CLAIMS

What is claimed is:

1. A ~~method of treatment of alcohol use disorder in a subject, comprising administering to the subject an~~ pharmaceutical formulation for intranasal ~~formulation~~ administration, formulated as an aqueous solution, comprising:

a) about 1% (w/v) to about 4% (w/v) ~~a therapeutically effective amount of~~ naltrexone or a pharmaceutically acceptable salt, hydrate, or solvate thereof;

b) about 0.1% (w/v) to about 0.5% (w/v) of dodecyl maltoside;

c) about 0.2% (w/v) to about 1.2% (w/v) of sodium chloride;

d) about 0.005% (w/v) to about 0.1% (w/v) of benzalkonium chloride;

e) about 0.2% (w/v) to about 0.3% (w/v) of disodium edetate; and

f) water in an amount sufficient to achieve a final volume of about 0.05 mL to about 0.2 mL;

wherein the pH of the formulation is about 3.5 to about 5.4.

2. The pharmaceutical ~~method as recited in claim 1, wherein the intranasal~~ formulation as recited in claim 1, wherein the formulation comprises~~ing~~ about 0.25% (w/v) of dodecyl maltoside~~naltrexone is administered prior to ingestion of alcohol~~.

3. The pharmaceutical ~~method as recited in claim 1, wherein the intranasal~~ formulation as recited in claim 1, comprising about 3% (w/v) naltrexone or a pharmaceutically acceptable salt, hydrate, or solvate thereof~~is administered about 1-2 hours prior to ingestion of alcohol~~.

4. ~~The method as recited in claim 1, wherein the intranasal formulation comprising naltrexone is administered about 0.5 to about 1 hours prior to ingestion of alcohol~~The pharmaceutical formulation as recited in claim 1, wherein the total volume of the formulation comprises between about 0.05 mL to about 0.2 mL.

5. ~~The method as recited in claim 1, wherein the intranasal formulation comprising naltrexone is administered about 10 to about 30 minutes prior to ingestion of alcohol~~The pharmaceutical formulation as recited in claim 1, wherein the total volume of the formulation comprises about 0.1 mL.

6. ~~The method as recited in claim 1, wherein the intranasal formulation comprising naltrexone is administered about 5 to about 10 minutes prior to ingestion of alcohol.~~A pharmaceutical composition for intranasal administration to a human subject in need thereof, comprising:

a) about 3 mg to about 4 mg of naltrexone or a pharmaceutically acceptable salt, hydrate, or solvate thereof;

b) about 0.25 mg of dodecyl maltoside;

c) water in an amount sufficient to total about 0.1 mL;

wherein the pH of the composition is between about 3.5 to about 5.4.

7. ~~The method as recited in claim 1, wherein the intranasal formulation comprising naltrexone is administered contemporaneously with the ingestion of alcohol.~~The pharmaceutical composition of claim 6, further comprising a preservative and an isotonicity agent.

8. ~~The method as recited in claim 1, wherein the intranasal formulation comprising naltrexone is administered within 0.5 hours after commencement of ingestion of alcohol.~~The pharmaceutical composition of claim 6, wherein upon administration to the subject of the pharmaceutical composition, the Tmax is 25 minutes or less.

9. ~~The method as recited in claim 1, wherein the intranasal formulation comprises an aqueous solution.~~The pharmaceutical composition of claim 6, wherein upon administration to the subject of the pharmaceutical composition, the Tmax is 20 minutes or less.

10. ~~The method as recited in any of claims 1-9, wherein each dose of the formulation comprises about 2 to about 12 mg naltrexone or a salt or hydrate thereof.~~The pharmaceutical composition of claim 6, wherein upon administration to the subject of the pharmaceutical composition, the Tmax is 15 minutes or less.

11. ~~The method as recited in claim 10, wherein each dose of the formulation comprises about 2 to about 8 mg naltrexone or a salt or hydrate thereof.~~The pharmaceutical composition of claim 6, wherein upon administration to the subject of the pharmaceutical composition, the AUC0-inf after administration of the composition is higher than the AUC0-inf of an intranasal formulation of about 3 mg to about 4 mg naltrexone or a pharmaceutically acceptable salt, hydrate, or solvate thereof that does not contain dodecyl maltoside.

12. ~~The method as recited in claim 11, wherein each dose of the formulation comprises about 4 mg naltrexone or a salt or hydrate thereof.~~The pharmaceutical composition of claim 6, wherein upon administration to the subject of the pharmaceutical composition, the AUC0-inf is about 50% higher than the AUC0-inf of the intranasal formulation of about 3 mg to about 4 mg naltrexone or a pharmaceutically acceptable salt, hydrate, or solvate thereof that does not contain dodecyl maltoside.

13. ~~The method as recited in any of claims 1-12, wherein about 0.05 – about 0.2 mL of said formulation is delivered to the subject.~~The pharmaceutical composition of claim 6,

wherein upon administration to the subject of the pharmaceutical composition, the AUC0-inf is about 50% to about 60% higher than the AUC0-inf of an intranasal formulation of about 3 mg to about 4 mg naltrexone or a pharmaceutically acceptable salt, hydrate, or solvate thereof that does not contain dodecyl maltoside.

14. ~~The method as recited in claim 13, wherein about 0.1 mL of said formulation is delivered to the subject.~~The pharmaceutical composition of claim 6, wherein upon administration to the subject of the pharmaceutical composition, the Cmax is about 2 to about 3 times higher than the Cmax of an intranasal formulation of about 3 mg to about 4 mg naltrexone or a pharmaceutically acceptable salt, hydrate, or solvate thereof that does not contain dodecyl maltoside.

15. ~~The method as recited in claim 13, wherein said formulation is at a concentration of 40mg/mL.~~The pharmaceutical composition of claim 6, wherein upon administration to a population of subjects of the pharmaceutical composition, the mean plasma concentration of naltrexone at about 5 minutes post-dose is about 12 ng/mL.

16. ~~The method as recited in any of claims 1-15, wherein the intranasal formulation is administered as a single administration to one nostril.~~The pharmaceutical composition of claim 6, wherein upon administration to a population of subjects of the pharmaceutical composition, the mean plasma concentration of naltrexone at about 15 minutes post-dose is about 10 ng/mL.

17. ~~The method as recited in any of claims 1-15, wherein the intranasal formulation is administered as two administrations, one to each nostril.~~The pharmaceutical composition of claim 6, wherein upon administration to a population of subjects of the pharmaceutical composition, the mean plasma concentration of naltrexone at about 30 minutes post-dose is about 7 ng/mL.

18. ~~The method as recited in any of claims 1-17 wherein the intranasal formulation additionally comprises an absorption enhancer.~~ The pharmaceutical composition of claim 6, wherein the total volume of the pharmaceutical composition comprises about 0.1 mL.

~~19. The method as recited in claim 18, wherein the absorption enhancer is selected from the group consisting of benzalkonium chloride, chitosans, cyclodextrins, deoxycholic acid, dodecyl maltoside, glycocholic acid, laureth-9, taurocholic acid, and taurodihydrofusidic acid.~~

~~20. The method as recited in claim 18, wherein the absorption enhancer is an alkylsaccharide.~~

~~21. The method as recited in claim 20, wherein the alkylsaccharide is chosen from dodecyl maltoside, tetradecyl maltoside (TDM) and sucrose dodecanoate.~~

~~22. The method as recited in claim 21, wherein the alkylsaccharide is Intravail® (dodecyl maltoside).~~

~~23. The method as recited in claim 22, wherein the intranasal formulation comprises between about 0.05% to about 2.5% of Intravail® (dodecyl maltoside).~~

~~24. The method as recited in claim 23, wherein the intranasal formulation comprises between about 0.1% to about 0.5% of Intravail® (dodecyl maltoside).~~

~~25. The method as recited in claim 24, wherein the intranasal formulation comprises about 0.25% of Intravail® (dodecyl maltoside).~~

~~26. The method as recited in claim 18, wherein the absorption enhancer is benzalkonium chloride.~~

~~27. The method as recited in claim 26, wherein the intranasal formulation comprises about 0.005% to about 0.015% of benzalkonium chloride.~~

~~28. The method as recited in claim 27, wherein the intranasal formulation comprises about 0.01% of benzalkonium chloride.~~

~~29. The method as recited in any of claims 1-28, wherein the intranasal formulation additionally comprises one or more excipients selected from sodium chloride, benzalkonium chloride, edetate disodium, and an acid.~~

~~30. The method as recited in claim 29, wherein the acid is sufficient to achieve a pH of 3.5-5.5.~~

~~31. The method as recited in any of claims 1-30, wherein the therapeutically effective amount comprises from about 4 mg to about 16 mg of naltrexone per day.~~

~~32. The method as recited in claim 31, wherein the therapeutically effective amount of naltrexone is administered in doses of about 4 mg throughout the day as needed by the subject.~~

~~33. The method as recited in claim 32, wherein the therapeutically effective amount of naltrexone is administered as a first dose of about 4 mg in the morning, and subsequent doses of about 4 mg as needed prior to consumption of alcohol.~~

~~34. The method as recited in any of claims 1-33, wherein the therapeutically effective amount comprises from about 4 mg to about 16 mg of naltrexone per day.~~

~~35. The method as recited in any of claims 1-33, wherein the therapeutically effective amount of naltrexone is administered in 4 mg doses throughout the day as needed by the subject.~~

~~36. The method as recited in any of claims 1-33, wherein the therapeutically effective amount of naltrexone is administered as a first 4 mg dose in the morning, and subsequent 4 mg doses as needed prior to exposure to an addictive substance or behavior.~~

~~37. A pharmaceutical formulation for intranasal administration, formulated as an aqueous solution, comprising an amount of naltrexone or a pharmaceutically acceptable salt thereof therapeutically effective for the treatment of alcohol use disorder.~~

~~38. The pharmaceutical formulation as recited in claim 37, comprising about 2.5 – about 12 mg naltrexone or a salt or hydrate thereof.~~

~~39. The pharmaceutical formulation as recited in claim 37, comprising about 2.5 – about 8 mg naltrexone or a salt or hydrate thereof.~~

~~40. The pharmaceutical formulation as recited in claim 39, comprising about 4 mg naltrexone or a salt or hydrate thereof.~~

~~41. The pharmaceutical formulation as recited in any of claims 37-40, wherein about 0.05 – about 0.2 mL of said formulation is delivered to the subject.~~

~~42. The pharmaceutical formulation as recited in claim 41, wherein about 0.1 mL of said formulation is delivered to the subject.~~

~~43. The pharmaceutical formulation as recited in any of claims 37-42 wherein the intranasal formulation additionally comprises an absorption enhancer.~~

~~44. The pharmaceutical formulation as recited in claim 43, wherein the absorption enhancer is selected from the group consisting of benzalkonium chloride, chitosans, cyclodextrins, deoxycholic acid, dodecyl maltoside, glycocholic acid, laureth-9, taurocholic acid, and taurodihydrofusidic acid.~~

~~45. The pharmaceutical formulation as recited in claim 43, wherein the absorption enhancer is an alkylsaccharide.~~

~~46. The pharmaceutical formulation as recited in claim 45, wherein the alkylsaccharide is chosen from dodecyl maltoside, tetradecyl maltoside (TDM) and sucrose dodecanoate.~~

~~47. The pharmaceutical formulation as recited in claim 46, wherein the alkylsaccharide is Intravail® (dodecyl maltoside).~~

~~48. The pharmaceutical formulation as recited in claim 47, wherein the intranasal formulation comprises between about 0.05% to about 2.5% of Intravail® (dodecyl maltoside).~~

49. The pharmaceutical formulation as recited in claim 48, wherein the intranasal formulation comprises between about 0.1% to about 0.5% of Intravail® (dodecyl maltoside).

50. The pharmaceutical formulation as recited in claim 49, wherein the intranasal formulation comprises about 0.25% of Intravail® (dodecyl maltoside).

51. The pharmaceutical formulation as recited in claim 44, wherein the absorption enhancer is benzalkonium chloride.

52. The pharmaceutical formulation as recited in claim 51, wherein the intranasal formulation comprises about 0.005% to about 0.015% of benzalkonium chloride.

53. The pharmaceutical formulation as recited in claim 52, wherein the intranasal formulation comprises about 0.01% of benzalkonium chloride.

54. The pharmaceutical formulation as recited in any of claims 37-53, wherein the intranasal formulation additionally comprises one or more excipients selected from sodium chloride, benzalkonium chloride, edetate disodium, and an acid.

55. The pharmaceutical formulation as recited in claim 54, wherein the acid is sufficient to achieve a pH of 3.5-5.5.

56. A multi-dose device adapted for nasal delivery of a pharmaceutical formulation to a subject suffering alcohol use disorder, comprising a plurality of doses each comprising an amount of naltrexone or a pharmaceutically acceptable salt thereof therapeutically effective for the treatment of alcohol use disorder.

57. The device as recited in claim 56, further comprising a dose counter.

58. The device as recited in claim 53, wherein the pharmaceutical formulation is formulated as an aqueous solution.

59. The device as recited in claim 56, configured for administration of each dose as a single administration to one nostril.

60. The device as recited in claim 56, configured for administration of each dose as two administrations, one to each nostril.

61. The device as recited in claim 56, configured for administration of each dose as four administrations, two to each nostril.

62. The device as recited in claim any of claims 56-61, comprising about 2.5 to about 12 mg naltrexone or a salt or hydrate thereof in each dose.

63. The device as recited in claim 62, comprising about 2.5 to about 8 mg naltrexone or a salt or hydrate thereof in each dose.

64. The device as recited in claim 63, comprising about 4 mg naltrexone or a salt or hydrate thereof in each dose.

65. The device as recited in any of claims 56-64, wherein about 0.05 to about 0.2 mL of said formulation is delivered to the subject in each dose.

66. The device as recited in claim 65, wherein about 0.1 mL of said formulation is delivered to the subject in each dose.

67. The device as recited in claim 65, wherein said formulation is at a concentration of 40mg/mL.

68. The device as recited in any of claims 56-67 wherein the intranasal formulation additionally comprises an absorption enhancer.

69. The device as recited in claim 68, wherein the absorption enhancer is selected from the group consisting of benzalkonium chloride, chitosans, cyclodextrins, deoxycholic acid, dodecyl maltoside, glycocholic acid, laureth-9, taurocholic acid, and taurodihydrofusidic acid.

70. The device as recited in claim 68, wherein the absorption enhancer is an alkylsaccharide.

71. The device as recited in claim 70, wherein the alkylsaccharide is chosen from dodecyl maltoside, tetradecyl maltoside (TDM) and sucrose dodecanoate.

72. The device as recited in claim 71, wherein the alkylsaccharide is Intravail® (dodecyl maltoside).

73. The device as recited in claim 69, wherein the intranasal formulation comprises between about 0.05% to about 2.5% of Intravail® (dodecyl maltoside).

74. The device as recited in claim 73, wherein the intranasal formulation comprises between about 0.1% to about 0.5% of Intravail® (dodecyl maltoside).

75. The device as recited in claim 74, wherein the intranasal formulation comprises about 0.25% of Intravail® (dodecyl maltoside).

76. The device as recited in claim 71, wherein the absorption enhancer is benzalkonium chloride.

77. The device as recited in claim 69, wherein the intranasal formulation comprises about 0.005% to about 0.015% of benzalkonium chloride.

78. The device as recited in claim 77, wherein the intranasal formulation comprises about 0.01% of benzalkonium chloride.

79. The device as recited in any of claims 56-78, wherein the intranasal formulation additionally comprises one or more excipients selected from sodium chloride, benzalkonium chloride, edetate disodium, and an acid.

~~80. The device as recited in claim 79, wherein the acid is sufficient to achieve a pH of 3.5-5.5.~~