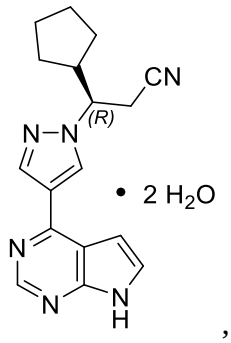
What is claimed is:

1. A solid form, which is crystalline ruxolitinib di-hydrate:



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wherein the solid form is substantially isolated.

2. The solid form of claim 1, wherein the solid form is characterized by having at least one XRPD peak, in terms of 2-theta (± 0.2 degrees), selected from 6.9, 10.6, 11.6, 12.9, 15.1, 15.4, 19.0, 21.8, 22.7, 23.1, 24.8, and 25.7 degrees.

3. The solid form of claim 1, wherein the solid form is characterized by having at least five XRPD peaks, in terms of 2-theta (± 0.2 degrees), selected from 6.9, 10.6, 11.6, 12.9, 15.1, 15.4, 19.0, 21.8, 22.7, 23.1, 24.8, and 25.7 degrees.

4. The solid form of any one of claims 1-3, wherein the solid form is characterized by having an XRPD pattern with characteristic peaks as substantially shown in FIG. 2.

5. The solid form of any one of claims 1-4, wherein the solid form is characterized by single crystal x-ray diffraction having a P212121 space group and cell formula units (Z) of 8.

6. The solid form of claim 5, wherein the solid form has unit cell parameters: a is about 9.97 Å, b is about 15.18 Å, c is about 23.64 Å, α is about 90°, β is about 90°, and γ is about 90°.

7. The solid form of any one of claims 1-6, wherein the solid form is characterized by having an endothermic peak with an onset temperature (± 5 ^{o}C) at 61 ^{o}C and a maximum temperature (± 5 ^{o}C) at 67 ^{o}C, in a DSC thermogram.

8. The solid form of any one of claims 1-6, wherein the solid form is characterized by having a DSC thermogram substantially as depicted in FIG. 3.

9. The solid form of any one of claims 1-8, wherein the solid form is characterized by having a TGA thermogram substantially as depicted in FIG. 4.

10. A solid form, which is anhydrous crystalline ruxolitinib free base.

11. The solid form of claim 10, wherein the solid form is substantially isolated.

12. The solid form of claim 10 or claim 11, wherein the solid form is characterized by having at least one XRPD peak, in terms of 2-theta (± 0.2 degrees), selected from 7.2, 11.5, 11.6, 13.2, 14.0, 15.4, 15.7, 18.2, 19.1, 19.6, 22.0, and 23.9 degrees.

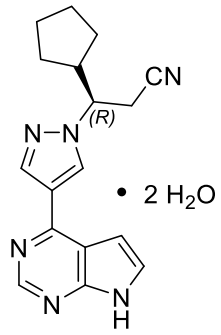
13. The solid form of any one of claims 10-12, wherein the solid form is characterized by having an XRPD pattern with characteristic peaks as substantially shown in FIG. 13.

14. The solid form of any one of claims 10-13, wherein the solid form is characterized by having an endothermic peak with an onset temperature (± 5 °C) at 83 °C and a maximum temperature (± 5 °C) at 93 °C, in a DSC thermogram.

15. The solid form of any one of claims 10-13, wherein the solid form is characterized by having a DSC thermogram substantially as depicted in FIG. 15 or FIG. 16.

16. The solid form of any one of claims 10-15, wherein the solid form is characterized by having a TGA thermogram substantially as depicted in FIG. 17 or FIG. 18.

17. A process of preparing a solid form of any one of claims 1-9, which is ruxolitinib di-hydrate:

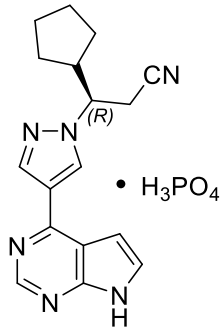


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comprising isolating the solid form from a solution comprising ruxolitinib free base and an aqueous solvent component.

18. The process of claim 17, wherein the aqueous solvent component comprises a polar protic solvent and water, wherein the polar protic solvent is isopropanol.

19. The process of claim 17 or claim 18, wherein the ruxolitinib free base is prepared by a process comprising reacting ruxolitinib phosphate:



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with a base in a solvent component, wherein:

the reacting of ruxolitinib phosphate with a base comprises using from about 2 to about 3 molar equivalents of the base relative to ruxolitinib phosphate;

the base is a hydroxide base; and

the solvent component comprises water, an ester solvent, a halogenated solvent, or a mixture thereof, wherein the ester solvent is ethyl acetate; and wherein the halogenated solvent is dichloromethane.

20. A process of preparing a solid form of any one of claims 10-16, comprising drying crystalline ruxolitinib di-hydrate.

21. The process of claim 20, wherein the drying comprising drying crystalline ruxolitinib di-hydrate in a jar with desiccant at about room temperature.

22. A pharmaceutical composition comprising the solid form of any one of claims 1-16.

23. The pharmaceutical composition of claim 22, which is an oral dosage form.

24. The pharmaceutical composition of claim 23, wherein the oral dosage form is an immediate dosage form.

25. The pharmaceutical composition of any one of claims 22-24, wherein the solid form is ruxolitinib di-hydrate, which is present in an amount of about 5 to about 25 mg on a free base basis.

26. The pharmaceutical composition of claim 23, wherein the oral dosage form is a sustained-release dosage form.

27. The pharmaceutical composition of any one of claims 22, 23 and 26, wherein the solid form is ruxolitinib di-hydrate, which is present in an amount of about 10 to about 50 mg on a free base basis.

28. The pharmaceutical composition of claim 22, wherein the composition is a topical formulation.

29. The pharmaceutical composition of claim 28, wherein the topical formulation is a cream formulation.

30. The pharmaceutical composition of claim 29, wherein the cream formulation comprises an oil-in-water emulsion.

31. The pharmaceutical composition of claim 30, wherein the cream formulation is prepared by incorporating ruxolitinib di-hydrate in the oil-in-water emulsion.

32. A process for releasing a batch of the topical pharmaceutical formulation of any one of claims 28-31, comprising (i) testing a sample of the topical pharmaceutical formulation for the absence of crystalline ruxolitinib di-hydrate; and, if the sample passes the test in step (i), then: (ii) releasing the batch for public use.

33. The process of claim 32, wherein the testing comprises observing a sample of the formulation under a light microscope in order to detect the absence or presence of crystals, wherein the sample passes the test when crystals are not detected.

34. Use of a pharmaceutical composition of any one of claims 22-31, in the manufacture of a medicament for the treatment of a disease, wherein the disease is myelofibrosis, polycythemia vera, acute graft versus host disease or chronic graft versus host disease.

35. Use of a pharmaceutical composition of any one of claims 22-31, in the manufacture of a medicament for the treatment of a skin disorder.

36. Use of a topical pharmaceutical formulation of any one of claims 28-31, in the manufacture of a medicament for the treatment of a skin disorder.

37. The use of claim 35 or claim 36, wherein the skin disorder is an autoimmune skin disease.

38. The use of claim 37, wherein the skin disorder is:

atopic dermatitis; or

lichen planus; or

hidradenitis suppurativa; or

psoriasis; or

skin rash, skin irritation, or skin sensitization; or

contact dermatitis or allergic contact dermatitis; or

bullous pemphigoid.