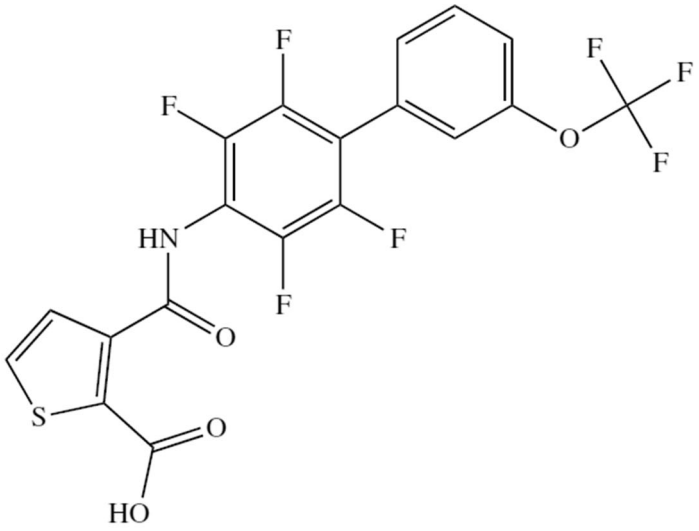
CLAIMS

1. A polymorph of 3-(2,3,5,6-tetrafluoro-3'-trifluoromethoxy-biphenyl-4-ylcarbamoyl)-thiophene-2-carboxylic acid as shown in Formula I:

Formula I



wherein the polymorph is

Form A comprising an X-ray powder diffraction (XRPD) comprising five or more 2θ values selected from 14.8±0.2, 15.6±0.2, 16.5±0.2, 19.6±0.2, 20.8±0.2, 25.6±0.2 and 26.1±0.2; or

Form B comprising an X-ray powder diffraction (XRPD) comprising five or more 2θ values selected from 14.9±0.2, 17.6±0.2, 19.3±0.2, 20.9±0.2, 24.0±0.2, 24.9±0.2 and 25.4±0.2.

2. The polymorph of claim 1, wherein the polymorph is Form A.

3. The polymorph of claim 2, wherein the polymorph comprises five or more 2θ values selected from 14.8±0.2, 15.6±0.2, 16.5±0.2, 19.6±0.2, 20.8±0.2, 25.6±0.2 and 26.1±0.2.

4. The polymorph of claim 2, wherein Form A comprises the XRPD pattern shown in FIG. 2A.

5. The polymorph of claim 2 further comprising one or more characteristics selected from:
   a. a DSC spectrum (5°C/min) comprising an endotherm onset at 178.3±1.0°C, and a second endotherm onset at 227.3±1.0°C;
   b. a DSC spectrum (10°C/min) comprising an endotherm onset at 177.6±1.0°C, and an endotherm onset at 227.9±1.0°C;
   c. a DSC spectrum (20°C/min) comprising an endotherm onset at 178.5±1.0°C, and an endotherm onset at 222.5±1.0°C and 224.3±1.0°C, followed by an endotherm onset at 227.8±1.0°C;
   d. a DSC spectrum (50°C/min) comprising double endotherm onsets at 88.0±1.0°C and 92.6±1.0°C, a second endotherm onset at 180.5±1.0°C, a sharp endo/exo onset at 224.7±1.0°C, and an endotherm onset at 229.5±1.0°C;
   e. a melt-quench-cool (MDSC) comprising an endotherm onset at 177.7±1.0°C, an endotherm onset at 227.8±1.0°C; or
   f. a VT-XRPD pattern with observable changes at 200°C.

6. The polymorph of claim 1, wherein the polymorph is Form B.

7. The polymorph of claim 6, wherein the polymorph comprises five or more 2θ values selected from 14.8±0.2, 17.6±0.2, 19.3±0.2, 20.9±0.2, 24.0±0.2, 24.9±0.2 and 25.4±0.2.

8. The polymorph of claim 6, wherein Form B comprises the XRPD pattern shown in FIG. 2B.

9. A pharmaceutical composition comprising the polymorph Form A or Form B of claim 1.

10. A kit comprising the polymorph Form A or Form B of claim 1.

11. A method of preparing polymorph Form A of 3-(2,3,5,6-tetrafluoro-3'-trifluoromethoxy-biphenyl-4-ylcarbamoyl)-thiophene-2-carboxylic acid, the method comprising:
    a) obtaining a sample comprising 3-(2,3,5,6-tetrafluoro-3'-trifluoromethoxy-biphenyl-4-ylcarbamoyl)-thiophene-2-carboxylic acid;
    b) dissolving the sample of (a) in a solvent comprising C_1-C_5 alcohol, C_1-C_5 ketone, or C_1-C_5 acetate solvent at 20°C to 60°C to form a solution, wherein the solution is greater than 80% C_1-C_5 alcohol, C_1-C_5 ketone, or C_1-C_5 acetate, wherein the C_1-C_5 alcohol is selected from methanol, ethanol, 1-propanol, isopropanol, 1-butanol, 2-butanol, 1-pentanol, 2-pentanol, or isopentanol, the C_1-C_5 ketone is selected from methyl ethyl ketone (MEK), methylisobutyl ketone (MIBK), or acetone, and the C_1-C_5 acetate is selected from methyl acetate, ethyl acetate, propyl acetate, butyl acetate, or pentyl acetate; and
    c) removing the solvent from the solution to obtain the polymorph Form A of claim 1.

12. The method of claim 11, wherein the C_1-C_5 alcohol is selected from methanol, ethanol, 1-propanol, isopropanol, the C_1-C_5 ketone is selected from methyl ethyl ketone (MEK), methylisobutyl ketone (MIBK), or acetone, and the C_1-C_5 acetate is selected from ethyl acetate or propyl acetate.

13. The method of claim 11, wherein the solution is greater than 90% C_1-C_5 alcohol, C_1-C_5 ketone, or C_1-C_5 acetate.

14. The method of claim 11, wherein the solution comprises 0% to 20% water.

15. The method of claim 11, wherein after the dissolving in (b), the solution is cooled to an incubation temperature of 1°C to 10°C for a period of time.

16. The method of claim 15, wherein the cooling to the incubation temperature is at a rate of 0.02°C/min to 1°C/min until the incubation temperature is reached.

17. The method of claim 15, wherein the period of time for the incubation temperature is 1 hour to 48 hours.

18. The method of claim 11, wherein the removing of the solvent is performed by evaporation.

19. The method of claim 18, wherein the evaporation occurs at about 20°C to about 35°C.

20. Use of a pharmaceutically effective amount of polymorph Form A of claim 1 in the manufacture of a medicament for treating or ameliorating an inflammatory disease or disorder.

21. A method of preparing polymorph Form A of 3-(2,3,5,6-tetrafluoro-3'-trifluoromethoxy-biphenyl-4-ylcarbamoyl)-thiophene-2-carboxylic acid, the method comprising:
    a) obtaining a sample comprising 3-(2,3,5,6-tetrafluoro-3'-trifluoromethoxy-biphenyl-4-ylcarbamoyl)-thiophene-2-carboxylic acid;
    b) dissolving the sample of (a) in a solvent comprising C_1-C_5 alcohol, C_1-C_5 ketone, or C_1-C_5 acetate solvent at 20°C to 60°C to form a solution;
    c) removing the solvent from the solution to obtain a resulting polymorph; and
    d) characterizing the resulting polymorph to confirm that it is solely polymorph Form A of Claim 1.