Patent claims:

1. A formulation for inhalation comprising a dry powder blend, wherein the dry powder blend comprises:

a) crystalline monohydrate form of (5S)-{[2-(4-carboxyphenyl)ethyl][2-(2-{[3-chloro-4'-(trifluoromethyl)biphenyl-4-yl]methoxy}phenyl)ethyl]-amino}-5,6,7,8-tetrahydroquinoline-2-carboxylic acid, wherein the crystalline monohydrate form has X-ray powder diffraction reflections at 12.8 ± 0.2 °2θ, 29.2 ± 0.2 °2θ, and at least one additional reflection at 6.9 ± 0.2 °2θ, 7.2 ± 0.2 °2θ, or 7.3 ± 0.2 °2θ using Cu K alpha radiation when measured at 25 °C; and

b) a lactose carrier.

2. The formulation of claim 1, wherein the crystalline monohydrate form has at least one additional reflection at 15.2 ± 0.2 °2θ or 23.0 ± 0.2 °2θ, using Cu K alpha radiation when measured at 25 °C.

3. A formulation for inhalation comprising a dry powder blend, wherein the dry powder blend comprises:

a) crystalline monohydrate form of (5S)-{[2-(4-carboxyphenyl)ethyl][2-(2-{[3-chloro-4'-(trifluoromethyl)biphenyl-4-yl]methoxy}phenyl)ethyl]-amino}-5,6,7,8-tetrahydroquinoline-2-carboxylic acid, wherein the crystalline monohydrate form has X-ray powder diffraction reflections at 12.8 ± 0.2 °2θ, 16.0 ± 0.2 °2θ, and 25.8 ± 0.2 °2θ, using Cu K alpha radiation when measured at 25 °C; and

b) a lactose carrier.

4. The formulation of claim 3, wherein the crystalline monohydrate form has at least one additional reflection at 6.9 ± 0.2 °2θ, 7.2 ± 0.2 °2θ, 7.3 ± 0.2 °2θ, or 15.2 ± 0.2 °2θ, using Cu K alpha radiation when measured at 25 °C.

5. A formulation for inhalation comprising a dry powder blend, wherein the dry powder blend comprises:

a) crystalline monohydrate form of (5S)-{[2-(4-carboxyphenyl)ethyl][2-(2-{[3-chloro-4'-(trifluoromethyl)biphenyl-4-yl]methoxy}phenyl)ethyl]-amino}-5,6,7,8-tetrahydroquinoline-2-carboxylic acid, wherein the crystalline monohydrate form has X-ray powder diffraction reflections at 12.8 ± 0.2 °2θ, 20.5 ± 0.2 °2θ, and 25.8 ± 0.2 °2θ, using Cu K alpha radiation when measured at 25 °C; and

b) a lactose carrier.

6. The formulation of claim 5, wherein the crystalline monohydrate form has at least one additional reflection at 6.9 ± 0.2 °2θ, 7.2 ± 0.2 °2θ, 7.3 ± 0.2 °2θ, 15.2 ± 0.2 °2θ, or 25.1 ± 0.2 °2θ, using Cu K alpha radiation when measured at 25 °C.

7. A formulation for inhalation comprising a dry powder blend, wherein the dry powder blend comprises:

a) crystalline monohydrate form of (5S)-{[2-(4-carboxyphenyl)ethyl][2-(2-{[3-chloro-4'-(trifluoromethyl)biphenyl-4-yl]methoxy}phenyl)ethyl]-amino}-5,6,7,8-tetrahydroquinoline-2-carboxylic acid, wherein the crystalline monohydrate form has at least three X-ray powder reflections selected from 5.7 ± 0.2 °2θ, 6.9 ± 0.2 °2θ, 7.2 ± 0.2 °2θ, 7.3 ± 0.2 °2θ, 9.9 ± 0.2 °2θ, 10.4 ± 0.2 °2θ, 10.6 ± 0.2 °2θ, 11.1 ± 0.2 °2θ, 11.5 ± 0.2 °2θ, 12.0 ± 0.2 °2θ, 12.3 ± 0.2 °2θ, 12.4 ± 0.2 °2θ, 12.8 ± 0.2 °2θ, 13.7 ± 0.2 °2θ, 14.1 ± 0.2 °2θ, 14.3 ± 0.2 °2θ, 15.2 ± 0.2 °2θ, 15.6 ± 0.2 °2θ, 16.0 ± 0.2 °2θ, 16.9 ± 0.2 °2θ, 17.2 ± 0.2 °2θ, 17.5 ± 0.2 °2θ, 17.7 ± 0.2 °2θ, 18.0 ± 0.2 °2θ, 18.4 ± 0.2 °2θ, 18.8 ± 0.2 °2θ, 19.2 ± 0.2 °2θ, 19.9 ± 0.2 °2θ, 20.2 ± 0.2 °2θ, 20.5 ± 0.2 °2θ, 20.7 ± 0.2 °2θ, 21.3 ± 0.2 °2θ, 21.9 ± 0.2 °2θ, 22.2 ± 0.2 °2θ, 22.5 ± 0.2 °2θ, 23.0 ± 0.2 °2θ, 23.4 ± 0.2 °2θ, 23.7 ± 0.2 °2θ, 24.1 ± 0.2 °2θ, 25.1 ± 0.2 °2θ, 25.8 ± 0.2 °2θ, 26.0 ± 0.2 °2θ, 26.4 ± 0.2 °2θ, 28.9 ± 0.2 °2θ, 29.2 ± 0.2 °2θ, 29.4 ± 0.2 °2θ, 30.6 ± 0.2 °2θ, 31.1 ± 0.2 °2θ, 32.2 ± 0.2 °2θ, and 35.3 ± 0.2 °2θ, using Cu K alpha radiation when measured at 25 °C; and

b) a lactose carrier.

8. The formulation of any one of claims 1-7, wherein the crystalline monohydrate is in a concentration by weight of from about 0.75% (w/w) to about 20% (w/w).

9. The formulation of any one of claims 1-8, wherein the lactose carrier is in a concentration by weight of from about 80% (w/w) to about 99.25% (w/w).

10. The formulation of any one of claims 1-9, wherein the crystalline monohydrate has a particle size of X50 of from about 1 μm to about 3 μm.

11. The formulation of any one of claims 1-10, wherein the lactose carrier is lactose monohydrate for inhalation.

12. The formulation of claim 11, wherein the lactose monohydrate has a particle size of X50 ≥ 50 μm.

13. The formulation of claim 12, wherein the lactose monohydrate comprises coarse lactose and fine lactose.

14. The formulation of claim 13, wherein:

i) the coarse lactose has a particle size of X50 ≥ 50 μm; and

ii) the fine lactose has a particle size of X50 < 10 μm.

15. The formulation of claim 14, wherein the coarse lactose content of the dry powder blend is from

about 70% to about 98.25% (w/w).

16. The formulation of any one of claims 1-15, wherein the crystalline monohydrate is in a concentration by weight of about 5%, about 10%, or about 20% (w/w).

17. The formulation of any one of claims 1-16, wherein the lactose is in a concentration by weight of about 95%, about 90%, or about 80% (w/w).

18. The formulation of claim 17, wherein the fine lactose is present in the total lactose concentration by weight of about 5% (w/w).

19. The formulation of claim 17 or claim 18, wherein the coarse lactose is present in the total lactose concentration by weight of about 90%, about 85%, or about 75% (w/w).

20. The formulation of claim 17, wherein the fine lactose is present from about 1% to about 10% (w/w).

21. The formulation of any one of claims 17-20, wherein the ratio of crystalline monohydrate to coarse lactose is from about 1:126 to about 1:3.8.

22. The formulation of any one of claims 17-21, wherein the ratio of crystalline monohydrate to fine lactose is from about 1:13 to about 1:0.1.

23. The formulation of any one of claims 17-22, wherein the ratio of coarse lactose to fine lactose is from about 445:5 to about 75:5.

24. The formulation for inhalation according to any one of claims 17-23, wherein the fine lactose is Lactohale® 300 or Lactohale® 230.

25. The formulation of any one of claims 1-24, wherein the crystalline monohydrate is at a nominal dose of from about 480 µg to about 4000 µg.

26. A capsule comprising the formulation of any one of claims 1-25, wherein the capsule is for administration via a dry powder inhaler.

27. A process for manufacturing the formulation of any one of claims 1-26, wherein:

a. in a first step 1) fine lactose is weighed and layered between two layers of coarse lactose prior to start of mixing both lactose components;

b. in a second step 2) the blending of the 2 components is carried out in a tumble mixer 2 times (2

cycles) at 72 rpm, 67 rpm or 34 rpm or 32 rpm or 30 rpm for 20 min and the pre-blend sieved through a 500µm sieve between the cycles;

c. in a third step 3) crystalline monohydrate (5S)-{[2-(4-carboxyphenyl)ethyl][2-(2-{[3-chloro-4'-(trifluoromethyl)biphenyl-4-yl]methoxy}phenyl)ethyl]-amino}-5,6,7,8-tetrahydroquinoline-2-carboxylic acid is pre-sieved through a 500 µm sieve and added to the lactose pre-blend as produced in step 1) and 2) and layered alternating with 10 layers of lactose pre-blend and 9 layers of active ingredient, 6 layers of lactose pre-blend and 5 layers of active ingredient (ex. 4) in between or 4 layers of lactose pre-blend and 3 layers of active ingredient (ex. 4) in between or 2 layers of lactose pre-blend and 1 layer of active ingredient (ex. 4) in between, preferably 6/5 layers prior to start of mixing;

d. in a fourth step 4) the pre-layered blend obtained in step 3) is mixed in a vessel (glass or stainless steel) in 3-5 cycles preferably 3 cycles at 72rpm, 67rpm, 34rpm or 32rpm preferably 32rpm for 20-30 minutes preferably 30 minutes (90min overall mixing time), with a rest time of 10 minutes between the mixing cycles, characterized in, that the product obtained in step 4) is mixed in a stainless steel container, wherein the blend is sieved between each mixing cycle or preferably without sieving the blend between mixing cycles;

e. in a fifth step 5) the product obtained in step 4) is left to rest at room temperature (15-25°C) and 35-65% relative humidity in a stainless steel container for a certain period of time, preferably 24-72 hours, more preferably 48h before blend uniformity sampling and final capsule filling is performed; and

f. in a sixth step 6) the dry powder blend obtained in step 5) is filled into a capsule.

28. Use of a formulation of any one of claims 1-24 in the manufacture of a medicament for the treatment of a cardiopulmonary disease or disorder.

29. The use of claim 28, wherein the cardiopulmonary disease or disorder is pulmonary arterial hypertension (PAH) or pulmonary hypertension (PH) associated with chronic lung disease (PH group 3).

30. The use of claim 29, wherein the pulmonary hypertension (PH) associated with chronic lung disease (PH group 3) is pulmonary hypertension in chronic obstructive pulmonary disease (PH-COPD) or pulmonary hypertension with idiopathic interstitial pneumonia (PH-IIP).