thereof.

Also provided by the disclosure is use of a compound which is ensifentrine or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating COPD, wherein the patient is susceptible to COPD exacerbations.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows the FEV_1 profile over 12 hours at Week 12.

DETAILED DESCRIPTION OF THE INVENTION

The compound decreases the frequency and/or severity of chronic obstructive pulmonary disease (COPD) exacerbations in a patient suffering from COPD. The compound may decrease the frequency of COPD exacerbations. For instance, the patient may suffer two or fewer (for instance one or zero) COPD exacerbations per year while being treated with the compound, for instance as a maintenance therapy. The number of COPD exacerbations experienced by the patient per year during treatment with the compound may be one to three fewer than the number of COPD exacerbations experienced by the patient per year prior to treatment with the compound.

The compound may increase the time to a first COPD exacerbation in the patient. Accordingly, the patient may not have yet experienced a COPD exacerbation and the compound may increase the time until the patient experiences a first COPD

CLAIMS

1. Use of a compound in the manufacture of a medicament for decreasing the frequency and/or severity of chronic obstructive pulmonary disease (COPD) exacerbations in a patient suffering from COPD, wherein the compound is ensifentrine or a pharmaceutically acceptable salt thereof.

2. Use according to claim 1, wherein the medicament is for decreasing the frequency of COPD exacerbations.

3. Use of a compound in the manufacture of a medicament for treating chronic obstructive pulmonary disease (COPD) in a patient, wherein:

the compound is ensifentrine or a pharmaceutically acceptable salt thereof; and

the patient is susceptible to COPD exacerbations.

4. Use according to any one of the preceding claims, wherein the COPD exacerbations comprise one or more of dyspnea, increased coughing, increased sputum volume, sputum purulence, wheezing, sore throat, a cold, and fever.

5. Use according to any one of the preceding claims, wherein the patient is a patient susceptible to COPD exacerbations and the patient susceptible to COPD exacerbations is suffering from one or more disease or condition selected from asthma, pulmonary hypertension, bronchiectasis, allergy, lung cancer, chest infection, cystic fibrosis, pulmonary fibrosis, pneumonia, hay fever, allergic rhinitis, bronchitis, emphysema, adult respiratory distress syndrome (ARDS), interstitial lung disease or tuberculosis.

6. Use according to claim 5, wherein the asthma is allergic asthma, steroid resistant asthma, severe asthma or paediatric asthma.

7. Use according to any one of the preceding claims, wherein the patient has suffered one or more COPD exacerbations in the year preceding first administration of the compound.

8. Use according to any one of the preceding claims, wherein the patient has suffered two or more COPD exacerbations in the year preceding first administration of the compound.

9. Use of according to any one of the preceding claims, wherein the compound is to be administered to the patient by inhalation.

10. Use according to any one of the preceding claims, wherein the compound is to be administered to the patient by inhalation by nebuliser.

11. Use according to any one of the preceding claims, wherein the compound is ensifentrine.

12. Use according to any one of the preceding claims, wherein the compound is to be administered to the patient once, twice or three times per day.

13. Use according to any one of the preceding claims, wherein the compound is to be administered to the patient twice a day.

14. Use according to any one of the preceding claims, wherein the compound is to be administered a total daily dose of from 0.5 to 10 mg

15. Use according to any one of the preceding claims, wherein the compound is to be administered a total daily dose of from 5 to 7 mg.

16. Use according to any one of the preceding claims, wherein the compound is to be administered to the patient twice a day in a first dose of from 2 to 4 mg and a second dose of from 2 to 4 mg.

17. Use according to any one of the preceding claims, wherein a dose of about 3 mg the compound is to be administered to the patient twice a day (3 mg BID)

18. Use according to any one of the preceding claims, wherein a dose of about 3 mg the compound is to be administered by nebuliser to the patient twice a day.

19. Use according to any one of the preceding claims, wherein the compound is to be administered to the patient at least once per day for at least 8 weeks

20. Use according to any one of the preceding claims, wherein the compound is to be administered to the patient at least once per day for at least 16 weeks.

21. Use according to any one of the preceding claims, wherein the compound is to be administered to the patient at least once per day for at least 24 weeks.

22. Use according to any one of the preceding claims, wherein an inhalable pharmaceutical composition comprising a suspension of particles of the compound in a diluent is to be administered.

23. Use according to any one of the preceding claims, wherein the compound is used in combination with a muscarinic receptor antagonist, a beta-adrenergic receptor agonist or an inhaled corticosteroid.

24. A suspension formulation having the composition:

Constituent	**Concentration (mg/mL)**
Ensifentrine particles (RPL554)	1.2
Polysorbate 20 (Tween 20)	0.50
Sorbitan Monolaurate (Span 20)	0.05
Sodium Dihydrogen Phosphate Dihydrate	0.744
Disodium Hydrogen Phosphate Dihydrate	0.853
Sodium Chloride	8.60
Water	q.s. to 1 mL