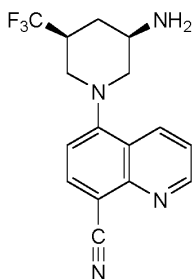


CRYSTALLINE FORM H1 OF 5-((3R,5S)-3-AMINO-5-TRIFLUOROMETHYL-PIPERIDIN-1-YL)-QUINOLINE-8-CARBONITRILE HEMIHYDRATE**FIELD**

[0001] A crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate is provided herein. Processes for preparing the polymorph and pharmaceutical composition comprising the polymorph are also disclosed.

BACKGROUND

[0002] 5-((3R,5S)-3-Amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile, also named Enpatoran, is a compound having the following structure:



[0003] Enpatoran is a potent and selective dual toll-like receptor (TLR) 7/8 inhibitor in clinical development, including for the treatment of cutaneous and systemic lupus erythematosus (CLE/SLE). The compound may be prepared according to the methods provided in WO 2017/106607.

[0004] Polymorphism refers to the occurrence of different crystalline forms of a single compound. A single compound may give rise to a variety of polymorphic forms, each having different solid-state physical properties, such as different solubility, melting point, stability, dissolution rates and/or different X-ray diffraction peaks. Due to the possibility of variable solubility and/or stability of different polymorph, identifying the existence of polymorphs of pharmaceutical compounds is important for providing pharmaceutical products having predictable solubility profiles. It may be desirable to investigate solid state forms of a drug, including polymorphic forms, and to determine the stability, dissolution and flow properties of each polymorphic form. Unfortunately, the existence of particular polymorphic forms and their physical properties is unpredictable.

[0005] When used for treating humans, it is important that a crystalline form of a therapeutic agent, like 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile, or a salt or hydrate thereof, retains appropriate polymorphic and chemical

stability, solubility, and other physicochemical properties over time and among various manufactured batches of the agent. If the physical or chemical properties vary with time and/or among batches, the administration of a therapeutically effective dose may become problematic and may lead to inconsistent dosages or to ineffective therapy. Therefore, it is important to choose a polymorphic form of the agent that is stable, is manufactured reproducibly, and has physicochemical properties favorable for its use as a therapeutic agent.

[0006] However, the art remains unable to predict which crystalline form of an agent will have a combination of the desired properties and will be suitable for human administration, and how to make the agent in such a crystalline form.

SUMMARY

[0007] In one aspect, the disclosure provides a crystalline polymorphic form of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate, termed herein Form H1. The polymorphic form described herein is useful in the treatment of immune disorders, including TLR7/8-related diseases, such as cutaneous and systemic lupus erythematosus (CLE/SLE).

[0008] In another aspect, the disclosure provides a composition comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1. An embodiment provides a pharmaceutical composition comprising Form H1 described herein, and one or more pharmaceutically acceptable carriers or excipients.

[0009] In another aspect, the disclosure provides methods of treating diseases responsive to the administration of a dual toll-like receptor (TLR) 7/8 inhibitor by the administration of a pharmaceutical dosage form comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1.

[0010] Another aspect provides methods of treating a disease or disorder modulated by TLR 7/8, comprising administering to a mammal in need of such treatment an effective amount of a composition comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1. The method may comprise the administration of a composition(s) comprising Form H1 alone or in combination with one or more additional polymorphs or compounds having inhibitory properties for TLR 7/8.

[0011] Another aspect provides the use of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 in the manufacture of a medicament for the treatment of an immune disorder.

BRIEF DESCRIPTION OF THE FIGURES

- [0012] Figure 1 shows the Powder X-ray diffractogram of Form H1.
- [0013] Figure 2 shows the single crystal structure of Form H1.
- [0014] Figure 3 shows the DSC scan of Form H1 (5 K/min).
- [0015] Figure 4 shows the TGA scan of Form H1 form (5 K/min).
- [0016] Figure 5 shows the Water Vapor Sorption Isotherm (25 °C) of Form H1.
- [0017] Figure 6 shows the SEM-Images of Form H1 (magnification: left: 100x; middle: 200x; right: 500x).

DETAILED DESCRIPTION

[0018] As used herein, the term “polymorph” or “polymorphic form” refer to a crystallographically distinct form of a substance. The practical physical characteristics of a polymorphic form are influenced by the conformation and orientation of molecules in the unit cell, which defines a particular polymorphic form of a substance. Different polymorphs of the same compound may have different physical, chemical, biological and/or spectroscopic properties. For example, and without limitation, different polymorphic forms may have different stability properties. A particular polymorphic form may be more sensitive to relative humidity, heat and/or light. In some cases, differences in stability result from changes in chemical reactivity, such as and without limitation, differential oxidation. Such properties may provide for more suitable product qualities such as a dosage form that is more resistant to discoloration when comprised of a particular polymorph.

[0019] Alternatively or additionally, a particular polymorphic form may have a different dissolution rate thereby providing, for example, a more desirable bioavailability. Alternatively or additionally, a particular polymorphic form may provide different compressibility and/or density properties, thereby providing more desirable characteristics for formulation and/or product manufacturing. Mechanical characteristics may differ between polymorphs also. For example and without limitation, tablets having a higher ratio of a particular polymorph may be more resistant to crumbling on storage. Also, the different physical properties of polymorphs may affect their processing. For example, a particular polymorph may be more or less likely to form solvates or may be more difficult to filter and/or wash.

[0020] Polymorphs can be detected, identified, classified and characterized using well-known techniques such as, but not limited to, powder X-ray diffractometry (PXRD), single

crystal X-ray diffractometry, differential scanning calorimetry (DSC), thermogravimetry (TGA), vibrational spectroscopy, solution calorimetry, solid state nuclear magnetic resonance (NMR), infrared (IR) spectroscopy, Raman spectroscopy, hot stage optical microscopy, scanning electron microscopy (SEM), electron crystallography, quantitative analysis, solubility, and rate of dissolution.

[0021] As used herein when referring to a spectrum and/or to data presented in a graph, the term “peak” refers a feature that one skilled in the art would recognize as not attributable to background noise.

[0022] In embodiments, the invention provides a crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 characterized by one or more peaks from the powder X-ray diffraction (PXRD) ($\text{Cu-K}\alpha_1$ radiation), presented in degrees $2\theta \pm 0.2^\circ$, wherein the peaks comprise 7.2, 9.7, 13.4, 14.3, 17.0, 17.8, 19.9, 20.6, 21.5, 21.9, 22.2, 22.6, 23.0, 23.5, 24.1, 25.1, 25.5, 25.8, 26.4 and 26.9. 7.2, 9.7, 13.4, 14.3, 17.0, 17.8, 19.9, 20.6, 21.5, 21.9, 22.2, 22.6, 23.0, 23.5, 24.1, 25.1, 25.5, 25.8, 26.4 and 26.9.

[0023] The crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 may be characterized by two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, eleven or more, twelve or more, thirteen or more, fourteen or more, fifteen or more, sixteen or more, seventeen or more, eighteen or more, nineteen or more, or each of the PXRD peaks 7.2, 9.7, 13.4, 14.3, 17.0, 17.8, 19.9, 20.6, 21.5, 21.9, 22.2, 22.6, 23.0, 23.5, 24.1, 25.1, 25.5, 25.8, 26.4 and 26.9. All PXRD peaks provided herein are measured with $\text{Cu-K}\alpha_1$ radiation in degrees 2θ and include ± 0.2 degrees.

[0024] The crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 may be characterized by PXRD peaks comprising a peak at 13.4.

[0025] The crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 may be characterized by PXRD peaks comprising peaks at 9.7 and 13.4.

[0026] The crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 may be characterized by PXRD peaks comprising peaks at 7.2, 9.7 and 13.4.

[0027] The crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 may be characterized by PXRD peaks comprising peaks at 7.2, 9.7, 13.4 and 22.2.

[0028] The crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 may be characterized by PXRD peaks comprising peaks at 7.2, 9.7, 13.4, 21.5 and 22.2.

[0029] The crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1 may additionally or alternatively be characterized by single crystal X-Ray diffraction. Crystal Form H1 crystallizes in the orthorhombic space group $P2_12_12_1$ with the lattice parameters $a = 10.7499 \pm 0.1 \text{ \AA}$, $b = 16.4119 \pm 0.1 \text{ \AA}$, $c = 17.5927 \pm 0.1 \text{ \AA}$, and $\alpha = \gamma = \beta = 90^\circ$.

[0030] In aspects, this disclosure provides compositions comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1. The composition comprising Form H1, may comprise Form H1 alone or in combination with one or more additional polymorphs or compounds having inhibitory properties for TLR 7/8.

[0031] Enpatoran compositions comprising crystalline polymorph Form H1 may comprise Form H1 in any quantity. Compositions may comprise less than about 1 % Form H1. Compositions may comprise 1 % to 100% of Form H1. Compositions may comprise 50 % to 100% of Form H1. Compositions may comprise 80 % to 100% of Form H1. Compositions may comprise 90 % to 100% of Form H1. Compositions may comprise 5% to 99% of Form H1. Compositions may comprise 10% to 95% Form H1. Compositions may comprise 15% to 95% Form H1. Compositions may comprise 1 % to 80% Form H1. Compositions may comprise 1% to 75% Form H1. Compositions may comprise 1 % to 70% Form H1. Compositions may comprise 1% to 65% Form H1. Compositions may comprise 1% to 60% Form H1. Compositions may comprise 1 % to 55% Form H1. Compositions may comprise 1 % to 50% Form H1. Compositions may comprise 1 % to 25% Form H1. Compositions may comprise 1 % to 20% Form H1. Compositions may comprise 1 % to 15% Form H1. Compositions may comprise 1 % to 10% Form H1. Compositions may comprise 1% to 5% Form H1.

[0032] Further aspects provide a pharmaceutical composition comprising Form H1 described herein, and one or more pharmaceutically acceptable carriers or excipients. The term “pharmaceutically acceptable carrier or excipient” refers to a non-toxic carrier, adjuvant, excipient or vehicle that does not interfere with the pharmacological activity of the compound with which it is formulated. Pharmaceutically acceptable carriers or excipients that may be

used in the pharmaceutical compositions of Form H1 include any such excipients known in the art.

[0033] Pharmaceutically acceptable compositions of this invention may be orally administered in any orally acceptable dosage form. Exemplary oral dosage forms are capsules, tablets, aqueous suspensions or solutions. In the case of tablets for oral use, carriers commonly used include lactose and corn starch. Lubricating agents, such as magnesium stearate, are also typically added. For oral administration in a capsule form, useful diluents include lactose and dried cornstarch. When aqueous suspensions are required for oral use, the active ingredient may be combined with emulsifying and suspending agents. If desired, sweetening, flavoring or coloring agents are optionally also added.

[0034] Solid dosage forms for oral administration include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound comprising Form H1 may be mixed with at least one inert, pharmaceutically acceptable excipient or carrier such as sodium citrate or dicalcium phosphate and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol, and silicic acid, b) binders such as, for example, carboxymethylcellulose, alginates, gelatin, polyvinyl pyrrolidinone, sucrose, and acacia, c) humectants such as glycerol, d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates, and sodium carbonate, e) solution retarding agents such as paraffin, f) absorption accelerators such as quaternary ammonium compounds, g) wetting agents such as, for example, cetyl alcohol and glycerol monostearate, h) absorbents such as kaolin and bentonite clay, and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate, and mixtures thereof. In the case of capsules, tablets and pills, the dosage form also optionally comprises buffering agents.

[0035] Solid compositions of a similar type are also employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like. The solid dosage forms of tablets, dragees, capsules, pills, and granules can be prepared with coatings and shells such as enteric coatings and other coatings well known in the pharmaceutical formulating art. They optionally contain opacifying agents and can also be of a composition that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions that can be used include polymeric substances and waxes. Solid compositions of a similar type are also employed as fillers in soft and hard-filled gelatin capsules using such excipients as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like.

[0036] In another aspect, the disclosure provides methods of treating diseases responsive to the administration of a dual toll-like receptor (TLR) 7/8 inhibitor by the administration to a patient in need thereof a pharmaceutical dosage form comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1. The term “patient” or “subject” as used herein, means an animal, preferably a mammal, and most preferably a human.

[0037] Another aspect provides methods of treating a disease or disorder modulated by TLR 7/8, comprising administering to a mammal in need of such treatment an effective amount of a composition comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile hemihydrate Form H1. The method may comprise the administration of a composition(s) comprising Form H1 alone or in combination with one or more additional polymorphs or compounds having inhibitory properties for TLR 7/8.

[0038] The present disclosure furthermore relates to a method for treating or preventing a disease or disorder in a subject, such as a TLR7/8 related disease or disorder, comprising administering to said subject an effective amount of a composition(s) comprising Form H1.

[0039] The disease or disorder to be treated or prevented by administering a composition comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile Form H1 may be an autoimmune disease, for instance, one characterized by joint pain, antinuclear antibody positivity, malar rash, or discoid rash. In some aspects, the autoimmune disease is associated with the skin, muscle tissue, and/or connective tissue. In some embodiments, the autoimmune disease is not evidenced in the individual by skin, muscle tissue, and/or connective tissue symptoms. In some embodiments, the autoimmune disease is systemic. Autoimmune diseases that may be treated or prevented by administering a composition comprising 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile Form H1 include, without limitation, rheumatoid arthritis (RA), autoimmune pancreatitis (AIP), lupus, such as systemic lupus erythematosus (SLE) or cutaneous lupus erythematosus (CLE), type I diabetes mellitus, multiple sclerosis (MS), antiphospholipid syndrome (APS), sclerosing cholangitis, systemic onset arthritis, irritable bowel disease (IBD), scleroderma, Sjogren's disease, vitiligo, myositis, such as dermatomyositis or polymyositis, pemphigus vulgaris, pemphigus foliaceus, inflammatory bowel disease including Crohn's disease and ulcerative colitis, autoimmune hepatitis, hypopituitarism, graft-versus-host disease (GvHD), autoimmune skin diseases, uveitis, pernicious anemia, and hypoparathyroidism. The autoimmune disease may also be, without limitation, polyangiitis overlap syndrome, Kawasaki's disease, sarcoidosis, glomerulonephritis, and cryopathies.

[0040] In some aspects, the autoimmune disease is selected from the group consisting of arthritis, pancreatitis, mixed connective tissue disease (MCTD), lupus, antiphospholipid syndrome (APS), systemic onset arthritis, and irritable bowel syndrome.

[0041] In other aspects, the autoimmune disease is selected from the group consisting of pancreatitis, glomerulonephritis, pyelitis, sclerosing cholangitis, and type I diabetes. In some aspects, the autoimmune disease is rheumatoid arthritis. In some aspects, the autoimmune disease is autoimmune pancreatitis (AIP). In some aspects, the autoimmune disease is glomerulonephritis. In some aspects, the autoimmune disease is pyelitis. In some aspects, the autoimmune disease is sclerosing cholangitis. In some aspects the autoimmune disorder is psoriasis. In some aspects, the autoimmune disease is a rheumatoid disease or disorder.

[0042] In other aspects, the autoimmune disease is selected from the group consisting of systemic lupus erythematosus (SLE), rheumatoid arthritis, autoimmune skin disease, and multiple sclerosis. The autoimmune disease may be cutaneous and systemic lupus erythematosus (CLE/SLE). In some aspects, any of the above-mentioned autoimmune diseases is a TLR7/8-related autoimmune disease.

EXAMPLES

Example 1: Preparation of Form H1

[0043] Approx. 220 mg of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile prepared according to the method of WO 2017/106607 (compound 73) were suspended in 0.8 mL water at 50 °C for 2 hours. After filtration, the solid was dried at ambient conditions for 18 hours.

Example 2: NMR data of Form H1

[0044] NMR data for Form H1: ¹H NMR (500 MHz, DMSO) δ 9.06 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.52 (dd, *J* = 8.6, 1.6 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 7.70 (dd, *J* = 8.6, 4.2 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 3.62 – 3.50 (m, 1H), 3.51 – 3.40 (m, 1H), 3.12 (tt, *J* = 10.7, 4.7 Hz, 1H), 3.09 – 2.95 (m, 1H), 2.86 (t, *J* = 11.5 Hz, 1H), 2.47 (d, *J* = 11.1 Hz, 1H), 2.18 (d, *J* = 12.2 Hz, 1H), 1.74 (s, 2H), 1.26 (q, *J* = 12.2 Hz, 1H).

Example 3: Crystallographic studies of Form H1

[0045] A Powder X-Ray Diffraction pattern was obtained by standard techniques as described in the European Pharmacopeia 6th Edition chapter 2.9.33, and is characterized by the X-ray powder diffractogram of Figure 1 (monochromatic Cu-K α_1 radiation, $\lambda = 1.5406 \text{ \AA}$, Stoe StadiP 611 KL transmission diffractometer) and having the following peaks:

No.	2θ (Cu-K α_1 radiation) $\pm 0.2^\circ$
1	7.2
2	9.7
3	13.4
4	14.3
5	17.0
6	17.8
7	19.9
8	20.6
9	21.5
10	21.9
11	22.2
12	22.6
13	23.0
14	23.5
15	24.1
16	25.1
17	25.5
18	25.8
19	26.4
20	26.9

[0046] Single crystal X-Ray structure data were obtained on Form H1 form (Oxford Diffraction Supernova Single Crystal X-ray Diffractometer with Graphite monochromator

and CCD Detector) at 298 K. Hemi-hydrate Form H1 crystallises in the orthorhombic space group $P2_12_12_1$ with the lattice parameters $a = 10.7499 \pm 0.1 \text{ \AA}$, $b = 16.4119 \pm 0.1 \text{ \AA}$, $c = 17.5927 \pm 0.1 \text{ \AA}$, and $\alpha = \gamma = \beta = 90^\circ$. As can be seen from the single crystal structure, Form H1 represents a hemi-hydrate form.

Example 4: Physical Properties of Form H1

[0047] Form H1 is characterised by the following physical properties. Thermal behaviour shows dehydration $<100^\circ\text{C}$, followed by melting of anhydrous form A1 at $\sim 165^\circ\text{C}$. TGA shows weight loss of $\sim 2.9\%$ (w/w) up to 130°C which can be clearly assigned to degradation of 0.5 mol water. DSC and TGA profiles are displayed in Figures 3 and 4, respectively. The DSC scan of Form H1 was acquired on a Mettler-Toledo DSC1 with a heating rate of 5 K/min, using nitrogen purge gas at 50 mL/min. The TGA scan of Form H1 was acquired on a Mettler-Toledo TGA 851 with a heating rate of 5 K/min, using nitrogen purge gas at 50 mL/min.

[0048] Water Vapour Sorption behaviour reveals water uptake levels $\sim 0.5\%$ (w/w) in the full relative humidity (RH) range 0-98% RH. Hemi-hydrate form H1 can be classified as non-hygroscopic according to Ph. Eur. criteria (section 5.11.). The Water Vapour Sorption isotherm (25°C) is displayed in Figure 5. Water Vapour Sorption isotherm was acquired on a DVS Intrinsic system from SMS.

[0049] SEM-Images of Form H1 prepared according to Example 1 are provided in Figure 6 (magnification: left: 100x; middle: 200x; right: 500x).

We Claim:

1. A crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile characterized by one or more peaks from the powder X-ray diffraction (PXRD), wherein the peaks, expressed in degrees $2\theta \pm 0.2^\circ$, comprise 7.2, 9.7, 13.4, 14.3, 17.0, 17.8, 19.9, 20.6, 21.5, 21.9, 22.2, 22.6, 23.0, 23.5, 24.1, 25.1, 25.5, 25.8, 26.4 and 26.9.
2. The crystalline polymorph of claim 1, wherein characterized by two or more, three or more, four or more, five or more, six or more, seven or more, eight or more, nine or more, ten or more, eleven or more, twelve or more, thirteen or more, fourteen or more, fifteen or more, sixteen or more, seventeen or more, eighteen or more, nineteen or more, or each of the PXRD peaks, expressed in degrees $2\theta \pm 0.2^\circ$, 7.2, 9.7, 13.4, 14.3, 17.0, 17.8, 19.9, 20.6, 21.5, 21.9, 22.2, 22.6, 23.0, 23.5, 24.1, 25.1, 25.5, 25.8, 26.4 and 26.9.
3. The crystalline polymorph of claim 1, characterized by PXRD peaks, expressed in degrees $2\theta \pm 0.2^\circ$, comprising a peak at 13.4.
4. The crystalline polymorph of claim 1, characterized by PXRD peaks, expressed in degrees $2\theta \pm 0.2^\circ$, comprising peaks at 9.7 and 13.4.
5. The crystalline polymorph of claim 1, characterized by PXRD peaks, expressed in degrees $2\theta \pm 0.2^\circ$, comprising peaks at 7.2, 9.7 and 13.4.
6. The crystalline polymorph of claim 1, characterized by PXRD peaks, expressed in degrees $2\theta \pm 0.2^\circ$, comprising peaks at 7.2, 9.7, 13.4 and 22.2.
7. The crystalline polymorph of claim 1, characterized by PXRD peaks, expressed in degrees $2\theta \pm 0.2^\circ$, comprising peaks at 7.2, 9.7, 13.4, 21.5 and 22.2.
8. A crystalline polymorph of 5-((3R,5S)-3-amino-5-(trifluoromethyl)piperidin-1-yl)quinoline-8-carbonitrile characterized by an orthorhombic space group $P2_12_12_1$ with the lattice parameters $a = 10.7499 \pm 0.1 \text{ \AA}$, $b = 16.4119 \pm 0.1 \text{ \AA}$, $c = 17.5927 \pm 0.1 \text{ \AA}$, and $\alpha = \gamma = \beta = 90^\circ$.
9. A pharmaceutical composition comprising a crystalline polymorph according to any one of claims 1 to 8 and one or more pharmaceutically acceptable carriers.
10. A pharmaceutical composition for use in a method of treating or preventing a TLR7/8-related autoimmune disease, the composition comprising a crystalline polymorph according to any one of claims 1 to 8 and one or more pharmaceutically acceptable carriers.

11. The pharmaceutical composition for use in a method according to claim 10, wherein the TLR7/8-related autoimmune disease is selected from the group consisting of rheumatoid arthritis, autoimmune pancreatitis, lupus, systemic lupus erythematosus, cutaneous lupus erythematosus, type I diabetes mellitus, multiple sclerosis, antiphospholipid syndrome, sclerosing cholangitis, systemic onset arthritis, irritable bowel disease, scleroderma, Sjogren's disease, vitiligo, myositis, dermatomyositis, polymyositis, pemphigus vulgaris, pemphigus foliaceus, inflammatory bowel disease, Crohn's disease, ulcerative colitis, autoimmune hepatitis, hypopituitarism, graft-versus-host disease, autoimmune skin diseases, uveitis, pernicious anemia, and hypoparathyroidism.