CLAIMS

1. A pharmaceutical composition deliverable from a metered dose inhaler, the pharmaceutical composition comprising:

a propellant of pharmaceutical grade (1*E*)-1,3,3,3-Tetrafluoro-1-propene (HFO-1234ze(E)) having a purity of at least about 99.90%;

a plurality of one or more species of active agent particles; and

a plurality of phospholipid particles comprising perforated microstructures;

wherein the one or more active agents are selected from a long-acting muscarinic antagonist (LAMA), a long-acting β2-agonists (LABA), a short-acting beta-agonists (SABA), an inhaled corticosteroid (ICS), and a non-corticosteroid anti-inflammatory agent, wherein the pharmaceutical composition comprises:

(i) a plurality of budesonide particles, and
a plurality of albuterol particles;

(ii) a plurality of glycopyrrolate particles, and
a plurality of formoterol particles; or

(iii) a plurality of budesonide particles, and
a plurality of formoterol particles.

2. The pharmaceutical composition according to claim 1, wherein (i) the SABA is present at a concentration in the range of about 0.04 mg/mL to about 2.25 mg/mL, (ii) the LABA is present at a concentration in the range of about 0.01 mg/mL to about 1 mg/mL, (iii) the ICS is present at a concentration in the range of about 0.1 mg/mL to about 20 mg/mL, (iv) the LAMA is present at a concentration in the range of 0.04 mg/mL to 2.25 mg/mL.

3. The pharmaceutical composition according to claim 1 or 2, wherein the perforated microstructures comprise 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC) and calcium chloride.

4. The pharmaceutical composition according to any one of claims 1 to 3, wherein the phospholipid particles are present at a concentration in the range of about 0.1 mg/mL to about 10 mg/mL.

5. The pharmaceutical composition according to any one of the preceding claims 1-4, wherein the albuterol particles are in the propellant at a concentration sufficient to provide a delivered dose of glycopyrrolate per actuation of the metered dose inhaler selected from between 5 µg and 50 µg per actuation, between 2 µg and 25 µg per actuation, and between 6 µg and 15 µg per actuation.

6. The pharmaceutical composition according to any one of claims 1-5, wherein the albuterol particles comprise albuterol sulfate.

7. The pharmaceutical composition according to claim 6, wherein the albuterol sulfate is micronized and crystalline albuterol sulfate.

8. The pharmaceutical composition according to any one of claims 1-7, wherein the formoterol particles are included in the composition at a concentration sufficient to provide a delivered dose of formoterol selected from between 1 µg and 30 µg, between 0.5 µg and 10 µg, between 2 µg and 5 µg, between 3 µg and 10 µg, between 5 µg and 10 µg, and between 3 µg and 30 µg per actuation of the metered dose inhaler.

9. The pharmaceutical composition according to any one of claims 1-8, wherein the formoterol particles comprise formoterol fumarate.

10. The pharmaceutical composition according to claim 9, wherein the formoterol fumarate is micronized and crystalline formoterol fumarate.

11. The pharmaceutical composition according to any one of claims 1-10, wherein the budesonide particles are included in the composition at a concentration sufficient to provide a delivered dose of budesonide selected from between 50 µg and 400 µg,

between 20 µg and 600 µg, between 30 µg and 100 µg, between 50 µg and 200 µg, and between 150 µg and 350 µg per actuation of the metered dose inhaler.

12. The pharmaceutical composition according to any of claims 1-11, wherein the budesonide particles comprise micronized budesonide.

13. The pharmaceutical composition according to any of claims 1-12, wherein the phospholipid particles are included in the composition at a concentration sufficient to provide a delivered dose of the phospholipid particles selected from between 50 µg and 400 µg.

14. A metered dose inhaler comprising a canister with an outlet valve including an actuator for dispensing a metered amount of a pharmaceutical composition according to any one of claims 1-13, wherein the canister contains the pharmaceutical composition.

15. The metered dose inhaler according to claim 14, wherein the outlet valve comprises a neck gasket and at least one seat gasket; and the neck gasket or the at least one seat gasket is composed of bromobutyl material.

16. The metered dose inhaler according to claim 14 or 15, exhibiting less than about 10%, 9%, 8%, 7%, 6%, or 5% reduced shot weight per actuation throughout emptying of the canister.

17. The metered dose inhaler according to any one of claims 14-16, exhibiting less than about 1.0%, 0.5%, 0.4%, 0.3%, 0.2%, or 0.1% weight loss at 25°C/60% RH per year.

18. The metered dose inhaler according to any one of claims 14-17, which exhibits a delivered dose uniformity (DDU) for the pharmaceutical formulation selected from a DDU of ± 20%, or better, a DDU of ± 15%, or better, and a DDU of ± 10%, or better, throughout emptying of the canister.

19. A pharmaceutical composition according to any one of claims 1-18 for use in the treatment of a pulmonary disease or disorder.

20. The pharmaceutical composition for use according to claim 19, wherein the treatment comprises a method of treating a pulmonary disease or disorder in a patient, the method comprising administering the pharmaceutical composition to the patient by actuating a metered dose inhaler; wherein the metered dose inhaler contains the pharmaceutical composition.

21. The pharmaceutical composition for use according to claim 19 or 20, wherein the pulmonary disease or disorder is asthma or COPD.

22. The pharmaceutical composition for use according to any one of claims 19-21, wherein the metered dose inhaler is described according to any one of the claims 14-18.