

COMPOUND FOR TREATING GOUT OR HYPERURICEMIA

CROSS-REFERENCE

[0001] This application claims benefit of U.S. Provisional Application No. 62/847,519, filed on May 14, 2019, which is herein incorporated by reference in its entirety.

BACKGROUND

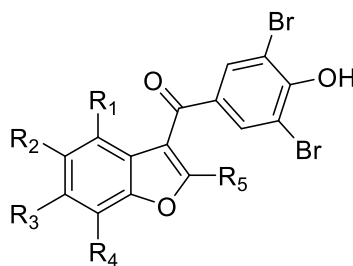
[0002] Hyperuricemia is caused by the overproduction or under-excretion of uric acid, and is considered to be a causative factor of several diseases that significantly impair the quality of life. For example, hyperuricemia is considered the causative factor of gout – the most prevalent form of inflammatory 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 one aspect of the present disclosure, there is provided a compound that is:

(i) (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7-d₃)methanone, or a pharmaceutically acceptable salt or solvate thereof;

(ii) a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof:



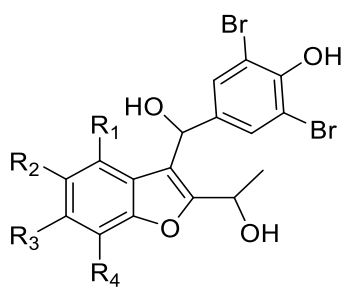
Formula (I):

wherein:

R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium; and

R₅ is -CH₂CH₂(OH) or -CH(OH)CH₂(OH); or

(iii) a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof:



Formula (II);

wherein:

R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium.

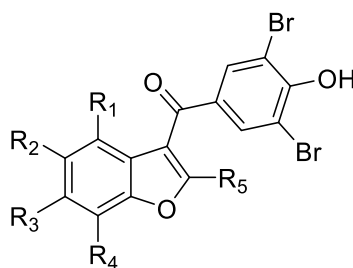
[0002b] In another aspect of the present disclosure, there is provided a use of a compound as disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating or preventing hyperuricemia or gout in an individual in need thereof.

[0002c] In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising a compound as disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.

[0002d] In another aspect of the present disclosure, there is provided a compound as disclosed herein, or a pharmaceutically acceptable salt or solvate thereof, for use in therapy.

[0003] In one aspectexample, described herein is a compound that is (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7-*d*₃)methanone, or a pharmaceutically acceptable salt or solvate thereof.

[0004] In another aspectexample, described herein is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof:



Formula (I);

wherein:

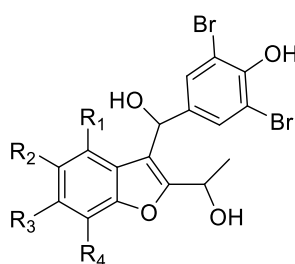
R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium;
and

R₅ is -CH₂CH₃, -CH₂CH₂(OH), or -CH(OH)CH₂(OH).

[0005] In some embodiment examples is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, wherein at least two of R₁, R₂, R₃, and R₄ is deuterium. In some

embodimentexamples is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, wherein at least three of R₁, R₂, R₃, and R₄ is deuterium. In some embodimentexamples is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, wherein R₁, R₂, R₃, and R₄ are deuterium. In some embodimentexamples is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, wherein R₅ is -CH₂CH₃. In some embodimentexamples is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, wherein R₅ is -CH₂CH₂(OH). In some embodimentexamples is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof, wherein R₅ is -CH(OH)CH₂(OH).

[0006] In another aspectexample, described herein is a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof:



Formula (II);

wherein:

R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium.

[0007] In some embodimentexamples is a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, wherein at least two of R₁, R₂, R₃, and R₄ is deuterium. In some embodimentexamples is a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, wherein at least three of R₁, R₂, R₃, and R₄ is deuterium. In some embodimentexamples is a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, wherein at least one of R₁, R₂, R₃, and R₄ is hydroxy.

[0008] In another aspectexample, described herein is a method for treating or preventing hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7-*d*₃)methanone, or a pharmaceutically acceptable salt or solvate thereof, described herein. In another aspectexample, described herein is a method for treating or preventing hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of a compound of Formula (I) or (II) described herein, or a pharmaceutically acceptable salt or solvate thereof. In some embodimentexamples is a method for treating or preventing hyperuricemia in an individual in need thereof. In some

embodimentexamples is a method for treating hyperuricemia in an individual in need thereof. In some embodimentexamples is a method for preventing hyperuricemia in an individual in need thereof. In some embodimentexamples is a method for treating or preventing gout in an individual in need thereof. In some embodimentexamples is a method for treating gout in an individual in need thereof. In some embodimentexamples is a method for preventing gout in an individual in need thereof. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is from about 3 mg to about 1500 mg. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is from about 3 mg to about 600 mg. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is from about 5 mg to about 300 mg. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is from about 10 mg to about 200 mg. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is from about 10 mg to about 100 mg. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered orally. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is taken with food. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is taken without food. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered to the individual once per day. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered to the individual twice per day. In some embodimentexamples, the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-

hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered with at least one additional therapeutic agent. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered with a xanthine oxidase inhibitor. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered with a xanthine oxidase inhibitor selected from allopurinol, oxypurinol, febuxostat, topiroxostat, and inositol. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered with a sodium-glucose co-transporter-2 (SGLT2) inhibitor. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered with an SGLT2 inhibitor selected from canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, and dapagliflozin/metformin. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered with a xanthine oxidase inhibitor and a SGLT2 inhibitor. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, is administered with a xanthine oxidase inhibitor and a SGLT2 inhibitor, wherein the xanthine oxidase inhibitor is selected from allopurinol, oxypurinol, febuxostat, topiroxostat, and inositol, and the SGLT2 inhibitor is selected from canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, and dapagliflozin/metformin.

[0009] In some [embodimentexamples](#) is a pharmaceutical composition comprising (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.

[0010] In some [embodimentexamples](#) is a pharmaceutical composition comprising a compound of Formula (I) or (II) described herein, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.

[0011] In another [aspectexample](#) is a pharmaceutical composition for the treatment or prevention of hyperuricemia or gout, wherein the pharmaceutical composition comprises a therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients. In another [aspectexample](#) is a pharmaceutical composition for the treatment or prevention of hyperuricemia or gout, wherein the pharmaceutical composition comprises a therapeutically effective amount of a compound of Formula (I) or (II) described herein, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients. In some [embodimentexamples](#) is a pharmaceutical composition for the treatment or prevention of hyperuricemia in an individual in need thereof. In some [embodimentexamples](#) is a pharmaceutical composition for the treatment of hyperuricemia in an individual in need thereof. In some [embodimentexamples](#) is a pharmaceutical composition for the prevention of hyperuricemia in an individual in need thereof. In some [embodimentexamples](#) is a pharmaceutical composition for the treatment or prevention of gout in an individual in need thereof. In some [embodimentexamples](#) is a pharmaceutical composition for the treatment of gout in an individual in need thereof. In some [embodimentexamples](#) is a pharmaceutical composition for the prevention of gout in an individual in need thereof. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is from about 3 mg to about 1500 mg. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is from about 3 mg to about 600 mg. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is from about 5 mg to about 300 mg. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is from about 10 mg to about 200 mg. In some [embodimentexamples](#), the therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate

thereof, is from about 10 mg to about 100 mg. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is formulated for oral, intravenous, intramuscular, or subcutaneous administration. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is formulated for oral administration. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is taken with food. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is taken without food. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is administered to the individual once per day. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, is administered to the individual twice per day. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, further comprises at least one additional therapeutic agent. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, further comprises a xanthine oxidase inhibitor. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, further comprises a xanthine oxidase inhibitor selected from allopurinol, oxypurinol, febuxostat, topiroxostat, and inositol. In some [embodimentexamples](#), the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-

hydroxyethyl)benzofuran-3-yl-4,5,7-*d*₃)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, further comprises an SGLT2 inhibitor. In some embodiment examples, the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7-*d*₃)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, further comprises an SGLT2 inhibitor selected from canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, and dapagliflozin/metformin. In some embodiment examples, the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7-*d*₃)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, further comprises a xanthine oxidase inhibitor and an SGLT2 inhibitor. In some embodiment examples, the pharmaceutical composition of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7-*d*₃)methanone, a compound of Formula (I), or a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof, further comprises a xanthine oxidase inhibitor and an SGLT2 inhibitor, wherein the xanthine oxidase inhibitor is selected from allopurinol, oxypurinol, febuxostat, topiroxostat, and inositol, and the SGLT2 inhibitor is selected from canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, and dapagliflozin/metformin.

INCORPORATION BY REFERENCE

[0012] 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.

DETAILED DESCRIPTION OF THE INVENTION

[0013] Benzbromarone is a uricosuric agent effective in lowering serum uric acid sUA and treating gout. It has been found that therapy using benzbromarone can lead to lowering of sUA even following a single dose and continue to be lowered following multiple doses, and that chronic therapy can bring sUA into target levels of <6 mg/dL. However, in certain patients, benzbromarone is associated with hepatotoxicity. A high proportion of these patients developed acute liver failure leading to death or emergency liver transplantation. As a result, benzbromarone was never approved for use in the United States. In addition, the hepatotoxicity of benzbromarone led to its withdrawal in Europe in 2003. Benzbromarone is converted to reactive metabolites by CYP2C9. Benzbromarone is metabolized to 5,6-

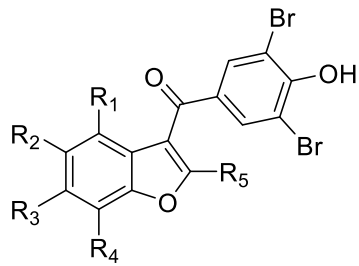
CLAIMS

We Claim:

1. A compound that is:

(i) (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof;

(ii) a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof:



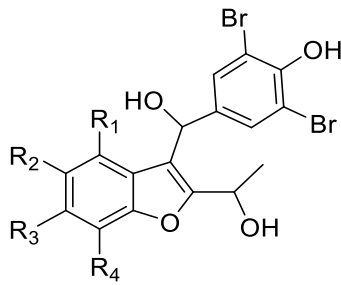
Formula (I):

wherein:

R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium; and

R₅ is -CH₂CH₂(OH) or -CH(OH)CH₂(OH); or

(iii) a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof:



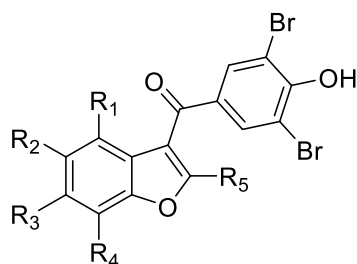
Formula (II):

wherein:

R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium.

2. The compound of claim 1, that is (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof.

2.3. A compound of claim 1, that is a compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof:



Formula (I);

wherein:

_____ R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium; and

_____ R₅ is ~~-CH₂CH₃~~, -CH₂CH₂(OH), or -CH(OH)CH₂(OH).

~~3.4.~~ The compound of claim ~~23~~, or a pharmaceutically acceptable salt or solvate thereof, wherein: at least two of R₁, R₂, R₃, and R₄ is deuterium.

~~4.5.~~ The compound of claim ~~23~~, or a pharmaceutically acceptable salt or solvate thereof, wherein: at least three of R₁, R₂, R₃, and R₄ is deuterium.

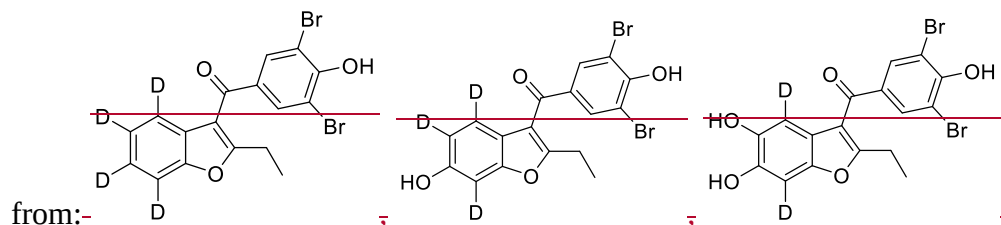
~~5.6.~~ The compound of claim ~~23~~, or a pharmaceutically acceptable salt or solvate thereof, wherein: R₁, R₂, R₃, and R₄ are deuterium.

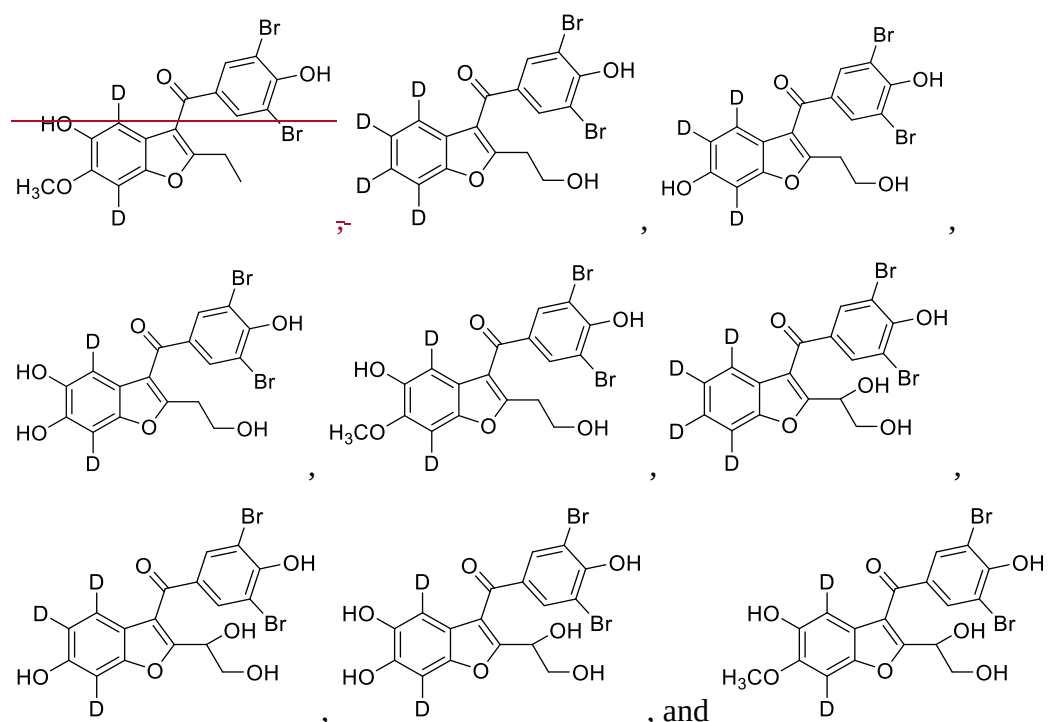
~~6. The compound of any one of claims 2-5, or a pharmaceutically acceptable salt or solvate thereof, wherein R₅ is -CH₂CH₃.~~

7. The compound of any one of claims ~~2-5~~3-6, or a pharmaceutically acceptable salt or solvate thereof, wherein:
R₅ is -CH₂CH₂(OH).

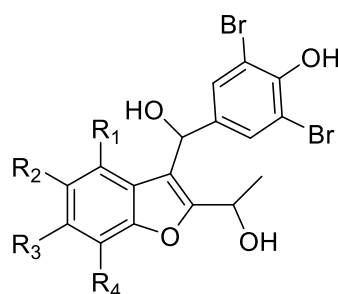
8. The compound of any one of claims ~~2-5~~3-6, or a pharmaceutically acceptable salt or solvate thereof, wherein:
R₅ is -CH(OH)CH₂(OH).

9. The compound of claim ~~32~~33, or a pharmaceutically acceptable salt or solvate thereof, selected





10. The compound of claim 1, that is a compound of Formula (II), or a pharmaceutically acceptable salt or solvate thereof:



Formula (II);

wherein:

R₁, R₂, R₃, and R₄ are each independently selected from a group consisting of hydrogen, deuterium, hydroxy, and methoxy; wherein at least one of R₁, R₂, R₃, and R₄ is deuterium.

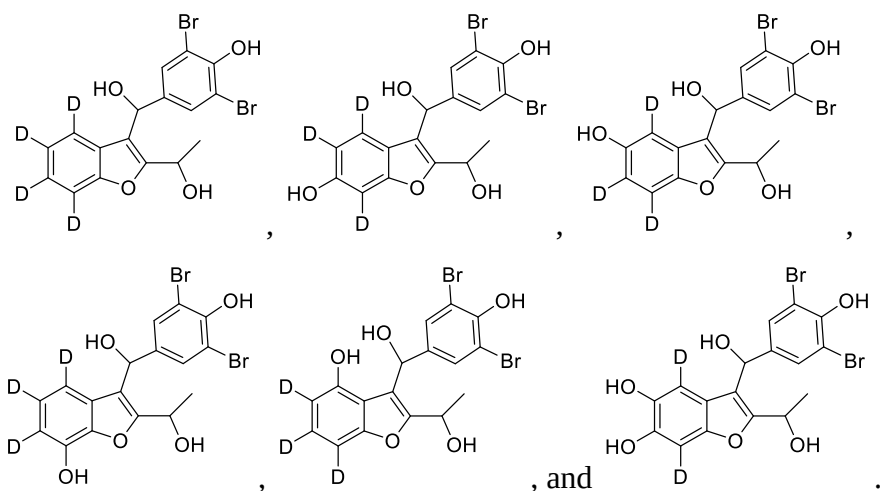
~~11.—The compound of claim 10, wherein at least two of R₁, R₂, R₃, and R₄ is deuterium.~~

~~12.—The compound of claim 10, wherein at least three of R₁, R₂, R₃, and R₄ is deuterium.~~

~~13.11.~~ The compound of ~~any one of claims 10-12~~claim 10, wherein:

_____ at least one of R₁, R₂, R₃, and R₄ is hydroxy.

~~14.12.~~ The compound of claim 10, or a pharmaceutically acceptable salt or solvate thereof, selected from:



15. ~~A method for treating or preventing hyperuricemia or gout in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl)-4,5,7-d₃-methanone, or a pharmaceutically acceptable salt or solvate thereof.~~

16.13. A method Use of a compound of any one of claims 1-12, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating or preventing hyperuricemia or gout in an individual in need thereof, ~~comprising administering to the individual a therapeutically effective amount of a compound of any one of claims 1-14, or a pharmaceutically acceptable salt or solvate thereof.~~

17. ~~The method of claim 15 or claim 16 for treating or preventing hyperuricemia in an individual in need thereof.~~

18. ~~The method of any one of claims 15-17 for treating hyperuricemia in an individual in need thereof.~~

19. ~~The method of any one of claims 15-17 for preventing hyperuricemia in an individual in need thereof.~~

20. ~~The method of claim 15 or claim 16 for treating or preventing gout in an individual in need thereof.~~

21. ~~The method of claim 20 for treating gout in an individual in need thereof.~~

22. ~~The method of claim 20 for preventing gout in an individual in need thereof.~~

23. ~~The method of any one of claims 15-22, wherein the therapeutically effective amount is from about 3 mg to about 1500 mg~~

24. ~~The method of any one of claims 15-23, wherein the therapeutically effective amount is from about 3 mg to about 600 mg.~~

25. ~~The method of any one of claims 15-24, wherein the therapeutically effective amount is from about 5 mg to about 300 mg.~~

- ~~26. The method of any one of claims 15-25, wherein the therapeutically effective amount is from about 10 mg to about 200 mg.~~
- ~~27. The method of any one of claims 15-26, wherein the therapeutically effective amount is from about 10 mg to about 100 mg.~~
- ~~28. The method of any one of claims 15-27, wherein (3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7-*d*₃)methanone is administered orally.~~
- ~~29. The method of claim 28, wherein the therapeutically effective amount is taken with food.~~
- ~~30. The method of claim 28, wherein the therapeutically effective amount is taken without food.~~
- ~~31. The method of any one of claims 15-30, wherein the therapeutically effective amount is administered to the individual once per day.~~
- ~~32. The method of any one of claims 15-31, wherein the therapeutically effective amount is administered to the individual twice per day.~~
- ~~33. The method of any one of claims 15-32, further comprising administering at least one additional therapeutic agent.~~
- ~~34. The method of any one of claims 15-33, further comprising administering a xanthine oxidase inhibitor.~~
- ~~35. The method of claim 34, wherein the xanthine oxidase inhibitor is allopurinol, oxypurinol, febuxostat, topiroxostat, or inositol.~~
- ~~36. The method of any one of claims 15-35, further comprising administering an SGLT2 inhibitor.~~
- ~~37. The method of claim 36, wherein the SGLT2 inhibitor is canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, or dapagliflozin/metformin.~~
- ~~38. A pharmaceutical composition comprising the compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.~~
- 39.14. A pharmaceutical composition comprising a compound of any one of claims 1-1412, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.
15. A compound of any one of claims 1-12, or a pharmaceutically acceptable salt or solvate thereof, for use in therapy.
- ~~40. A pharmaceutical composition for the treatment or prevention of hyperuricemia or gout, wherein the pharmaceutical composition comprises a therapeutically effective amount of~~

~~(3,5-dibromo-4-hydroxyphenyl)(6-hydroxy-2-(1-hydroxyethyl)benzofuran-3-yl-4,5,7- d_3)methanone, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.~~

- ~~41.— A pharmaceutical composition for the treatment or prevention of hyperuricemia or gout, wherein the pharmaceutical composition comprises a therapeutically effective amount of a compound of any one of claims 1-14, or a pharmaceutically acceptable salt or solvate thereof, and at least one inactive ingredient selected from pharmaceutically acceptable carriers, diluents, and excipients.~~
- ~~42.— The pharmaceutical composition of claim 40 or claim 41 for the treatment or prevention of hyperuricemia in an individual in need thereof.~~
- ~~43.— The pharmaceutical composition of any one of claims 40-42 for the treatment of hyperuricemia in an individual in need thereof.~~
- ~~44.— The pharmaceutical composition of any one of claims 40-42 for the prevention of hyperuricemia in an individual in need thereof.~~
- ~~45.— The pharmaceutical composition of claim 40 or claim 41 for the treatment or prevention of gout in an individual in need thereof.~~
- ~~46.— The pharmaceutical composition of claim 45 for the treatment of gout in an individual in need thereof.~~
- ~~47.— The pharmaceutical composition of claim 45 for the prevention of gout in an individual in need thereof.~~
- ~~48.— The pharmaceutical composition of any one of claims 40-47, wherein the therapeutically effective amount is from about 3 mg to about 1500 mg.~~
- ~~49.— The pharmaceutical composition of any one of claims 40-48, wherein the therapeutically effective amount is from about 3 mg to about 600 mg.~~
- ~~50.— The pharmaceutical composition of any one of claims 40-49, wherein the therapeutically effective amount is from about 5 mg to about 300 mg.~~
- ~~51.— The pharmaceutical composition of any one of claims 40-50, wherein the therapeutically effective amount is from about 10 mg to about 200 mg.~~
- ~~52.— The pharmaceutical composition of any one of claims 40-51, wherein the therapeutically effective amount is from about 10 mg to about 100 mg.~~
- ~~53.— The pharmaceutical composition of any one of claims 40-52 formulated for oral, intravenous, intramuscular, or subcutaneous administration.~~

- ~~54.—The pharmaceutical composition of any one of claims 40-53 formulated for oral administration.~~
- ~~55.—The pharmaceutical composition of claim 54, wherein the therapeutically effective amount is taken with food.~~
- ~~56.—The pharmaceutical composition of claim 54, wherein the therapeutically effective amount is taken without food.~~
- ~~57.—The pharmaceutical composition of any one of claims 40-56, wherein the therapeutically effective amount is administered once per day.~~
- ~~58.—The pharmaceutical composition of any one of claims 40-56, wherein the therapeutically effective amount is administered twice per day.~~
- ~~59.—The pharmaceutical composition of any one of claims 40-58, further comprising at least one additional therapeutic agent.~~
- ~~60.—The pharmaceutical composition of any one of claims 40-59, further comprising a xanthine oxidase inhibitor.~~
- ~~61.—The pharmaceutical composition of claim 60, wherein the xanthine oxidase inhibitor is allopurinol, oxypurinol, febuxostat, topiroxostat, or inositol.~~
- ~~62.—The pharmaceutical composition of any one of claims 40-61, further comprising an SGLT2 inhibitor.~~
- ~~63.—The pharmaceutical composition of claim 62, wherein the SGLT2 inhibitor is canagliflozin, dapagliflozin, empagliflozin, empagliflozin/linagliptin, empagliflozin/metformin, or dapagliflozin/metformin.~~