CRYSTALLINE FORMS OF A COMPOUND FOR TREATING OR PREVENTING GOUT OR HYPERURICEMIA

CROSS-REFERENCE

[0001] This application claims benefit of PCT/CN2018/119567, filed on December 6, 2018, which is herein incorporated by reference in its entirety.

BACKGROUND

[0002] Hyperuricemia is caused by the overproduction or under-excretion of uric acid, and is considered to be a causative factor of several diseases that significantly impair the quality of life. For example, hyperuricemia is considered the causative factor of gout – the most prevalent form of inflammatory arthritis, characterized by severe pain and tenderness in joints caused by urate crystal accumulation. The identification of a gout/hyperuricemia drug effective in lowering serum uric acid (sUA) with reduced toxicity represents an unmet medical need that would have beneficial impact on patients.

SUMMARY OF THE INVENTION

[0002a] In an aspect of the present disclosure, there is provided a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 3 having at least one of the following properties:

(a) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 6.8° 2-Theta, 13.6° 2-Theta, 14.6° 2-Theta, 21.2° 2-Theta, 24.2° 2-Theta, 24.7° 2-Theta, 26.7° 2-Theta, and 27.5° 2-Theta;

(b) a DSC thermogram with an endotherm having an onset at about 147°C; or

(c) combinations thereof.

[0002b] In another aspect of the present disclosure, there is provided a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 2 having at least one of the following properties:

(a) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 8.3° 2-Theta, 10.7° 2-Theta, 16.6° 2-Theta, 19.7° 2-Theta, 23.7° 2-Theta, 25.0° 2-Theta, 25.6° 2-Theta, and 27.1° 2-Theta;

(b) a DSC thermogram with an endotherm having an onset at about 139°C; or

(c) combinations thereof.

[0002c] In a further aspect of the present disclosure, there is provided a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 1 having at least one of the following properties:

(a) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.6° 2-Theta, 11.5° 2-Theta, 13.8° 2-Theta, 14.3° 2-Theta, 17.0° 2-Theta, 18.9° 2-Theta, 27.9° 2-Theta, and 31.4° 2-Theta;

(b) a DSC thermogram with an endotherm having an onset at about 80°C; or

(c) combinations thereof.

[0002d] In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the crystalline form disclosed herein, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.

[0002e] In a further aspect of the present disclosure, there is provided a use of a crystalline form disclosed herein, in the manufacture of a medicament for treating hyperuricemia or gout in an individual in need.

[0002f] In another aspect of the present disclosure, there is provided a crystalline form disclosed herein, for use in therapy.

[0003] In one example, described herein is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof.

[0004] In one example, is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 3 having at least one of the following properties:

(a) an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 1**;

(b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 6.8° 2-Theta, 13.6° 2-Theta, 14.6° 2-Theta, 21.2° 2-Theta, 24.2° 2-Theta, 24.7° 2-Theta, 26.7° 2-Theta, and 27.5° 2-Theta;

(c) a thermo-gravimetric analysis (TGA) substantially similar to the one set forth in **Figure 2**;

(d) a DSC thermogram substantially similar to the one set forth in **Figure 3**;

(e) a DSC thermogram with an endotherm having an onset at about 147°C;

(f) non-hygroscopicity; or

(g) combinations thereof.

[0005] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline

form has an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 1**.

[0006] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 6.8° 2-Theta, 13.6° 2-Theta, 14.6° 2-Theta, 21.2° 2-Theta, 24.2° 2-Theta, 24.7° 2-Theta, 26.7° 2-Theta, and 27.5° 2-Theta.

[0007] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 2**.

[0008] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a DSC thermogram substantially similar to the one set forth in **Figure 3**.

[0009] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a DSC thermogram with an endotherm having an onset at about 147°C.

[0010] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is non-hygroscopic.

[0011] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is characterized as having properties: (a) an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 1**; (b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 6.8° 2-Theta, 13.6° 2-Theta, 14.6° 2-Theta, 21.2° 2-Theta, 24.2° 2-Theta, 24.7° 2-Theta, 26.7° 2-Theta, and 27.5° 2-Theta; (c) a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 2**; (d) a DSC thermogram substantially similar to the one set forth in **Figure 3**; (e) a DSC thermogram with an endotherm having an onset at about 147°C; and (f) non-hygroscopicity.

[0012] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is obtained from toluene, toluene/heptane, or ethyl acetate/heptane.

[0013] In another example, is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline

form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 2 having at least one of the following properties:

(a) an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 4**;

(b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 8.3° 2-Theta, 10.7° 2-Theta, 16.6° 2-Theta, 19.7° 2-Theta, 23.7° 2-Theta, 25.0° 2-Theta, 25.6° 2-Theta, and 27.1° 2-Theta;

(c) a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 5**;

(d) a DSC thermogram substantially similar to the one set forth in **Figure 6**;

(e) a DSC thermogram with an endotherm having an onset at about 139°C;

(f) non-hygroscopicity; or

(g) combinations thereof.

[0014] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 4**.

[0015] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 8.3° 2-Theta, 10.7° 2-Theta, 16.6° 2-Theta, 19.7° 2-Theta, 23.7° 2-Theta, 25.0° 2-Theta, 25.6° 2-Theta, and 27.1° 2-Theta.

[0016] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 5**.

[0017] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a DSC thermogram substantially similar to the one set forth in **Figure 6**.

[0018] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a DSC thermogram with an endotherm having an onset at about 139°C.

[0019] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is non-hygroscopic.

[0020] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is characterized as having properties: (a) an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 4**; (b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 8.3° 2-Theta, 10.7° 2-Theta, 16.6° 2-Theta, 19.7° 2-Theta, 23.7° 2-Theta, 25.0° 2-Theta, 25.6° 2-Theta, and 27.1° 2-Theta; (c) a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 5**; (d) a DSC thermogram substantially similar to the one set forth in **Figure 6**; (e) a DSC thermogram with an endotherm having an onset at about 139°C; and (f) non-hygroscopicity.

[0021] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is obtained from heptane or ethyl acetate/heptane.

[0022] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form is unsolvated.

[0023] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form is anhydrous.

[0024] In another example, is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 1 having at least one of the following properties:

(a) an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 7**;

(b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.6° 2-Theta, 11.5° 2-Theta, 13.8° 2-Theta, 14.3° 2-Theta, 17.0° 2-Theta, 18.9° 2-Theta, 27.9° 2-Theta, and 31.4° 2-Theta;

(c) a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 8**;

(d) a DSC thermogram substantially similar to the one set forth in **Figure 9**;

(e) a DSC thermogram with an endotherm having an onset at about 80°C; or

(f) combinations thereof.

[0025] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 7**.

[0026] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.6° 2-Theta, 11.5° 2-Theta, 13.8° 2-Theta, 14.3° 2-Theta, 17.0° 2-Theta, 18.9° 2-Theta, 27.9° 2-Theta, and 31.4° 2-Theta.

[0027] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 8**.

[0028] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a DSC thermogram substantially similar to the one set forth in **Figure 9**.

[0029] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form has a DSC thermogram with an endotherm having an onset at about 80°C.

[0030] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is characterized as having properties: (a) an X-ray powder diffraction (XRPD) pattern substantially the same as shown in **Figure 7**; (b) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.6° 2-Theta, 11.5° 2-Theta, 13.8° 2-Theta, 14.3° 2-Theta, 17.0° 2-Theta, 18.9° 2-Theta, 27.9° 2-Theta, and 31.4° 2-Theta; (c) a thermogravimetric analysis (TGA) substantially similar to the one set forth in **Figure 8**; (d) a DSC thermogram substantially similar to the one set forth in **Figure 9**; and (e) a DSC thermogram with an endotherm having an onset at about 80°C.

[0031] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, wherein the crystalline form is obtained from methanol, ethanol, isopropanol, toluene, water, acetonitrile, heptane, acetone, *tert*-butyl methyl ether, 2-butanone, ethyl acetate, isopropyl acetate, tetrahydrofuran, or combinations thereof.

[0032] In some examples is a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, for use in medicine.

[0033] In some examples is (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is amorphous.

[0034] In another example, described herein is a pharmaceutical composition comprising a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.

[0035] In another example, described herein is a pharmaceutical composition comprising a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, formulated for oral, intravenous, intramuscular, or subcutaneous administration.

[0036] In another example, described herein is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein. In some examples is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, wherein (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is administered orally. In some examples is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, wherein the therapeutically effective amount is taken with food. In some examples is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, wherein the therapeutically effective amount is taken without food. In some examples is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof,

described herein, wherein (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is administered to the individual once per day. In some examples is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, wherein (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is administered to the individual twice per day.

[0037] In some examples, described herein is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, further comprising administering at least one additional therapeutic agent. In some examples, described herein is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, further comprising administering a xanthine oxidase inhibitor. In some examples, described herein is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, further comprising administering a xanthine oxidase inhibitor, wherein the xanthine oxidase inhibitor is allopurinol, oxypurinol, febuxostat, topiroxostat, or inositol. In some examples, described herein is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, further comprising administering a sodium-glucose co-transporter-2 (SGLT2) inhibitor. In some examples, described herein is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, further comprising administering an SGLT2 inhibitor, wherein the SGLT2 inhibitor is selected from canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, and dapagliflozin/metformin. In some examples, described herein

is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, further comprising administering a xanthine oxidase inhibitor and an SGLT2 inhibitor. In some examples, described herein is a method for treating hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, or solvate thereof, described herein, further comprising administering a xanthine oxidase inhibitor and an SGLT2 inhibitor, wherein the xanthine oxidase inhibitor, wherein the xanthine oxidase inhibitor is allopurinol, oxypurinol, febuxostat, topiroxostat, or inositol, and the SGLT2 inhibitor is selected from canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, and dapagliflozin/metformin.

INCORPORATION BY REFERENCE

[0038] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the extent applicable and relevant and to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE FIGURES

[0039] Figure 1. Illustrates an X-ray powder diffraction (XRPD) pattern of crystalline (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone (Compound 1), Form 3.

[0040] Figure 2. Illustrates a thermogravimetric analysis (TGA) thermogram of crystalline (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone (Compound 1), Form 3.

[0041] Figure 3. Illustrates a differential scanning calorimetry (DSC) thermogram of crystalline (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone (Compound 1), Form 3.

[0042] Figure 4. Illustrates an X-ray powder diffraction (XRPD) pattern of crystalline (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone (Compound 1), Form 2.

[0043] Figure 5. Illustrates a thermogravimetric analysis (TGA) thermogram of crystalline (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone (Compound 1), Form 2.

CLAIMS

We Claim:

1. A crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 3 having at least one of the following properties:
   (a) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 6.8° 2-Theta, 13.6° 2-Theta, 14.6° 2-Theta, 21.2° 2-Theta, 24.2° 2-Theta, 24.7° 2-Theta, 26.7° 2-Theta, and 27.5° 2-Theta;
   (b) a DSC thermogram with an endotherm having an onset at about 147°C; or
   (c) combinations thereof.
2. The crystalline form of claim 1, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 6.8° 2-Theta, 13.6° 2-Theta, 14.6° 2-Theta, 21.2° 2-Theta, 24.2° 2-Theta, 24.7° 2-Theta, 26.7° 2-Theta, and 27.5° 2-Theta.
3. The crystalline form of claim 1 or claim 2, wherein the crystalline form has a DSC thermogram with an endotherm having an onset at about 147°C.
4. The crystalline form of claim 1, wherein the crystalline form is characterized as having properties (a) and (b).
5. A crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 2 having at least one of the following properties:
   (a) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 8.3° 2-Theta, 10.7° 2-Theta, 16.6° 2-Theta, 19.7° 2-Theta, 23.7° 2-Theta, 25.0° 2-Theta, 25.6° 2-Theta, and 27.1° 2-Theta;
   (b) a DSC thermogram with an endotherm having an onset at about 139°C; or
   (c) combinations thereof.
6. The crystalline form of claim 5, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 8.3° 2-Theta, 10.7° 2-Theta, 16.6° 2-Theta, 19.7° 2-Theta, 23.7° 2-Theta, 25.0° 2-Theta, 25.6° 2-Theta, and 27.1° 2-Theta.
7. The crystalline form of claim 5, wherein the crystalline form has a DSC thermogram with an endotherm having an onset at about 139°C.

8. The crystalline form of claim 5, wherein the crystalline form is characterized as having properties (a) and (b).
9. A crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone, wherein the crystalline form of (3,5-dibromo-4-hydroxyphenyl)(2-(1-hydroxyethyl)benzofuran-3-yl-4,5,6,7-d_4)methanone is Form 1 having at least one of the following properties:
   (a) an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.6° 2-Theta, 11.5° 2-Theta, 13.8° 2-Theta, 14.3° 2-Theta, 17.0° 2-Theta, 18.9° 2-Theta, 27.9° 2-Theta, and 31.4° 2-Theta;
   (b) a DSC thermogram with an endotherm having an onset at about 80°C; or
   (c) combinations thereof.
10. The crystalline form of claim 9, wherein the crystalline form has an X-ray powder diffraction (XRPD) pattern with characteristic peaks at 5.6° 2-Theta, 11.5° 2-Theta, 13.8° 2-Theta, 14.3° 2-Theta, 17.0° 2-Theta, 18.9° 2-Theta, 27.9° 2-Theta, and 31.4° 2-Theta.
11. The crystalline form of claim 9, wherein the crystalline form has a DSC thermogram with an endotherm having an onset at about 80°C.
12. The crystalline form of claim 11, wherein the crystalline form is characterized as having properties (a) and (b).
13. A pharmaceutical composition comprising the crystalline form of any one of claims 1-12, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.
14. Use of a crystalline form of any one of claims 1-12, in the manufacture of a medicament for treating hyperuricemia or gout in an individual in need.
15. A crystalline form of any one of claims 1-12, for use in therapy.