is specifically disclosed in the application as a potent pan-JAK inhibitor.

To effectively use this compound as a therapeutic agent, it would be desirable to have a crystalline solid-state salt form. For example, it would be highly desirable to have a physical form that is thermally stable at reasonably high temperature, thereby facilitating processing and storage of the material. Crystalline solids are generally preferred over amorphous forms, for enhancing purity and stability of the manufactured product. However, the formation of crystalline forms of organic compounds is highly unpredictable. No reliable methods exist for predicting which, if any, form of an organic compound will be crystalline. Moreover, no methods exist for predicting which, if any, crystalline form will have the physically properties desired for use as pharmaceutical agents.

No crystalline salt forms of compound **1** have previously been reported. Accordingly, a need exists for crystalline salt forms of compound **1.**

SUMMARY OF THE INVENTION

In one aspect, the present disclosure provides crystalline hydrates of the oxalate and succinate salts of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol (**1**).

The crystalline hydrate of the oxalate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol has been found to have a melting temperature in the range of about 266 ºC to about 276 ºC and to exhibit total moisture uptake of about 1 % when exposed to a range of relative humidity between about 30 % and about 90 % at room temperature.

In another aspect, there is provided a crystalline hydrate of the succinate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol found to have a melting temperature in the range of about 180 ºC to about 190 ºC and to exhibit total moisture uptake of about 2 % when exposed to a range of relative humidity between about 5 % and about 90 % at room temperature.

Among other uses, the crystalline solid forms of the invention are expected to be useful for preparing pharmaceutical compositions for treating or ameliorating disease amenable to treatment with a JAK inhibitor, in particular respiratory disease. Accordingly, in another of its composition aspects, the invention provides a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and an active agent selected from the crystalline hydrate of the oxalate salt of 5-ethyl-2-fluoro-4-

(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol and the crystalline hydrate of the succinate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol.

In another aspect, there is provided a method of preparing the crystalline hydrate of the oxalate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol, the method comprising:

(a) dissolving a 1:1 mixture of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol: oxalic acid in a 1:1 mixture of tetrahydrofuran:water at room temperature,

(b) adding a 1:1:2 mixture of tetrahydrofuran:water:acetonitrile to produce a suspension,

(c) stirring the suspension for about one day, and

(d) isolating the crystalline hydrate of the oxalate salt from the suspension.

The invention also provides a method of treating respiratory disease, in particular, asthma, in a mammal, the method comprising administering to the mammal a crystalline solid form or a pharmaceutical composition of the invention. In separate and distinct aspects, the invention also provides synthetic processes useful for preparing the crystalline forms of the invention.

The invention further provides a method of treating an ocular inflammatory disease in a mammal, the method comprising administering to the eye of the mammal, a crystalline solid form or a pharmaceutical composition of the invention.

The invention also provides a crystalline solid form of the invention as described herein for use in medical therapy. In yet another aspect, there is provided the use of a crystalline solid form of the invention in the manufacture of a formulation or medicament for treating respiratory disease in a mammal.

In a further aspect, there is provided a use of the crystalline oxalate hydrate described herein or the crystalline succinate hydrate described herein in the manufacture of a medicament for the treatment of an ocular disease in a mammal.

BRIEF DESCRIPTION OF THE DRAWINGS

Various aspects of the present invention are illustrated by reference to the accompanying drawings.

Figure 1 shows a powder x-ray diffraction (PXRD) pattern of the crystalline hydrate of the oxalate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol (hereinafter 'oxalate hydrate').

Figure 2 shows a differential scanning calorimetry (DSC) thermogram of the oxalate hydrate of the invention.

Figure 3 shows a thermal gravimetric analysis (TGA) plot of the oxalate hydrate of the invention.

Figure 4 shows a dynamic moisture sorption (DMS) isotherm of the oxalate hydrate of the invention observed at a temperature of about 25 ºC.

Figure 5 shows a powder x-ray diffraction (PXRD) pattern of the crystalline succinate hydrate of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol (hereinafter 'succinate hydrate').

Figure 6 shows a differential scanning calorimetry (DSC) thermogram of the succinate hydrate of the invention.

WHAT IS CLAIMED IS:

1. A crystalline hydrate of the oxalate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol.

2. The crystalline oxalate hydrate of Claim 1, wherein the crystalline oxalate hydrate is characterized by a powder X-ray diffraction pattern comprising diffraction peaks at 2θ values of 6.77±0.20, 12.13±0.20, 13.54±0.20, 17.23±0.20, and 18.00±0.20.

3. The crystalline oxalate hydrate of Claim 2 wherein the powder X-ray diffraction pattern is further characterized by having two or more additional diffraction peaks at 2θ values selected from 11.56±0.20, 14.29±0.20, 19.51±0.20, 21.38±0.20, and 23.63±0.20.

4. The crystalline oxalate hydrate of Claim 1, wherein the crystalline oxalate hydrate is characterized by a powder X-ray diffraction pattern in which the peak positions are substantially in accordance with the peak positions of the pattern shown in Figure 1.

5. The crystalline oxalate hydrate of Claim 1 wherein the crystalline oxalate hydrate is characterized by a differential scanning calorimetry trace recorded at a heating rate of 10 ºC per minute which shows a maximum in endothermic heat flow at a temperature between 266 ºC and 276 ºC.

6. The crystalline oxalate hydrate of Claim 1, wherein the crystalline oxalate hydrate is characterized by a differential scanning calorimetry trace substantially in accordance with that shown in Figure 2.

7. A crystalline hydrate of the succinate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol.

8. The crystalline succinate hydrate of Claim 7, wherein the crystalline succinate hydrate is characterized by a powder X-ray diffraction pattern comprising diffraction peaks at 2θ values of 4.81±0.20, 9.66±0.20, 14.93±0.20, and 16.78±0.20.

9. The crystalline succinate hydrate of Claim 8 wherein the powder X-ray diffraction pattern is further characterized by having two or more additional diffraction peaks at 2θ values selected from 10.46±0.20, 16.21±0.20, 17.45±0.20, 22.87±0.20, and 24.77±0.20.

10. The crystalline succinate hydrate of Claim 7, wherein the crystalline succinate hydrate is characterized by a powder X-ray diffraction pattern in which the peak positions are substantially in accordance with the peak positions of the pattern shown in Figure 5.

11. The crystalline succinate hydrate of Claim 7 wherein the crystalline succinate hydrate is characterized by a differential scanning calorimetry trace recorded at a heating rate of 10 ºC per minute which shows a maximum in endothermic heat flow at a temperature between 180 ºC and 190 ºC.

12. The crystalline succinate hydrate of Claim 7, wherein the crystalline succinate hydrate is characterized by a differential scanning calorimetry trace substantially in accordance with that shown in Figure 6.

13. A pharmaceutical composition comprising a crystalline oxalate hydrate of any one of Claims 1 to 6 or a crystalline succinate hydrate of any one of Claims 7 to 12 and a pharmaceutically-acceptable carrier.

14. A method of preparing the crystalline hydrate of the oxalate salt of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol, the method comprising:

(a) dissolving a 1:1 mixture of 5-ethyl-2-fluoro-4-(3-(5-(1-methylpiperidin-4-yl)-4,5,6,7-tetrahydro-1*H*-imidazo[4,5-c]pyridin-2-yl)-1*H*-indazol-6-yl)phenol: oxalic acid in a 1:1 mixture of tetrahydrofuran:water at room temperature,

(b) adding a 1:1:2 mixture of tetrahydrofuran:water:acetonitrile to produce a suspension,

(c) stirring the suspension for about one day, and

(d) isolating the crystalline hydrate of the oxalate salt from the suspension.

15. Use of the crystalline oxalate hydrate of any one of Claims 1 to 6 or the crystalline succinate hydrate of any one of Claims 7 to 12 in the manufacture of a medicament for the treatment of a respiratory disease in a mammal.

16. The use of Claim 15 wherein the respiratory disease is asthma, chronic obstructive pulmonary disease, cystic fibrosis, pneumonitis, idiopathic pulmonary fibrosis, acute lung injury, acute respiratory distress syndrome, bronchitis, emphysema or bronchiolitis obliterans.

17. The useof Claim 15 wherein the respiratory disease is bronchiolitis obliterans.

18. The use of Claim 15 wherein the respiratory disease is asthma or chronic obstructive pulmonary disease.

19. The use of Claim 18 wherein the respiratory disease is asthma.

20. The use of Claim 15 wherein the medicament is to be administered by inhalation.

21. The use of Claim 15 wherein the respiratory disease is a lung infection, a helminthic infection, pulmonary arterial hypertension, sarcoidosis, lymphangioleiomyomatosis, bronchiectasis, or infiltrative pulmonary disease.

22. The use of Claim 15 wherein the respiratory disease is drug-induced pneumonitis, fungal induced pneumonitis, allergic bronchopulmonary aspergillosis, hypersensitivity pneumonitis, eosinophilic granulomatosis with polyangiitis, idiopathic acute eosinophilic pneumonia, idiopathic chronic eosinophilic pneumonia,

hypereosinophilic syndrome, Löffler syndrome, bronchiolitis obliterans organizing pneumonia, or immune-checkpoint-inhibitor induced pneumonitis.

23. Use of the crystalline oxalate hydrate of any one of Claims 1 to 6 or the crystalline succinate hydrate of any one of Claims 7 to 12 in the manufacture of a medicament for the treatment of an ocular disease in a mammal.