

powder diffraction diagram is measured at about 5%, at about 20%, at about 50%, or at about 95% relative humidity and at a temperature of about 25°C.

In another aspect, the present disclosure provides a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid as disclosed herein, for use as a medicament.

In a further aspect, the present disclosure provides a pharmaceutical composition comprising as active ingredient a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid as disclosed herein, and at least one pharmaceutically acceptable carrier.

In yet another aspect, the present disclosure provides a use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid as disclosed herein, or a pharmaceutical composition as disclosed herein, in the manufacture of a medicament, for the prevention or treatment of diseases selected from the group consisting of chronic and acute allergic/immune diseases/disorders, comprising

asthma, allergic asthma, eosinophilic asthma, severe asthma, rhinitis, allergic rhinitis, angioedema, insect venom allergy, drug allergies, allergic sinusitis, allergic nephritis, allergic conjunctivitis, atopic dermatitis, bronchial asthma, food allergy, systemic mast cell disorders, anaphylactic shock, urticaria, eczema, ulcerative colitis, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease, rheumatoid arthritis, and nasal polyposis;

eosinophil-related diseases comprising small vessel vasculitides like Churg-Strauss syndrome, Wegener's granulomatosis, microscopic polyangiitis (and organ-specific subsets of the latter), hypereosinophilic syndromes like eosinophilic pneumonia, eosinophilic esophagitis, reflux esophagitis, eosinophilic endocarditis (Loeffler's endocarditis), eosinophilia-myalgia syndrome, eosinophilic fasciitis, eosinophilic pustular folliculitis (Ofuji's disease), eosinophilic ulcers, angiolymphoid hyperplasia with eosinophilia (ALHE), eosinophilic cellulitis (Wells syndrome), chronic eosinophilic leukemia, DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symptoms), and Still's disease (systemic onset juvenile idiopathic arthritis); basophil-related diseases, comprising basophilic leukemia and basophilic leucocytosis; and cystic fibrosis.

In another aspect, the present disclosure provides a use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid as disclosed herein in the manufacture of a pharmaceutical composition, for the prevention or treatment of diseases selected from the group consisting of chronic and acute allergic/immune diseases/disorders, comprising asthma, allergic asthma, eosinophilic

asthma, severe asthma, rhinitis, allergic rhinitis, angioedema, insect venom allergy, drug allergies, allergic sinusitis, allergic nephritis, allergic conjunctivitis, atopic dermatitis, bronchial asthma, food allergy, systemic mast cell disorders, anaphylactic shock, urticaria, eczema, ulcerative colitis, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease, rheumatoid arthritis, and nasal polyposis; eosinophil-related diseases comprising small vessel vasculitides like Churg-Strauss syndrome, Wegener's granulomatosis, microscopic polyangiitis (and organ-specific subsets of the latter), hypereosinophilic syndromes like eosinophilic pneumonia, eosinophilic esophagitis, reflux esophagitis, eosinophilic endocarditis (Loeffler's endocarditis), eosinophilia-myalgia syndrome, eosinophilic fasciitis, eosinophilic pustular folliculitis (Ofuji's disease), eosinophilic ulcers, angiolymphoid hyperplasia with eosinophilia (ALHE), eosinophilic cellulitis (Wells syndrome), chronic eosinophilic leukemia, DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symptoms), and Still's disease (systemic onset juvenile idiopathic arthritis); basophil-related diseases, comprising basophilic leukemia and basophilic leucocytosis; and cystic fibrosis.

In another aspect, the present disclosure provides a use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid as described herein in the manufacture of a medicament for the prevention or treatment of diseases selected from the group consisting of asthma, eosinophilic asthma, allergic rhinitis, atopic dermatitis, nasal polyposis, food allergy, urticaria, eosinophilic esophagitis, Churg Strauss Syndrome, hypereosinophilic syndrome, eosinophilic pneumonia, DRESS syndrome, Still's disease, COPD and cystic fibrosis.

In another aspect, the present disclosure provides a use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid as described herein in the manufacture of a medicament for the prevention or treatment of nasal polyposis.

It has surprisingly been found that COMPOUND has significantly improved properties in an *in-vitro* cytotoxicity assay in primary cultured rat hepatocytes. It is thus expected that COMPOUND has an improved toxicity profile *in-vivo*.

It has now been found that certain crystalline forms of COMPOUND may under certain conditions be found. Said crystalline forms of COMPOUND are novel and may have advantageous properties in view of the potential use of COMPOUND as active pharmaceutical ingredient. Such advantages may include better flow properties; less

Claims

1. A crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid, characterized by the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6°, 14.0°, and 21.1°, wherein the X-ray powder diffraction diagram is measured at about 5%, at about 20%, at about 50%, or at about 95% relative humidity and at a temperature of about 25°C.
2. A crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to claim 1, characterized by:
 - a. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6°, 14.0°, 19.8°, 20.0°, 21.1° and 26.4°, wherein the X-ray powder diffraction diagram is measured at about 5% relative humidity and at a temperature of about 25°C; or
 - b. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6°, 14.0°, 19.7°, 21.1° and 26.4°, wherein the X-ray powder diffraction diagram is measured at about 20% relative humidity and at a temperature of about 25°C; or
 - c. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6°, 14.0°, 19.5°, 21.1°, 21.4° and 26.1°, wherein the X-ray powder diffraction diagram is measured at about 50% relative humidity and at a temperature of about 25°C; or
 - d. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6°, 14.0°, 19.5°, 21.1°, 21.5° and 26.0°, wherein the X-ray powder diffraction diagram is measured at about 95% relative humidity and at a temperature of about 25°C.
3. A crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to claim 1, characterized by:
 - a. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6°, 14.0°, 15.6°, 19.8°, 20.0°, 21.1°, 23.7°, 26.4°, 27.5° and 28.4°, wherein the X-ray powder diffraction diagram is measured at about 5% relative humidity and at a temperature of about 25°C; or
 - b. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6°, 14.0°, 15.6°, 19.7°, 21.1°, 23.3°, 23.6°, 26.4°, 27.4°, and 28.4°, wherein the X-ray powder diffraction diagram is measured at about 20% relative humidity and at a temperature of about 25°C; or

- c. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6° , 14.0° , 15.2° , 16.1° , 19.5° , 21.1° , 21.4° , 23.0° , 26.1° , and 27.0° , wherein the X-ray powder diffraction diagram is measured at about 50% relative humidity and at a temperature of about 25°C ; or
- 5 d. the presence of peaks in the X-ray powder diffraction diagram at the following angles of refraction 2θ : 12.6° , 14.0° , 16.2° , 18.9° , 19.5° , 21.1° , 21.5° , 22.9° , 26.0° , and 27.0° , wherein the X-ray powder diffraction diagram is measured at about 95% relative humidity and at a temperature of about 25°C .
4. A crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to claim 1,
- 10 a. which essentially shows the X-ray powder diffraction pattern as depicted in Fig. 1, wherein the X-ray powder diffraction diagram is measured at about 5% relative humidity and at a temperature of about 25°C ; or
- b. which essentially shows the X-ray powder diffraction pattern as depicted in Fig. 2,
- 15 wherein the X-ray powder diffraction diagram is measured at about 20% relative humidity and at a temperature of about 25°C ; or
- c. which essentially shows the X-ray powder diffraction pattern as depicted in Fig. 3, wherein the X-ray powder diffraction diagram is measured at about 50% relative humidity and at a temperature of about 25°C ; or
- 20 d. which essentially shows the X-ray powder diffraction pattern as depicted in Fig. 4, wherein the X-ray powder diffraction diagram is measured at about 95% relative humidity and at a temperature of about 25°C .
- a)
5. A crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 4, which
- 25 shows an endothermal event in the range of about 260°C to 276°C as determined by differential scanning calorimetry.
6. A crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 5, which
- 30 essentially shows a gravimetric moisture sorption profile as depicted in Fig. 5, wherein the gravimetric moisture sorption profile is measured at 25°C .

7. A crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 6, for use as a medicament.

8. A pharmaceutical composition comprising as active ingredient a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 6, and at least one pharmaceutically acceptable carrier.

9. Use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 6, or a pharmaceutical composition according to claim 8, in the manufacture of a medicament, for the prevention or treatment of diseases selected from the group consisting of chronic and acute allergic/immune diseases/disorders, comprising asthma, allergic asthma, eosinophilic asthma, severe asthma, rhinitis, allergic rhinitis, angioedema, insect venom allergy, drug allergies, allergic sinusitis, allergic nephritis, allergic conjunctivitis, atopic dermatitis, bronchial asthma, food allergy, systemic mast cell disorders, anaphylactic shock, urticaria, eczema, ulcerative colitis, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease, rheumatoid arthritis, and nasal polyposis; eosinophil-related diseases comprising small vessel vasculitides like Churg-Strauss syndrome, Wegener's granulomatosis, microscopic polyangiitis (and organ-specific subsets of the latter), hypereosinophilic syndromes like eosinophilic pneumonia, eosinophilic esophagitis, reflux esophagitis, eosinophilic endocarditis (Loeffler's endocarditis), eosinophilia-myalgia syndrome, eosinophilic fasciitis, eosinophilic pustular folliculitis (Ofuji's disease), eosinophilic ulcers, angiolymphoid hyperplasia with eosinophilia (ALHE), eosinophilic cellulitis (Wells syndrome), chronic eosinophilic leukemia, DRESS syndrome (Drug Rash with Eosinophilia and Systemic Symptoms), and Still's disease (systemic onset juvenile idiopathic arthritis); basophil-related diseases, comprising basophilic leukemia and basophilic leucocytosis; and cystic fibrosis.

10. Use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 6 in the manufacture of a pharmaceutical composition, for the prevention or treatment of diseases selected from the group consisting of chronic and acute allergic/immune diseases/disorders, comprising asthma, allergic asthma, eosinophilic asthma, severe asthma, rhinitis, allergic rhinitis, angioedema, insect venom allergy, drug allergies, allergic sinusitis, allergic nephritis, allergic conjunctivitis, atopic dermatitis, bronchial asthma, food allergy, systemic mast cell disorders, anaphylactic shock, urticaria, eczema, ulcerative colitis,

chronic obstructive pulmonary disease (COPD), inflammatory bowel disease, rheumatoid arthritis, and nasal polyposis; eosinophil-related diseases comprising small vessel vasculitides like Churg-Strauss syndrome, Wegener's granulomatosis, microscopic polyangiitis (and organ-specific subsets of the latter), hypereosinophilic syndromes like
 5 eosinophilic pneumonia, eosinophilic esophagitis, reflux esophagitis, eosinophilic endocarditis (Loeffler's endocarditis), eosinophilia-myalgia syndrome, eosinophilic fasciitis, eosinophilic pustular folliculitis (Ofuji's disease), eosinophilic ulcers, angiolymphoid hyperplasia with eosinophilia (ALHE), eosinophilic cellulitis (Wells syndrome), chronic eosinophilic leukemia, DRESS syndrome (Drug Rash with Eosinophilia and Systemic
 10 Symptoms), and Still's disease (systemic onset juvenile idiopathic arthritis); basophil-related diseases, comprising basophilic leukemia and basophilic leucocytosis; and cystic fibrosis.

11. Use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 6
 15 in the manufacture of a medicament for the prevention or treatment of diseases selected from the group consisting of asthma, eosinophilic asthma, allergic rhinitis, atopic dermatitis, nasal polyposis, food allergy, urticaria, eosinophilic esophagitis, Churg Strauss Syndrome, hypereosinophilic syndrome, eosinophilic pneumonia, DRESS syndrome, Still's disease, COPD and cystic fibrosis.

12. Use of a crystalline form of (S)-2-(8-((5-chloropyrimidin-2-yl)(methyl)amino)-2-fluoro-6,7,8,9-tetrahydro-5H-pyrido[3,2-b]indol-5-yl)acetic acid according to any one of claims 1 to 6
 20 in the manufacture of a medicament for the prevention or treatment of nasal polyposis.