CLAIMS

1. A pharmaceutical composition comprising a crystalline polymorph of 5-(2-{[6-(2,2-difluoro-2-phenylethoxy)hexyl]amino}-1*(R)*-hydroxyethyl)-8-hydroxyquinolin-2(1*H*)-one heminapadisylate and a pharmaceutically acceptable carrier,

wherein the crystalline polymorph is a hydrate polymorph and the hydrate polymorph has:

a) an X-Ray Powder Diffraction (XRPD) pattern with peaks at 13.3, 16.1 and 19.2 degrees 2θ (± 0.1 degrees 2θ); and/or

b) a Differential Scanning Calorimetery (DSC) trace which shows a first endotherm in the range 75-120 ºC (± 5 ºC) and a second endotherm with an onset at 190 ºC (± 1 ºC).

2. A pharmaceutical composition according to claim 1, wherein the hydrate polymorph is obtainable by:

a) adding a solution of naphthalene-1,5-disulfonic acid tetrahydrate in methanol/acetic acid (1:1) to a solution of 5-(2-{[6-(2,2-difluoro-2-phenylethoxy)hexyl]amino}-1*(R)*-hydroxyethyl)-8-hydroxyquinolin-2(1*H*)-one in methanol/acetic acid (1:1),

b) stirring the reaction mixture at reflux for 30 minutes and leaving the reaction mixture to cool down to 20-25 ºC, then stirring at room temperature, preferably 20-25 ºC, for 20 hours,

c) isolating, filtrating and washed with methanol and drying, preferably in vacuum, at 50ºC.

3. A pharmaceutical composition according to claim 1 or 2, wherein the X-Ray Powder Diffraction (XRPD) pattern of the hydrate polymorph additionally has one or more peaks at 9.9, 11.5, 12.7, 14.4, 15.2, 16.7, 19.6, 20.2, 21.9, 22.7, 23.1, 24.2, 25.6, 27.0, 27.6, 28.9, 30.5, 31.7, 33.4 and 37.0 degrees 2θ (± 0.1 degrees 2θ), preferably wherein the X-Ray Powder Diffraction (XRPD)

pattern of the hydrate polymorph has peaks at 9.9, 11.5, 12.7, 13.3, 14.4, 15.2, 16.1, 16.7, 19.2, 19.6, 20.2, 21.9, 22.7, 23.1, 24.2, 25.6, 27.0, 27.6, 28.9, 30.5, 31.7, 33.4 and 37.0 degrees 2θ (± 0.1 degrees 2θ).

4. A crystalline polymorph 5-(2-{[6-(2,2-difluoro-2-phenylethoxy)hexyl]amino}-1 (R) hydroxyethyl)-8-hydroxyquinolin-2(1 H)-one heminapadisylate, which is a type β polymorphobtainable by drying the hydrate polymorph as defined in claim 1, wherein the type β polymorph has:

a) an X-Ray Powder Diffraction (XRPD) pattern with a peak at 19.1 degrees 2θ (± 0.1 degrees 2θ); and/or

b) a Differential Scanning Calorimetery (DSC) trace which shows an endotherm with an onset at 190 °C (± 1 °C).

5. A crystalline polymorph according to claim 4, wherein the type β polymorph is obtainable by drying the hydrate polymorph as defined in claim 1 at 105 ºC for 20 hours, preferably in a vacuum.

6. A crystalline polymorph according to claim 4 or 5, wherein the X-ray powder diffraction (XRPD) pattern of the type β polymorph additionally has one or more peaks at 10.0, 11.6, 12.7, 13.5, 14.5, 16.1, 19.7, 20.3, 22.0, 22.8, 23.8, 24.2. 25.8, 27.1, 27.7, 29.2 and 39.4 degrees 2θ (± 0.1 degrees 2θ),

preferably wherein the X-ray powder diffraction (XRPD) pattern of the type β polymorph has peaks at 10.0, 11.6, 12.7, 13.5, 14.5, 16.1, 19.1, 19.7, 20.3, 22.0, 22.8, 23.8, 24.2. 25.8, 27.1, 27.7, 29.2 and 39.4 degrees 2θ (± 0.1 degrees 2θ).

7. A type β crystalline polymorph of 5-(2-{[6-(2,2-difluoro-2-phenylethoxy)hexyl]amino}-1*(R)*-hydroxyethyl)-8-hydroxyquinolin-2(1*H*)-one heminapadisylate, which has:

a) an X-Ray Powder Diffraction (XRPD) pattern with peaks at 19.1, 19.7 and 22.8 degrees 2θ (± 0.1 degrees 2θ); and/or

b) a Differential Scanning Calorimetery (DSC) trace which shows a first endotherm with an onset at 190 ºC (± 1 ºC), and which preferably has:

a) an X-Ray Powder Diffraction (XRPD) pattern as defined in claim 6.

8. A crystalline polymorph according to any one of claims 4 to 7, which is the type β polymorph and which is isolated in a pure form or is admixed with a polymorph selected from the hydrate polymorph as defined in any one of claims 1 to 3 and the type α polymorph.

9. A pharmaceutical composition comprising the type β crystalline polymorph as defined in any one of claims 4 to 7 and a pharmaceutically acceptable carrier.

10. A pharmaceutical composition according to any one claims 1 to 3 and 9, wherein the pharmaceutical composition is formulated for administration by inhalation,

preferably wherein the composition comprises less than 0.1 wt% of an additive for improving the Fine Particle Fraction (FPF).

11. A pharmaceutical composition according to any one of claims 1 to 3, 9 and 10, wherein the composition further comprises a therapeutically effective amount of one or more other therapeutic agent.

12. The pharmaceutical composition according to claim 11 wherein the other therapeutic agent is a corticosteroid, an anticholinergic agent, and/or a PDE4 inhibitor, preferably wherein:

(a) the other therapeutic agent is a corticosteroid selected from the group consisting of prednisolone, methylprednisolone, dexamethasone, dexamethasone acetate, dexamethasone cipecilate, naflocort, deflazacort, halopredone acetate, budesonide, beclomethasone dipropionate, hydrocortisone, triamcinolone acetonide, fluocinolone

acetonide, fluocinonide, clocortolone pivalate, methylprednisolone aceponate, dexamethasone palmitoate, tipredane, hydrocortisone aceponate, prednicarbate, alclometasone dipropionate, halometasone, methylprednisolone suleptanate, mometasone, mometasone furoate, rimexolone, prednisolone farnesylate, ciclesonide, butixocort propionate, deltacortisone, NO-Prednisolone, NO-Budesonide, etiprednol dicloacetate, deprodone propionate, fluticasone, fluticasone propionate, fluticasone furoate, halobetasol propionate, loteprednol etabonate, betamethasone butyrate propionate, flunisolide, prednisone, dexamethasone sodium phosphate, triamcinolone, betamethasone 17-valerate, betamethasone, betamethasone dipropionate, 21-Chloro-11beta-hydroxy-17alpha-[2-(methylsulfanyl)acetoxy]-4-pregnene-3,20-dione, desisobutyrylciclesonide, hydrocortisone acetate, hydrocortisone sodium succinate, prednisolone sodium phosphate and hydrocortisone probutate, prednisolone sodium metasulfobenzoate and clobetasol propionate; or

(b) the other therapeutic agent is an anticholinergic agent selected from the group consisting of tiotropium salts, oxitropium salts, flutropium salts, ipratropium salts, glycopyrronium salts, trospium salts, zamifenacin, revatropate, espatropate, darotropium bromide, 3-[2-Hydroxy-2,2-bis(2-thienyl)acetoxy]-1-(3-phenoxypropyl)-1-azoniabicyclo[2.2.2]octane salts (in particular aclidinium salts, more preferably aclidinium bromide), 1-(2-Phenylethyl)-3-(9H-xanthen-9-ylcarbonyloxy)-1-azoniabicyclo[2.2.2]octane salts, 2-oxo-1,2,3,4-tetrahydroquinazoline-3-carboxylic acid endo-8-methyl-8-azabicyclo[3.2.1]oct-3-yl ester salts (DAU-5884), 3-(4-Benzylpiperazin-1-yl)-1-cyclobutyl-1-hydroxy-1-phenylpropan-2-one (NPC-14695), N-[1-(6-Aminopyridin-2-ylmethyl)piperidin-4-yl]-2(R)-[3,3-difluoro-1(R)-cyclopentyl]-2-hydroxy-2-phenylacetamide (J-104135), 2(R)-Cyclopentyl-2-hydroxy-N-[1-[4(S)-methylhexyl]piperidin-4-yl]-2-phenyl-acetamide (J-106366), 2(R)-Cyclopentyl-2-hydroxy-N-[1-(4-methyl-3-pentenyl)-4-piperidinyl]-2-phenylacetamide (J-104129), 1-[4-(2-Aminoethyl)piperidin-

1-yl]-2(R)-[3,3-difluorocyclopent-1(R)-yl]-2-hydroxy-2-phenylethan-1-one (Banyu-280634), N-[N-[2-[N-[1-(Cyclohexylmethyl)piperidin-3(R)-ylmethyl]carbamoyl]ethyl]carbamoylmethyl]-3,3,3-triphenylpropionamide (Banyu CPTP), 2(R)-Cyclopentyl-2-hydroxy-2-phenylacetic acid 4-(3-azabicyclo[3.1.0]hex-3-yl)-2-butynyl ester (Ranbaxy 364057), 3(R)-[4,4-Bis(4-fluorophenyl)-2-oxoimidazolidin-1-yl]-1-methyl-1-[2-oxo-2-(3-thienyl)ethyl]pyrrolidinium iodide, N-[1-(3-Hydroxybenzyl)-1-methylpiperidinium-3(S)-yl]-N-[N-[4-(isopropoxy-carbonyl)phenyl]carbamoyl]-L-tyrosinamide trifluoroacetate, 7-endo-(2-hydroxy-2,2-diphenylacetoxy)-9,9-dimethyl-3-oxa-9-azoniatricyclo[3.3.1.0(2,4)]-nonane salts, 3(R)-[4,4-Bis(4-fluorophenyl)-2-oxoimidazolidin-1-yl]-1-methyl-1-(2-phenyl-ethyl)pyrrolidinium iodide, trans-4-[2-[Hydroxy-2,2-(dithien-2-yl)acetoxy]-1-methyl-1-(2-phenoxyethyl)piperidinium bromide from Novartis (412682), 7-(2,2-diphenylpropionyloxy)-7,9,9-trimethyl-3-oxa-9-azoniatricyclo[3.3.1.0*2,4*]nonane salts, 7-hydroxy-7,9,9-trimethyl-3-oxa-9-azoniatricyclo[3.3.1.0*2,4*]nonane 9-methyl-9H-fluorene-9-carboxylic acid ester salts, all of them optionally in the form of their racemates, their enantiomers, their diastereomers and mixtures thereof, and optionally in the form of their pharmacologically-compatible acid addition salts; or

(c) the other therapeutic agent is a PDE4 inhibitor selected from the group consisting of benafentrine dimaleate, etazolate, denbufylline, rolipram, cipamfylline, zardaverine, arofylline, filaminast, tipelukast, tofimilast, piclamilast, tolafentrine, mesopram, drotaverine hydrochloride, lirimilast, roflumilast, cilomilast, oglemilast, apremilast, tetomilast, revamilast, ronomilast, (R)-(+)-4-[2-(3-Cyclopentyloxy-4-methoxyphenyl)-2-phenylethyl]pyridine (CDP-840), N-(3,5-Dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide (GSK-842470), 9-(2-Fluorobenzyl)-N6-methyl-2-(trifluoromethyl)adenine (NCS-613), N-(3,5-Dichloro-4-pyridinyl)-8-methoxyquinoline-5-carboxamide (D-4418), 3-[3-(Cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-iso-propyl-3H-purine hydrochloride (V-11294A), 6-[3-(N,N-Dimethylcarbamoyl)-phenyl-

sulfonyl]-4-(3-methoxyphenylamino)-8-methylquinoline-3-carboxamide hydrochloride (GSK-256066), 4-[6,7-Diethoxy-2,3-bis(hydroxymethyl)naphthalen-1-yl]-1-(2-methoxy-ethyl)pyridin-2(1H)-one (T-440), (-)-trans-2-[3'-[3-(N-Cyclopropylcarbamoyl)-4-oxo-1,4-dihydro-1,8-naphthyridin-1-yl]-3-fluorobiphenyl-4-yl]cyclopropanecarboxylic acid, 2-carbomethoxy-4-cyano-4-(3-cyclopropylmethoxy-4-difluroromethoxyphenyl)cyclohexan1-one, *cis* [4-cyano-4-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)cyclohexan-1-ol and 5(S)-[3-(Cyclopentyloxy)-4-methoxyphenyl]-3(S)-(3-methylbenzyl)piperidin-2-one (IPL-455903); or

(d) the other therapeutic agent is selected from the group consisting of mometasone furoate, ciclesonide, budesonide, fluticasone propionate, fluticasone furoate, tiotropium salts, glycopirrolium salts, 3-[2-Hydroxy-2,2-bis(2-thienyl)acetoxy]-1-(3-phenoxypropyl)-1-azoniabicyclo[2.2.2]octane salts, 1-(2-Phenylethyl)-3-(9H-xanthen-9-ylcarbonyloxy)-1-azoniabicyclo[2.2.2]octane salts, rolipram, roflumilast and cilomilast.

13. A combination comprising a crystalline polymorph as defined in any one of claims 1 to 7 and one or more other therapeutic agents as defined in claim 11 or claim 12.

14. A crystalline polymorph as defined in any one of claims 1 to 7, or a pharmaceutical composition as defined in any one of claims 1 to 3 and 9 to 12, for use in the treatment of asthma or chronic obstructive pulmonary disease.

15. Use of a crystalline polymorph as defined in any one of claims 1 to 7, or a pharmaceutical composition as defined in any one of claims 1 to 3 and 9 to 12, in the manufacture of a medicament for the treatment of asthma or chronic obstructive pulmonary disease.