X-ray diffraction pattern, IR spectrum, and solid state ^{13}C NMR spectrum. One or more of these techniques may be used to distinguish different polymorphic forms of a compound.

Different salts and crystalline forms (including solvated forms) of an active pharmaceutical ingredient may possess different properties. Such variations in the properties of different salts and crystalline forms and solvates may provide a basis for improving formulation and/or clinical properties. Different salts and solvates of an active pharmaceutical ingredient may also give rise to a variety of polymorphs or crystalline forms.

SUMMARY

In an aspect, there is provided a crystalline form of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof.

In another aspect, there is provided a pharmaceutical composition comprising the crystalline form disclosed herein and a pharmaceutically acceptable carrier.

There is provided a method for treating cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the crystalline form disclosed herein, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition comprising a crystalline form disclosed herein and a pharmaceutically acceptable carrier.

In another aspect, there is provided use of the crystalline form disclosed herein, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition disclosed herein in the manufacture of a medicament for treating cancer.

There is provided a method for treating cancer in a subject in need thereof, the method comprising (a) determining that the cancer is associated with a dysregulation of a *PIK3CA* gene, a PI3Kα protein, or expression or activity or level of any of the same; and (b) administering to the subject a therapeutically effective amount of the crystalline form disclosed herein, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition comprising a crystalline form disclosed herein and a pharmaceutically acceptable carrier.

In another aspect, there is provided use of of the crystalline form disclosed herein, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition disclosed herein in the manufacture of a medicament for treating cancer, wherein the cancer is determined to be associated with a dysregulation of a *PIK3CA* gene, a PI3Kα protein, or expression or activity or level of any of the same.

There is provided a method of treating a PI3Kα-associated cancer in a subject, the method comprising administering to a subject identified or diagnosed as having a PI3Kα-associated cancer a therapeutically effective amount of the crystalline form disclosed herein, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition comprising a crystalline form disclosed herein and a pharmaceutically acceptable carrier.

In another aspect, there is provided use of the crystalline form disclosed herein or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition disclosed herein in the manufacture of a medicament for treating a PI3Kα-associated cancer.

There is provided a method for modulating PI3Kα in a mammalian cell, the

method comprising contacting the mammalian cell with an effective amount of the crystalline form disclosed herein, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition comprising a crystalline form disclosed herein and a pharmaceutically acceptable carrier.

In another aspect, there is provided an in vitro method for modulating PI3Kα in a mammalian cell, the method comprising contacting the mammalian cell with an effective amount of the crystalline form disclosed herein, or a pharmaceutically acceptable salt and/or solvate thereof.

In another aspect, there is provided a pharmaceutical composition comprising about 1 mg to about 200 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof, and a pharmaceutically acceptable carrier.

In another aspect, there is provided a pharmaceutical composition comprising about 0.1% to about 50% weight percent 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, and a pharmaceutically acceptable carrier.

In another aspect, there is provided a pharmaceutical composition comprising about 20 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

In another aspect, there is provided a pharmaceutical composition comprising about 40 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

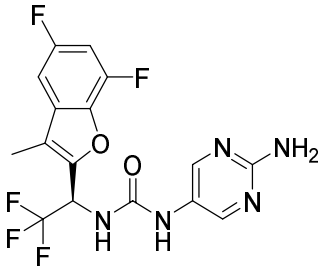
In another aspect, there is provided a pharmaceutical composition comprising about 60 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

In another aspect, there is provided a pharmaceutical composition comprising about 80 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

In another aspect, there is provided a pharmaceutical composition comprising about 100 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

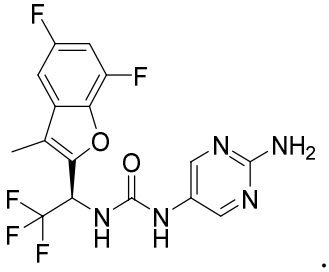
In another aspect, there is provided a pharmaceutical composition comprising about 25% weight percent (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

In another aspect, there is provided a hydrate of the compound of the formula



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In another aspect, there is provided a hemi-hydrate of the compound of the formula



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In another aspect, there is provided use of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof, in the manufacture of a medicament for treating a PI3Kα-associated cancer, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 1 mg to about 200 mg per day.

In another aspect, there is provided the crystalline form disclosed herein or a pharmaceutically acceptable salt and/or solvate thereof, the pharmaceutical composition disclosed herein, the hydrate disclosed herein, or the hemi-hydrate disclosed herein, for use in therapy.

Additional Definitions

To facilitate understanding of the disclosure set forth herein, a number of additional terms are defined below. Generally, the nomenclature used herein and the laboratory procedures in organic chemistry, medicinal chemistry, and pharmacology described herein are those well-known and commonly employed in the art. Unless defined otherwise, all technical and scientific terms used herein generally have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Each of the patents, applications, published applications, and other publications that are mentioned throughout the specification and the attached appendices are incorporated herein by reference in their entireties.

The term “about” when referring to a number or a numerical range means that the number or numerical range referred to is an approximation, for example, within experimental variability and/or statistical experimental error, and thus the number or numerical range may vary up to ±10% of the stated number or numerical range.

The term “acceptable” with respect to a formulation, composition or ingredient, as used herein, means having no persistent detrimental effect on the general health of the subject being treated.

The term "inhibit” or “inhibition of” means to reduce by a measurable amount, or to prevent entirely (e.g., 100% inhibition).

The terms “polymorph” and “polymorphic form” are used interchangeably and refer to different crystalline forms of a single compound. That is, polymorphs are distinct solids sharing the same molecular formula, yet each polymorph may have distinct solid state physical properties. Therefore, a single compound may give rise to a variety of polymorphic forms where each form has different and distinct solid state physical properties, such as different solubility profiles, dissolution rates, melting point temperatures, flowability, and/or different X-ray diffraction peaks.

The term “amorphous” means a solid in a non-crystalline state. Amorphous solids are disordered arrangements of molecules and therefore possess no distinguishable crystal lattice or

WHAT IS CLAIMED IS:

1. A crystalline form of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof.

2. The crystalline form of claim 1, wherein the (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea is present in the form of a pharmaceutically acceptable solvate.

3. The crystalline form of claim 1 or 2, wherein the crystalline form is Form 1 characterized by an X-ray powder diffraction (XRPD) pattern having a peak at 18.3 ± 0.2 degrees 2θ.

4. The crystalline form of claim 1 or 2, wherein the crystalline form is Form 1, and wherein the XRPD pattern has peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3.

5. The crystalline form of claim 1 or 2, wherein the crystalline form is Form 1, and wherein the XRPD pattern has peaks (± 0.2 degrees 2θ) at 6.4, 14.6, 15.8, 18.3, 19.3, 20.8, 22.3, 24.0, 26.9, 28.3, 29.2 and 31.3.

6. The crystalline form of claim 1 or 2, wherein the crystalline form is Form 1, characterized by an XRPD pattern substantially the same as that shown in FIG. 4.

7. The crystalline form of any one of claims 1-6, wherein the crystalline form is Form 1 having a thermogravimetric analysis (TGA) curve characterized by a weight loss of about 2.3% at about 112.5 ^{o}C.

8. The crystalline form of any one of claims 1-7, wherein the crystalline form is Form 1 having a TGA curve characterized by a weight loss of about 17.6% at about 245 ^{o}C.

9. The crystalline form of any one of claims 1-8, wherein the crystalline form is Form 1 having a TGA curve that is substantially the same as that shown in FIG. 28.

10. The crystalline form of any one of claims 1-9, wherein the crystalline form is Form 1 prepared by a method comprising:

(a) dissolving (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof in isopropanol to form a solution;

(b) adding water to the solution to form a mixture;

(c) reducing the temperature of the mixture then maintaining the temperature for a first period of time;

(d) increasing the temperature of the mixture then maintaining the temperature for a second period of time;

(e) reducing the temperature of the mixture then maintaining the temperature for a third period of time; and

(f) isolating Form 1 from the mixture.

11. The crystalline form of any one of claims 1-4, wherein the crystalline form is Form 1 prepared by a method comprising:

(a) dissolving (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof in methanol to form a solution;

(b) adding water to the solution to form a first mixture;

(c) adding (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea Form 1 to the first mixture to form a second mixture;

(d) agitating the second mixture;

(e) adding water to the second mixture to form a third mixture;

(f) agitating the third mixture; and

(g) isolating Form 1 from the third mixture.

12. The crystalline form of claim 11, wherein isolating Form 1 from the third mixture comprises:

(i) filtering the third mixture to provide a solid;

(ii) rinsing the solid with methanol and water; and

(iii) drying the solid to provide Form 1.

13. A pharmaceutical composition comprising the crystalline form of any one of claims 1-12 and a pharmaceutically acceptable carrier.

14. The pharmaceutical composition of claim 13, wherein the composition is in the form of a tablet.

15. The pharmaceutical composition of claim 13 or 14, wherein the composition comprises microcrystalline cellulose, mannitol, croscarmellose sodium, colloidal silicon dioxide, sodium stearyl fumarate, or any combination thereof.

16. Use of the crystalline form of any one of claims 1-12, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition of any one of claims 13-15 in the manufacture of a medicament for treating cancer.

17. Use of the crystalline form of any one of claims 1-12, or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition of any one of claims 13-15 in the manufacture of a medicament for treating cancer, wherein the cancer is determined to be associated with a dysregulation of a *PIK3CA* gene, a PI3Kα protein, or expression or activity or level of any of the same.

18. Use of the crystalline form of any one of claims 1-12 or a pharmaceutically acceptable salt and/or solvate thereof, or a pharmaceutical composition of any one of claims 13-15 in the manufacture of a medicament for treating a PI3Kα-associated cancer.

19. An in vitro method for modulating PI3Kα in a mammalian cell, the method comprising contacting the mammalian cell with an effective amount of the crystalline form of any one of claims 1-12, or a pharmaceutically acceptable salt and/or solvate thereof.

20. The use of claim 18, wherein the PI3Kα-associated cancer is PI3Kα-associated breast cancer.

21. The use of claim 20, wherein the PI3Kα-associated breast cancer is PI3Kα-associated HR+, HER2- breast cancer.

22. A pharmaceutical composition comprising about 1 mg to about 200 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof, and a pharmaceutically acceptable carrier.

23. The pharmaceutical composition of claim 22, comprising about 1 mg to about 100 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

24. The pharmaceutical composition of claim 22, comprising about 20 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

25. The pharmaceutical composition of claim 22, comprising about 40 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

26. The pharmaceutical composition of claim 22, comprising about 60 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

27. The pharmaceutical composition of claim 22, comprising about 80 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

28. The pharmaceutical composition of claim 22, comprising about 100 mg of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

29. A pharmaceutical composition comprising about 0.1% to about 50% weight percent 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, and a pharmaceutically acceptable carrier.

30. The pharmaceutical composition of claim 29, comprising about 0.1% to about 25% weight percent 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutical acceptable salt and/or solvate thereof.

31. The pharmaceutical composition of any one of claims 22-30, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

32. The pharmaceutical composition of any one of claims 22-30, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hydrate.

33. The pharmaceutical composition of any one of claims 22-30, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate.

34. The pharmaceutical composition of any one of claims 22-30, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3.

35. The pharmaceutical composition of any one of claims 22-30, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 14.6, 15.8, 18.3, 19.3, 20.8, 22.3, 24.0, 26.9, 28.3, 29.2 and 31.3.

36. A pharmaceutical composition comprising about 20 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea

hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

37. A pharmaceutical composition comprising about 40 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

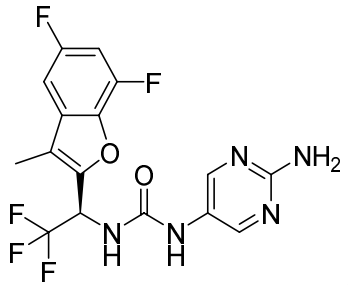
38. A pharmaceutical composition comprising about 60 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

39. A pharmaceutical composition comprising about 80 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

40. A pharmaceutical composition comprising about 100 mg of (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

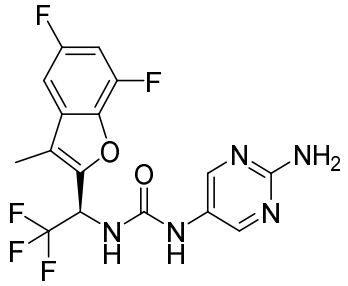
41. A pharmaceutical composition comprising about 25% weight percent (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3, and a pharmaceutically acceptable carrier.

42. A hydrate of the compound of the formula



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43. A hemi-hydrate of the compound of the formula



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44. The hemi-hydrate of claim 43, characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3.

45. The hemi-hydrate of claim 43, characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 14.6, 15.8, 18.3, 19.3, 20.8, 22.3, 24.0, 26.9, 28.3, 29.2 and 31.3.

46. Use of 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof, in the manufacture of a medicament for treating a PI3Kα-associated cancer, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea, or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 1 mg to about 200 mg per day.

47. The use of claim 46, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 1 mg to about 100 mg per day.

48. The use of claim 46, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 20 mg per day.

49. The use of claim 46, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 40 mg per day.

50. The use of claim 46, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 60 mg per day.

51. The use of claim 46, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 80 mg per day.

52. The use of claim 46, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof, is formulated to be administered in an amount of about 100 mg per day.

53. The use of any one of claims 46-52, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or a pharmaceutically acceptable salt and/or solvate thereof.

54. The use of any one of claims 46-52, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hydrate.

55. The use of any one of claims 46-52, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically

acceptable salt and/or solvate thereof is (R)-1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea hemi-hydrate.

56. The use of any one of claims 46-52, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 15.8, and 18.3.

57. The use of any one of claims 46-52, wherein the 1-(2-aminopyrimidin-5-yl)-3-(1-(5,7-difluoro-3-methylbenzofuran-2-yl)-2,2,2-trifluoroethyl)urea or pharmaceutically acceptable salt and/or solvate thereof is characterized by an X-ray powder diffraction (XRPD) pattern having peaks (± 0.2 degrees 2θ) at 6.4, 14.6, 15.8, 18.3, 19.3, 20.8, 22.3, 24.0, 26.9, 28.3, 29.2 and 31.3.

58. The use of any one of claims 46-57, wherein the PI3Kα-associated cancer is PI3Kα-associated breast cancer.

59. The use of claim 58, wherein the PI3Kα-associated breast cancer is PI3Kα-associated HR+, HER2- breast cancer.

60. The crystalline form of any one of claims 1-12 or a pharmaceutically acceptable salt and/or solvate thereof, the pharmaceutical composition of any one of claims 13-15 or 22-41, the hydrate of claim 42, or the hemi-hydrate of any one of claims 43-45, for use in therapy.