the compound are described in WO 2011/097602. To move a drug candidate such as (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one to a viable pharmaceutical product, it can be important to understand whether the drug candidate has polymorph forms, as well as the relative stability and interconversions of these forms under conditions likely to be encountered upon large-scale production, transportation, storage and pre-usage preparation. The ability to control and produce a stable polymorph with a robust manufacturing process can be key for regulatory approval and marketing. Large scale production processes for high purity 5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-*de*]phthalazin-3(7*H*)-one are sought, which is hampered by the fact that parameters affecting the stability of this compound are not known and polymorphic forms of the compound have not been available.

BRIEF SUMMARY

[0005] In one aspect, the present invention refers to a crystalline tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one having an X-Ray Powder Diffraction pattern comprising peaks at 2θ angle degrees ± 0.2 of 7.5, 20.1, and 24.1.

[0005a] In another aspect, the present invention refers to a crystalline tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one exhibiting a solid state ^{13}C NMR spectrum with peaks at 143.2, 136.0, 131.8, 123.9, 112.2, 105.2, and 100.3 ppm ± 0.2 ppm.

[0005b] In yet another aspect, the present invention refers to a pharmaceutical composition comprising the crystalline tosylate salt of the present invention and a pharmaceutically acceptable excipient.

[0005c] In yet another aspect, the present invention refers to the use of a therapeutically effective amount of the crystalline tosylate salt of the present invention for the manufacture of a medicament for treating a subject with cancer.

[0005d] In one example, provided herein is a tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one. In some examples the tosylate salt is in a crystalline form. In some examples, provided herein are solid forms of a tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-

methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one, including crystalline forms, amorphous forms, or mixtures thereof.

[0006] In another example, provided herein are methods of synthesizing (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one in a free base form ("free base").

[0007] In another example, a method of preparing a tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one is provided. In certain examples, the tosylate salt is prepared from a suspension in tetrahydrofuran (THF).

[0008] In another example, the present disclosure provides a pharmaceutical composition comprising a tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one, or a solid form thereof, as described herein.

[0009] In another example, the present disclosure provides a method of treating cancer with a tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one, in another example a crystalline form thereof, or a composition thereof.

DESCRIPTION OF THE DRAWINGS

[0010] **Fig.1** provides an overlay of five examples of powder X-ray powder diffraction (XRPD) patterns of crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt.

[0011] **FIG. 2a** provides a differential scanning calorimetric (DSC) graph of a crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt polymorph, 8, from acetone-THF preparation.

[0012] **Fig. 2b** provides a thermogravimetric analysis (TGA) graph of a crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt polymorph, 8, from acetone-THF preparation.

[0013] **FIG. 3a** provides a DSC graph of a crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt polymorph, 5, from DCM-ACN preparation.

[0014] **Fig. 3b** provides a TGA graph of a crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt polymorph, 5, from DCM-ACN preparation.

[0015] **FIG. 4a** provides a DSC graph of a crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt polymorph, 6, from acetone preparation.

[0016] **Fig. 4b** provides a TGA graph of a crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt polymorph, 6, from acetone preparation.

[0017] **FIG. 5a** provides a DSC graph of a crystalline (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one tosylate salt polymorph, 7, from THF preparation.

WHAT IS CLAIMED:

1. A crystalline tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one having an X-Ray Powder Diffraction pattern comprising peaks at 2θ angle degrees ± 0.2 of 7.5, 20.1, and 24.1.

2. The crystalline tosylate salt of claim 1, having an X-ray powder diffraction pattern comprising peaks at 2θ angle degrees ± 0.2 of 7.5, 15.1, 18.1, 20.1, 20.5, 22.6, and 24.1.

3. A crystalline tosylate salt of (8*S*,9*R*)-5-fluoro-8-(4-fluorophenyl)-9-(1-methyl-1*H*-1,2,4-triazol-5-yl)-8,9-dihydro-2*H*-pyrido[4,3,2-de]phthalazin-3(7*H*)-one exhibiting a solid state ^{13}C NMR spectrum with peaks at 143.2, 136.0, 131.8, 123.9, 112.2, 105.2, and 100.3 ppm ± 0.2 ppm.

4. A pharmaceutical composition comprising the crystalline tosylate salt of claim 1 and a pharmaceutically acceptable excipient.

5. A pharmaceutical composition comprising the crystalline tosylate salt of claim 3 and a pharmaceutically acceptable excipient.

6. Use of a therapeutically effective amount of the crystalline tosylate salt of claim 1 for the manufacture of a medicament for treating a subject with cancer.

7. The use of claim 6, where the cancer is bladder cancer, breast cancer, cervical cancer, colon cancer, colorectal cancer, Burkitt's lymphoma, nasopharyngeal carcinoma, EBV+ gastric cancer, endometrial cancer, gastrointestinal stromal tumor, glioblastoma, head and neck cancer, hepatocellular carcinoma, kidney cancer, leukemia, lung cancer, lymphoma, medulloblastoma, melanoma, meningioma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, small cell lung carcinoma, thyroid cancer, or uterine cancer.

8. Use of a therapeutically effective amount of the crystalline tosylate salt of claim 3 for the manufacture of a medicament for treating a subject with cancer.

9. The use of claim 8, where the cancer is bladder cancer, breast cancer, cervical cancer, colon cancer, colorectal cancer, Burkitt's lymphoma, nasopharyngeal carcinoma, EBV+ gastric cancer, endometrial cancer, gastrointestinal stromal tumor, glioblastoma, head and neck cancer, hepatocellular carcinoma, kidney cancer, leukemia, lung cancer, lymphoma, medulloblastoma, melanoma, meningioma, ovarian cancer, pancreatic cancer, prostate cancer, renal cancer, small cell lung carcinoma, thyroid cancer, or uterine cancer.