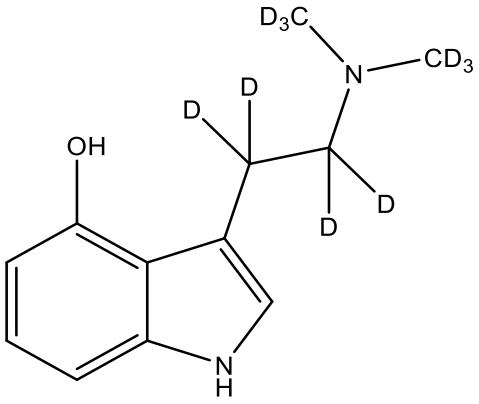
CLAIMS

1. Use of a compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof, in the manufacture of a medicament for the treatment of a depressive disorder in a subject,



(I-3)

wherein the medicament is to be orally administered at about 8 mg to about 16 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof.

2. The use of claim 0, wherein the medicament is to be orally administered at : (i) about 12 mg to about 16 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof; or (ii) about 12 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof; or (iii) about 14 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof; or (iv) about 16 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof.

3. The use of claim 1 or 2, wherein the medicament comprises a pharmaceutically acceptable salt of the compound of Formula (I-3).

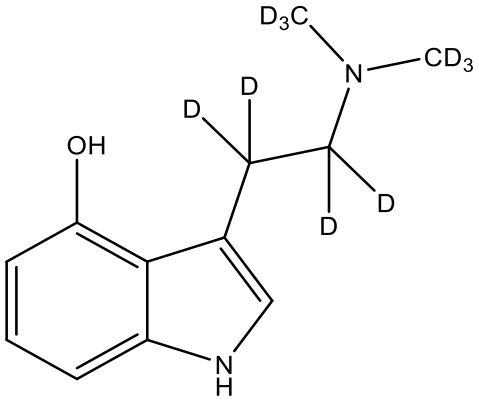
4. The use of claim 3, wherein the pharmaceutically acceptable salt of the compound of Formula (I-3) is selected from the group consisting of a benzenesulfonate, a tartrate, a hemi-fumarate, an acetate, a citrate, a malonate, a fumarate, a succinate, an oxalate, a benzoate, a

salicylate, an ascorbate, a hydrochloride, a maleate, a malate, a methanesulfonate, a toluenesulfonate, a glucuronate, and a glutarate salt, of the compound of Formula (I-3).

5. The use of claim 3 or 4, wherein the pharmaceutically acceptable salt of the compound of Formula (I-3) is a crystalline benzenesulfonate salt (I-3a), characterized by an X-ray powder diffraction pattern containing at least three characteristic peaks selected from 7.023, 7.767, 11.822, 12.550, 12.860, 13.994, 15.521, 18.436, 19.503, 20.760, 21.070, 22.007, 22.745, 23.340, 24.187, 25.532, 26.880, 27.856, 28.163, 31.267, 33.024, 35.030, 36.835, 39.3 12, 40.545, and 40.988 °2θ (±0.2° 2θ).

6. A pharmaceutical composition, comprising:

about 8 mg to about 16 mg (free base equivalence) of a compound of Formula (I-3)



(I-3)

or a pharmaceutically acceptable salt, polymorph, or solvate thereof; and

a pharmaceutically acceptable vehicle.

7. The pharmaceutical composition of claim 6, wherein the pharmaceutical composition comprises: (i) about 12 mg to about 16 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof; or(ii) about 12 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof; or(iii) about 14 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof; or (iv) about 16 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof.

8. The pharmaceutical composition of claim 6 or 7, wherein the pharmaceutical composition comprises a pharmaceutically acceptable salt of the compound of Formula (I-3).

9. The pharmaceutical composition of claim 8, wherein the pharmaceutically acceptable salt of the compound of Formula (I-3) is selected from the group consisting of a benzenesulfonate, a tartrate, a hemi-fumarate, an acetate, a citrate, a malonate, a fumarate, a succinate, an oxalate, a benzoate, a salicylate, an ascorbate, a hydrochloride, a maleate, a malate, a methanesulfonate, a toluenesulfonate, a glucuronate, and a glutarate salt, of the compound of Formula (I-3).

10. The pharmaceutical composition of claim 8 or 9, wherein the pharmaceutically acceptable salt of the compound of Formula (I-3) is a crystalline benzenesulfonate salt (I-3a), characterized by an X-ray powder diffraction pattern containing at least three characteristic peaks selected from 7.023, 7.767, 11.822, 12.550, 12.860, 13.994, 15.521, 18.436, 19.503, 20.760, 21.070, 22.007, 22.745, 23.340, 24.187, 25.532, 26.880, 27.856, 28.163, 31.267, 33.024, 35.030, 36.835, 39.312, 40.545, and 40.988 °2θ (±0.2° 2θ).

11. The pharmaceutical composition of any one of claims 6 to 10, wherein the pharmaceutically acceptable vehicle comprises an organic acid agent.

12. The pharmaceutical composition of claim 11, wherein the organic acid agent is: (i) citric acid;(ii) present in the pharmaceutical composition in an amount of at least 2% by weight and up to 10% by weight, based on a total weight of the pharmaceutical composition (on a dry basis); or both (i) and (ii).

13. The pharmaceutical composition of any one of claims 6 to 12, wherein the pharmaceutical composition is in a solid dosage form adapted for oral administration.

14. The pharmaceutical composition of claim 13, wherein the solid dosage form is a powder in capsule dosage form.

15. The pharmaceutical composition of any one of claims 6 to 12, wherein the pharmaceutical composition is an oral liquid dosage form.

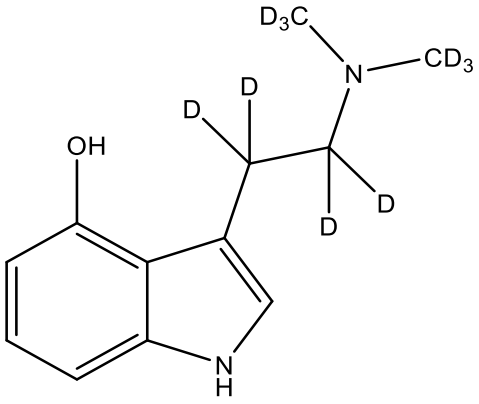
16. Use of a pharmaceutical composition of any one of claims 6 to 15 in the manufacture of a medicament for the treatment of a depressive disorder in a subject.

17. The use of claim 16, wherein the medicament is to be orally administered.

18. The use of claim 16 or 17, wherein the medicament is reconstituted from the pharmaceutical composition in solid dosage form in a pharmaceutically acceptable aqueous medium to form an oral liquid dosage form, and is to be orally administered in the liquid dosage form.

19. The use of any one of claims 0 to 5, or 16 to 18 wherein the subject is taking antidepressant medication as part of ongoing treatment and the treatment with the medicament is to be adjunctive therapy.

20. Use of a compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof, in the manufacture of a medicament for adjunctive therapy for the treatment of a depressive disorder in a subject taking an antidepressant medication,



(I-3)

wherein the medicament for adjunctive therapy is to be administered at about 8 mg to about 16 mg (free base equivalence) of a compound of Formula (I-3) or a pharmaceutically acceptable salt, polymorph, or solvate thereof.

21. The use of any one of claims 1 to 5, or 16 to 20 wherein the depressive disorder is major depressive disorder (MDD).

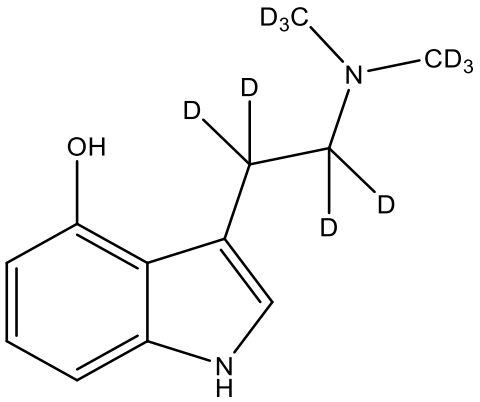
22. The use of claim 21, wherein, prior to treatment, the subject has: (i) been diagnosed with moderate to severe major depressive disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5);(ii) scored greater than or equal to 21 on the Montgomery-Åsberg Depression Scale (MADRS); or both (i) and (ii).

23. The use of any one of claims 0 to 5, or 16 to 19, or 20 to 22 wherein the medicament is to be orally administered as a first dose and a second dose, each being about 8 mg to about 16 mg (free base equivalence) of the compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof, (i) one to four weeks apart (± 3 days); or (ii) three weeks apart (± 3 days).

24. The use of any one of claims 19 to 23, wherein the antidepressant medication is a selective serotonin reuptake inhibitor (SSRI), a serotonin and noradrenaline reuptake inhibitor (SNRI), or a combination thereof.

25. The use of any one of claims 20 to 24, wherein the medicament for adjunctive therapy is to be orally administered.

26. Use of a benzenesulfonate salt of a compound of Formula (I-3) in the manufacture of a capsule for the treatment of major depressive disorder (MDD) in a subject,

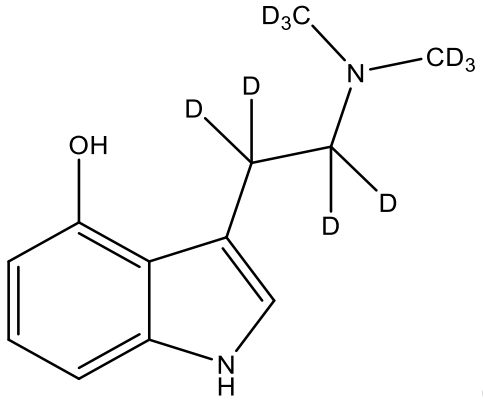


(I-3),

wherein the capsule comprises about 8 mg to about 16 mg (free base equivalence) of the benzenesulfonate salt of the compound of Formula (I-3).

27. Use of a compound of Formula (I-3), or a pharmaceutically acceptable salt, polymorph, or solvate thereof, in the manufacture of an oral liquid dosage form for the treatment of major depressive disorder (MDD) in a subject, wherein the oral liquid dosage form comprises:

(i) about 8 mg to about 16 mg (free base equivalence) of the compound of Formula (I-3)



(I-3)

or a pharmaceutically acceptable salt, polymorph, or solvate thereof; and

(ii) a pharmaceutically acceptable aqueous medium.